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EDITORIAL

Editorial: Patient Earth is critically ill

Simon Paul Attard Montalto

If planet earth was a patient she would be diagnosed with multi-organ failure and transferred immediately to intensive care. The list of problems afflicting 'Earth' would include runaway hyperthermia despite numerous attempts to control this, respiratory failure and decreasing ability to maintain proper oxygenation, circulatory failure with multiple thromboses in major arteries, and renal and hepatic failure with inexorable accumulation of body wastes. On top of all of these ailments, intermittent bouts of extreme dehydration alternating with fluid overload as well as sporadic unexpected infections would have contributed to a steady decline in her health over the past few decades, culminating in the need for life support.

Simon Paul Attard Montalto
Editor
Malta Medical Journal

COVER PICTURE

'Veccia at night'

Lino Said is a retired dentist who is also a self-taught artist. His preferred media are acrylics and pastels.

Born in 1962, Dr Said attended St Albert the Great College, before graduating from the Faculty of Dentistry, University of Malta in 1985. He is currently attending a Diploma course in Archival and Ecclesiastical Patrimony.

His other interests include Maltese history and archaeology. He also manages a local boutique winery.

He has been involved in a number of fund-raising activities for various charities.

Real earth, the planet not the patient, is in fact experiencing uncontrolled global warming which, year-on-year is projected to get worse.[1] Numerous major multi-national conventions, profound declarations and pledged commitments have not reversed the trend: indeed, the projected rate of global temperature rise is forever re-adjusted upwards.[1,2] Climate control conferences have become an annual depressing if not predictable exercise in failed diplomacy and international pretend-cooperation.[1] Erudite and researched orations are inevitably followed by petty squabbling resulting in no meaningful resolutions (or none that are sufficiently supported to make a difference). For Earth, the patient, multiple remedies exist but are unavailable, have expired, are too expensive, not approved . . . . etc., etc. Despite the consequences of this temperature rise having been documented scientifically ad nauseam, many continue to ignore or even, incredibly, deny this phenomenon. Sadly, these include some world leaders and significantly influential bodies that, in turn, allow those for whom it is expedient to continue harmful practices to continue doing so. This includes, amongst others, massive-scale logging, mining, burning of fossil fuels, dumping of waste into waterways, etc.[3-5] The knock-on effects of global warming are immense and self-perpetuating: hence, as the planet warms, glaciers and the sea-ice retreat resulting in rising sea levels, havoc for many coastline and fragile eco-systems,[6] but also warming and release of vast amounts of methane from thawing permafrost.[7] Methane is a major and more permanent greenhouse gas than CO_2 and billions of tons-worth is currently locked into frozen permafrost in the tundra regions of the planet. It's release, together with fast disappearing rainforests – more than 50% of the earth's total rainforests, the earth's natural lung and greatest carbon trap, have disappeared[8] – will result in a huge upturn in global warming.[9] If the downward spiral of further warming causing further melting (permafrost, glaciers, sea-ice, etc.) is not stopped and reversed, it will tip beyond the point of no return within a few decades or less.

Man-driven air pollution 'took off' during the industrial revolution in Victorian times, but has continued apace despite accrued knowledge of its harmful effects over the past two centuries. Indeed, the negative impact of air pollution that had occurred over such a tiny period of Earth's lifetime, around 5.4 billion years, is quite staggering. In practice, in 2024, air pollution in some cities is so bad that the population are regularly advised to stay indoors![10] Continuing massive-scale industrial emissions, continuing use of fossil-burning machines, wildfires secondary to global warming etc., will ensure that patient Earth is in dire need of ventilatory support.

Polluted oceans and waterways are the norm in almost all large cities or anywhere where there has been industrialization.[11] Many rivers are virtual sewers and plastic and micro-plastics are present everywhere, including in the little-explored abyssal depths of the oceans.[12] The problem of clean, unpolluted water is massive and destined to worsen again, as adequate measures are implemented, sometimes in part only, by just a few countries. In this regard, patient Earth has reached the point of requiring renal replacement therapy.

Arterial congestion is a universal problem particularly to those utilizing these roads, although the pollution ensuing from clogged arteries poses an even greater health risk to the planet. Even emission-free electric transport comes with its own baggage, not least as a result of the extremely damaging and wasteful means of extracting lithium from the earth and problems with its disposal once spent.[13]

A reversal to natural healing remedies may be the answer: solar energy is natural and hugely abundant. But for Earth, is it a suitable homeopathic alternative? Not quite: it remains expensive, not widely available and insufficiently supported by authorities who intermittently offer incentives/grants/sweeteners of varying 'substance/attractiveness'.

Earth, the patient, is undoubtedly sick, indeed, sick enough to be on intensive care. It behoves everyone with a modicum of understanding and in a position of influence, including doctors, to support clean/green measures wherever possible, and to lobby those in power to propose and enforce earth-friendly measures in relation to air quality, waterways, oceans, agriculture, farming, land use, forestry, energy production, etc. In a tiny overcrowded island with multiple apartment blocks, why don't we cover all public buildings of no historical/architectural value, schools, reservoirs, warehouses, etc., with solar panels and lease these to those living in properties who cannot/do not wish to install their own? The energy generated would be passed onto the grid, but offset against the domestic bills of all lease-holders. One small step for man . . . one tiny step towards Earth's recovery!

REFERENCES

1. 2023 Global Climate Summary. Copernicus EU Highlights. 2024. https://climate.copernicus.eu/global-climate-highlights-2023#:~:text=More%20specifically%2C%20the%20WMO%20reported,updated%20report%20published%20in%202023.
2. Sudova D. The UN Conference on climate change COP27: Disappointment or historic win? Czech Centre for Human Rights and Democracy. 2023. https://www.humanrightscentre.org/blog/un-conference-climate-change-cop27-disappointment-or-historic-win
3. What is the role of deforestation in climate change and how can 'Reducing Emissions from Deforestation and Degradation' (REDD+) help? London School of Economics and Political Science. Feb 2023. https://www.lse.ac.uk/granthaminstitute/explainers/whats-redd-and-will-it-help-tackle-climate-change/
4. Fossil fuels and climate change: the facts. ClientEarth Commun Feb 2022. https://www.clientearth.org/latest/news/fossil-fuels-and-climate-change-the-facts/
5. Aquatic trash. US Environmental Protection Agency. 2023. https://www.epa.gov/trash-free-waters/learn-about-aquatic-trash#:~:text=Mismanaged%20trash%20that%20escapes%20into,on%20for%20tourism%20and%20recreation.
6. Magnan AK, Oppenheimer M, Garschagen M, et al. Sea level rise risks and societal adaptation benefits in low-lying coastal areas. Nature Scientific Reports. 2022; 12: 10677.
7. Rößger N, Sachs T, Wille C, et al. Seasonal increase of methane emissions linked to warming in Siberian tundra. Nature Climate Change. 2022; 12: 1031–1036.
8. Rain forest threats. National Geographic. https://www.nationalgeographic.com/environment/article/rainforest threats#:~:text=Logging%20interests%20cut%20down%20rain,techniques%20to%20clear%20ranch%20land.
9. Smith C, Baker JCA, Spracklen DV. Tropical deforestation causes large reductions in observed precipitation. Nature. 2023; 615: 270-275.
10. Abbasi K, Ali P, Barbour V, et al. Time to treat the climate and nature crisis as one indivisible global health emergency. npj Primary Care Respiratory Medicine volume 33, Article number: 37.(2023)
11. Top water contamination disasters that shook the world. Onya Mag 2023. https://www.onyamagazine.com/australian-affairs/top-water-contamination-disasters-that-shook-the-world/
12. Chiba S, Saito H, Fletcher R et al. Human footprint in the abyss: 230 year records of deep-sea plastic debris. Marine Pol Science Direct. 2018; 96: 204-212.
13. Tedesco M. State of the Planet. The paradox of lithium. Climate Earth Society. 2023, Jan 18. https://news.climate.columbia.edu/2023/01/18/the-paradox-of-lithium/#:~:text=These%20side%20effects%20include%3A%20use,interests%20at%20stake%20are%20enormous.

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ORIGINAL ARTICLE

Maternal Admissions at Central Delivery Suite in Mater Dei Hospital

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Background

Central Delivery Suite is a specialised ward in Mater Dei Hospital (MDH) dedicated for intra-partum care. It consists of nine delivery rooms, an admission room, an operating theatre and a neonatal resuscitation room. Currently, all pregnant mothers of 22 weeks gestation and above are reviewed in this ward. The aim of this audit is to assess the management of bed space at Central Delivery Suite in the absence of a maternity unit triage room.

Methods

All Central Delivery Suite admissions, over a 4 week period, were logged using the labour ward admission book. Data collected included demographic data, reasons for (planned as well as acute presentations), whether delivery was achieved or not and whether patient was admitted or not. Reasons for acute presentations between the admitted and non-admitted population were compared.

Results

Out of 488 patients, 122 patients (25%) had an elective LSCS or IOL. 366 patients (75%) presented to the labour ward with an acute complaint. Of these, 224 patients (61.2%) were admitted and 142 patients (38.8%) were discharged after review. Out of the 224 patients that were admitted, 171 patients (76.3%) delivered during that admission and 53 patients (23.7%) did not deliver.

Conclusion

This audit showed that 53.3% of women who had an unplanned presentation to Central Delivery Suite did not need to block a bed in the labour ward and could have been assessed in a maternity assessment unit. This means better management and utilisation of beds and resources.

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Central Delivery Suite is a specialised ward in Mater Dei Hospital (MDH) dedicated for intra-partum care. It consists of nine delivery rooms which are single rooms with individual bathroom facilities. There is also an operating theatre equipped for caesarean sections and other birth procedures, as well as a neonatal resuscitation room. A team of midwives is responsible for caring of mothers during their temporary stay in this ward. It is not just mothers in labour who are admitted here, but any expecting mother from 22 weeks gestation onwards may be referred for assessment and will be reviewed by an obstetric team and discharged or admitted as necessary. Unfortunately, this puts additional stress on the bed availability and may lead to burnout of the team members.[1] The various functions of the labour ward demand a sound organisational structure to maximise the limited resources available whilst providing the best care. This could be optimised by providing a maternity unit triage room prior to admission to Central Delivery Suite.

AIMS

The aim of this audit is to assess the management and utilisation of bed space at Central Delivery Suite in the absence of a maternity unit triage room.

MATERIALS AND METHODS

Audit Design

This is a quantitative prospective analysis of all women admitted at Central Delivery Suite in MDH over a 4 week period. Data protection approval was obtained from the Data Protection Office at MDH. Labour ward admissions were logged in on a daily basis using the labour ward admission book. All data collection was anonymised and no direct patient contact was required. A Microsoft Excel spreadsheet was used to log all collected data. Every patient was assigned an individual numerical code. Patient demographic data, including maternal age, gestational age, parity and previous mode of delivery were collected. Reasons for admission to the labour ward were noted. These included women who had a planned lower-section cesarean section (LSCS) and induction of labour (IOL) as well as different acute presentations (contractions, decreased fetal movements, bleeding per vagina, high blood pressure, query spontaneous rupture of membranes (?SROM), motor vehicle accidents (MVAs), itching, vomiting and/or diarrhoea, abdominal pain, show, cardiotocography (CTG) monitoring). Other rarer presentations were put under the heading "others". For each acute presentation it was noted whether delivery was achieved or not and whether the patient was admitted or not.

Data analysis

The total number of patients present in the labour ward for a 4 week period was noted. Mean maternal age was calculated. Those that had a planned LSCS and IOL were excluded from the total. The number of acute presentations were categories into; those admitted (which was further subdivided into those that were admitted and delivered and those admitted that did not deliver) and not admitted.

Finally, reasons for acute presentations for women that were admitted were compared with those that were not admitted.

RESULTS

Admission and delivery statistics

490 patients were admitted in the 4 week collection period in this audit. Two patients had to be excluded as not enough information was documented for the purposes of this audit. As a result 488 patients were eligible for this audit. Out of these, 122 patients (25%) had an elective LSCS or IOL.

366 patients (75%) presented to the labour ward with an acute complaint. Of these, 224 patients (61.2%) were admitted and 142 patients (38.8%) were discharged after review by basic specialist trainee (BST) or above.

Out of the 224 patients that were admitted, 171 patients (76.3%) delivered during that admission and 53 patients (23.7%) did not deliver. Figure 1 is a flow diagram that outlines the structure of the audit.

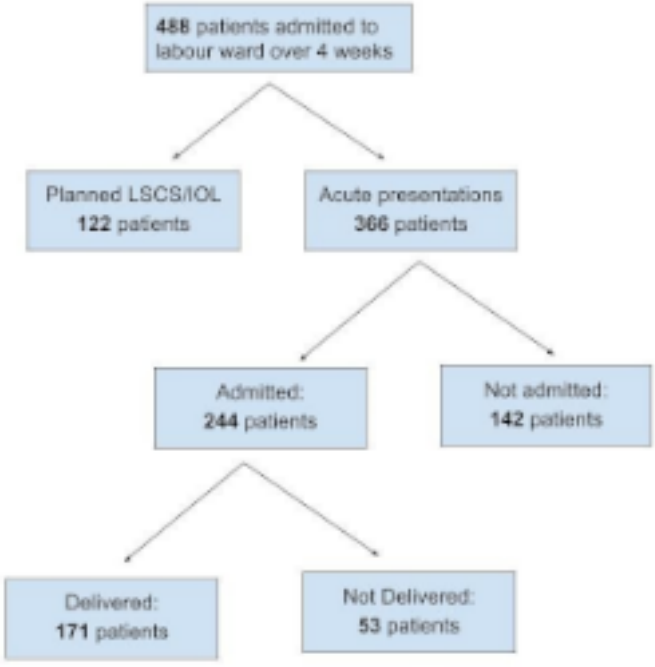

Figure 1 Audit results flow diagram

Table 1 Comparison of reasons of acute presentations between the admitted and non-admitted

Reason	Admitted	Not admitted
contractions	100	31
decreased fetal movements	12	37
bleeding pv	10	6
high blood pressure	5	2
?SROM	72	27
following MVAs	0	5
itching	0	4
vomiting and/or diarrhoea	4	3
abdominal pain	17	20
show	3	5
CTG monitoring	3	6
Others	6*	13**

* Others: High HGT - 1, lower limb oedema-1, intrauterine growth restriction (IUGR) - 2, referred from antenatal clinic as cervix was 1cm long - 1, Eclampsia day 3 post-LSCS – 1

** Others - IUGR- 1,premature rupture of membranes (PROM) - 1, Pessary insertion - 1, lethargy -1, headache - 1, amnioreduction -1, dexamethasone administration - 1, investigations - 1, removal of cerclage - 1, dizziness - 1,white cells on dipstick ?urinary tract infection - 1, sciatic pain- 1, external cephalic version – 1

Reasons For Acute Presentations In The Admitted Population Vs Non-Admitted Population

Out of the 244 patients that were admitted, the number of times the following presenting complaints were documented, as seen in Table 1.

DISCUSSION

For the past few years there has been increasing concern about better utilisation of the limited bed space at Central Delivery Suite.

Currently, there is one admission room in Central Delivery Suite which is used to review pregnant women at 22 weeks gestation or more who self-admit or are referred by the caring obstetric team either because one is in active labour or needs intrapartum management of a pregnancy related complications.

122 women (25%) of these had a planned admission into the labour ward (either a planned LSCS or IOL). The remaining 366 (75%) were acute presentations.

42 women (38.8%) presented with an acute complaint to the labour ward and were discharged after initial assessments. The vast majority of these women occupied a delivery room which could have been available to women that really needed it. Furthermore, out of the 224 women (61.2%) that were admitted following an acute presentation, 53 of them (23.7%) did not deliver but were kept in the room for observation or transferred to an obstetric ward. These women were also blocking a delivery bed and could have been managed elsewhere and in doing so preserving these limited beds and human resources in the labour ward for women that were actually in labour and needed a delivery room.

A maternity triage unit situated next to the labour ward aims to assess women who are 22 weeks or more gestation as well as women who are 14 days postpartum and have an urgent clinical complaint relating to pregnancy and delivery. This is an assessment area staffed by a team of midwives and obstetricians. Women who come with acute complaints are assessed on a priority of care basis. The midwife takes a thorough history to identify antenatal risk factors, take basic parameters including blood pressure, pulse, temperature and send urine for urinalysis and/or cultures depending on the situation. Abdominal examination followed by bimanual vaginal examination (if applicable) will complete the initial assessment. Obstetricians are always involved before women are admitted or discharged. The triage midwife in conjunction with the obstetric team would then come to a decision of whether the index case needs immediate attention at Central Delivery Suite, admission to hospital for further management or can be safely discharged home.

A maternity triage unit may also provide a telephone service, accessible by healthcare professionals such as GPs and community midwives who need advice, as well as pregnant women who have queries. The midwife can provide appropriate advice over the phone and support accordingly or refer to a doctor when necessary. This service would optimise utilisation of beds as well as human resources in Central Delivery Suite.

Apart from being an assessment area to evaluate labour symptoms, care for urgent pregnancy complaints and additional procedures may be performed such as blood tests, CTGs, parameter monitoring, internal examinations and ultrasound when required. The number of delivery rooms on a labour ward are limited so a maternity triage room in MDH will ensure that these beds are assigned to women who are in active labour and/or need urgent

intrapartum management.[1,2] Apart from optimal utilisation of high-dependency beds, a maternity triage system offers other advantages; it reduces waiting and transfer times, it improves patient satisfaction, it reduces unplanned admissions or readmissions within the first 48 hours, it provides a mechanism to reduce complications arising from emergency presentations and improves overall health and wellbeing.[3]

Common presentations that were documented in this audit could have been handled in a maternity triage room. Most of the presentations were of low acuity. 38.8% of acute presentations did not need an admission and were discharged after initial review. Their assessment in a triage unit would have been enough and delivery rooms need not be used. Also, 23.7% of the admitted women following an acute presentation did not deliver. These women could have been directed directly to an obstetric ward instead of occupying a room in the delivery suite for their assessment. This means that 53.3% of women in this audit who had an unplanned admission to the labour ward could have been handled in a maternity triage room and did not need to block a bed in the labour ward. If MDH had this system we would be using our limited delivery room beds better. This room could be situated adjacent to the labour ward in the ground floor, blue block and it should have two private assessment areas.

An issue that might arise could be that one triage room may not be sufficient, as simultaneous admissions do commonly occur. To prevent overcrowding in this room a number of systems have to be in place. One needs to aim to reduce the inflow of patients. This can be achieved by having a proper telephone service as mentioned earlier. Pregnant women and GPs can phone for queries. Midwives and obstetricians can re-direct non-urgent cases (such as early labour or rupture of membranes>37 weeks, vaginal spotting, minor trauma (e.g. domestic fall), reduced FM and gastrointestinal symptoms) which are the majority of the acute presentations. One must also ensure that an efficient triage system is in place. Midwives should be trained properly in triaging and a doctor ideally senior should be present at triage to evaluate the situation upon encounter and treat immediately without any delays. A fast track system should be in place. Patients that have low acuity presentations should be assessed in one room by a team of midwives that when necessary involve an obstetrician. Patients with high acuity presentations (such as cord prolapse, fitting patients, altered level of consciousness, imminent birth, constant abdominal pain with or without bleeding and active bleeding should be assessed in another room directly by more senior members of the obstetric team [3] This will prevent prolonged waiting when there are simultaneous admissions and prevent adverse effects for the mother and the child as well as improving their safety and patient satisfaction. This would mean that less pressure is put on labour ward as only women who really need to be admitted will be present. Additional equipment like US and CTG machines are also required. Another counter argument would be patient satisfaction of care. In a single delivery suite women reported more satisfaction of care for a number of reasons including the delivery room setting and its privacy, improved continuity of midwifery care and avoidance of transfers.[4,5]

Another concern with having a triage room would be the risk of an emergency being delayed due to transit in a triage room. There is little literature discussing this issue. However, the aim of this room is to triage acute presentations into different levels of urgencies. A system should be in place to properly categorise emergencies. One system that has been validated is the Canadian Triage and Acuity Scoring System (CATS) for the initial assessment and triaging of patients.[6] This system classifies patients into a 5-tier level based on the acuity of their condition. Conditions such as cord prolapse and placental abruption are classified as resuscitation cases and are seen immediately. Cases like severe hypertension (BP>160/110mmHg) or symptomatic hypertension, sepsis and major trauma are classified as an emergency and patients have to be seen within 15 mins. Urgent cases such as hypertension (BP>140-90 to <160/110mmHg), signs of active labour, reduced FM etc have to be seen within 30mins. Less urgent and non-urgent cases are seen within 60min and 120 min respectively. Such a system in place ensures that the acute emergencies are seen without any delay.[3] The location of a triage room also plays a role in reducing delays in transit as it should be situated adjacent to delivery suite.

The commonest acute presentation to the labour ward were contractions, which was documented 131 times. 76.3% of the time, women were admitted. The remaining 23.7% occupied a bed in the labour ward for initial assessment and were then discharged home. In obstetrics, accurate diagnosis of onset of labour is a real challenge as criteria to accurately diagnose labour are not scientifically validated and incorrect diagnosis leads to poor management i.e either prolonged labour or unnecessary induction. In low-risk women, later hospital admission (for example at 4cm or more cervical dilation) has an increased rate of spontaneous vaginal births.[7] But to be able to safely offer later admission a precise

framework for diagnosis is necessary, to avoid discharging women in real labour. Premature diagnosis of labour means longer hospital admissions, increased rates of interventions such as induction and cesarean sections.[8] Hence, strict criteria to diagnose labour should be in place. Having a maternity triage room in place would allow midwives and obstetricians to prevent the remaining 23.7% of women presenting with contractions to occupy a bed, as they would be discharged safely home or monitored until they were into real labour and a bed in delivery suite would be warranted. [9]

?SROM was the second most common presentation, with 99 times being documented. 27.3% of the cases were not confirmed SROM. Diagnosis of SROM or PROM is based on maternal history and a speculum examination which shows a pool of clear fluid in the posterior fornix of the vagina. This is the gold standard for the diagnosis and no further tests are required. When a pool of amniotic fluid is not obviously visualised, different biochemical markers (such as IGFBP-1 or PAMG-1) that have a high sensitivity and specificity, are available to help and make the diagnosis. These are all used in conjunction with the womens' history and risk factors. This is a basic examination that can be done in a maternity assessment unit. It requires no fancy equipment except for a sterile speculum plus or minus an IGFBP-1 or PAMG-1 test to guide further management. Hence having this room will prevent blocking the limited beds available and only women with confirmed SROM will occupy a delivery suite.[10]

Decreased FM was the third commonest presentation in this audit. It was documented 49 times with 75.5% of the times women were not admitted and wrongly occupied a room in the labour ward. Management of decreased FM in singleton pregnancies can be performed in a maternity triage room. A proper history including duration of decreased FM, risk factors for stillbirth and fetal growth restrictions. On examining the women the main objective is to confirm fetal viability. Hand-held doppler or real-time ultrasound can be used to objectively assess fetal viability. The ideal duration of recording is 20–30 minutes, with the mother in a semi-recumbent position. Small for gestational age (SGA) fetus assessment should include an abdominal palpation, measurement of symphysis–fundal height and ultrasound biometry. The latter is most useful in assessing fetal size in women with a raised body mass index as clinical assessment is likely to be less accurate in these cases. Measurement of BP and urine for proteinuria should also be included in the assessment as pre-eclampsia is a cause of SGA.[11]

CTG monitoring, initially for 20 mins, is an easy and cheap way of detecting fetal compromise, if pregnancy is over 28 weeks gestation. This is something that can be easily done in a maternity assessment room and no beds in the labour ward need to be blocked in doing so. Admission CTG is useful as one can compare to changes that happen later on. However studies have shown that there was no evidence of benefit for low risk women. It increases the risk of LSCS and invasive fetal monitoring during labour.[12]

US in women presenting with reduced FM is indicated if the perception of reduced FM persists despite a normal CTG or if there are any additional risk factors for stillbirth. It should include measurements of abdominal circumference, amniotic fluid, estimated fetal weight and/or assessment of fetal morphology to identify SGA fetuses.[11] Hence, having a maternity assessment unit equipped with a CTG machine and an US will allow assessment of a common complaint to the labour ward ~ reduced FM, which does not require a labour ward room.

All other presentations could be assessed in a maternity triage room, with basic investigations to assess the health of the mother and wellbeing of the fetus. After initial assessments are done and working diagnoses are formulated women can be directed to the appropriate level of care i.e. discharged home, an obstetric ward or in labour ward. This will minimise wasting limited resources (delivery room) and better utilisation of these beds.

CONCLUSION

The presence of a maternity unit triage room adjacent to the labour ward in MDH will better utilise the limited number of delivery rooms. This audit showed that 53.3% of women who had an unplanned presentation to Central Delivery Suite did not need to block a bed in the labour ward and could have been assessed in a maternity unit triage room This means that by having a maternity unit triage room, there will be better management and utilisation of labour ward and resources are used appropriately for those most in need.

ACKNOWLEDGEMENT

For this audit to be possible, we would like to thank the secretary of Central delivery Suite who kept all the files of women discharged for us to review and log our data. We would also like to thank the midwives working in Central Delivery Suite who kept the admission book updated most of the time with all the data required for this audit.

SUMMARY BOX

What is already known about this subject

- Most maternity units in the UK there is a maternity triage room, where all incoming pregnant women with acute presentations are assessed.
- Telephone referrals from women who have queries, GPs and community midwives are also taken by the team of midwives in the maternity triage room.
- Apart from being an assessment area, additional procedures may be performed. These include blood tests, CTGs, BP monitoring, internal examinations and US if this is required.

What are the new findings

- 3% of women in this audit who had an unplanned admission to the labour ward could have been handled in a maternity triage room and did not need to block a bed in the labour ward.(38.8% of acute presentations did not need an admission and were discharged after initial review and 23.7% of the admitted women following an acute presentation did not deliver).
- The commonest acute presentation to the labour ward were contractions, ?SROM and decreased fetal movement.
- 5% of women presenting with decreased fetal movements were not admitted and wrongly occupied a room in the labour ward. Management of decreased FM in singleton pregnancies can be performed in a maternity triage room.

REFERENCES

1. Austin, R..\(2018\) Patient information obstetrics and gynaecology maternity triage services. Retrieved November 12, 2021, from https://www.uhcw.nhs.uk/download/clientfiles/files/Patient%20Information%20Leaflets/Women%20and%20Children_s/Maternity/118310_Maternity_Triage_Services_(1253)_-_October_pdf
2. Mid Cheshire, H..\(2021\) Maternity triage. Retrieved November, 14, 2021, from https://www.mcht.nhs.uk/information-for-patients/departmentsandservices/maternity/maternity-triage/
3. Saleh H, Al Monsoori Z, Serour A, Oniya O, Konje JC. Improving Emergency Care Through a Dedicated Redesigned Obstetrics and Gynecology Emergency Unit at the Women's Hospital, Doha, Qatar. AJOG Global Reports 2022:100053.
4. Janssen, P. A., Klein, M. C., Harris, S. J., Soolsma, J., & Seymour, L. C..\(2000\) Single room maternity care and client satisfaction. Birth, 27,(4) 235-243.
5. Pereira, S., Portela, F., Santos, M. F., Machado, J., & Abelha, A..\(2015\) Predicting pre-triage waiting time in a maternity emergency room through data mining. Icsh, pp. 105-117.
6. Smithson DS, Twohey R, Rice T, Watts N, Fernandes CM, Gratton RJ. Implementing an obstetric triage acuity scale: interrater reliability and patient flow analysis. Obstet Gynecol 2013;209: (4)287-293.

7. Jackson, D. J., Jeffrey,Lang JM FAU - Ecker, Ecker J FAU - Swartz, William,H., Tim,Swartz WH FAU - Heeren, & Heeren, T. Impact of collaborative management and early admission in labor on method of delivery
8. Quenby, S., Pierce, S. J., Brigham, S., & Wray, S..\(2004\) Dysfunctional labor and myometrial lactic acidosis. Obstetrics & Gynecology, 103,(4) 718-723.
9. Ragusa, A., Mansur, M., Zanini, A., Musicco, M., Maccario, L., & Borsellino, G..\(2005\) Diagnosis of labor: A prospective study. MedGenMed : Medscape General Medicine, 7,(3) 61.
10. Thomson, A., & Royal College of Obstetricians and Gynaecologists..\(2019\) Care of women presenting with suspected preterm prelabour rupture of membranes from 24 0 weeks of gestation: Green-top guideline no. BJOG: An International Journal of Obstetrics & Gynaecology, 126,(9) e152-e166.
11. Royal College of Obstetricians & Gynaecologists..\(2011\) Reduced fetal movements,(green-top guidelines no. 57). Hentet Fra Https://www.Rcog.Org.uk/globalassets/documents/guidelines/gtg_57.Pdf,
12. Devane, D., Lalor, J. G., Daly, S., McGuire, W., Cuthbert, A., & Smith, V..\(2017\) Cardiotocography versus intermittent auscultation of fetal heart on admission to labour ward for assessment of fetal wellbeing. Cochrane Database of Systematic Reviews, (1)

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ORIGINAL ARTICLE

Knowledge on the use of adrenaline autoinjectors among healthcare professionals

Caroline Gouder, Darren Borg, Stefano Corso, Ivan Debono, Stephen Montefort

Background

Adrenaline auto-injectors are indicated in the emergency treatment of allergic reactions including anaphylaxis prescribed to patients at increased risk for anaphylaxis, intended for immediate self-administration as emergency supportive therapy only and not a substitute for immediate medical care. The objective of this audit was to study the knowledge of indications for prescription and administration, mode of administration and post-administration management of an adrenaline autoinjector among health care professionals at our local hospital.

Method

86 medical doctors across various working grades in the Department of Medicine and 16 pharmacists were asked to complete a questionnaire in the presence of the investigator in July 2018 at Mater Dei Hospital, Malta.

Results

The mean age was 27.5years and 57% were females. 21 participants had previously prescribed an EpipenÂ®. Questions answered correctly were as follows: dosage in adults 63% and children 54%; correct indication for prescription 73%; correct indication for administration 100%; correct injection end of autoinjector 79.4%; incorrect patient positioning for injection 13%; correct site of administration 99%; correct duration of injection 56.8%; common side effects 73.5%; referral to A&E post-administration 75%; timing of repeat injection 80%; contraindications 86.7%. 68.6% participants did not feel confident explaining to patients when to use it while 72.5% participants did not feel confident explaining how to use it.

Conclusion

It is evident that education is urgently needed among health care professions on the indications for prescription, mode of administration as well as post-administration management of this potentially life-saving medication.

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Adrenaline administration intramuscularly is the first-line, most important drug for the treatment of anaphylaxis,[1-4] and the only one with proven lifesaving properties if received in a correct and timely manner, while simultaneously discontinuing exposure to the potential trigger.[4] Anaphylaxis is defined as a 'severe, life-threatening systemic hypersensitivity reaction' characterized by its rapidity in onset with potentially life-threatening airway, breathing, or circulatory problems, usually but not always, associated with skin and mucosal changes[2] which is potentially fatal if left untreated.[4] Anaphylaxis is usually IgE-mediated, but other non-IgE mediated mechanisms are also said to play a role.[4] Diagnosis and management are challenging since reactions may be quick, often unexpected and severe, with no single test to diagnose anaphylaxis in routine clinical practice.[5] The most common triggers are food, insect stings, and drugs.[4] Despite the clinical importance of anaphylaxis and a recent increase in its occurrence, studies regarding epidemiology and risk factors are poorly described.[6] The results of 10 European studies suggest an incidence of 1.5 to 7.9 per 100,000 person-years[2] while United Kingdom report an annual incidence of 8.4 per 100,000.[7] Recent studies in the United Kingdom show an increase in admissions with anaphylaxis over the last couple of decades.[2]

Adrenaline is an emergency supportive therapy only, and not a substitute for immediate medical care. The safety profile of intramuscular adrenaline is excellent although some patients may experience transient pallor, palpitations, and headache. Once received, patients are expected to seek medical help as soon as possible after the event in view of a possible biphasic reaction a few hours later. Self-administered adrenaline is the main out-of-hospital treatment for anaphylaxis[8] and is usually available as a pre-filled syringe.[9] Rapid administration of the drug is of utmost importance since delayed administration has been associated with a poor prognosis.[10] The European Academy of Allergy and Clinical Immunology Taskforce on Anaphylaxis recommends that all healthcare professionals should be familiar with recognition and acute and ongoing management of anaphylaxis since it is a clinical emergency with potentially fatal consequences.[2,3,11]

It is widely recognized that education and training of how to use adrenaline auto-injectors is important for effective management of anaphylaxis[12]and preventing fatalities,[11] and training should be offered to all professionals dealing with patients at risk of anaphylaxis.[2] For this important medication to be administered timely and appropriately, patients and their relatives must also be educated on adrenaline auto-injector usage. Once prescribed, patients should be trained by the prescribing professional to learn promptly and correctly, use of the device[8] in case of anaphylaxis occurring in the absence of expert help.

Despite accurate training identified in an Italian survey, it is reported that many patients are still unable to use the adrenaline auto-injector properly.[8] Studies in the paediatric population have shown that both doctors and patients themselves may use the adrenaline auto-injector improperly and that usage skills are improved by training.[13]It is recommended that allergists should ensure that technique is reviewed and re-explained to the patients each time a renewal of the auto-injector is prescribed.[2,8] However, at our local hospital in the absence of an allergy service, the prescribing doctor should be responsible for this. Estimates of the incidence of anaphylaxis are not available locally and there is no data on adrenaline auto-injector prescribing rates either.

In a study in Toronto performed on medical convention's delegates and emergency department personnel as well as pharmacists of the target hospitals and retail pharmacists, only 25% of the study participants were able to demonstrate the steps of injection correctly.[14] In a study in Brussels, it was concluded that the low rate of doctors prescribing adrenaline auto-injectors in the emergency department setting underlines the need to train doctors in various fields on the management of anaphylaxis in close collaboration with allergologists.[15] Such studies demonstrate a lack of allergy knowledge in primary care, especially the recognition and treatment of anaphylaxis were problematic and that national guidelines are often not followed.[16]

The objective of this audit was to study the knowledge of indications for prescription and administration, mode of administration and post-administration management of an adrenaline autoinjector among health care professionals at our local hospital.

MATERIALS AND METHODS

Eighty-six random consecutive medical doctors across various working grades in various specialities in the Department of Medicine and 16 consecutive pharmacists who agreed to participate, were asked to complete a questionnaire during one month at Mater Dei Hospital, Malta. Acceptance rate to participate was 100%. Epipen® was the only adrenaline auto-

Table 1 *Questions answered for clinical indications for adrenaline auto-injector prescription (n=102)*

Clinical Indications	Correct	Incorrect	No answer
Adrenaline auto-injector is indicated following a first anaphylactic reaction, n(%)	90 (88.2)	12 (11.8)	0 (0)
Food allergy and chronic asthma, n(%)	45 (44.1)	55 (53.9)	2 (1.9)
Food allergy with trace amounts of food, n(%)	79 (69.6)	31(30.4)	0 (0)
Nut allergy, n(%)	94 (92.1)	8 (7.9)	0 (0)

injector available locally during the time of recruitment. Questions and their respective answers were therefore designed based on the Summary of Product Characteristics of the adult Epipen®.[17]

The questionnaire (Supplement File 1) was divided into the following sections: age, gender, working grade, whether the professional ever received training on adrenaline auto-injectors and whether the subject ever prescribed such treatment, indications for prescription, dosing regimen, mode of administration as well as how confident the professional felt about prescribing or explaining the use of adrenaline auto-injector to the patient.

The questionnaire was completed in the presence of the investigator so as to ensure that the participants did not search for the answers. The questionnaires were kept anonymous. Patient demographics and responses to the questionnaires were inputted and calculated using Microsoft Excel®.

RESULTS

Our cohort included a total of 102 participants, 86 medical doctors and 16 pharmacists. The mean age was 27.5years and 57% were females. Only 16.7% reported that they had been trained on how to administer an adrenaline auto-injector and 20.6% of doctors reported that they had ever prescribed an adrenaline autoinjector.

Table 1 shows the percentage of participants who answered the questions in the clinical indications for prescription section of the questionnaire. The majority of responders recognized the necessity for adrenaline in a first anaphylactic reaction and in nut allergy but not so frequently in the other indications.

Table 2 shows the percentage of participants who answered the questions for the prescription of an adrenaline auto-injector. The dosage for both adults and children was incorrect for 62.7% and 39.2% respectively. Timing for adrenaline administration was correct in the majority of responses.

Table 3 shows the responses to methods of administration of an adrenaline auto-injector. Most responders thought that adrenaline in such indications could be erroneously administered intravenously in the deltoid or buttocks and most were not aware that the injector must be kept intramuscularly for 10 seconds post-administration.

Table 2 *Questions answered for prescription details of adrenaline auto-injector (n=102).*

Prescription details	Correct	Incorrect	No answer
The dose of adrenaline in adults over 20kg is 0.5mg, n(%)	32 (31.4)	64 (62.7)	6 (5.9)
In children 10 to 20kg, the adrenaline dose is 0.15mg, n(%)	55 (53.9)	40 (39.2)	7 (6.9)
Adrenaline should be administered immediately every time the patient notices he ingested an allergen, n(%)	102 (100)	0 (0)	0 (0)
Adrenaline should be administered immediately if patient exposed to allergen, is asymptomatic, but far away from hospital, n(%)	95 (93.1)	6 (5.9)	1 (0.1)

Table 3 *Questions answered for mode of administration of adrenaline auto-injector (n=102)*

Mode of Administration	Correct	Incorrect	No answer
Blue end of the EpiPen® is site which contains injection, n(%)	82 (80.4)	19 (18.6)	1 (0.98)
Orange end of the EpiPen® is site which contains injection, n(%)	70 (68.6)	25 (24.5)	7 (6.8)
Adrenaline can be injected standing up, n(%)	81 (79.4)	14 (13.7)	7 (6.8|)
Adrenaline can be given intravenously, n(%)	13 (12.7)	85 (83.3)	4 (3.9)
Adrenaline cannot be injected through clothes, n(%)	96 (94.1)	4 (3.9)	2 (1.9)
One of the injection sites is the buttock, n(%)	43 (42.2)	59 (57.8)	0 (0)
One of the injection sites is the thigh, n(%)	100 (98)	2 (1.9)	0 (0)
One of the injection sites is the deltoid muscle, n(%)	65 (63.7)	37 (36.2)	0 (0)
The injector must be kept inside the area for 10 seconds, n(%)	26 (25.5)	76 (74.5)	0 (0)

Table 4 shows the responses to management after administration of an adrenaline auto-injector.

When asked these questions, 68.6% of participants did not feel confident explaining to patients when to use an adrenaline auto-injector while 72.5% of participants did not feel confident explaining to patients how to use it.

DISCUSSION

Few studies have assessed medical professionals' knowledge and ability to use adrenaline auto-injectors. This has never been done locally. In recent years, self-administered adrenaline auto-injector pens have become commonly prescribed for patients at risk of anaphylaxis or severe allergic reactions.[18] EpiPen® was the only epinephrine auto-injector at the time of data collection in Malta. We included pharmacists in our survey since these professionals too play an important role when dispensing an auto-injector to ensure that a patient is provided with sufficient knowledge.

In a survey among members of the American College of Allergy, Asthma and Immunology to assess their self-reported practices and procedures in the management of anaphylaxis, adherence to practice parameter recommendations was not surprisingly high.[11] On the other hand, a small study in

Table 4 *Questions answered for post-administration management of adrenaline auto-injector (n=102)*

Post-Administration	Correct	Incorrect	No answer
A localised erythematous skin reaction is a common side-effect, n(%)	101 (99)	1 (0.9)	0 (0)
It is advised to massage the area after injection, n(%)	19 (18.6)	83 (81.4)	0 (0)
It is common to have pruritus in the area post-injection, n(%)	58 (56.9)	38 (37.3)	4 (3.9)
Injection can be repeated at least after 1 minute, n(%)	21 (20.6)	78 (76.5)	3 (2.9)
Injection can be repeated at least after 5 minutes, n(%)	97 (95.1)	4 (3.9)	1 (0.9)
Injection can be repeated at least after 8 minutes, n(%)	67 (65.7)	32 (31.4)	3 (2.9)
After injection it's not always necessary for patient to go to A&E, n(%)	49 (48)	50 (49.1)	3 (2.9)

Netherlands using an online questionnaire sent to pharmacists, a country were pharmacists supply adrenaline auto-injectors to patients and instruct patients how and when to use it, only 8% respondents gave correct answers concerning the proper adrenaline auto-injector demonstration to food-allergic patients.[16]

Risk factors for an anaphylactic reaction were defined as follows: a previously severe anaphylactic reaction to a food requiring emergency treatment or hospitalization, asthma or asthmatic reactions to food, adolescent or young adult age, systemic reaction to traces of food allergen, and having a peanut or nut allergy.[19] There are six absolute clinical indications for an adrenaline auto-injector prescription as follows : previous anaphylaxis with food, latex, aeroallergens such as animals or other unavoidable triggers, exercise-induced anaphylaxis, previous idiopathic anaphylaxis, co-existent unstable or moderate-to-severe persistent asthma with food allergy, venom allergy in adults with previous systemic reactions underlying mast cell disorders.[2] Not all respondents were aware that adrenaline must be given always even with a first anaphylactic reaction. Less than half of respondents were aware of the necessity to prescribe adrenaline in patients with food allergy and co-existent asthma. Co-existing asthma is a risk factor for anaphylaxis and fatal anaphylaxis, especially if it is severe and uncontrolled.[2] Foods are the most common anaphylaxis trigger in infants, children, teens, and young adults. A meta-analysis with data from 34 studies reported an incidence rate of food-induced anaphylaxis to be 0.14 per 100 person-years at all ages, and up to 7 per 100 person-years in children aged 0 to 4 years.[20]

The dose of adrenaline during an anaphylactic reaction in adults or children was poorly known. Intramuscular adrenaline(1mg/ml) should be given at a dose of 0.01ml/kg of body weight to a maximum total dose of 0.5mg. Patients weighing between 7.5 to 25 kg should receive 0.15 mg dose with patients being moved to 0.3 mg dose at 25 to 30 kg.[2,21] At the time of the survey, the adrenaline auto-injectors were available as 0.15 or 0.3mg only. There is no data as to which patients should receive a 0.5mg dose auto-injector when this is available. The same dose could be repeated every 5 to 15 minutes as necessary.[2]

In a survey conducted among 674 Japanese physicians regarding timing of adrenaline administration it was concluded that they did not necessarily understand the importance of timing of adrenaline administration.[22] Early injection of adrenaline for anaphylaxis, defined as initial injection before emergency department arrival, significantly reduced the hospital admissions, compared with injection post-arrival.[20] A large series of anaphylaxis-related fatalities were reported when delayed injection of adrenaline was reported when only 23% of 92 individuals received it prior to cardiac arrest.[20] Timing of administration was not questioned in our survey. The correct end of the colour-coded adrenaline injector was not known to all interviewed. This could be dangerous in view of possible injection of the administrator's digit instead of the patients' musculature. However, adrenaline auto-injectors tend to have very clear instructions on the cover of the injector, facilitating and providing readily available instructions for correct administration during an emergency.13.7% of our respondents replied that adrenaline can be administered standing up. This should not be allowed in view of the risk of developing 'empty ventricle syndrome' which can precipitate a profound loss of blood pressure and resultant death during the anaphylactic reaction.[21] 83.3% said that the adrenaline during the anaphylactic reaction could be given intravenously. Adrenaline during anaphylaxis should ideally be given intramuscularly. Not only is it important to promptly self-administer an autoinjector using the correct technique, but the exact location of adrenaline deposition is also very important. Significantly faster peak plasma concentrations due to more rapid absorption are achieved via the intramuscular route when compared to the subcutaneous route[21,24]or intramuscularly in the upper arm.[22] The site of administration was correctly recognised as the anterolateral thigh but other sites such as the deltoid were also erroneously considered. Many failed to recognise the importance of keeping the injection in for 10seconds. In a study in Toronto aimed at assessing community-based professionals' knowledge of epinephrine auto-injector use. The most common problem with the use of the auto-injector trainer device was forgetting to hold the auto-injector in site for 10 seconds(n=122).[14]

In a study by Lowe et al 18% of respondents would not routinely inform patients of the need to seek immediate medical attention in the event of having to use a pen.[18] Only 48% of our respondents were aware that patients still need to be referred to the emergency department post-adrenaline administration. Treatment of anaphylaxis is not complete following resolution of an acute episode.[20] Biphasic anaphylactic reactions have been reported to develop in up to 20% of reactions.[2] In order to decrease anaphylaxis morbidity and

mortality in the community, referral to an allergist is recommended so as to reduce the risk of future severe anaphylaxis requiring hospital admission.[20] Specialist advice from an allergist is essential during a follow-up visit is essential to investigate possible triggers and potential cofactors, to perform a risk assessment and to provide advice including avoidance measures so as to prevent future episodes.[2] It is recommended that to prevent future anaphylactic reaction, the mainstays of long-term management include developing a personalized risk reduction strategy using a formalised anaphylaxis action plan with an adrenaline auto-injector and a personalized emergency response plan is crucial.[2,4,22] Patients should be equipped to treat recurrences that occur despite attempts to avoid trigger exposure in the community.[3] Research has shown that specific interventions by allergists may improve patient adherence to recommendations for managing anaphylaxis.[11]

The lack of confidence reported by our participants when explaining how to use an adrenaline auto-injector indicated a limited knowledge on its therapeutic indication, also reflected in the questions related to clinical indications for its use. In an international survey, less than half of general practitioners felt confident in their use and only 359(65%) of those who had prescribed adrenaline pens would arrange demonstration of when and how to use them.[18] Recommendations state that doctors have a responsibility to ensure that patients know how and when to take any prescribed medication, and it is unacceptable to prescribe a dangerous drug with no demonstration on how to use it.[25]

Upon prescription of an adrenaline auto-injector, healthcare providers familiar with adrenaline autoinjectors must instruct the patient on how and when to use the device, together with regular review of technique is vital for patients who have been prescribed these devices.[22,26] Studies have shown that usage skills for an auto-injector tend to decrease with time. Sicherer et alreported a decline after one year after the initial training in food allergies[27]while a study by Topal et alwho compared skills between 3 and 6 months after initial training, skills were stable after 3 months but worse skills were reported after 6 months.[13] These studies emphasize the need for repeat training in patients at risk of anaphylaxis.

Limitations of this study include the small sample size particularly among the pharmacist group, which did not allow comparison between both health care professionals and between medical doctors across the various working grades. The fact that the investigator was present during completion of the questionnaire could have imposed a degree of psychological pressure on the respondent. However, the questionnaire was posted into a box, which was only opened on completion of data collection.

Our survey results indicate that education is urgently needed among health care professions on the indications for prescription, mode of administration as well as post-administration management of this potentially life-saving medication. With the development of an emergency action plan to be distributed among healthcare professionals for readily available distribution among patients, together with the delivery of lectures to healthcare professionals on adrenaline auto-injector use, we aim to increase the knowledge of adrenaline auto-injectors locally and hence provide a better service to our vulnerable allergic patients.

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REFERENCES

1. Kemp SF, Lockey RF, Simons FE; World Allergy Organization ad hoc Committee on Epinephrine in Anaphylaxis. Epinephrine: the drug of choice for anaphylaxis. A statement of the World Allergy Organization. Allergy. 2008 Aug;63:(8)1061-70.
2. Muraro A, Roberts G, Worm M, Bilò MB, Brockow K, Fernández Rivas M et al EAACI Food Allergy and Anaphylaxis Guidelines Group. Anaphylaxis: guidelines from the European Academy of Allergy and Clinical Immunology. Allergy. 2014 Aug;69:(8)1026-45.
3. Simons FE, Ardusso LR, Bilò MB, El-Gamal YM, Ledford DK, Ring J et al World Allergy Organization. World Allergy Organization anaphylaxis guidelines: summary. J Allergy Clin Immunol. 2011 Mar;127:(3)587-93.
4. Rutkowski K, Dua S, Nasser S. Anaphylaxis: current state of knowledge for the modern physician. Postgrad Med J. 2012 Aug;88(1042):458-64.

5. Waserman S, Chad Z, Francoeur MJ, Small P, Stark D, Vander Leek TK et al Management of anaphylaxis in primary care: Canadian expert consensus recommendations. Allergy. 2010 Sep;65:(9)1082-92.
6. Lieberman P, Camargo CA Jr, Bohlke K, Jick H, Miller RL, Sheikh A et al Epidemiology of anaphylaxis: findings of the American College of Allergy, Asthma and Immunology Epidemiology of Anaphylaxis Working Group. Ann Allergy Asthma Immunol. 2006 Nov;97:(5)596-602.
7. Peng MM, Jick H. A population-based study of the incidence, cause, and severity of anaphylaxis in the United Kingdom. Arch Intern Med. 2004 Feb 9;164:(3)317-9.
8. Ridolo E, Montagni M, Bonzano L, Savi E, Peveri S, Costantino MT, et al How far from correct is the use of adrenaline auto-injectors? A survey in Italian patients. Intern Emerg Med. 2015 Dec;10:(8)937-41.
9. Ewan P, Brathwaite N, Leech S, Luyt D, Powell R, Till S et al Prescribing an adrenaline auto-injector - personalized care recommended. Clin Exp Allergy. 2016 Dec;46:(12)1621-1622.
10. [Braganza SC, Acworth JP, Mckinnon DR, Peake JE, Brown AF. Paediatric emergency department anaphylaxis: different patterns from adults. Arch Dis Child. 2006 Feb;91:(2)159-63.
11. Fineman S, Dowling P, O'Rourke D. Allergists' self-reported adherence to anaphylaxis practice parameters and perceived barriers to care: an American College of Allergy, Asthma, and Immunology member survey. Ann Allergy Asthma Immunol. 2013 Dec;111:(6)529-36.
12. Gosbee LL. Nuts! I can't figure out how to use my life-saving epinephrine auto-injector! Jt Comm J Qual Saf. 2004 Apr;30:(4)220-3.
13. Topal E, Bakirtas A, Yilmaz O, Karagol IH, Arga M, Demirsoy MS, Turktas I. When should we perform a repeat training on adrenaline auto-injector use for physician trainees? Allergol Immunopathol (Madr). 2014 Sep-Oct;42:(5)472-5.
14. Grouhi M, Alshehri M, Hummel D, Roifman CM. Anaphylaxis and epinephrine auto-injector training: who will teach the teachers? J Allergy Clin Immunol. 1999;104:(1)190-3.
15. Mostmans Y, Grosber M, Blykers M, Mols P, Naeije N, Gutermuth J. Adrenaline in anaphylaxis treatment and self-administration: experience from an inner city emergency department. Allergy. 2017 Mar;72:(3)492-497.
16. Saleh-Langenberg J, Dubois AE, Groenhof F, Kocks JW, van der Molen T, Flokstra-de Blok BM. Epinephrine auto-injector prescriptions to food-allergic patients in primary care in The Netherlands. Allergy Asthma Clin Immunol 2015;15;11:28.
17. Summary of Product Characteristics of the adult Epipen®. Available from: https://www.medicines.org.uk/emc/product/4289/smpc#gref. Accessed 1st October 2020.
18. Lowe G, Kirkwood E, Harkness S. Survey of anaphylaxis management by general practitioners in Scotland. Scott Med J. 2010 Aug;55:(3)11-4.
19. Muraro A, Roberts G, Clark A, Eigenmann PA, Halken S, Lack G et al EAACI Task Force on Anaphylaxis in Children. The management of anaphylaxis in childhood: position paper of the European academy of allergology and clinical immunology. Allergy. 2007 Aug;62:(8)857-71.
20. Simons FE, Ebisawa M, Sanchez-Borges M, Thong BY, Worm M, Tanno LK, Lockey RF, El-Gamal YM, Brown SG, Park HS, Sheikh A. 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. World Allergy Organ J. 2015 Oct 28;8:(1)32.
21. Fischer D, Vander Leek TK, Ellis AK, Kim H. Anaphylaxis. Allergy Asthma Clin Immunol. 2018 Sep 12;14(Suppl 2):54.
22. Imai T, Sugizaki C, Ebisawa M. [Physicians' knowledge with regard to the timing of adrenaline administration for anaphylaxis in Japan]. Arerugi. 2013 Nov;62:(11)1515-21. Japanese.
23. Frew AJ. What are the 'ideal' features of an adrenaline (epinephrine) auto-injector in the treatment of anaphylaxis? Allergy. 2011 Jan;66:(1)15-24.
24. Davies H, Harris J, Kakoo A. Treatment of acute anaphylaxis. Patients should be taught how to inject adrenaline. BMJ. 1996 Mar 9;312(7031):638.
25. McLean-Tooke AP, Bethune CA, Fay AC, Spickett GP. Adrenaline in the treatment of anaphylaxis: what is the evidence? BMJ. 2003 Dec 6;327(7427):1332-5.
26. Sicherer SH, Vargas PA, Groetch ME, Christie L, Carlisle SK, Noone S, Jones SM. Development and validation of educational materials for food allergy. J Pediatr. 2012 Apr;160:(4)651-6.

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ORIGINAL ARTICLE

Audit of Inpatient Chronic Urinary Retention Management

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Background

Chronic urinary retention (CUR) occurs when urine accumulates in the bladder secondary to incomplete voiding. The aim of this audit was to assess compliance to the Mater Dei Hospital Urinary Retention Management Guidelines in a cohort of patients admitted between August 2019 and February 2020.

Methodology

Patients admitted because of CUR were included. Data was acquired from medical files, discharge letters, hospital electronic record systems and urology outreach records.

Standard used

The Urinary Retention Management Guidelines, published in 2018, were considered standard for outcome comparison.

Results

The quantitative results included data on clinical presentation, inpatient management and medium-term outcomes. 55% had a successful TWOC after CUR. 45% were treated pharmacologically, 35% had a trans-urethral resection of the prostate, 10% started a self-intermittent catheterisation (SIC) programme, 5% remained with a long-term catheter and 5% required a re-trial without catheter (TWOC).

Conclusion

Compliance to MDH guidelines was suboptimal in some cases. This audit highlights CUR management issues which can be optimised and also current outcomes of patients presenting in CUR. 55% of patients presented with a degree of acute kidney injury. Nephrology specialists were rarely involved in the management of these patients.

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Urinary retention is defined as the incapability of voluntary complete bladder voiding, resulting in accumulation of urine in the bladder.[1] Chronic urinary retention (CUR) is described as painless retention accompanied by an increased post void residual (PVR).[2] In July 2018 local guidelines for the management of urinary retention were published, delineating the clinical features of CUR, necessary investigations and management according to findings, including discharge plans. The aim of this audit was to evaluate compliance to the Urinary Retention Management Guidelines (Supplementary File 1), in a cohort of patients suffering from CUR The evaluation included assessment of patient's presentation, investigations chosen and eventual treatment plans.

METHODOLOGY

All patients admitted with CUR in the period between August 2019 to February 2020, were included in the audit. The data was predominantly obtained from patient's medical files (current and old notes), discharge letters, hospital electronic systems and urology outreach records. The information obtained from all sources comprising, patient demographics, investigations, management and treatment plans, were inputted into a database accordingly.

RESULTS

Demographics

A total of 20 patients were included in the audit, 19 (95%) of which were male and 1 (5%) female. The maximum age was that of 84 years and the minimum age 57 years, with an average age of 71.6 years.

Referral Source

Patients were predominantly referred from the Accident and Emergency department, 18 (90%). Other referral sources included, 1 (5%) from another surgical firm and 1 (5%) from the community (Figure 1).

Clinical Features

Of the patients included, only 8 (40%) had significant lower urinary tract symptoms (LUTS). 14 (70%) were found to be in painful urinary retention, while 6 (30%) were in painless retention. 9 (45%) had a previous history of urinary retention and only 1 (5%) had a preceding transurethral resection of the prostate (TURP).

On presentation 85% of patients were already on pharmacological treatment, of which, 11 were on a combination of Dutasteride and Tamsulosin (Combodart), 4 on Tamsulosin and 2 on Finasteride.

Post-void residual volume (PVR) was measured in 90% of cases. The minimum PVR was 350ml and the maximum PVR was 2300ml, with an average of 1075.1ml.

Investigations

In 80% of cases, urinalysis and microscopy was sent. Renal profile was taken and sent in 95% of cases. The minimum eGFR was 6 ml/min/1.73m^2 and the maximum 125 ml/min/1.73m^2, with an average of 55.95 ml/min/1.73m^2. 45% of patients had an eGFR of >60 ml/min/1.73m^2, while the remaining 55% had some degree of acute kidney injury (AKI).

An ultrasound of the kidneys, ureters and bladder (US KUB) was performed in 35% of cases. 15% of patients were found to have signs of hydronephrosis on US KUB None of the patients who underwent US KUB

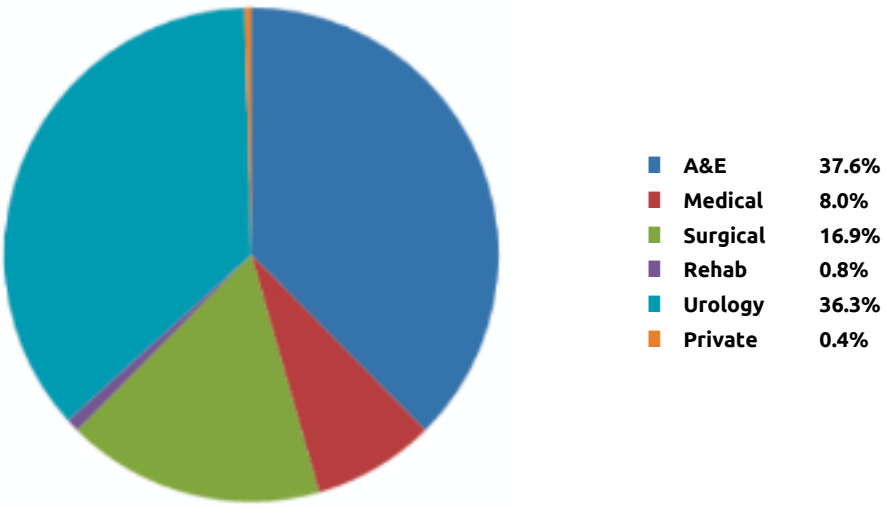

Figure 1 *Source of Referral*

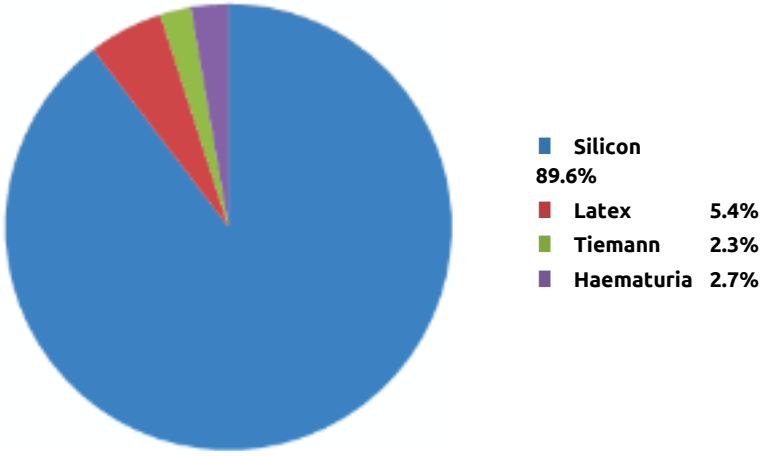

Figure 2 *Type of catheter inserted*

had signs of renal atrophy. Renal Replacement Therapy (RRT) was not required in any instance.

Management

In 90% of cases a urinary catheter was inserted, 13 (72.2%) of which were silicone catheters, 4 (22.2%) haematuria catheters and 1 (5.5%) latex catheter. Of the catheters inserted 50% were 16F in size (Figure 2).

Type Of Catheter Inserted

Post-obstructive diuresis (POD), defined as >200ml urine output over 2 hours or >3 L urine output over 24 hours, was noted in 45% of cases. The maximum duration of POD (>3l/24hrs) was 5 days, with an average duration of 2.75 days. The total urine output over the first 24 hours on average was 2,327.3 ml.

Intravenous fluid replacement was set up in 60% of cases. Serum electrolytes and serum creatinine 12 hourly were only taken in 25% of patients. Moreover, urine samples for measurement of urinary sodium, potassium and osmolality were sent for as little as 10% of patients. Daily weight of patient was not recorded throughout. Nephrologists were consulted in just one case.

Pharmacological Treatment

45% of patients were started on drug treatment for benign prostatic hyperplasia (BPH). 8 (40%) individuals were already being treated for BPH, 3 (15%) of which had their treatment changed accordingly.

85% of the cohort were discharged on various pharmacological treatment. 11 (55%) were discharged on Combodart, 4 (20%) on Tamsulosin and 2 (10%) on Finasteride (Figure 3).

Trial without Catheter (TWOC)

The average amount of days spent with a bladder catheter was 17.17, with a minimum of 4 days and a maximum of 86 days. In 13 patients TWOC was only

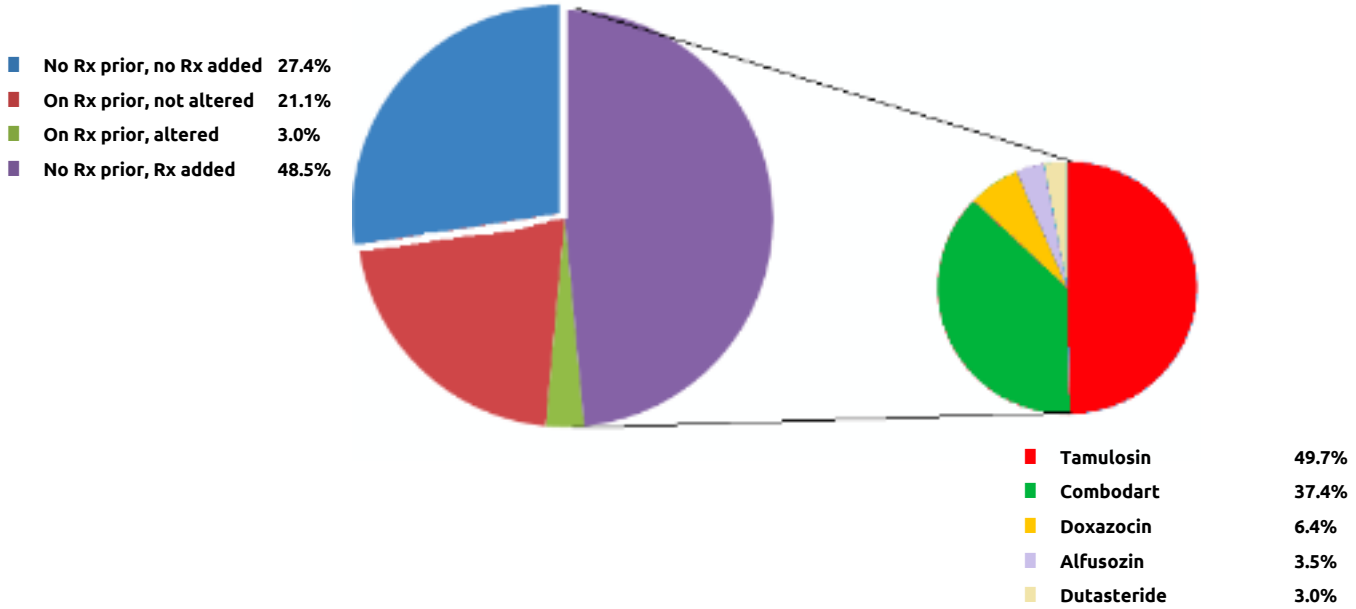

Figure 3 *Treatment changes and type of treatment started*

attempted once, while in the remaining patients there were 2 or 3 attempts. TWOC was successful in 55% of cases. The average PVR following TWOC was that of 188.67ml, with a maximum of 700ml and a minimum of 0ml. In the 45% who failed TWOC, the average catheter residual was 525 ml (maximum of 700 ml and a minimum of 350ml).

Outcome

The average length of stay for patients admitted with CUR was 585 days. Nine (45%) patients were discharged on medical treatment and followed up at outpatients. Seven (35%) patients underwent TURP. One (5%) remained with a long-term catheter and in another patient (5%) TWOC was reattempted. The remaining two patiens (10%) were introduced to self-intermittent catheterization (SIC).

DISCUSSION

Chronic urinary retention is the inability to void the bladder, which is usually painless, as opposed to acute urinary retention. The PVR is a measurement used to distinguish chronic from acute urinary retention. It is easily quantified by an ultrasound scan of the bladder post-micturition. Up till now, there has been no agreement on a defined PVR value, over which chronic urinary retention is diagnosed. Most agree that a significant PVR is between 300 to 1000ml[3] While Abrams et al, used a diagnostic minimum PVR value of 300ml.[4], the American Urological Association defines non-neurogenic CUR as a PVR of more than 300ml, persisting for a minimum of 6 months and documented on at least 2 or more instances[5] The PVRs in the patients included range from a minimum of 350ml and a maximum of 2300ml.

CUR mostly affects men rather than women and mostly targets the elderly.[6] 95% of our cohort were male while only 5% were female and the average age was around 71 years, with the lowest being 57 years. Only 30% were found to be in painless CUR The remaining had painful retention. This could be due to acute-on-chronic urinary retention where a person suffering from CUR suddenly stops voiding.[7]

Recognizing CUR is not always a simple task. Some points in the history-taking which are useful are the presence of lower urinary tract symptoms such as voiding difficulties, frequency, nocturia and nocturnal enuresis. A previous history of a urinary tract infection, constipation or previous episodes of CUR helps in reaching a CUR diagnosis. Medications which hint towards CUR include alpha adrenergic blockers, 5 alpha reductase inhibitors and anticholinergics; 85% were already on some. NICE also recommends a patient examination comprised of an abdominal, a genital and a digital rectal examination.[7]

CUR can be divided into 2 categories: low pressure CUR (LPCUR) and high-pressure CUR (HPCUR). Bladder pressures post-micturition of 30cm H2O and above are classified as HPCUR while pressures of around 20 or less fall under LPCUR Patients with HPCUR are at increased risk of developing upper urinary tract involvement such as hydronephrosis or a decline in renal function shown by a rising creatinine. Differentiating between the two is essential since patients with HPCUR need urgent catheterisation.[8] HPCUR always requires catheterisation as opposed to LPCUR According to a randomised controlled trial conducted by Boettcher et al, slow, or gradual bladder decompression does not confer additional benefits, such as minimising the risk of circulatory collapse or haematuria, when compared to rapid decompression. Thus, rapid decompression is preferred.[9]

As mentioned above a rising creatinine and hydronephrosis are both important indicators for urgent catheterization. During this audit a renal profile was taken in 95% of cases, with 55% having some degree of AKI However, US KUB was only done in 35% of cases, with 15% of those having hydronephrosis. This high level of non- compliance means that possible upper urinary tract involvement was missed.

A urinary catheter was used in 90%, with the majority having a 16F silicone catheter inserted. When inserting a urinary catheter, output charting must be done to identify the potential development of POD This was noted in 45%. The Urinary Retention Management Guidelines of 2018, state that if POD is diagnosed the following are advised: a daily weight, 12-hourly renal profiles, testing the urine for electrolytes and osmolality, nephrology consultations and setting up an IVI if POD continues after reaching haemostasis.[10]

The results show that no daily weights were taken, only one case was discussed with a nephrologist, 12-hourly renal profiles taken in 25% and a minimum of 10% checked for urinary electrolytes and osmolality. On the other hand, intravenous fluid replacement was set up for 60% of cases. Despite satisfactory levels of input-output charting and identification of POD, it was still inadequately managed in most cases.

Moreover, the fact that urinary electrolytes were only checked in 10% of patients, reveals that fluid types may have not been chosen appropriately.

Studies have shown that in patients with benign prostatic hyperplasia (BPH), a successful TWOC is more likely to be achieved when starting alpha adrenergic blockers with catheterisation and attempting a TWOC 3 days after.[11] In this cohort, a minimum of 4 days passed before a TWOC was attempted.

Pharmacological intervention is essential in managing CUR As BPH is one of the leading causes of CUR in males, drugs targeting this have been widely used. Alpha-1 adrenergic antagonists, such as tamsulosin, relax the bladder neck and the prostate capsule while 5-alpha reductase inhibitors like finasteride work as anti-androgenics to reduce prostatic tissue mass. When used together, they significantly reduce BPH progression hence decreasing CUR[12] 85% were discharged with pharmacological treatment, with the majority discharged on Combodart, which is a 5-alpha reductase inhibitor and alpha-1 adrenergic antagonist combination.

A total of 35% underwent TURP while 10% had SIC introduced. A study comparing TURP with SIC showed that both are effective for symptom relief with SIC showing to be useful for recovery of bladder function. SIC was shown to be useful before TURP in cases of LPCUR while those with HPCUR had good outcomes from surgery.[13]

RECOMMENDATIONS

Every patient presentation should be assessed clinically and managed according to the appropriate pathway. US kidneys and renal profiles should be performed in all CUR patients. When opting for urethral catheterization, urine residuals and urine output need to be measured and recorded diligently. More education regarding POD, its potential complications and management is required. Emphasising the importance of adequate investigations, fluid replacement and involvement of nephrologists when necessary. Improving knowledge of guidelines and coordination between clinicians and health professionals, can lead to better patient outcomes. Patients should also be educated, encouraged to comply to pharmacological treatment and involved in their own catheter care.

CONCLUSION

The audit carried out showed that the guidelines were only partially followed in most cases. Inadequate management of CUR may lead to several complications, which may include chronic kidney disease and hence life-long repercussions. Improving compliance to, and application of these guidelines in all patients presenting with CUR,

will result in standardisation of care and preferable end results. This will be achieved by organizing teaching sessions for healthcare professionals, based in both wards and the emergency department, and reauditing once teaching has been completed.

REFERENCES

1. Health Quality Ontario, 2019. Intermittent catheters for chronic urinary retention: A health technology assessment. *Ontario health technology assessment series*, *19*,(1) p.1.
2. Selius, BA and Subedi, R, 2008. Urinary retention in adults: diagnosis and initial management. *American family physician*, *77*,(5) pp.643-650.
3. Negro, CL and Muir, GH, 2012. Chronic urinary retention in men: how we define it, and how does it affect treatment outcome. BJU international, 110,(11) pp.1590-1594.
4. Abrams, PH, Dunn, M and George, N, 1978. Urodynamic findings in chronic retention of urine and their relevance to results of surgery. Br Med J, 2(6147), pp.1258-1260.
5. Stoffel, J, Lightner, D, Peterson, A, Sandhu, J, Suskind, A, Wei, J, Bertsch, J, Hubbard, H, Pope, S and Wilder, MV, 2016. Non-neurogenic chronic urinary retention: consensus definition, management strategies, and future opportunities. AUA White Paper. Linthicum, MD: American Urological Association.
6. Serlin, DC, Heidelbaugh, JJ and Stoffel, JT, 2018. Urinary retention in adults: evaluation and initial management. American family physician, 98,(8) pp.496-503.

7. National Institute for Health and Care Excellence, 2015. Lower urinary tract symptoms in men: management.
8. Martin, J, Chandler, W and Speakman, M, 2019. Investigating chronic urinary retention. bmj, 366, p.l4590.
9. Boettcher, S, Brandt, AS, Roth, S, Mathers, MJ and Lazica, DA, 2013. Urinary retention: benefit of gradual bladder decompression-myth or truth? A randomized controlled trial. Urologia internationalis, 91,(2) pp.140-144.
10. Sciberras, J, Pace, K, Busuttil, G, Piscopo, T, 2018. Urinary Retention Management Guidelines.
11. Selius, BA and Subedi, R, 2008. Urinary retention in adults: diagnosis and initial management. American family physician, 77,(5) pp.643-650.
12. Tarter, TH and Vaughan Jr, ED, 2006. Inhibitors of 5α-reductase in the treatment of benign prostatic hyperplasia. Current pharmaceutical design, 12,(7) pp.775-783.
13. Ghalayini, IF, Al-Ghazo, MA and Pickard, RS, 2005. A prospective randomized trial comparing transurethral prostatic resection and clean intermittent self-catheterization in men with chronic urinary retention. BJU international, 96,(1) pp.93-97.

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ORIGINAL ARTICLE

Assessment of obstructive sleep apnea among Malaysians with open-angle glaucoma using the STOP-Bang Questionnaire

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Introduction

Glaucoma is the most common cause of irreversible loss of vision worldwide. Numerous studies have confirmed an association between open-angle glaucoma (OAG) and obstructive sleep apnea (OSA) among Caucasian and Chinese populations; however, there has been no published study from South East Asia on this subject.

Materials and Methods

Therefore, our objectives were to use the STOP-BANG questionnaire (SBQ) to determine the factors (socio-demography, medical comorbidities) associated with the risk of OSA among patients with OAG and the association between glaucoma parameters and OSA. The SBQ was used for classifying patients as OSA low risk (score ≤ 2) to moderate/high risk (score ≥ 3).

Results

We found that the mean patient age was 64.2 ± 8.9 years, of which 55.4% (245 subjects) were males. The prevalence of moderate/high risk of OSA among the open angle glaucoma patients was 247 (55.9%), which comprised of mostly males(n=196,44.34%) compared to females (n=51,11.54%). Multiple logistic regression analysis showed that the predictors of moderate/high risk of OSA were males [odds ratio (OR) = 189.7, 95% confidence interval (CI) = 55.21, 651.69], high body mass index (OR = 1.23, 95% CI = 1.14, 1.33), diabetes (OR = 3.1, 95% CI = 1.45, 6.63) and hypertension (OR = 70.73, 95% CI = 22.59,221.50).

Conclusion

The identification of modifiable risk factors will be beneficial in the prevention of visual loss from glaucoma. The prevalence of moderate to high risk OSA risk was 56.9% among patients with OAG, that supports the vascular theory causing glaucomatous damage.

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Glaucoma remains a major global health problem with the risk for irreversible loss of vision.[1] It is known as the "Silent thief of sight" as it steals vision slowly and painlessly, therefore, most patients present late with permanent visual disability.[2] Identifying modifiable risk factors for this disorder is of vital importance as it will delay it progression and reduce the cost of treatment for patients. The objective of this study was to determine the prevalence of moderate and high-risk OSA among patients with open-angle glaucoma (OAG) and also determine the co-morbidity of these patients. This would bridge the gap of knowledge, raise the awareness among clinicians, enable the implementation for early intervention and prevent complications of OSA.

MATERIALS AND METHODS

A cross-sectional study was conducted from November 2019 - January 2021 to determine the factors (socio-demographic and medical comorbidities) associated with OSA risk among the OAG patients attending the ophthalmology clinic in Hospital Pengajar Universiti Putra Malaysia (HPUPM). Respondents were also assessment for the association between the severity of OSA with their most recent glaucoma parameters. Ethical approval was obtained from the relevant ethical boards. We used the STOP-BANG questionnaire, which consists of eight (yes, no) questions and according to the patient's response, the dependent variable in this study is the obstructive sleep apnea among patients with open-angle glaucoma and the independent variable are demographic characteristics, medical and co-morbidities factors, and glaucoma parameters.[3] The comparison of numerical categories between the two separate groups, usually normally distributed, was tested using the T-test, while the Chi-square and Fisher Test were used for two independent categorical groups. Version 25.0 of the Statistical Package for the Social Sciences (SPSS) was used to analyse the results.

This study classified the risk of having OSA as low for those scored ≤ 2, moderate for those scored 3-4 and high for those who scored 5-8. The study included patients aged ≥40 years with OAG or normotensive glaucoma (NTG) in one or both eyes who were able to give consent and who attended the ophthalmology clinic. Patients confirmed as having OSA by questionnaire were also examined by an ear, nose and throat (ENT) specialist to exclude any other pathology for their symptoms. We excluded from the study patients with secondary glaucoma, such as post-traumatic, uveitis, and surgical complication, also closed-angle glaucoma; patients who were unable to perform reliable visual field testing; patients with pulmonary disease, chronic steroid use, with previous diagnosis of OSA, diuretics or fluid restriction for congestive cardiac failure or chronic renal failure; patients on anticoagulants, atrial fibrillation or myocardial infarction in the last 6 months; patients with central and mixed sleep apnoea, and insomnia.

RESULTS

A total of 442 patients aged >40 years participated in this study. The mean participant age was 64.2 ± 9.0 years; of which 55.4% were male. Malay was the most common ethnicity (40.3%), followed by Chinese (38.2%) then Indians (21.3%) (Table 1 and Figure 1). More than half of the participants had secondary education (43.9%) and tertiary education (29.4%). The majority of participants were non-smokers (83.7%) and did not drink alcohol (93.9%). Family history of glaucoma was absent in most participants (82.6%).

Hypertension (71.2%) was the most prevalent comorbidity among the patients, followed by hyperlipidaemia (67.2%) and diabetes mellitus (54.3%) (Table 2). Other than these comorbidities, less than one-fifth of the participants had ischemic heart disease, chronic kidney disease, asthma, migraine, stroke, or peripheral vascular disease, and less than 1% had hypothyroidism and depression.

Being male ($p < 0.001$), still working ($p = 0.026$), in the M40 income stratum ($p = 0.018$), high body mass index (BMI) ($p < 0.001$), smoking ($p < 0.001$) and alcohol drinking ($p = 0.002$) all were highly associated with moderate and high risk of OSA as assessed with the STOP-BANG questionnaire among glaucoma

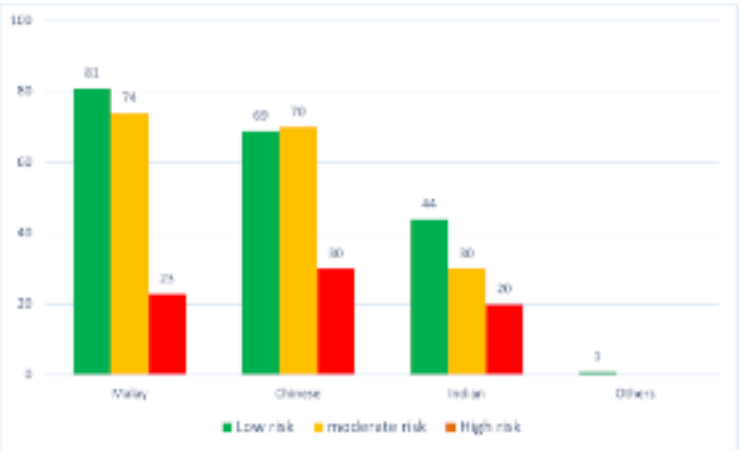

Figure 1 Distribution of OSA risk among glaucoma patients by ethnicity using SBQ N=442

Table 1 *Socio-demographic characteristics of the respondents. (N= 442)*

		Frequency (n)	Percentage (%)
Gender	Male	245	55.4
	Female	197	44.6
Ethnicity	Malay	178	40.3
	Chinese	169	38.2
	Indian	94	21.3
	Others	1	0.2
Education level	None	18	4.1
	Primary	100	22.6
	Secondary	194	43.9
	Tertiary	130	29.4
Occupation	Retiree or housewives	320	72.6
	Working	121	27.4
	Commercial vehicle driver	75	17.0
Body mass index, (BMI)	Underweight	9	2.0%
Male (n= 245), 26.31±4.89	Normal	87	19.7%
Female (n=197), 27.14±5.17	Overweight	184	41.6%
	Obese	162	36.7%
Smokers	Yes	72	16.3%
	No	370	83.7%
Alcohol drinkers	Yes	27	6.1%
	No	415	93.9%
Family history of OSA	Yes	77	17.4%
	No	365	82.6%
Income group	B40 <RM5,000)	390	88.2%
	M40 (>RM5,000)	52	11.8%
Age (Mean± SD) = 64.20±8.95 years			

Table 2 *The frequency of medical comorbidities among the respondents. (N= 442)*

Medical comorbidities	Frequency (n)	Percentage (%)
Diabetes mellitus	240	54.3
Hypertension	314	71.2
Hyperlipidemia	298	67.4
Ischaemic heart disease	74	16.7
Stroke	19	4.3
Migraine	21	4.8
Peripheral vascular disease	10	2.3
Chronic kidney disease	40	9.0
Hypothyroidism	4	0.9
Depression	2	0.5
Asthma	32	7.2

Table 3 Association between the respondents' socio-demographic factors and OSA risk (N = 442)

Variable		Low-risk OSA STOP-BANG ≤2 (195) N (%)	Moderate & high risk OSA STOP-BANG ≥3 (247) N (%)	p-value
Age (Mean± SD)	63.35±9.44	64.87±8.50	0.081	
Gender	Male	49 (20.0)	196 (80.0)	*<0.001*
	Female	146 (74.1)	51 (25.9)	
Ethnicity	Chinese	69 (40.8)	100 (59.2)	0.489
	Malay	81 (45.5)	97 (54.5)	
	Indian	44 (46.8)	50 (53.2)	
	Others	1 (100.0)	0 (0.0)	
Education level	None	13 (72.2)	5 (27.8)	*0.050*
	Primary	47 (47.0)	53 (53.0)	
	Secondary	85 (43.8)	109 (56.2)	
	Tertiary	50 (38.5)	80 (61.5)	
Occupation	Retiree or housewives	152 (47.4)	109 (52.6)	*0.026*
	Working	43 (35.5)	78 (64.5)	
Income group	B40 (<RM5,000)	180 (46.1)	210 (53.9)	*0.018*
	M40 (>RM5,000)	15 (28.8)	37 (71.2)	
Body mass index, kg/m² (Mean± SD) Male 25.49±4.30 Female 27.62±5.36	Underweight	9	2.0%	*<0.001*
	Normal	87	19.7%	
	Overweight	184	41.6%	
	Obese	162	36.7%	
Smokers	Yes	11 (15.3)	61 (84.7)	*<0.001*
	No	184 (49.7)	186 (50.3)	
Alcohol drinkers	Yes	4 (14.5)	23 (85.2)	*0.002*
	No	191 (46.0)	224 (54.0)	
Family history of OSA	Yes	27 (35.1)	50 (64.9)	0.078
	No	168 (46.0)	197 (54.0)	

patients who attended the Hospital Pengajar UPM ophthalmology clinic (Table 3).

Having hypertension ($p < 0.001$), diabetes ($p = 0.026$), hyperlipidaemia ($p = 0.018$), ischaemic heart disease ($p < 0.001$), smoking ($p < 0.001$) and alcohol drinking ($p = 0.002$) all were also significantly associated with moderate and high risk of OSA as assessed with the STOP-BANG questionnaire among glaucoma patients who attended the Hospital Pengajar UPM ophthalmology clinic (Table 4).

Multiple logistic regression analysis showed that the predictors of moderate/high risk of OSA were males [odds ratio (OR) = 189.7, 95% confidence interval (CI) = 55.21 - 651.69], high body mass index (OR = 1.23, 95% CI = 1.14, 1.33), diabetes (OR = 3.1, 95% CI = 1.45 - 6.63) and hypertension (OR = 70.73, 95% CI = 22.59 - 221.50).

DISCUSSION

To the best of our knowledge, this study is the first to evaluate the prevalence of OSA in OAG patients in Malaysia. Here, we used the STOP-BANG questionnaire to identify the risk of OSA in OAG patients who attended the ophthalmology clinic, and included 442 patients with OAG. The STOP-BANG questionnaire has been validated in the local language in Malaysia and therefore was a suitable instrument to determine the objectives of this study.[4] In addition, it has good sensitivity and specificity.[5-6] The questionnaire requires just a few minutes to complete and its sensitivity using a cut-off score of > 3 are 84% to 100% in detecting sleep apnea, depending on its severity.[5-6]The specificity is also acceptable, ranging from 37% to 56.4%, once again depending on the severity of the sleep apnea.[5-6]

Table 4 Association between the respondents' medical comorbidities and OSA risk (N = 442)

Variable		Low-risk OSA STOP-BANG ≤2 (195) N (%)	Moderate & high risk OSA STOP-BANG ≥3 (247) N (%)	p-value
Diabetes mellitus	Yes	87 (36.3)	153 (63.7)	*<0.001*
	No	108 (53.5)	94 (46.5)	
Hypertension	Yes	101 (32.2)	213 (67.8)	*<0.001*
	No	94 (73.4)	34 (26.6)	
Hyperlipidemia	Yes	112 (37.5)	187 (62.5)	*<0.001*
	No	83 (58.0)	60 (42.0)	
Ischemic heart disease	Yes	24 (32.4)	50 (67.6)	*0.027*
	No	171 (46.5)	197 (53.5)	
Stroke	Yes	5 (26.3)	14 (73.7)	0.110
	No	190 (44.9)	233 (55.1)	
Migraine	Yes	10 (47.6)	11 (52.4)	0.741
	No	185 (43.9)	236 (56.1)	
Peripheral vascular disease	Yes	3 (30.0)	7 (70.0)	0.363
	No	192 (44.4)	240 (55.6)	
Chronic kidney disease	Yes	16 (40.0)	24 (60.0)	0.582
	No	179 (44.5)	223 (55.5)	
Hypothyroidism	Yes	3 (75.0)	1 (25.0)	0.325
	No	192 (43.8)	246 (56.2)	
Depression	Yes	2 (100.0)	0 (0.0)	0.111
	No	193 (43.9)	247 (56.1)	
Asthma	Yes	14 (43.8)	18 (56.2)	0.965
	No	181 (44.1)	229 (55.9)	

We found that the prevalence of moderate to severe OSA among the patients was 56.9%. Male gender (odds ratio (OR) = 189.7), BMI (OR = 1.23), diabetes (OR = 3.1) and hypertension (OR = 70.73) were predictors of moderate to high risk of OSA in the OAG patients; we also found that the prevalence of NTG was 59.5% compared to OAG.[7] These findings are consistent with the results of previous global literature, which had also reported that people with OAG and diabetes mellitus had higher odds for moderate to high risk of OSA symptoms as compared to non-diabetics.[8] Our findings are also consistent with several previous studies in which the OR of diabetes mellitus for OSA was 1.23–1.78.[9-10] Diabetes may disturb vascular autoregulation of the retina, and the resulting vascular dysfunction, which induces glaucomatous optic neuropathy diabetes also disturb glial cell function and neuronal metabolism.[11] The high relation between OSA and diabetes mellitus could be because diabetes affects the control of respiration and the upper airway neural reflexes, which in turn lead to respiratory disorders during sleep.[12] Therefore, OSA is common among diabetics, with a prevalence of 54.50%. A lower prevalence of OSA has been reported in men (63.26%) compared to women (66.22%).[13] Diabetes may stimulate OSA via many mechanisms, as patients with diabetes mellitus also have high oxidative stress, inflammation and sympathetic activation with hypothalamic-pituitary-adrenal hyperactivity.[14] OSA in diabetic patients could be also mediated by decreased physical activity and changes related to lung volume.[15] There is evidence that non-diabetic and overweight (OR = 2.2) and obese (OR = 8.29) are associated with OSA; furthermore, diabetic patients with relatively high BMI have increased odds for OSA (OR = 1.1) in comparison to patients with low BMI.[9] Patients with hypertension had 70 times greater odds of developing moderate to high risk of OSA than normotensive patients. As is the case in obesity and

diabetes mellitus, hypertension and OSA have a bidirectional relationship, and a fairly high proportion (50%) of hypertensive people also have associated OSA, where hypertensive patients had 1.32 greater odds of having OSA than normotensive patients.[9,16] Males have 2.27 greater odds for OSA risk; this finding can be explained by the clear statistically significant difference of the mean STOP-BANG score between men (3.36) and women (2.12).[9] Furthermore, among the findings were the increased proportion of smokers among men (29.4%) compared to women (0.0%), as well as the higher number of alcohol drinkers among men (12.7%) than women (0.5%). From an anatomical and physical viewpoint, a higher percentage of men (24.1%) had neck circumference > 40 cm, and this is much higher by about 3-fold compared to that in women (7.6%). So, according to gender-stratified analysis, it is unsurprising that males with OAG were predicted to have moderate to severe OSA. Men are 2–3 times more prone to OSA than women, and the prevalence in both increases with age. This may indicate that sex hormones play a role OSA development. Estimates of sex differences for OSA have been made globally. In the USA, 24% of men and 9% of women have an apnoea-hypopnea index ≥ 5. A highly interesting case was that women with polycystic ovary syndrome, secreting high testosterone, are at higher risk of developing OSA. This may be due to sex hormone- and sex-related anatomical distribution of fatty tissue deposition around the respiratory passages.[17] Sex hormones determine the deposition of fatty tissue around the airway structures.

An interesting finding in the present study was that the prevalence of NTG was much more common (59.5%) compared to OAG in the patients (N = 442), and this is consistent with the previous literature. A recent population-based study stated that NTG prevalence is higher in Asia (76.3%) compared to the white population (33.7%), whatever the glaucoma parameters (intraocular pressure (IOP), IOP above the target, Hodapp-Parrish visual field damage, cup/disc ratio, visual field index, visual acuity, clinical progression); compared to OSA in this study, the p-value was not significant (>0.05).[18]

The main limitation was as it is cross-sectional study and observed the problem temporary in one time make it difficult to find the causality of the effect and therefore there is a possible association between OSA and glaucoma but not a definite link, the second is that most of the patients were old and they had their own conditions and not easy for them to be attended regularly to the clinic to be rechecked. Thirdly, any of the patients had secondary glaucoma who were excluded from the study.

CONCLUSION

This study was conducted among open-angle glaucoma patients, to assess their risk for OSA using the validated STOP-BANG questionnaire. We found that male gender, high BMI, hypertension and diabetes mellitus were highly significantly associated with moderate to high risk of OSA among patients with OAG; the prevalence of moderate to high OSA risk was 56.9% in those with OAG; the prevalence of NTG was 59.5% versus that of primary angle glaucoma (40.5%). Finally, our findings are all consistent with all of the previous findings on this subject.

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ETHICS APPROVAL

Ethical approval was obtained from the Medical Research and Ethics Committee of the Ministry of Health Malaysia, reference number NMRR-18-2796-43737 ('IR) and by the Ethics Committee for Human Study of Universiti Putra Malaysia.

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REFERENCES

1. 1Weinreb RN, Aung T, Medeiros FA. The pathophysiology and treatment of glaucoma: a review. JAMA [Internet]. 2014 May 14;311:(18)1901–11.
2. Patel D. A Review Of Recent Advances Pharmacolotherapy Of Glaucoma. EJPDCR 2013;2:112-120
3. Chung F, Yegneswaran B, Liao P. et ah STOP questionnaire: a tool to screen patients for obstruetive sleep apnea. Anesthesiology. 2008;108:(5)812–21.
4. Abdullah B, Idris AI, Mohammad ZW, Mohamad H. Validation of Bahasa Malaysia STOP-BANG questionnaire for identification of obstructive sleep apnea. Sleep Breath. 2018 Dec;22:(4)1235-1239.
5. Chung F, Yegneswaran B, Liao P, Chung SA, Vairavanathan S, Islam S, Khajehdehi A, Shapiro CM. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. The Journal of the American Society of Anesthesiologists. 2008 May 1;108:(5)812-21.
6. Chung F, Abdullah HR, Liao P. STOP-Bang questionnaire: a practical approach to screen for obstructive sleep apnea. Chest. 2016 Mar 1;149:(3)631-8.
7. Balbay EG, Balbay O, Annakkaya AN, Suner KO, Yuksel H, Tunç M, et al Obstructive sleep apnoea syndrome in patients with primary open-angle glaucoma. Hong Kong Med J. 2014;20:(5)379–85.
8. Bonsignore MR, Baiamonte P, Mazzuca E, Castrogiovanni A, Marrone O. Obstructive sleep apnea and comorbidities: a dangerous liaison. Multidiscip Respir Med [Internet]. 2019;14:(1)8.
9. Subramanian A, Adderley NJ, Tracy A, Taverner T, Hanif W, Toulis KA, et al Risk of incident obstructive sleep apnea among patients with type 2 diabetes. Diabetes Care. 2019;42:(5)954–63.
10. Huang T, Lin BM, Stampfer MJ, Tworoger SS, Hu FB, Redline S. A population-based study of the bidirectional association between obstructive sleep apnea and type 2 diabetes in three prospective U.S. Cohorts. Diabetes Care. 2018;41:(10)2111–9.
11. Rivera CE, Cantor E, Castillo A, Martinez A, Newball L, Rueda JC, et al Prevalence of Primary Open Angle Glaucoma among Patients with Diagnosis of Systemic Hypertension and Diabetes Mellitus: The Colombian Glaucoma Study. 2020;99–114.
12. Reutrakul S, Mokhlesi B. Obstructive Sleep Apnea and Diabetes: A State of the Art Review. Chest [Internet]. 2017;152:(5)1070–86.
13. Fallahi A, Jamil DI, Karimi EB, Baghi V, Gheshlagh RG. Prevalence of obstructive sleep apnea in patients with type 2 diabetes: A systematic review and meta-analysis. Diabetes Metab Syndr Clin Res Rev [Internet]. 2019;13:(4)2463–8.
14. Rajan P, Greenberg H. Nature and Science of Sleep Dovepress Obstructive sleep apnea as a risk factor for type 2 diabetes mellitus. Nat Sci Sleep [Internet]. 2015;7–113.
15. Lecube A, Simó R, Pallayova M, Punjabi NM, López-Cano C, Turino C, et al Pulmonary function and sleep breathing: Two new targets for type 2 diabetes care. Endocr Rev. 2017;38:(6)550–73.
16. Ahmad M, Makati D, Akbar S. Review of and Updates on Hypertension in Obstructive Sleep Apnea. Int J Hypertens. 2017;2017.
17. Snyder B, Cunningham RL. Sex differences in sleep apnea and comorbid neurodegenerative diseases. Steroids. 2018;133:28–33.
18. Kim KE, Park KH. Update on the prevalence, etiology, diagnosis, and monitoring of normal-tension glaucoma. Asia-Pacific J Ophthalmol. 2016;5:(1)23–31.

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ORIGINAL ARTICLE

Patients' quality of life after Bipolar Transurethral Enucleation & Laparoscopic Simple Prostatectomy for large Benign Prostatic Hyperplasia

Quality of life after surgical treatment of large BPH

Mladen Doykov, Gancho Kostov

Background

The purpose of this study was to assess the changes in storage, voiding, and post-micturition LUTS and disease-related QoL in patients with large benign prostatic hyperplasia (BPH) who underwent either bipolar transurethral enucleation (B-TUEP) or laparoscopic simple prostatectomy (LSP).

Methods

This was a prospective study, involving 112 men, aged 58 -78, with BPH > 80m/L, of whom 55 were treated through B-TUEP and 57 through LSP.

Results

Both patient groups experienced a significant reduction in LUTS ($p < 0.001$ for all); however, the LSP patients had a higher reduction in storage, voiding, and post-micturition symptoms ($p < 0.001$ for all comparisons). Overall, LUTS decreased by 76±5.8% in the LSP group and by 70±7.8% in the B-TUEP group. The percentage improvement in QoL was 61.66±15.74% in the LSP group versus 52.69±17.85% in the B-TUEP group, $p = 0.006$. There was a significant association between reduction in LUTS and improvement in disease-related QoL (rs =- 0.463, 95% CI: -0.293 to -0.605). The advantages of B-TUEP were shorter operative duration, hospital stay, and catheter duration ($p < 0.001$).

Conclusions

Our results suggest that both B-TUEP and LSP are effective surgical treatments for patients with BPH > 80m/L, which contribute to significant reductions in LUTS and improved QoL. Yet, the extent of improvement was greater in the LSP group, whereas B-TUEP required less operative time, hospital stay, and catheter duration.

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Benign prostatic hyperplasia (BPH) is a common urinary system disease in older men worldwide.[1,2] It has been linked to lower urinary tract symptoms (LUTS) which according to the International Continence Society are categorized into: (a) storage symptoms - increased daytime frequency, urgency, nocturia, and urinary incontinence; (b) voiding symptoms – weak flow, urinary intermittency, hesitancy, straining, and terminal dribble; and (c) post-micturition symptoms - incomplete bladder emptying and post-terminal dripping.[3] Lower urinary tract symptoms have a negative impact on men's physical, emotional, and social well-being, as well as overall quality of life (QoL).[4]

Treatment options vary according to the size of the prostatic hyperplasia and/or the severity of the symptoms. For patients with moderate-to-severe drug-resistant LUTS and BPH-related complications, surgical therapy is recommended.[4,5] The European Association of Urology (EAU) guidelines endorse three surgical procedures for large size benign BPH (>80 mL), including an open simple prostatectomy (OSP), holmium laser enucleation (HoLEP), and bipolar-transurethral enucleation (B-TUEP).[6]

Although OSP remains the gold standard for surgical treatment of BPH > 80 mL[7], the EAU guidelines define it as the most invasive method and recommend B-TUEP and HoLEP when available.[6] Several randomized controlled trials (RCTs) have found that B-TUEP is as effective as OSP but has a better safety profile.[8-11]

Laparoscopic simple prostatectomy (LSP) is a minimally invasive procedure that is listed in the EAU guidelines as a viable alternative to OP, HoLEP, and B-TUEP for surgical treatment of large benign prostatic hyperplasia.[6]

Most of the research on surgical treatments for high-volume enlarged prostate has compared the efficacy of alternative methods to open simple prostatectomy (OSP), with fewer comparisons between alternative methods. The improvement in patients' quality of life (QoL) is usually reported as changes in the international prostate symptom score (IPSS) and the quality of life (QoL) score. However, full-spectrum accounts of the extent of improvement in individual lower urinary tract symptoms (LUTS) and/or subcategories of LUTS are rare.

The primary goal of this study was to assess and compare the changes in storage, voiding, and post-micturition LUTS and disease-related QoL in patients with high-volume enlarged prostate prostatic hyperplasia (> 80m/L) who underwent either bipolar transurethral enucleation (B-TUEP) or laparoscopic simple (LSP) prostatectomy. We sought to get empirical evidence about the effect of each type of treatment that could be used in the preoperative period for patient advisement and treatment planning. The objectives were as follows:

1. Estimate and compare the reduction in storage, voiding, post-micturition symptoms, and overall LUTS between B-TUEP and LSP.
2. Evaluate and compare the improvement in the patients' disease-related QoL between B-TUEP and LSP.
3. Examine whether a reduction in storage, voiding, post-micturition symptoms, and overall LUTS is associated with an improvement in patients' disease-related QoL.

MATERIALS AND METHODS

This was a single-center prospective study, conducted in the Department of Urology at the University General Hospital "Kaspela" in Plovdiv, Bulgaria. The target population were patients with high-volume enlarged prostate (> 80 m/L) and persistent LUT symptoms who had not responded to conservative medical treatment. The pre-operative protocol for patient evaluation and diagnosis included physical examination, digital rectal examination, transrectal ultrasonography(TRUS), uroflowmetry (Qmax), and laboratory measurements of the prostate-specific antigen (PSA) and hemoglobin concentration (HGB).

The research project was approved by the Committee for Scientific Ethics at the University General Hospital "Kaspela" in Plovdiv, Bulgaria (IRB document No. 72, issued on October 15th, 2019). The data was gathered in accordance with the Helsinki Declaration\(1964\) and its revised version (Edinburgh, 2000). Patients were informed about the procedure's purpose, benefits, and risks and were asked to sign a written informed consent form for their voluntary participation in the study.

To be included in the study, patients had to satisfy the following criteria:(1) BPH > 80 m/L;.[2] moderate-to-severe lower tract symptoms;[3] written informed consent for participation in the study. The exclusion criteria were:[1] BPH < 80m/L;[2] previous prostatic or urethral surgery; [3]prostate or bladder tumors;[4] severe comorbidities;[5] refusal to provide written consent for inclusion in the study;[6] incomplete data.

In the period between October 2019 and November 2021, 112 patients satisfied the inclusion and exclusion criteria for participation in the study. Of them, 55 were treated with B-TUEP and 57 with LSP. The surgeries were performed by two surgeons with recognized expertise and substantial experience in both B-TUEP and LSP at a university hospital clinic of urology.

Surgical Procedures

The patients were randomly allocated to one of the two surgical treatments.

Bipolar Transurethral Enucleation

B-TUEP was performed using the Karl Storz38T -38T 38TAUTOCON 38TIII bipolar generator, a bipolar working element with a 12° HOPKINS telescope, saline continuous flow irrigation, a 'hybrid' type vapo-resection electrode, and the UNIDRIVE S III morcellator. The procedure followed the standard steps of laser enucleation. During the first endoscopic stage, after an initial cysto-urethroscopic assessment of the prostatic bulk, the median lobe was enucleated using 5 and 7 o'clock incisions starting from the bladder neck and continuing up to the verumontanum. In the next step, a deep incision at 12 o'clock was made, resulting in the complete separation of the two lateral lobes and their enucleation in a descendant direction, beginning from the 1 and 11 o'clock positions. The process continued from the 5 and 7 o'clock incisions in an ascendant sense until the respective lobes were gradually detached from the prostatic capsule and pushed back into the bladder. The remaining adenoma tissue was then ablated by simple plasma vaporization, and the procedure was concluded with the careful coagulation of any hemorrhagic sources. Last, BPH tissue morcellation was performed under clear endoscopic vision and control. The procedure resulted in a large prostatic fossa with no irregularities, debris, or obstruction and was completed with the placement of a Foley catheter.

Laparoscopic simple prostatectomy

LSP was performed through 5 ports using the extraperitoneal and transvesical approaches. A rectal enema was administered one night before surgery as standard pre-operative care to prepare the intestines. In addition, all patients received antibioprophylaxis and anticoagulant therapy to prevent venous thromboembolism. A 20Fr Foley catheter was inserted into the patient's modified Trendelenburg position on the operating table. For the camera port, a 2-cm long transverse incision was made just under the umbilicus (Hassan port). The preperitoneal space was exposed with a gentle blunt finger dissection and dilated with 700 mL of air using a balloon dissector.

Subsequently, other ports were inserted under direct view. The second and third ports, 12 mm each, were placed on the right and on the left symmetry. On both the right and left sides, fourth and fifth ports of 5 mm each were inserted around 2 fingers long superomedial of the spina iliaca anterior superior. Using a harmonic scalpel (Ethicon, USA), a transverse incision was made at the vesicoprostatic junction of the bladder. After the bladder was opened and the prostate was approached, a mucosal incision was performed between the surgical capsule and the adenoma. Adenoma was enucleated with the assistance of a harmonic scalpel, an aspiration cannula, and a claw grasper. Following a 3-0 V-Lock trigonisation application, a three-way 22F Dufour catheter was inserted and the bladder was closed again with a 3-0 V-lock in one layer suture, in a running continuous fashion. The operation was finalized after the retropubic placement of one redon drain.

Pre-And Post-Operative Data

The preoperative data included patients' age, prostate volume (m/L), maximum urinary flow rate (Qmax), prostate-specific antigen (PSA), residual urine volume (RUV), and haemoglobin concentration (HGB). The post-operative data comprised operation duration, hospital stay, duration of catheter use, Qmax, PSA, RUV, and HGB, and complications according to the Clavian-Dindo classification. The patients also completed the International Prostatic Symptom Score (IPSS) questionnaire before surgery and six months after undergoing either bipolar-transurethral enucleation or laparoscopic simple enucleation. The frequency and severity of each symptom were assessed and compared separately and in categories (storage, voiding, and post-micturition), along with the overall IPSS and QoL scores.

Statistical Analysis

The statistical analyses were performed using the Statistical Package for the Social Sciences IBM SPSS version 27 (SPSS Inc., Chicago, IL, USA). The continuously measured variables were described with the mean values and standard deviations (SDs) if they met the assumption of normality according to the Shapiro-Wilk's test, and with the median values and interquartile ranges (IQR) in the absence of normality. The categorical variables were presented as frequencies and percentages (%). Between-group

Table 1 *Preoperative data*

Parameters	B-TUEP (n = 55)	LSP (n = 57)	p-value
Age (years) Median (IQR) Minimum - Maximum	 65 (8) 58 - 78	 68 (9.50) 58 - 78	0.271[U]
Prostate volume (mL) Median (IQR) Minimum-Maximum	 96.12 (8.91) 85.20 – 115.30	 97.95 (5.77) 85.12 – 116.55	0.225[U]
PSA (ng/ml) Median (IQR)	 3.66 (0.99)	 3.67 (0.98)	0.349[U]
Qmax (mL/s) Median (IQR)	 8 (2)	 8 (3)	0.304[U]
RUV (mL) Mean (±SD)	 148.34 (±38.97)	 143.40 (±34.64)	0.479[t]
HGB (g/Dl) Median (IQR)	 139 (15)	 133 (14.50)	0.530[U]

PPSA- prostate-specific antigen; Qmax - maximum urinary flow rate; RUV - residual urine volume; HGB - haemoglobin concentration; U-Mann-Whitney U test; t- independent-samples t-test

comparisons were carried out using the independent-samples t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. Paired-samples t-tests were used for comparing data within each group. A Spearman rank-order correlation was performed to examine the relationship between changes in patients' disease-related QoL and LUTS after the treatments. Associations between categorical variables were examined through the chi-square test or the Fisher exact test. All tests were two-tailed and the results were interpreted as significant at Type I error alpha = 0.05 ($p < 0.05$).

RESULTS

The statistical comparisons of the preoperative data between the two groups revealed no significant differences in age, prostate volume, PSA level, Qmax, RUV, and HGB (Table 1).

Postoperative data

All surgical procedures were completed successfully, without the need for open surgery. The LSP treatment was associated with significantly longer median operative time ($p < 0.001$), hospital stay ($p < 0.001$), and Foley catheter duration ($p < 0.001$) than the B-TUEP treatment. The two groups did not differ significantly in the median post-operative HGB concentration, mean HGB drop, or the percentage of patients with HGB drop (Table 2).

Complications according to the Clavien-Dindo Classification

The rate of complications according to the Clavien-Dindo classification was low and mostly of Grade I in both treatment groups, with no significant

Table 2 *Postoperative data*

Parameters	B-TUEP (n = 55)	LSP (n = 57)	p-value
Operative time (min) Median (IQR) Minimum - Maximum	 77 (11) 65 - 110	 106 (11.50) 97 - 120	*<0.001*[U]
Hospital stay (days) Median (IQR) Minimum-Maximum	 4 (2) 3 – 7	 6 (2) 5 – 8	*< 0.001*[U]
Catheter duration (days) Median (IQR) Minimum-Maximum	 7 (2) 5 - 15	 8 (5) 6-15	*<0.001*[U]
HGB (g/Dl) Median (IQR)	 127 (15)	 125 (6)	0.347[U]
HGB drop Mean (±SD) % of patients	 -9.80 (15.83) 61.80%	 -8.12 (16.35) 71.40%	0.587[t] 0.318[f]

HGB - haemoglobin concentration; U-Mann-Whitney U test; t- independent-samples t-test; f – Fisher's exact test

Table 3 *Complications of B-TUEP and LSP according to the Clavien-Dindo system*

Complications	B-TUEP n = 55	LSP n = 57	p
Grade 1 n (%)	7 (12.70%)	5 (8.75%)	0.554
Hyponatremia	2 (3.63%)	2 (3.50%)	1.000
Acute urinary retention	1 (1.81%)	1 (1.75%)	1.000
Bladder neck stenosis	2 (3.63%)	1 (1.75%)	0.615
Incontinence at 1st month	2 (3.63%)	1 (1.75%	0.615
Grade 2	1(1.81%)	1 (1.75%)	1.000
Blood transfusion	1(1.81%)	1 (1.75%)	1.000
Grade 3	2 (3.63%)	0 (0.00%)	0.239
Bleeding requiring surgery	1 (1.81%)	0 (0.00%)	0.491
Urethral stricture	1 (1.81%)	0 (0.00%)	0.491
Grade 4	0 (0.00%)	0 (0.00%)	-
Grade 5	0 (0.00%)	0 (0.00%)	-
Total	10 (18.14%)	6 (10.50%)	0.289

differences (Table 3). Grade II complications occurred in two patients, one from the B-TUEP group and one from the LSP group, both of whom required blood transfusions. Grade III complications were observed in two patients from the B-TUEP group and in none

Table 4 *Changes in lower urinary tract symptoms perioperatively*

LUTS		Pre- operative	Post-operative	Mean diff. (±SD)	Paired samples p-value!
Storage					
Frequency	B-TUEP	3.75 (±0.86)	1.27 (±0.87)	-2.48(±1.16) -	*<0.001*
	LSP	3.91 (±0.76)	1.27 (±0.95)	2.64 (±1.40)	*<0.001*
Urgency	B-TUEP	3.69 (±0.92)	1.32 (±0.96)	-2.37(±1.12) -	*<0.001*
	LSP	3.89 (±0.72)	1.10 (±0.76)	2.79 (±0.98)*	*<0.001*
Nocturia	B-TUEP	3.83 (±0.85)	1.14 (±0.73)	-2.69(±1.10) -	*<0.001*
	LSP	4.03 (±0.73)	1.14 (±0.98)	2.89(±1.12)	*<0.001*
Voiding					
Weak stream	B-TUEP	3.61 (±0.87)	1.18 (±0.74)	-2.43 (±1.11) -	*<0.001*
	LSP	4.00 (±0.88)	1.21 (±0.89)	2.79 (±1.35)**	*<0.001*
Intermittency	B-TUEP	3.45 (±1.08)	1.20 (±0.82)	-2.25 (±1.51) -	*<0.001*
	LSP	3.72 (±0.78)	0.94 (±0.67)	2.78 (±1.11)**	*<0.001*
Straining	B-TUEP	3.41 (±0.85)	1.12 (±0.77)	-2.29 (±0.97) -	*<0.001*
	LSP	3.81 (±0.79)	1.09 (±0.92)	2.72 (±1.16)***	*<0.001*
Post-micturition					
Incomplete emptying	B-TUEP	3.74 (±0.75)	1.38 (±0.84)	-2.36 (±1.19) -	*<0.001*
	LSP	4.03 (±0.73)	1.05 (±0.77)	2.98(±1.02)**	*<0.001*
IPSS (total)	B-TUEP	25.50 (±2.58)	7.45 (±1.85)	-18.05 (±3.03) -	*<0.001*
	LSP	27.41 (±1.86)	6.61 (±1.64)	20.80 (±2.14)***	*<0.001*

! – paired-samples t-test shows the p-value for the change in the occurrence of a given symptom between baseline and the 6th month posoperatively in each group (horizontally); * - Significantly larger reduction in a given symptom in comparison to the other group (vertically) at $p < 0.05$; **-- Significantly larger reduction in a given symptom in comparison to the other group (vertically) at $p < 0.01$; *** - Significantly larger reduction in a given symptom in comparison to the other group (vertically) at $p < 0.001$

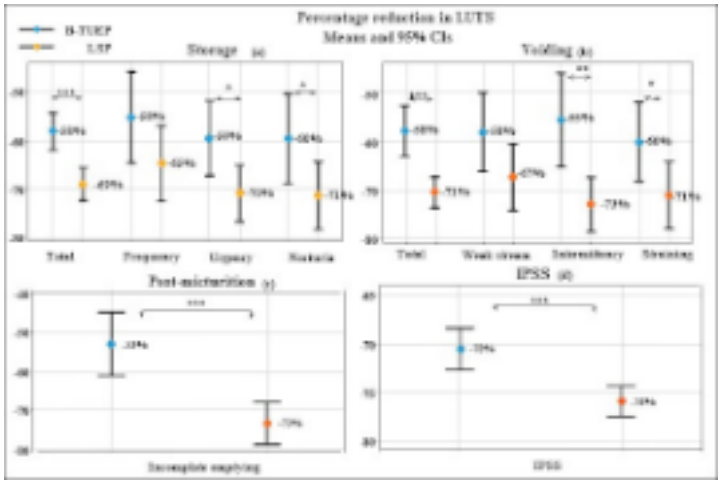

Figure 1 Percentage reduction in lower urinary tract symptoms 6 months after B-TUEP and LSP

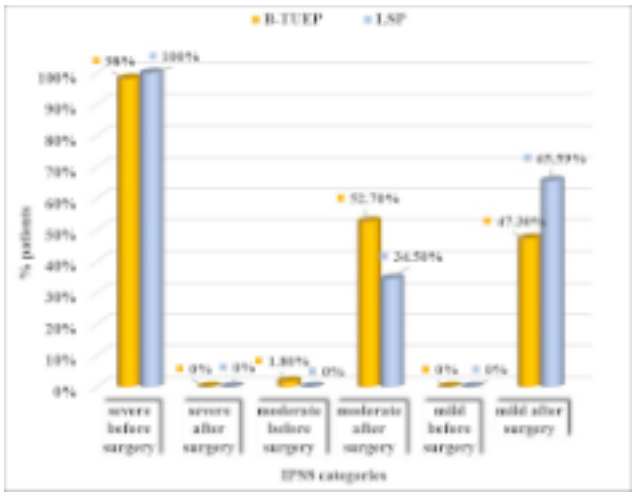

Figure 2 *Distribution of the patients across IPSS* categories before and 6 months after the surgical treatment

from the LSP group. Grades IV and V complications were not registered in either of the two groups.

Change In LUTS Perioperatively

Both groups of patients experienced significant reductions in storage, voiding, and post-micturition symptoms six months after the surgical treatment ($p < 0.001$ for all paired comparisons). However, the patients who underwent LSP had a significantly higher reduction in urgency ($p = 0.037$), weak stream ($p = 0.001$), intermittency ($p = 0.001$), straining ($p = 0.004$), and incomplete emptying ($p = 0.004$).

The postoperative 6-month IPSS decreased significantly in both patient groups - by 18.05 units in the B-TUEP group and by 20.80 units in the LSP group, with a significantly larger reduction in the LSP group, $p < 0.001$ (Table 4).

Percentage Reduction In LUTS

The percentage reduction in lower urinary tract symptoms six months after the surgical treatments is illustrated in Figure 1. In the LSP group, the mean % reduction in storage symptoms was 69±12% versus 58 ±15% in the B-TUEP group ($p < 0.001$). For each symptom in this category, the results were: frequency ($p = 0.121$), urgency ($p = 0.021$), and nocturia ($p = 0.046$) (Panel A).

Post-micturition symptoms (incomplete emptying) were reduced by 73±20% in the LSP group versus 53±29% in the B-TUEP group, $p < 0.001$ (Panel C). Overall, IPSS decreased by 76±5.8% in the LSP group and by 70±7.8% in the B-TUEP group, $p < 0.001$ (Panel D).

According to the IPSS categorization ranges (1 to 7 – mild; 8 to 19 – moderate; 20 to 35 – severe), 98.20% of the B-TUEP group and 100% of the LSP group had severe symptoms prior to surgery. Six months after surgery, 0.0% of the patients had severe symptoms; 57.70% of the B-TUEP and 34.50% of the LSP improved to moderate symptoms; 47.30% of the B-TUEP group and 65.59% of the LSP group improved to mild symptoms. The distribution of the patients across IPSS categories did not differ significantly between the groups, $p = 0.056$ (Figure 2).

Change in the Patients' Disease-Related Quality Of Life

The QoL question is categorized into 7 levels with the following descriptions: 0 = delighted, 1 = pleased, 2 = mostly satisfied, 3 = mixed, 4 = mostly dissatisfied, 5 = unhappy, 6 = terrible. Both groups of patients had a mean QoL score close to 5 (unhappy) prior to surgery (B-TUEP 4.69±0.71; LSP 4.73±0.69), with no significant difference ($p = 0.731$). Six months after surgery, both groups improved, with mean QoL scores close to 2 (mostly satisfied) – (TUEP 2.16±0.73; LSP 1.80±0.73). However, the LSP group showed a significantly greater improvement (-2.96±0.96) than the B-TUEP group (-2.52±1.06), $p = 0.026$ (Figure 3). The mean percentage improvement in the LSP group was 61.66±15.74% versus 52.69±17.85% in the B-TUEP group, $p = 0.006$.

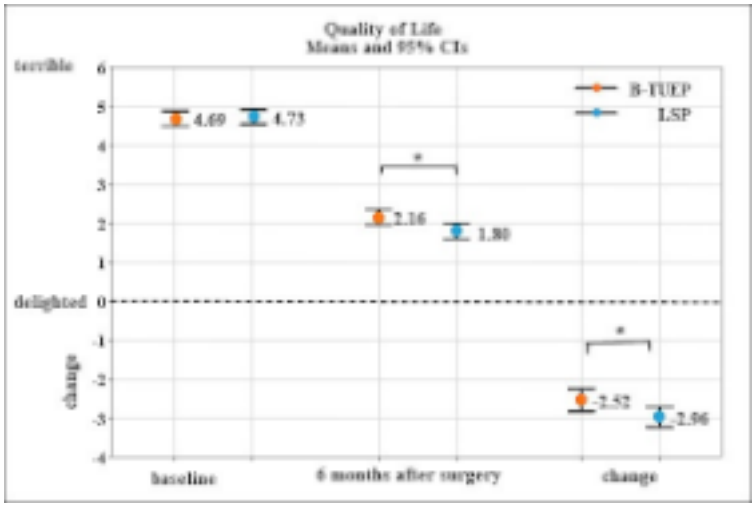

Figure 3 *Change in the patients' quality of life 6 months after the surgical treatment*

Relationship between LUTS And Disease-Related Qol after Surgical Treatment With B-TUEP And LSP

We examined the relationship between the percentage reduction in LUTS and the improvement in the patients' disease-related QoL for the entire sample of 112 patients. Three significant negative correlations were observed between the % improvement in QoL and the % reduction in: IPSS (rs =- 0.463, 95% CI: -0.293 to -0.605, p< 0.001); storage symptoms (rs = - 0.333, 95% CI: -0.150 to -0.493, p< 0.001); and voiding symptoms (rs = - 0.300, 95% CI: -0.115 to -0.465, p =0.001). No significant association was found with post-micturition symptoms/ incomplete emptying (rs = - 0.130, 95% CI: -0.310 to -0.060, p =0.176) (Figure 4: a, b, and c).

DISCUSSION

The incidence of BPH increases in aging men. By the age of 85, approximately 90% of men in this age group are affected by BPH and develop lower urinary symptoms, which have a negative impact on their physical and mental health [4,12] The main purpose of the present study was to provide a comprehensive assessment of the improvement in lower urinary track symptoms and disease-related quality of life in patients with high- volume enlarged prostate (> 80m/L) treated with either bipolar transurethral enucleation or laparoscopic simple prostatectomy.

Both B-TUEP and LSP are recommended as minimally invasive alternatives to OSP for patients with high-volume enlarged prostate.[6] in the EAU guidelines, with comparable effectiveness, improved safety, and fewer complications than OSP [8, 13, 14]. Our findings revealed that both treatments were effective, with a low rate of Clavien-Dindo complications, mostly of Grade 1.

Except for one patient in the B-TUEP group, all patients had severe LUT symptoms prior to surgery. Six months after surgery, both groups of patients experienced a significant reduction in LUTS, which improved from severe to moderate or mild, with a 76% improvement rate in the LSP group and a 70% improvement rate in the B-TUEP group.

The LSP treatment produced superior results in reducing storage, voiding, and post-micturition symptoms. The improvement in storage symptoms was 11% higher, in voiding it was 13% higher, and in post-micturition it was 20% higher.

Irrespective of the surgical treatment, reduction in IPSS was significantly associated with an improvement in the patients' disease-related QoL. In the existing literature, some studies found that storage symptoms correlated more closely with disease-related QoL than voiding symptoms [15-18], whereas in other studies the reversed result was reported [19] In our study, reductions in both storage and voiding symptoms were moderately associated with an improvement in the patients' disease-related quality of life, with a slightly stronger link between storage symptoms and disease-related QoL.

Prior to surgery, the mean disease-related QoL score in both groups indicated that the patients were "unhappy" with their urinary condition. Six months

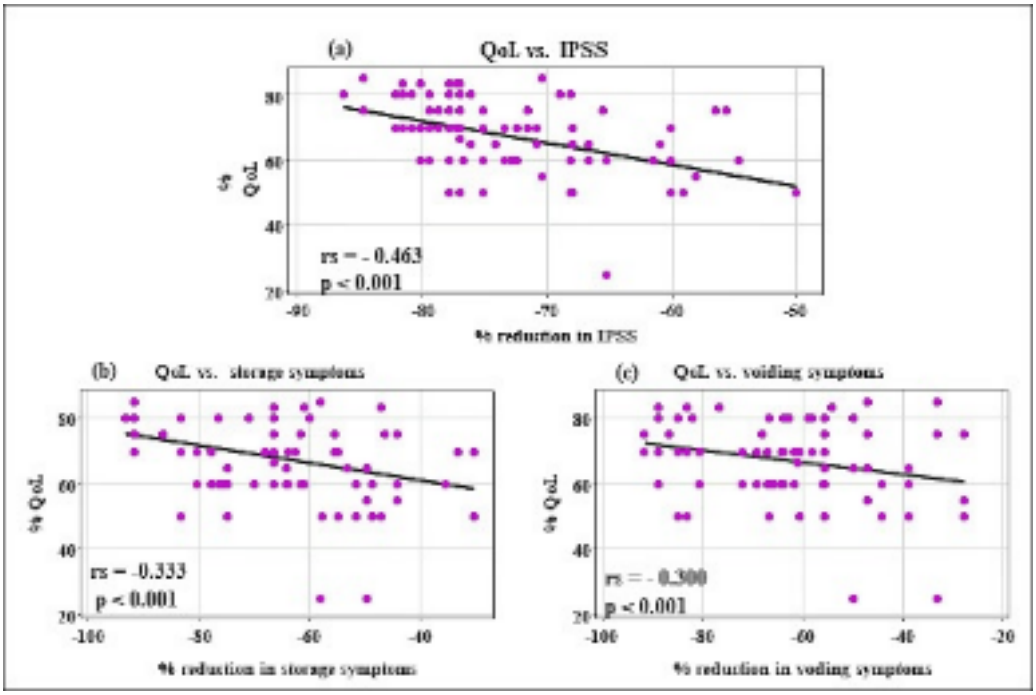

Figure 4 Relationship between changes in LUTS and QoL after surgical treatment with B-TUEP and LSP

SUMMARY BOX

What is already known about this subject

- Benign prostatic hyperplasia (BPH) is a common urinary system disease that negatively impacts the physical and mental well-being of the patients.
- Bipolar transurethral enucleation (B-TUEP) and laparoscopic simple prostatectomy are commonly used as minimally invasive alternatives to open simple prostatectomy (OSP) for the treatment of BHP.
- Previous reports on patients' quality of life after surgical treatment of high-volume enlarged prostate mostly reported the total IPSS (International Prostatic Symptom Score) and QoL scores, but did not track the changes in specific lower urinary tract symptoms (LUTS) and/or sub-categories of symptoms.

What are the new findings?

- The importance of our study is that it provides a detailed evaluation of the extent of improvement in storage, voiding, and post-micturition lower urinary symptoms in patients with BPH > 80m/L after treatment with B-TEUP or LSP.
- Our results showed that the extent of LUTS reduction and improvement in the patients' QoL was significantly greater in the LSP group. On the other hand, the B-TUEP procedure required shorter operative time, hospital stay, and catheter use.
- The findings suggest that LSP would be a better option for patients with high-volume enlarged prostate and severe to very severe LUTS, whereas B-TUEP can be used to treat men with high-volume enlarged prostate and mild to moderate LUTS.
- Our study also adds to the relatively small body of research on the link between lower urinary tract symptoms and the disease-related quality of life of patients with large BPH.

after treatment, the overall perception improved to "mostly satisfied." The improvement in the patients' well-being was higher in the LSP group, 73% of whom were pleased or mostly satisfied with their urinary health versus 60% of the B-TUEP group.

Mariano et al concluded, based on a six-year experience, that using a laparoscopic approach in the treatment of large benign prostatic hyperplasia was not only effective, but also reduced the hospital stay and recovery time for the patients.[20] In our study, LSP was found to be more effective than B-TUEP in reducing LUTS and improving the disease-related quality of life of the patients. However, LSP was associated with significantly longer operative time, hospital stay, and Foley catheter duration than the B-TUEP treatment. The difference with the findings of Mariano et al can be explained by the fact that they compared LSP to the standard OSP procedure, whereas we compared two minimally invasive procedures.

Our study has several limitations. One of them refers to the short-term follow-up time, spanning only the first six months after the surgical treatments. We are aware that the observed trends may not hold for longer postoperative periods. Due to the COVID-19 pandemic, there were several government-imposed lockdowns during which planned surgeries were postponed to later dates. For this reason, we are still in the process of completing the data collection for the 12 and 18-month postoperative periods. Another limitation is that, being a single-center study, we had no access to larger populations of men with BHP > 80m/L, and the relatively small sample sizes might limit the strength of our conclusions. The reported trends need to be validated by longitudinal data and bigger samples.

CONCLUSION

Previous studies have demonstrated the efficacy of minimally invasive surgical treatments for patients with high-volume enlarged prostate. In line with their findings, in our study, both B-TUEP and LSP were shown as effective surgical alternatives to OSP for men with BPH > 80m/L. Irrespective of the treatment, the patients experienced significant reductions in storage, voiding, and post-micturition symptoms, and their disease-related QoL improved significantly. However, the extent of LUTS reduction and improvement in patients' QoL was significantly greater in the LSP group. On the other hand, the B-TUEP procedure required shorter operative time, hospital stay and catheter use. These findings have practical implications for clinical practice, patient counselling, and treatment planning. Based on our results, LSP would be a better option for patients with very severe LUTS, whereas B-TUEP can be used to treat men with large BHP and less severe LUTS.

REFERENCES

1. Launer, BM; McVary, KT; Ricke, WA; Lloyd, GL. The rising worldwide impact of benign prostatic hyperplasia. *British Journal of Urology International* 2021;127,722-728.
2. Zhu, C; Wang, DQ; Zi, H; Huang, Q et al Epidemiological trends of urinary tract infections, urolithiasis and benign prostatic hyperplasia in 203 countries and territories from 1990 to 2019. *Military Medical Research* 2021;8, 64.
3. Abrams, P; Cardozo, L, Fall, M et al Standardisation Sub-committee of the International Continence Society. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. *Neurourology and Urodynamics* 2002; 21,167-78.
4. Chughtai, B; Forde, JC; Thomas, DD et al Benign prostatic hyperplasia. *Nature Reviews Disease Primers* 2016; 2, 16031.
5. Foster, HE; Barry, MJ; Dahm, P et al Surgical Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA Guideline. *Journal of Urology* 2018; 200,612-619.
6. Oelke, M; Bachmann, A; Descazeaud, A et al European Association of Urology. EAU guidelines on the treatment and follow-up of non-neurogenic male lower urinary tract symptoms including benign prostatic obstruction. *European Urology* 2013; 64,118-40.
7. Millin, T. Retropubic prostatectomy: a new extravesical technique report on 20 cases. 1945. *Journal of Urology* 2002;167(2 Pt 2):976-9; discussion 980.
8. Geavlete, B; Stanescu, F; Iacoboaie, C; Geavlete, P. Bipolar plasma enucleation of the prostate vs open prostatectomy in large benign prostatic hyperplasia cases - a medium term, prospective, randomized comparison. *British Journal of Urology International* 2013;111,793-803.
9. Geavlete, B; Bulai, C; Ene, C; Checherita, I; Geavlete, P. Bipolar vaporization, resection, and enucleation versus open prostatectomy: optimal treatment alternatives in large prostate cases? *Journal of Endourology* 2015; 29, 323-31.
10. Ou, R; Deng, X; Yang, W; Wei, X; Chen, H; Xie, K. Transurethral enucleation and resection of the prostate vs transvesical prostatectomy for prostate volumes >80 mL: a prospective randomized study. *British Journal of Urology International* 2013; 112, 239-45.
11. Rao, JM; Yang, JR; Ren, YX; He, J; Ding, P; Yang, JH. Plasmakinetic enucleation of the prostate versus transvesical open prostatectomy for benign prostatic hyperplasia >80 mL: 12-month follow-up results of a randomized clinical trial. *Urology* 2013; 82, 176-81.
12. Egan, KB. The Epidemiology of Benign Prostatic Hyperplasia Associated with Lower Urinary Tract Symptoms: Prevalence and Incident Rates. *Urologic Clinics of North America* 2016; 43,289-97.
13. Li, J; Cao, D; Peng, L; Ren, Z; Gou, H; Li, Y; Wei, Q. Comparison Between Minimally Invasive Simple Prostatectomy and Open Simple Prostatectomy for Large Prostates: A Systematic Review and Meta-Analysis of Comparative Trials. *Journal of Endourology* 2019; 33,767-776.
14. Higazy, A; Tawfeek, AM; Abdalla, HM; Shorbagy, AA; Mousa, W; Radwan, AI. Holmium laser enucleation of the prostate versus bipolar transurethral enucleation of the prostate in management of benign prostatic hyperplasia: A randomized controlled trial. *International Journal of Urology* 2021; 28, 333-338.
15. Marklund-Bau, H; Edéll-Gustafsson, U; Spångberg, A. Bothersome urinary symptoms and disease-specific quality of life in patients with benign prostatic obstruction. *Scandinavian Journal of Urology and Nephrol*ogy 2007; 41, 32-41.
16. Engström, G; Henningsohn, L; Walker-Engström, ML; Leppert, J. Impact on quality of life of different lower urinary tract symptoms in men measured by means of the SF 36 questionnaire. *Scandinavian Journal of Urology and Nephrol*ogy 2006; 40, 485-94.

17. Coyne, KS; Wein, AJ; Tubaro, A et al The burden of lower urinary tract symptoms: evaluating the effect of LUTS on health-related quality of life, anxiety and depression: EpiLUTS. *British Journal of Urology International* 2009;103 Suppl 3, 4-11.

18. Sountoulides, P; van Dijk, MM; Wijkstra, H; de la Rosette, JJ; Michel, MC. Role of voiding and storage symptoms for the quality of life before and after treatment in men with voiding dysfunction. *World Journal of Urology* 2010; 28, 3-8.

19. Araki, I; Tsuchida, T; Nomura, T et al Differential impact of lower urinary tract symptoms on generic and disease-specific quality of life in men and women. *Urology International* 2008; 81, 60-5.

20. Mariano, MB; Tefilli, MV; Graziottin, TM; Morales, CM; Goldraich, IH. Laparoscopic prostatectomy for benign prostatic hyperplasia--a six-year experience. *European Urology* 2006; 49, 127-31; discussion 131-2.

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ORIGINAL ARTICLE

Gentamicin therapeutic drug monitoring in neonates: an observational study

Paul Torpiano, David Pace

Background

Gentamicin is important in the treatment of suspected neonatal sepsis, while also potentially oto- and nephrotoxic. Therapeutic drug monitoring of serum gentamicin levels (SGL) helps to prevent this. We present an investigation into the influence of birthweight, gestational age, and appropriateness-for-gestational age on the rates of high SGLs amongst neonates treated for suspected sepsis.

Methods

Case notes of neonates admitted to the neonatal and paediatric intensive care unit from 2013-2017 who received intravenous gentamicin treatment were reviewed. The dosing regimen, SGL, and demographic details were recorded. Trough SGLs ≥2mg/L before the 2nd gentamicin dose were taken as indicative of unsafe levels. Mean SGLs and percentage of safe SGLs were compared for each category (birthweight, gestational age, appropriateness-of-weight-for-gestational age) using odds ratios (Student's t-test), 'N-1' Chi squared test, and correlation coefficient.

Results

In total 170 neonatal gentamicin results were analysed. Nineteen (11.2%) of these were 32mg/L. Stratifying the results according to birthweight showed significantly higher mean gentamicin levels in neonates weighing <1.5kg (1.34mg/L; 95% CI: 1.16-1.53) and 1.5-3kg (1.33mg/L; 95% CI: 1.13-1.52), compared to those weighing >3kg (0.71mg/L; 95% CI 0.57-0.85). Premature neonates born at 28 weeks' gestation or less had significantly higher mean gentamicin levels (1.69mg/L; 95% CI: 1.33-2.04) than those born at term (0.84mg/L; 95% CI: 0.68-0.99mg/L).

Conclusions

While the current gentamicin dosing guidelines are safe, extremely premature neonates born under 28 weeks are at higher risk for high gentamicin trough levels and potential toxicity. Extended interval gentamicin dosing may have a role in mitigating for this.

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The initial empirical treatment of neonatal sepsis should include an aminoglycoside such as gentamicin.[1] This antimicrobial exhibits concentration-dependent bactericidal activity against gram-negative bacteria, as well as synergistic activity against important gram-positive organisms when combined with a penicillin.[2,3] This useful addition to the broad-spectrum coverage in treating neonatal sepsis comes at the risk of oto- and nephrotoxicity, both known adverse effects associated with aminoglycoside use.[4] Although toxicity studies in neonates are rare, there is no evidence that aminoglycoside toxicity should be different in neonates compared with adults, in whom toxicity has been extensively studied.[5] Therefore, in order to minimise toxicity, therapeutic drug monitoring (TDM) is recommended to guide gentamicin treatment that extends beyond 3 days.[6] Gentamicin trough levels of 2mg/l or more, taken 1 hour before the second dose, are associated with toxicity, while peak concentrations <5mg/L are associated with reduced efficacy.[7,8]

Dosing regimens for gentamicin in neonatal sepsis have changed considerably over the years, and there remains significant variation in aminoglycoside dosing and TDM guidelines across neonatal units worldwide.[9] Despite this, most dosing guidelines recommended a dose of 4-5mg/kg of gentamicin administered every 24-48 hours, with subsequent doses adjusted according to TDM.[5] Local guidelines implemented at the neonatal and paediatric intensive care unit at Mater Dei Hospital in Malta (the only neonatal unit locally) recommend a gentamicin dose of 5mg/kg, administered at 24-36 hour intervals in neonates born at a gestation of 32 weeks or more, and at 36-hourly intervals in neonates born at a gestation of under 32 weeks.[10] These follow the British National Formulary and National Institute of Clinical Excellence recommendations for dosing of gentamicin in neonatal sepsis.[11] The safety of this regimen is monitored using TDM of SGLs taken 1 hour before the second gentamicin dose.[12]

We present an investigation into the influence of birthweight, gestational age, and appropriateness-for-gestational age on the rates of high SGLs amongst neonates treated for suspected sepsis.

MATERIAL AND METHODS

All neonates admitted to the neonatal and paediatric intensive care unit (NPICU) at Mater Dei Hospital in Malta from 2013 to 2017 and treated with at least 2 doses of intravenous gentamicin for suspected neonatal sepsis, and for whom TDM of trough serum gentamicin levels was done 1 hour before the second gentamicin dose, were included. In these cases, the gentamicin dosing regimen used was 5mg/kg every 36 hours in neonates born at under 32 weeks' gestation, while those born at 32 weeks' gestation or above were treated with 5mg/kg gentamicin every 24 hours. Clinical case notes for each of these patients were consulted, including the dedicated gentamicin treatment chart currently in use in the NPICU, and the following details documented: gender, date of birth, gestation in weeks, birthweight in kilograms, risk factors for gentamicin toxicity, antibiotic regimen used, age at start of gentamicin treatment, gentamicin start date, duration of treatment, and date of completion, date, timing, and result of trough serum gentamicin level, date, timing, and dose of previous gentamicin dose, the effect of TDM on subsequent gentamicin dosing, and documented potential reason for an inappropriately raised serum gentamicin level of >2mg/l. SGLs taken in neonates who received inappropriate doses of gentamicin, or that were sampled at inappropriate times in relation to the gentamicin dose, were excluded from subsequent analysis. Factors considered to increase the risk of gentamicin toxicity were clinical dehydration, diarrhoea or persistent vomiting, renal impairment (reduced urine output of <1ml/kg/hour; raised serum creatinine >120µmol/L in preterm neonates and >90µmol/l in term neonates), poor cardiac output, sepsis requiring inotropic support, a history of perinatal asphyxia, and concomitant medications (cephalosporins such as cefotaxime, vancomycin, amphotericin, furosemide, non-steroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors).[10] World Health Organisation standardised centile charts were consulted to identify the patients' centile for weight, and categorise the patients as small-for-gestational age, appropriate-for-gestational age, and large-for-gestational age. Serum samples taken for therapeutic drug monitoring were transported immediately to the laboratory, and stored at 4°C for up to 12 hours. Serum gentamicin levels were obtained using a gentamicin enzyme immunoassay (Emit 2000 Gentamicin Plus Assay, Beckman Coulter, CA, USA). Serum gentamicin levels equal to or above 2mg/l were taken as abnormally high. Ethical approval for this research was sought and obtained from the Faculty Research Ethics Committee at the University of Malta (FRECMDS_1920_196).

Mean, median and range were used to describe continuous variables, including gestation and trough serum gentamicin level, while percentages were used for categorical variables. 95% confidence intervals were calculated on Statistical Package for Social Sciences using binomial exact method. Odds ratios for mean gentamicin levels and gestations were calculated using Student's t-test, while proportions were compared using 'N-1' Chi squared test. p values of less than 0.05 were taken to indicate statistical

significance. Correlation coefficients were used to compare the relationship between birthweight, gestation, and serum gentamicin level.

RESULTS

A total of 183 neonatal trough serum gentamicin levels were recorded, of which 20 were above the safe threshold of ≥2mg/l (10.9%; 95% C.I. 6.8-16.4%). Six gentamicin levels were excluded from subsequent analysis as they were taken from patients receiving inappropriate doses of gentamicin (less or more than 5mg/kg), while a further 7 levels were excluded as the timing of the trough serum gentamicin level was deemed inappropriate. Of the 170 levels included in the final analysis, the mean and median gestation were 34.6 (95% C.I. 33.9-35.4) and 36 weeks respectively (range: 24-45.1 weeks), with a M:F ratio of 1.6:1. Birthweights ranged from 0.47kg to 5.18kg, with a mean and median of 2.32kg (95% C.I. 2.16-2.49kg) and 2.49kg respectively. Eight patients were commenced on gentamicin therapy beyond the age of 7 days (range: 7-26 days), while the majority (n=117; 68.8%, 95% C.I. 61.3-75.7%) were commenced on the first day of life. Nineteen of 170 results included in the final analysis were above or equal to 2mg/l (11.2%; 95% C.I. 6.9-16.9%), ranging from 2mg/l to 4.4mg/l. Amongst the raised serum gentamicin levels, the mean level was 2.51mg/l (95% C.I. 2.21-2.81mg/l). The serum gentamicin levels showed a negative correlation with both birthweight (R=-0.38; p<0.0001) and gestation (R=-0.4, p<0.0001).

The results were stratified according to 3 main categories: birthweight, gestation, and appropriateness for gestational age (Table 1). There was a significantly lower rate of safe SGLs in the neonates born under 28 weeks compared to both term neonates born >37 weeks (57.9% vs 95.9%, p<0.0001) and the overall cohort (57.9% vs 88.8%,

Table 1 Trough serum gentamicin levels in the study group stratified according to birthweight, gestation, and appropriateness for gestational age. (SGA = small for gestational age; AGA = appropriate for gestational age; LGA = large for gestational age; brackets = 95% confidence intervals)

Patient category	Safe trough levels (n, %) (95% CI)	Mean gestation (weeks) (95% CI)	Median gestation (weeks)	Mean gentamicin level (mg/l) (95% CI)	Range gentamicin level (mg/l)	Mean high gentamicin level (mg/l) (95% C.I.)	Range high gentamicin level (mg/l)
a. All (n=170)							
	151, 88.8% (83.1-93.1)	34.6 (33.9-35.4)	36	1.13 (1.02-1.23)	0-4.4	2.5 (2.21-2.81)	2-4.4
b. Birthweight							
<1.5kg (n=56)	46, 82.1% (69.6-91.1)	29.1 (28.4-29.9)	29.1	1.34 (1.16-1.53)	0-3.64	2.49 (2.13-2.84)	2.1-3.64
1.5-3kg (n=57)	49, 86% (74.2-93.7)	35.7 (35-36.5)	36	1.33 (1.14-1.52)	0-4.4	2.57 (1.89-3.25)	2-4.4
>3kg (n=57)	56, 98.2% (90.6-100)	38.9 (38.6-39.4)	38.9	0.71 (0.57-0.85)	0-2.8	2.2	2.2
c. Gestation							
<28 weeks (n=19)	11, 57.9% (33.5-79.7)	26.1 (25.6-26.6)	26	1.69 (1.33-2.04)	0.47-3.1	2.4 (2.14-2.65)	2.15-3.1
28-32 weeks (n=29)	28, 96.6% (82.2-99.9)	29.8 (29.3-30.2)	30	1.17 (0.94-1.4)	0-3.64	3.64	3.64
32-37 weeks (n=48)	41, 85.4% (72.2-93.9)	34.2 (33.7-34.6)	34	1.32 (1.14-1.5)	0-2.9	2.34 (2.01-2.67)	2.05-2.9
>37 weeks (n=74)	71, 95.9% (88.6-99.2)	39 (38.7-39.4)	38.9	0.84 (0.68-0.99)	0-4.4	2.83 (0-6.21)	2-4.4
d. Appropriateness for gestational age							
SGA (n=39)	34, 87.2% (72.7-95.7)	33.2 (31.5-34.9)	33	1.24 (0.95-1.53)	0-4.4	3.05 (1.85-4.24)	2.1-4.4
AGA (n=118)	105, 89% (81.9-94)	34.9 (34.1-35.8)	36.6	1.11 (0.99-1.23)	0-3.1	2.32 (2.12-2.52)	2-3.1
LGA (n=13)	12, 92.3% (64-99.8)	36.4 (34.5-38.2)	36.9	0.91 (0.53-1.29)	0-2.2	2.2	2.2

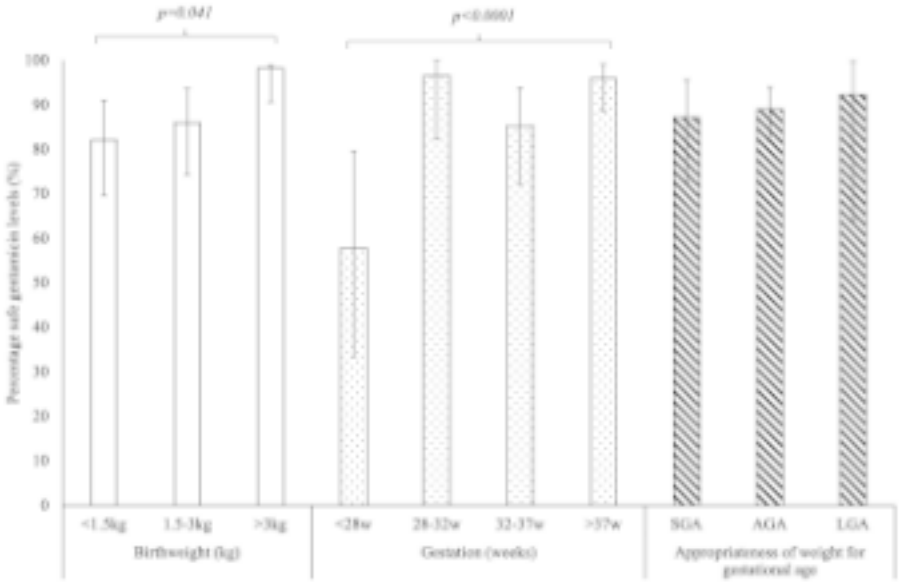

Figure 1 Percentage safe trough serum gentamicin levels amongst neonates in different birthweight, gestation, and appropriateness of weight-for-age categories.

p=0.0003). This was also seen when comparing neonates born weighing <1.5kg with those born over 3kg (82.1% vs 98.2%, p=0.0041). These differences were not seen when comparing the rates of safe SGLs amongst small for gestational age (SGA) with appropriate for gestational age (AGA) and large for gestational age (LGA) neonates. Focusing on the mean trough SGL, the mean SGL of neonates born at under 28 weeks' gestation was significantly higher than that of the overall cohort (1.69mg/l vs 1.13mg/l, p<0.0014) and of neonates born beyond 37 weeks' gestation (1.69mg/l vs 0.84mg/l, p<0.0001). Again, this is paralleled to a lesser extent in a comparison between neonates born <1.5kg and those 1.5kg and above (1.34mg/l vs 1.02mg/l, p=0.047), but not seen in the comparison of mean SGL in SGA with LGA or AGA infants (1.24mg/l vs 1.09mg/l, p=0.265).

While neonates born weighing <1.5kg were more likely to have unsafe SGLs than those >3kg (OR = 12.17 [95% C.I. 1.5-98.6]; p=0.019), they were not at a higher risk for unsafe SGLs than neonates weighing 1.5kg or more overall (OR=2.54 [95% C.I. 0.97-6.66]; p=0.059). Neonates born under 28 weeks were more likely than those born at >28 weeks (OR = 9.26 [95% C.I. 3.09-27.76]; p=0.0001), 28-32 weeks (OR = 20.37 [95% C.I. 2.27-182.46]; p=0.0071), 32-37 weeks (OR = 4.26 [95% C.I. 1.27-14.33]; p=0.0192), >32 weeks (OR = 8.15 [95% C.I. 2.67-24.9]; p=0.0002), and >37 weeks (OR = 17.21 [95% C.I. 3.95-74.94]; p=0.0001) to have unsafe trough SGLs. This contrasts with SGA infants who were not found to be at increased risk for unsafe SGLs compared with the AGA and LGA groups combined (OR = 1.23 [95% C.I. 0.41-3.66]; p=0.71) (Figure 1).

DISCUSSION

Despite the known risk of oto- and nephrotoxicity, aminoglycosides remain an important part of the treatment of neonatal sepsis in association with a penicillin and, incases of suspected Gram-negative meningitis, a third generation cephalosporin.[1] Fortunately, since efficacy and toxicity of aminoglycosides show a strong correlation with serum concentrations, TDM has proven helpful in monitoring therapy with this class of antimicrobials.[5] A dosing interval of 36 to 48 h in neonates is generally able to maintain safe trough SGLs of ≤2 mg/L..[6] Nonetheless, unexpectedly high SGLs can still occur, and the long-term effects of such high serum concentrations remain uncertain [13] The overall rate of safe trough SGLs of 88.8% (95% C.I. 83.1-93.1%) taken in our centre compares favourably with similar studies elsewhere, with Rocha et al Krishnamoorthy et al and Vervelde et alreporting safe levels in 59%, 67% and 95% of neonates respectively.[14–16]

Dosing recommendations for gentamicin in neonatal sepsis have changed considerably over the years: gentamicin was previously administered in doses of 2.5mg/kg/12h, before evidence showed once daily dosing at 4-5mg/kg/day to provide higher peak and

lower trough SGLs [17–19]. Most recently, extending the dose interval to 36-48 hours with a dose of 5mg/kg has been recommended, particularly in very low birthweight (VLBW) or extremely premature neonates [20–23]. Tailoring the dose according to gestation and birthweight is another recent advancement in the field, with recommendations for a gentamicin dose of 5mg/kg/48h in neonates with a gestational age of ≤29 weeks, a dose of 4.5mg/kg/36h in neonates with a gestational age of 30 to 34 weeks, and a dose of 4mg/kg/day when the gestational age is ≥35 weeks.[24] While extending the gentamicin dosing interval to 48 hours in neonates born ≤29 weeks has been adopted in some centres, this is not yet reflected in the British National Formulary gentamicin dosing recommendations, upon which local gentamicin dosing guidelines are based. This reflects concerns around a potential risk for suboptimally-treated neonatal sepsis in patients treated with gentamicin administered every 48 hours rather than every 36 hours. Future revisions of the local gentamicin dosing guidelines could consider this practice, however, as a means to mitigate for the increased risk of high SGLs reported here in those born ≤29 weeks. Stratifying for birthweight, Begg et alshowed that neonates of a birthweight of <1.5kg, 1-2.49kg and ≥2.5kg could be optimally treated with doses administered at intervals of 48h, 36h, and 24h respectively.[25] These data suggest that amending the local guidelines to include specific dosing recommendations for VLBW or extremely-premature neonates may result in safer gentamicin administration. Consistent with findings in this study, Krishnamoorthy et alreported lower rates of safe SGLs in neonates born weighing under 2.5kg in Singapore.[15]

Despite evidence for the safety and efficacy of extending interval doses to 48 hours in specific neonatal subgroups, there remains considerable variation across dosing guidelines on how to do this, with doses varying from 4-6mg/kg/dose, dosing intervals ranging from 24-48 hours, and total daily doses ranging from 2.5-6mg/kg/day.[6,20,22,26] Complicating matters further, aminoglycoside pharmacokinetic studies also vary in the recommended acceptable threshold for SGL, varying from 0.5mg/L to 2mg/L.[5] Furthermore, there is evidence that making dosing guidelines more complex may increase the incidence of dosing errors related to prescription, dilution, manipulation and administration, and showing that underdosing with aminoglycosides in the neonatal intensive care setting is common.[27,28] Future research should focus on whether the variations in SGLs we have shown correlate in practice with a higher rate of long-term oto- and nephrotoxicity, and identifying a more unified approach to gentamicin dosing that can be easily applied in clinical practice without increasing dosing errors, and that caters for specific patient subgroups such as VLBW and extremely premature neonates.

The data collection in this research was dependent on proper in-hospital documentation, so that documentation errors or missing information may have influenced the analysis and results. Furthermore, the categorisation of infants according to appropriateness-for-gestational age was based on international centile charts, as similar charts tailored to the local population are unavailable. Therefore, normal variation in the local birthweight compared with that in other populations may have impacted the comparisons of raised SGLs in SGA, AGA, and LGA infants. The authors did not make any distinction between suspected and confirmed sepsis, the latter of which may itself influence gentamicin pharmacokinetics.[29] This research also makes no attempt at extending conclusions on raised SGLs to those on the long-term clinical impact on neonates, as data on subsequent rates of deafness or renal function are not presented. This type of analysis would require a much longer term surveillance period with follow up of patients into adulthood, but would be important since previous studies have questioned the relationship between SGLs and

SUMMARY BOX

What is already known about this subject

- Gentamicin is often used in the empirical treatment of suspected neonatal sepsis.
- Gentamicin therapy is potentially oto- and nephrotoxic.
- Therapeutic drug monitoring of trough serum gentamicin levels helps to prevent toxicity.

What are the new findings

- There is a negative correlation between birthweight, gestation, and trough serum gentamicin levels taken one hour before the next dose.
- Extremely premature neonates born under 28 weeks have a higher risk of raised gentamicin levels and potential toxicity than those born beyond 28 weeks when gentamicin is administered at 36-hourly intervals.

clinical toxicity, and shown neonates to have a lower risk of oto- and nephrotoxicity compared with adult patients.[4,30]

CONCLUSION

Gentamicin is important in the treatment of suspected neonatal sepsis, but is also potentially oto- and nephrotoxic. Therapeutic drug monitoring of gentamicin levels helps prevent this. This study confirms that while the current gentamicin dosing guidelines are safe, extremely premature neonates born under 28 weeks are at higher risk for higher gentamicin trough levels and potential toxicity. Extended interval gentamicin dosing for this gestational category has been adopted in some centres for this reason, and may have a role locally. The long-term effects of high SGLs remain uncertain, and should be a focus of future research.

ABBREVIATIONS

AGA Appropriate for gestational age

LGA Large for gestational age

NPICU Neonatal & paediatric intensive care unit

SGA Small for gestational age

SGL Serum gentamicin level

TDM Therapeutic drug monitoring

VLBW Very low birthweight

ETHICS APPROVAL

Ethical approval for this research was sought and obtained from the Faculty Research Ethics Committee at the University of Malta (FRECMDS_1920_196). The study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its amendments.

REFERENCES

1. Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. Lancet 2017; 390:1770–1780
2. Brunton LL, Lazo JS, Parker KL. Goodman and Gilman's The Pharmacological Basis of Therapeutics, 11th ed. McGraw Hill: New York; 2006
3. Darmstadt GL, Miller-Bell M, Batra M, et al Extended-interval dosing of gentamicin for treatment of neonatal sepsis in developed and developing countries. J Health Popul Nutr 2008;26:163–82
4. Kent A, Turner MA, Sharland M, Heath PT. Aminoglycoside toxicity in neonates: Something to worry about? Expert Rev. Anti. Infect. Ther 2014;12:319–331
5. Touw DJ, Westerman EM, Sprij AJ. Therapeutic drug monitoring of aminoglycosides in neonates. Clin. Pharmacokinet 2009;48:71–88
6. Van Donge T, Pfister M, Bielicki J, et al Quantitative analysis of gentamicin exposure in neonates and infants calls into question its current dosing recommendations. Antimicrob Agents Chemother 2018; 62:(4) e02004-17.
7. Rougier F, Claude D, Maurin M, Maire P. Aminoglycoside nephrotoxicity. Curr. Drug Targets - Infect. Disord. 2004;4:153–162
8. Kovarik JM, Hoepelman IM, Verhoef J. Once-daily aminoglycoside administration: new strategies for an old drug. Eur J Clin Microbiol Infect Dis 1989;8:761–9.
9. Kadambari S, Heath PT, Sharland M, et al Variation in gentamicin and vancomycin dosage and monitoring in UK neonatal units. J Antimicrob Chemother 2011;66:2647–2650.
10. Pace D, Attard-Montalto S, Paracandalo R, et al Neonatal intravenous gentamicin dosing protocol, Department of Child and Adolescent Health, Mater Dei Hospital, Malta; 2013
11. Joint Formulary Committee. British National Formulary for Children, BNF 77. Pharmaceutical Press, London; 2019
12. NICE. Neonatal infection (early onset): antibiotics for prevention and treatment; 2020 https://www.nice.org.uk/guidance/cg149/chapter/1-Guidance. Accessed 14 Jun 2020

13. Samiee-Zafarghandy S, Van Den Anker JN. Aminoglycosides and ototoxicity in neonates: Is there a relation with serum concentrations? Int. J. Clin. Pharmacol. Ther. 2013;51:993–994
14. Rocha MJ, Almeida AM, Afonso E, et al The Kinetic Profile of Gentamicin in Premature Neonates. J Pharm Pharmacol 2000;52:1091–1097.
15. Krishnamoorthy SS, Nair A, Furness J, Sanderson J. Gentamicin use in neonates: Should we have a change of practice? Scott Med J 2013;58:241–245.
16. Vervelde ML, Rademaker CMA, Krediet TG, et al Population pharmacokinetics of gentamicin in preterm neonates: Evaluation of a once-daily dosage regimen. Ther Drug Monit 1999;21:514–519.
17. Hindmarsh KW, Nation RL, Williams GL, et al Pharmacokinetics of gentamicin in very low birth weight preterm infants. Eur J Clin Pharmacol 1983;24:649–653.
18. Rao SC, Srinivasjois R, Moon K . One dose per day compared to multiple doses per day of gentamicin for treatment of suspected or proven sepsis in neonates. Cochrane Database Syst. Rev; 2016
19. Miron D. Once daily dosing of gentamicin in infants and children. Pediatr Infect Dis J 2001;20:1169–1173.
20. Rastogi A, Agarwal G, Pyati S, Pildes RS. Comparison of two gentamicin dosing schedules in very low birth weight infants. Pediatr Infect Dis J 2002;21:234–240.
21. Avent ML, Kinney JS, Istre GR, Whitfield JM. Gentamicin and tobramycin in neonates: comparison of a new extended dosing interval regimen with a traditional multiple daily dosing regimen. Am J Perinatol 2002;19:413–20.
22. Lanao JM, Calvo MV, Mesa JA, et al Pharmacokinetic basis for the use of extended interval dosage regimens of gentamicin in neonates. J Antimicrob Chemother 2004;54:193–198.
23. Mercado MCK, Brodsky NL, McGuire MK, Hurt H. Extended Interval Dosing of Gentamicin in Preterm Infants. Am J Perinatol 2004;21:73–77.
24. Young TE, Mangum B. The antibiotics. Neofax: a manual of drugs used in neonatal care, 20th ed. Thomson Healthcare, MOntvale, NJ, USA; 2007
25. Begg EJ, Vella-Brincat JWA, Robertshawe B, et al Eight years' experience of an extended-interval dosing protocol for gentamicin in neonates. J Antimicrob Chemother 2009;63:1043–1049.
26. Alshaikh B, Dersch-Mills D, Taylor R, et al Extended interval dosing of gentamicin in premature neonates ≤ 28-week gestation. Acta Paediatr Int J Paediatr 2012;101:1134–1139.
27. Allegaert K, Cossey V, van den Anker J. Dosing Guidelines of Aminoglycosides in Neonates: A Balance Between Physiology and Feasibility. Curr Pharm Des 2015;21:5699–5704.
28. Nunes BM, Xavier TC, Martins RR. Antimicrobial drug-related problems in a neonatal intensive care unit. Rev Bras Ter Intensiva 2017;29:331–336.
29. Lingvall M, Reith D, Broadbent R. The effect of sepsis upon gentamicin pharmacokinetics in neonates. Br. J. Clin. Pharmacol. 2005;59:54–61
30. Setiabudy R, Suwento R, Rundjan L, et al Lack of a relationship between the serum concentration of aminoglycosides and ototoxicity in neonates. Int J Clin Pharmacol Ther 2013; 51:401–406.

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ORIGINAL ARTICLE

Retrospective audit of Active Surveillance practice in favourable risk Prostate Cancer in a local patient cohort

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Background

The aim of this audit is to review the local monitoring of favourable risk prostate cancer (CaP) patients under active surveillance (AS), the primary endpoints being determining cancer-specific survival (CSS), rate of development of metastatic disease, mortality and percentage of patients who required definitive treatment.

Methods

Men diagnosed with CaP between January 2010 and December 2015 who were candidates for AS were included. Prostate specific antigen (PSA) values, imaging and histology results were recorded. The standard used is European Association of Urology 2021 guideline on AS and landmark papers published in the past decade.

Results

56.3% of patients had biochemical, radiological or histological progression. Overall survival is 85.4%. CSS is 97.9%. Mortality is 2.1%, whilst 4.2% of patients developed metastatic disease. From the audited population, 36.4% eventually required radical treatment. There is a statistically significant difference between the vital status groups' PSA level at diagnosis (p=0.002), PSA velocity (p=0.0001) and PSA density (p=0.029). The mean length of follow-up is 6.33years.

Conclusion

The high CSS rate is testimony to the success of local AS programs. The wide range of cancer stage, grade and PSA levels of patients chosen for AS should raise the question of whether our selection criteria for AS are stringent enough.

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Active surveillance (AS) is a management option for men with localized, well-differentiated prostate cancer (CaP) considered to be at low risk of progression, in which invasive treatment is deferred till there is evidence of disease progression, or the patient expresses a desire for definitive treatment.[1] This avoids toxicity from overtreatment of clinically insignificant cancers without compromising long-term cancer-specific survival (CSS), by attempting to achieve the ideal timing for initiation of curative treatment. Through AS, patients are closely monitored by serum prostate specific antigen (PSA) levels, multiparametric magnetic resonance imaging (mpMRI) and prostate biopsies. When pre-defined thresholds are reached that signify curable but more serious disease, the patient should be offered definitive treatment.

OBJECTIVES

The aim of this audit is to review how favourable risk CaP patients under AS were monitored over recent years and to determine the proportion of men who had stable disease or eventually progressed to potentially life-threatening disease. The primary endpoints are to calculate CSS in patients on AS, rate of development of metastatic disease, mortality and to determine the percentage of patients who eventually switched to definitive treatment. The secondary outcomes of the audit are to record demographics and cancer characteristics of Maltese men diagnosed with favourable risk CaP such as age at diagnosis, histology and PSA kinetics and to develop correlations between this data and disease progression. Finally, we aim to determine whether the modalities used in follow-up, namely imaging, transrectal prostate biopsies and PSA serum levels are being performed locally in accordance to established guidelines and contemporary literature.

MATERIALS AND METHODS

This retrospective audit includes data on 96 Maltese patients diagnosed with favourable risk CaP enrolled onto AS within a 6 year period. Data protection clearance was obtained prior to data collection. All data was anonymised in a database. Data was collected by analysing all prostate biopsy histology reports showing adenocarcinoma of the prostate graded Gleason 6 (3+3), Gleason 7 (3+4) and Gleason 7 (4+3), issued by the histopathology department at Mater Dei Hospital between January 2010 and December 2015. All men diagnosed with favourable risk CaP who were candidates for AS during that time period were included in the study. Patient demographics, PSA values, imaging and histology results were manually retrieved from iSoft Clinical Manager. Censor date was taken to be either date of patient death or date of last follow-up appointment with the urologist or oncologist. Descriptive analyses were performed using Access Database. Statistical Package for the Social Sciences (SPSS) software was used for statistical analysis tests. The standard referred to is European Association of Urology (EAU) 2021 guideline on AS, along with landmark papers published in the past 10 years which were utilized in the development of the same guideline.

RESULTS

Baseline Demographics

The mean age at diagnosis with favourable risk CaP in the selected population was 69.4 years. The youngest patient was diagnosed at 49 years and the oldest at 86 years.

The mean PSA at diagnosis was 7.86 ng/ml. The PSA density was worked out as the PSA value divided by prostate volume, and the mean value was found to be 0.19 ng/ml^2 The mean PSA velocity was 0.9 ng/ml per year.

Only 11.5% of patients (11 individuals) had a pre-biopsy mpMRI performed. The tumour volume on diagnostic MRI was reported only in rare instances, but the mean tumour volume from the available reports was found to be 2ml. The prostate gland volume ranged widely from 20ml to 227ml, with the mean volume being 51.8ml. With regards to local staging on mpMRI, 20.8% of patients (20 men) had T2a disease, 1% (1 patient) T2b, 8.3% (8 patients) T2c and 2.1% (2 patients) T3a. Local staging was noted available for 67.7% of patients (65 cases).

The histological diagnosis in 85 patients was obtained through transrectal systematic biopsies. Four patients had fusion targeted biopsies. In the remaining 7 patients, adenocarcinoma was diagnosed incidentally from transurethral resection of the prostate (TURP) chippings. The majority of patients on AS (83 men, 86.5%), as expected, had Gleason 6 (3+3) tumours at diagnosis. Eight patients had Gleason 7 (3+4) disease at diagnosis, whilst the remaining 5 patients had higher grade Gleason 7 (4+3) tumours. A mean number of 10.7 cores were taken at biopsy. On average, there were 2.3 positive cores. The maximum cancer core length was not always specified in the histology report, however from the available data, the mean value was found to be 5.56mm.

Table 1 Biochemical, radiological and histological progression count

PSA progression	MRI progression	Histological progression	Count
Yes	Yes	Yes	4
Yes	Yes	No	11
Yes	No	Yes	5
Yes	No	No	23
No	Yes	Yes	3
No	Yes	No	7
No	No	Yes	1
No	No	No	42

Table 2 Vital status per PSA at diagnosis

Vital status	PSA at diagnosis		
	Minimum	Maximum	Mean
Alive - stable disease	1	23	7.25
Alive - progressive disease	1	25	9.13
Dead - cancer	8	8	8.00
Dead - other cause	5	9	7.11
Dead - unknown cause	15	19	17.33

Outcomes

In terms of biochemical follow-up, 44.8% of patients (43 men) had PSA progression. The mean level of PSA at progression was 13.3 ng/ml. The mean interval to PSA progression was 8.3 years.

With regards to radiological follow-up, our results show that 63.5% of the population (61 patients) had at least 1 follow-up MRI within the study period. This ranged from a minimum of 1 MRI to a maximum of 5 within 6 years, the mean being 2 MRIs. Out of all mpMRIs requested, 43 were as per AS protocol, whilst another 21 requests were prompted by PSA progression. One MRI was performed as follow-up to a previous MRI showing tumour progression. In 1 case, the indication for repeat MRI was not clear. Twenty-five patients were found to have tumour progression on MRI – 7 patients were re-staged at T2a, 3 at T2b, 10 T2c, 4 T3a and 1 patient was re-staged at T3b. The mean time to MRI progression was 8.9 years.

With regards to follow-up prostate biopsies, 30.2% of patients (29 individuals) underwent a repeat biopsy during the follow-up period. In 11 patients, biopsy was performed in view of PSA progression, in 8 patients in view of MRI progression, 4 as per proctocol, whilst no clear indication was found in 6 cases. When it comes to the type of biopsies performed, 19 were random biopsies, 8 were targeted and 2 were TURP specimens. The maximum number of follow-up biopsies in a single patient was 2. The mean number of repeat biopsies per patient from the subgroup that underwent follow-up biopsy was 1.04. Thirteen out of the 29 patients (44.8%) who had repeat biopsy were found to have histological progression – 8 patients progressed to Gleason 7 (3+4), 1 patient to Gleason 7 (4+3), 1 patient to Gleason 8 (4+4), 2 patients to Gleason 9 (4+5) and 1 patient progressed to Gleason 10. The mean time interval to histological progression was 3.98 years.

Table 1 shows that 56.3% of patients (54 individuals) had biochemical, radiological or histological progression. In the group with stable disease, the mean age at diagnosis was 55.9 years. The mean age at diagnosis of the group with disease progression was higher, at 62.6 years. Table 2 shows vital status counts per PSA level at diagnosis. Using the ANOVA (Analysis of Variance) test, allowing 95% confidence intervals, it was found that there is a statistically significant difference between the vital status groups' PSA level at diagnosis (p=0.002). Tables 3 and Table 4 correlate PSA kinetics and density with outcome. Using the ANOVA test, a statistically significant difference in PSA velocity was found between the vital status groups, allowing for confidence intervals of 95% (p=0.0001). There was also a statistically significant difference between groups in terms of PSA density (p=0.029, confidence intervals 95%). Table 5 gives further information on vital status per age at diagnosis. Table 6 show

Table 3 Outcome per PSA velocity

Vital status	Mean PSA velocity	Count
Alive - stable disease	0.27	67
Alive - progressive disease	2.99	15
Dead - cancer	5.11	2
Dead - other cause	-0.17	9
Dead - unknown cause	7.68	3

Table 4 Outcome per PSA density

Vital status	Count	Mean PSA density
Alive - stable disease	67	0.14
Alive - progressive disease	15	0.28
Dead - cancer	2	n/a
Dead - other cause	9	n/a
Dead - unknown cause	3	0.55

Table 5 Vital status per age at diagnosis

Vital status	Mean age
Alive - stable disease	68.8
Alive - progressive disease	69.3
Dead - cancer	78.2
Dead - other cause	69.6
Dead - unknown cause	76.8

Table 6 Disease progression per Gleason score at diagnosis

Diagnostic Gleason score	Stable disease no progression	Count
3+3	Yes	29
3+3	No	54
3+4	Yes	5
3+4	No	3
4+3	Yes	2
4+3	No	3

progression per Gleason score at diagnosis. Vital status of the various Gleason scores at diagnosis and of Gleason score at progression are found in Table 7 and Table 8.

A total of 35 patients (36.4 %) eventually required radical treatment, 32 in view of disease progression and 3 as per patient request. Definitive treatment consisted of external beam radiotherapy (EBRT) and androgen deprivation therapy (ADT) for 22 patients, EBRT alone in 2 patients, ADT alone in 7 patients and 4 men underwent radical prostatectomy (RP).

Final follow-up results show that 69.8% of patients (67 individuals) are alive with stable disease and 15.6% (15 patients) are alive with progressive

Table 7 Vital status per Gleason score at diagnosis

Gleason score at diagnosis	Vital status	Count
3+3	Alive - stable disease	62
3+3	Alive - progressive disease	14
3+3	Dead - other cause	6
3+3	Dead - unknown cause	1
3+4	Alive - stable disease	3
3+4	Dead - cancer	1
3+4	Dead - other cause	2
3+4	Dead - unknown cause	2
4+3	Alive - stable disease	2
4+3	Alive - progressive disease	1
4+3	Dead - cancer	1
4+3	Dead - other cause	1

Table 8 Vital status per Gleason score at progression

Gleason at progression	Vital status	Count
3+3	Alive - stable disease	62
3+3	Alive - progressive disease	10
3+3	Dead - cancer	1
3+3	Dead - other cause	7
3+3	Dead - unknown cause	3
3+4	Alive - stable disease	3
3+4	Alive - progressive disease	4
3+4	Dead - other cause	1
4+3	Alive - stable disease	1
4+4	Dead - other cause	1
9	Alive - progressive disease	1
9	Dead - cancer	1
10	Alive - stable disease	1

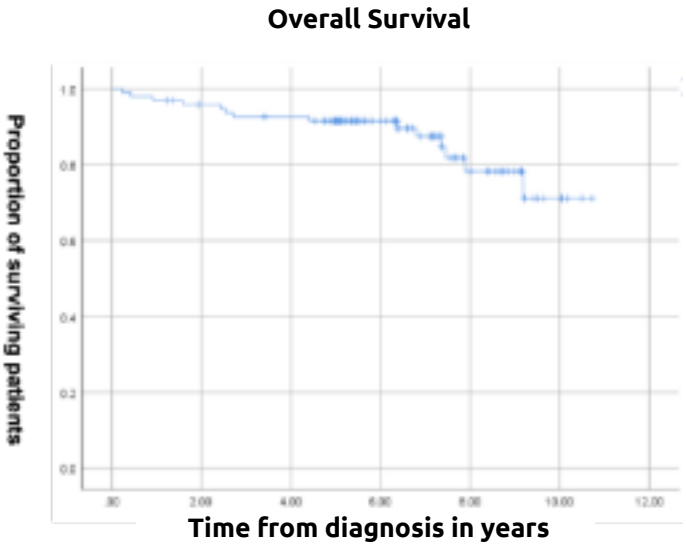

Figure 1 Kaplan-Meier curve showing overall survival

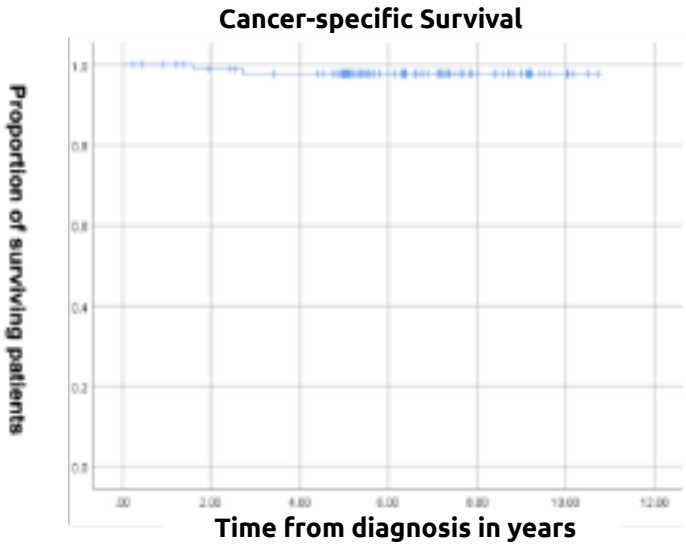

Figure 2 Kaplan-Meier curve showing cancer-specific survival

disease. Mortality from CaP cause is 2.1% (2 individuals), whereas 9.4% of patients (9 individuals) died from non-cancer related illness. Finally, 3.1% of patients (3 men) died from unknown cause. Overall survival (OS) was found to be 85.4%, as per Kaplan Meier curve in Figure 1. The Kaplan-Meier curve in Figure 2 shows CaP-specific survival which was worked out to be 97.9%. A total of 4 patients (4.2%) developed metastatic disease, of whom 2 are deceased of cancer cause and 2 are still alive. The mean time interval to the development of metastatic disease is 4.04 years. The mean length of follow-up for the entire population was 6.33 years.

DISCUSSION

CaP is one of the leading cancers worldwide and its incidence is expected to increase due to screening and early detection.[2] Life expectancy and health status play a crucial role in treatment decision. CaP is commoner in older men, the quoted mean age of diagnosis being 68 years.[3] This concurs with our findings, where the mean age at diagnosis was 69.4 years.

Uncertainties persists regarding optimal patient selection for AS and reliable progression criteria.[4] The eligibility criteria most often applied are International Society of Urological Pathology (ISUP) grade-1, tumour stage pT1c or pT2a, PSA<10ng/mL and PSA density<0.15ng/mL/cc. These criteria are supported by the DETECTIVE consensus, which also concluded that favourable ISUP-2 cancer (PSA<10 ng/mL, stage<pT2a, low number of positive cores) may be considered for AS but ISUP-3 disease should never be included.[5] There is significant variation between other studies regarding patient selection. In our cohort, selected men older than 70 years with intermediate-risk CaP (ISUP-2 and 3) were candidates for AS. This is justified by the fact that frail elderly patients with a poorer baseline health status gain less in terms of cancer-specific mortality with active treatment. Curative treatment is reserved for men with a life expectancy of at least 10 years.[6] From our results, at least 11 men had tumours more advanced than T2a at diagnosis and 17 patients had PSA higher than 10, yet were still considered for AS. Our local criteria for AS therefore seem to be more flexible than those traditionally recommended.

The surveillance protocol employed by Tosoian et al emphasized annual biopsy to avoid missing upgrading of cancers.[7] Locally, this is not standard practice since re-biopsy is usually prompted a rise in PSA or increase tumour burden on mpMRI. Thurtle et al report that MRI and PSA changes as sole triggers for re-biopsy detected 70% of progressions, whereas biopsy per protocol detected histological upgrading in only 7% of cases.[8] The DETECTIVE study concluded that repeat biopsies are indicated in case of progression on DRE, PSA or MRI; evidence for protocol-mandated biopsies is less robust.[5] Similarly, present guidelines are unclear on whether protocol mpMRI should be performed without clinical indication of progression. According to EAU guidelines, regular MRIs are increasingly used but their benefit and whether biopsy may be omitted based on MRI findings is controversial. The population audited here between 2010 and 2015 was managed mostly without the benefit of mpMRI, especially at diagnosis. This is a slightly different scenario to the current picture due to mpMRI being a more widely available resource nowadays. Nowadays,

most patients have a pre-biopsy MRI and regular MRIs thereafter whilst on AS.

Cancer grade is the most important factor for the prediction of CSS. A limitation of AS is that a significant proportion of patients with ISUP-1 cancer in fact harbour higher-grade disease. Definitive treatment is often recommended in the event of disease re-classification on biopsy.[7] From our results, 44.8% of patients who had repeat biopsy, had disease up-grading. In all cases, except for 3 patients, curative treatment was started. Literature states that 10% of patients on AS eventually request definitive treatment due to anxiety about their diagnosis.[9] Our results show a lower conversion rate (3.1%) from AS to active management strictly as per patient desire. The options of EBRT, RP or ADT were offered depending on co-morbidities and patient preference.

In the prospective series by Tosoian et al, 0.4% of patients on AS died from CaP or developed metastatic disease.[7] Our population, enrolled using less restrictive criteria and with less intensive monitoring, especially in terms of repeat biopsies, showed results more comparable to the study by Klotz et al[10] This reported that 3% of patients with low or intermediate risk CaP died or developed metastases at a median follow-up of 6 years. The local mortality rate of 2.1% and rate of metastatic disease of 4.2% are therefore consistent with expected outcome for low risk and select intermediate risk CaP. Mortality during AS highlights the attempt to balance overtreatment of cancer with the small, but real, risk of underestimating its fatality. Contemporary literature consistently shows excellent long-term OS and CSS of CaP patients on AS. Klotz et al report 10-year OS of 85%, comparable to our local OS of 85.4%.[10] They report CSS to be 98.1%, whilst our results show CSS of 97.9%. Tosoian et al report OS of 93% and CSS of 99.9%.[7] VanAs et al and Carter et al both report 10-year OS of 98% and CSS of 100%.[11,12]

A limitation of this audit is missing data which is crucial in determining adequacy of follow-up (e.g.if DRE was performed during visits, frequency at which PSA was taken). Radiological staging information is absent for 67% of patients. This is explained by the fact that up till recently, diagnosis of CaP relied on PSA levels and transrectal biopsies, without the benefit of mpMRI. Given the long natural history of CaP, follow-up is incomplete, despite the mean follow-up period of 6.33 years. The lack of pre-defined criteria in the recommendation for AS means that patients with higher grade disease who are normally not offered AS were included. This makes the cohort too heterogenous to derive solid conclusions on the safety of local AS programs.

CONCLUSION

AS is an ever-evolving strategy. There are no approved standards in follow-up protocols such as frequency of imaging with mpMRI, frequency of prostate biopsies, measurement of PSA kinetics and frequency of clinical examination with DRE, or when curative treatment should be initiated (i.e. re-classification criteria). Moreover, there is no consensus regarding which outcome measures are the best indicators of the disease progression and should therefore be prioritized. Individualized risk-based approaches to date replace protocol-based management of CaP patients on AS.

The value of this audit is that it provides the opportunity to compare our local practices in AS with those recommended by current guidelines and to recognize the areas that call for improvement. The high CSS rate is testimony to the success of local AS programs but could also be a reflection of the indolent behaviour of favourable risk CaP. On the other hand, scrutiny of cancer stage, grade and PSA levels of patients chosen for AS shows that the range is simply too wide. This should perhaps raise the question of whether our selection criteria for AS are stringent enough.

ABBREVIATIONS

ADT	androgen deprivation therapy
ANOVA	analysis of variance
AS	active surveillance
CaP	prostate cancer
CSS	cancer-specific survival
DRE	digital rectal examination
EAU	European Association of Urology
EBRT	external beam radiotherapy
ISUP	International Society of Urological Pathology
mpMRI	multi-parametric magnetic resonance imaging
OS	overall survival
PSA	prostate specific antigen
RP	radical prostatectomy
SPSS	Statistical Package for the Social Sciences
TURP	transurethral resection of the prostate

REFERENCES

1. Bruinsma SM, Roobol MJ, Carroll PR et al Semantics in active surveillance for men with localized prostate cancer — results of a modified Delphi consensus procedure. Nat Rev Urol 2017 May;14:(5)312–22.
2. Smith BD, Smith GL, Hurria A et al Future of cancer incidence in the United States: burdens upon an aging, changing nation. J Clin Oncol Off J Am Soc Clin Oncol 2009 Jun 10;27:(17)2758–65.
3. Arnold M, Karim-Kos HE, Coebergh JW et al Recent trends in incidence of five common cancers in 26 European countries since 1988: Analysis of the European Cancer Observatory. Eur J Cancer Oxf Engl 1990 2015 Jun;51:(9)1164–87.
4. Thomsen FB, Brasso K, Klotz LH et al Active surveillance for clinically localized prostate cancer-a systematic review. J Surg Oncol 2014 Jun;109:(8)830–5.
5. Lam TBL, MacLennan S, Willemse P-PM et al EAU-EANM-ESTRO-ESUR-SIOG Prostate Cancer Guideline Panel Consensus Statements for Deferred Treatment with Curative Intent for Localised Prostate Cancer from an International Collaborative Study (DETECTIVE Study). Eur Urol 2019 Dec;76:(6)790–813.
6. Liu D, Lehmann HP, Frick KD et al Active Surveillance Versus Surgery for Low Risk Prostate Cancer: A Clinical Decision Analysis. J Urol 2012 Apr;187:(4)1241–6.
7. Tosoian JJ, Mamawala M, Epstein JI et al Intermediate and Longer-Term Outcomes From a Prospective Active-Surveillance Program for Favorable-Risk Prostate Cancer. J Clin Oncol Off J Am Soc Clin Oncol 2015 Oct 20;33:(30)3379–85.
8. Thurtle D, Barrett T, Thankappan-Nair V et al Progression and treatment rates using an active surveillance protocol incorporating image-guided baseline biopsies and multiparametric magnetic resonance imaging monitoring for men with favourable-risk prostate cancer. BJU Int 2018 Jul;122:(1)59–65.
9. Klotz L, Zhang L, Lam A et al Clinical results of long-term follow-up of a large, active surveillance cohort with localized prostate cancer. J Clin Oncol Off J Am Soc Clin Oncol 2010 Jan 1;28:(1)126–31.
10. Klotz L, Vesprini D, Sethukavalan P et al Long-term follow-up of a large active surveillance cohort of patients with prostate cancer. J Clin Oncol Off J Am Soc Clin Oncol 2015 Jan 20;33:(3)272–7.
11. van As NJ, Norman AR, Thomas K et al Predicting the probability of deferred radical treatment for localised prostate cancer managed by active surveillance. Eur Urol 2008 Dec;54:(6)1297–305.
12. Carter HB, Kettermann A, Warlick C et al Expectant management of prostate cancer with curative intent: an update of the Johns Hopkins experience. J Urol 2007 Dec;178:(6)2359–64; discussion 2364-2365.

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ORIGINAL ARTICLE

Hip Fractures in Older Persons in Malta

an epidemiological study

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Background

Hip fractures are a common cause of morbidity and mortality in older adults, and may sometimes be the result of the inability to cope with arising medical problems. The purpose of this study is dual; it is primarily a local epidemiological study of hip fractures in older persons in Malta. The secondary purpose of this study is to identify the number of patients who have had a significant hospital visit in the three months preceding the hip fracture.

Method

Data was collected over a period of 6 months from the national general hospital of Malta; Mater Dei Hospital. Patients included were 70 years and older, and sustained a proximal hip fracture.

Results

The incidence of hip fractures in Malta in persons aged 70 and over is 7.29 per 1000 persons per year in females and 4.66 per 1000 persons per year in males. The 1 year mortality rate was found to be 22%. In over one quarter of the cases, there was a significant hospital visit within the 3 months prior to the hip fracture incident, one fifth of whom had a falls related visit.

Conclusion

Hip fractures in older persons in Malta resulted in a high mortality rate and rate of admission to care homes. Incidence rate in Malta matched incidence rates in central Europe. While case prevention is still limited, we suggest an age and sex-matched control study to assess the significance of hospital visits occurring prior to hip fractures, in order to guide a direction for case prevention.

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Proximal femoral fractures are associated with great morbidity and mortality in older adults. In fact, it is estimated that 25% of patients die within 1 year of a proximal femoral fracture, 76% will have impaired mobility, 50% will have a decline in their ability to perform activities of daily living (ADL) and 22% will require institutionalization within 1 year of having sustained the fracture.[2] There are various risk factors for proximal femoral fractures. In fact, an inability to cope with acute medical or surgical problems, can lead to falls and fractures.[16]

As a result, this study has two main objectives. The primary objective includes the collection of local epidemiological data on proximal femoral fractures in older persons in Malta, including the incidence of proximal femoral fractures, the average length of stay in the acute hospital, discharge destination, in-patient mortality rate, 6-month mortality rate and 1 year mortality rate. The secondary objective involves the identification of visits to the emergency department or significant hospital visits in the three months preceding the proximal femoral fracture which could potentially identify and possibly reduce the risk of falls and fractures.

MATERIALS AND METHODS

The patient population consisted of people aged 70 years and over who were admitted to hospital with a proximal femur fracture confirmed by bone imaging. Data was collected over a 6-month period from May 2019 until October 2019 and patients were followed up for 1 year post proximal femoral fracture. Cases were identified from two over-lapping sources to ensure a high pick-up rate: (i) the surgical PACS trauma list and (ii) the orthogeriatric team's census. The orthogeriatric team covers all proximal femoral fracture cases aged 70 years and over in the orthopaedic wards at Mater Dei Hospital, whether candidates for theatre or not. The surgical PACS trauma list includes all cases of operated proximal femoral fractures in Mater Dei Hospital as well as Gozo General Hospital.

Data was collected retrospectively via electronic case summaries, iSOFT clinical manager and CPAS. The following data was collected:

- The patient's demographics including gender and age
- The patient's residential location prior to hospitalization and after discharge,
- The proximal femoral fracture incident,
- Any emergency department visits or admissions to the acute hospital 3 months prior to the fracture,
- The nature of the hospital admission (i.e., medical pathology, surgical pathology, ophthalmic pathology or falls),
- Mortality status at 6 months and 1 year after the proximal femoral fracture incident.

RESULTS

Proximal Femoral Fracture Demographics

Over a period of 6 months, the total number of patients aged 70 years and over with a proximal femoral fracture, amounted to 195 with an average of 32.5 cases per month. The average age was 83 years, with an age range of 70 to 100; 70 being the minimum age of inclusion in the study. Thirty-four percent of the cases were males, while 66% of the case were females with a female: male ratio of 2:1. This ratio increased with age; the male cases peaked at age 70-74, and the female cases peaked at age 80-89. One hundred and forty-seven of the proximal femoral fracture incidents (75%) occurred in patients who were residing at their own home, while the remaining 25% of cases occurred in patients who were residing in institutions prior to the proximal femoral fracture. Of the 195 cases, 6 cases were lost to follow up, as the patients were not local residents (shown in Table 1, and Figure 1).

Table 1 Proximal Femur Fractures over the age of 70 years at Mater Dei Hospital over a period of 6 months

Age – years		
mean ± standard deviation	82.8 ± 6.95	
range	70 – 100	
Gender - number (%)		
Male	65 (34%)	
Female	130 (66%)	
Number of cases		
May 2019 until October 2019	195	
Average per month	32.5	
Patient location prior to fracture		
Own home	147 (75%)	
Care home	47 (24%)	
Rehabilitation Hospital	1 (1%)	
Patient location after fracture	**6 months after fracture**	**1 year after fracture**
Lost to follow up	6	6
Included in results	189	189
Own home	92 (49%)	86 (45%)
Care home	64 (34%)	62 (33%)
Death	33 (17%)	41 (22%)

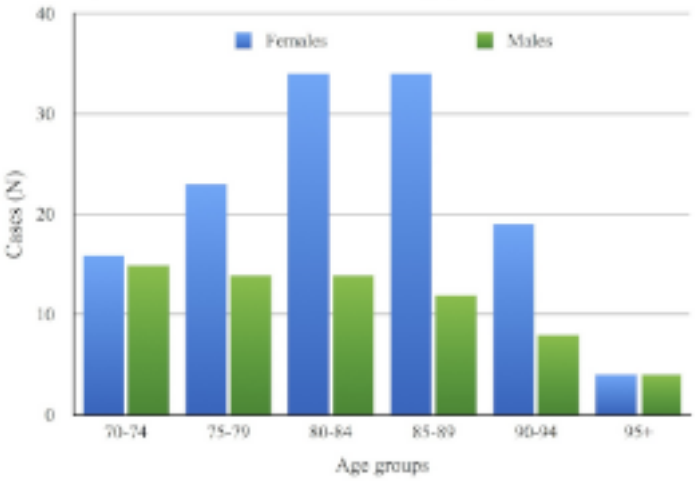

Figure 1 Female:Male ratio in different age groups

Figure 2 Approximate outcome at 6 months after a proximal hip fracture in older adults previously living at home prior to fracture

Estimated Incidence Rates

Data from the Maltese national statistics office from 2018 was used to establish the population size. The estimated incidence of proximal femoral fractures in Malta in persons aged 70 years and over was found to be 7.29 per 1000 persons per year in females and 4.66 per 1000 persons per year in males. In the age group 70 -79 years, the incidence was found to be 3.09 per 1000 persons per year. In females this was 3.43 per 1000 persons per year, and in males this was 2.71 per 1000 persons per year. The incidence rate rose dramatically with age, with a rate of 10.47 per 1000 persons per year in those aged 80 – 89 years, and 24.23 per 1000 persons per year in those aged 90 years and over, shown in Table 2, Supplementary File 1, and Supplementary File 2.

Mortality Rates

Mortality rate showed a plateaued curve, with a total of 11 deaths out of the 189 patients (5.8%) in the first 30 days from the proximal femoral fracture. This increased to 33 deaths (17%) at 6 months from the proximal femoral fracture and 41 (22%) deaths at 1 year from the proximal femoral fracture, shown in Supplementary File 3.

Rate of Institutionalization

Of the 147 patients who were residing at home prior to the proximal femoral fracture, 6 were lost to follow up at 6 months. Of the remaining 141 cases, 26 (18%) were living in a care home within 6 months of the proximal femoral fracture (Figure 2).

Hospital Encounters Prior to Proximal Femoral Fracture

Just over one quarter of the cases, 27% (n=52), had contact with the hospital emergency department, or were discharged after a hospital admission, within the 90 days preceding the proximal femoral fracture. Of these, 15 (29%) were seen at the emergency

Table 2 Estimated incidence rates of proximal femoral fractures in older adults in the Maltese islands

	Males	Females	Total
Aged 70 - 79			
cases per 1000 person years	2.71	3.43	3.09
one year % incidence	0.27%	0.34%	0.31%
Aged 80 - 89			
cases per 1000 person years	7.39	12.45	10.47
one year % incidence	0.74%	1.25%	1.05%
Aged 90 and over			
cases per 1000 person years	27.30	22.89	24.23
one year % incidence	2.73%	2.29%	2.42%

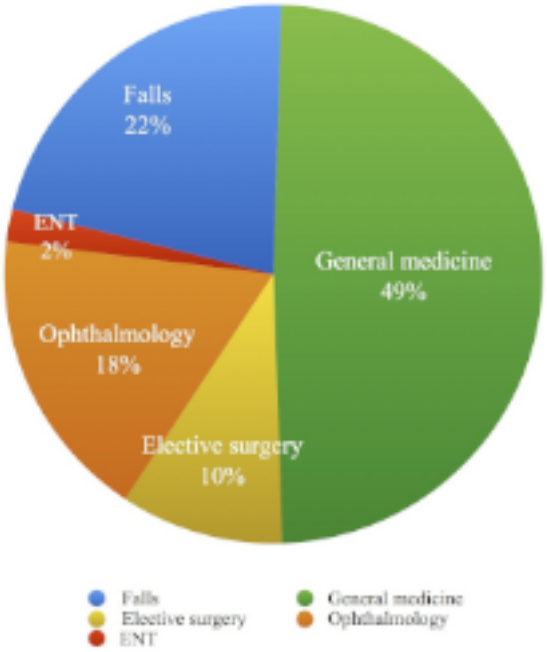

Figure 3 Admissions 90 days prior to proximal hip fracture sorted into categories

department and sent home, 24 (46%) were discharged from under the care of a medical firm, 13 (25%) were discharged from under the care of a surgical firm. 21% of the visits were related to falls, 17% of the visits were related to ophthalmic problems including elective ophthalmic surgery, 10% of the visits were for elective surgery excluding ophthalmic surgery (Figure 3 and Supplementary File 4).

Duration In Acute Hospital

The average length of stay in the acute hospital was 20.1 days, ranging from 4 to 183 days. Patients who did not have a hospital encounter in the 3 months prior to a proximal femoral fracture had an average length of stay of 18.6 days. Patients who did have a hospital encounter in the 3 months prior to proximal femoral fracture had a longer average length of stay of 24.7 days.

DISCUSSION

Proximal Femoral Fracture Demographics

This study showed a clear trend of proximal femoral fractures by gender, with a female to male ratio of 2:1 for proximal femur fractures. The review conducted by Rapp et al[9], explored the epidemiology of proximal femoral fractures in Germany. They also concluded that age-standardized difference between women and men is about 2:1 in most countries of the world, with that in Germany being 1.72:1.

Estimated Incidence Rates

Proximal femoral fracture incidence rates show a wide geographical variation. The estimated incidence rate from this study in Malta are similar to the incidence rates in central Europe; the Netherlands, Germany and Austria as noted in the review by Dhanwall et al.[6] Rey-Rodriguez et al[10] also showed a similar proximal femoral fracture incidence rate in Southern Spain of 2.28 per 1000 persons per year, where the incidence was higher in women (3.13 per 1000 women per year compared to 1.25 per 1000 men per year).

Mortality Rates

An incremental rise in mortality was noted from in-patient up to 1 year after a proximal femoral fracture. In fact, there was a mortality of 5.8% at 30 days and 22% at 1 year. This coincides with results from the study carried out in Malta by Zammit et al[15], which showed a 30-day mortality of 5.9% and a mortality of 23.9% at 1 year.

Rate of Institutionalization

In their review Rapp et al[9], showed that in high income countries, 10–20% of proximal femoral fracture patients will end up in a long-term facility following a proximal femoral fracture. This coincides with our results where 18% of the patients were living in a care home at 6 months from the proximal femoral fracture. This result also highlights how a proximal femoral fracture is often a major life event, having both a medical and social impact.

Hospital Encounters prior to Proximal Femoral Fracture

Part of our study identified how many patients had a significant hospital contact prior to sustaining a proximal femoral fracture. This was done with an aim to identify any potential risk factors which could have been identified and possibly managed.

A large proportion of the proximal femoral fracture cases did have a hospital encounter in the 90 days prior to their proximal femoral fracture. Among these, the commonest mechanism of injury was secondary to a fall. In fact, 90% of proximal femoral fractures result from falls but only 1% of falls result in proximal femoral fractures[2] Moreover, osteoporosis is an independent risk factor for both falls and fractures.[5] Table 3 gives a list of the risk factors for proximal femoral fractures, falls and osteoporosis.

This study showed that most emergency visits or hospital admission at 90 days preinjury, were due to

Table 3 Risk factors for proximal femoral fractures

Risk factors for osteoporosis[7]	Fall Characteristics
• Increasing Age • Family history • Certain medical conditions including endocrine disorders, menopause, renal and liver impairment and gastrointestinal conditions leading to malabsorption and malnutrition. • Smoking • Medications including antiepileptics, anticoagulants, chemotherapy, gonadotrophic-releasing hormone agonists/antagonists. • Low BMI • High alcohol consumption • Reduced mobility and physical inactivity • Low dietary intake of calcium and vitamin D • Personal history of fragility fracture **Risk factors for falls**[1] • Female gender • Advancing age • Multimorbidity • Conditions leading to gait and balance disturbances • Conditions leading to dizziness/syncope • Acute disease process • Polypharmacy especially sedatives, antihypertensives and neuroleptics. • Visual Impairment • Impaired mobility • Sensory impairment including tactile-proprioceptive and vestibular impairment • Environmental hazards including inappropriate footwear • Risk taking behaviour • Cognitive impairment, especially delirium • Psychosocial problems including anxiety, depression and fear of falling. • History of recurrent falls	**Mechanism of fall**[1] • Higher risk of proximal femoral fracture if unable to break the fall, example in loss of consciousness or syncope. **Factors involved in falls descent:** (Berry SD and Miller RR, 2008) • A greater height of descent results in a greater force of impact to the ground. • The direction of fall: Proximal femoral fractures are more common when people land on their side. **Factors involved with fall impact:**[3] • The amount of subcutaneous fat and soft tissue: A greater BMI or fall on the buttocks is associated with reduced proximal femoral fracture risk. • The surface of impact: Harder or uneven surfaces like stairs are associated with greater risk when compared to softer surfaces like carpeted or matted floors.

medical problems (48%) followed by falls (21%). This is expected since multiple medical pathologies are risk factors for both osteoporosis and falls as shown in Table 3, thereby increasing the risk of sustaining a proximal femoral fracture after a fall. Moreover, certain medical pathologies might lead to a more dangerous mechanism of injury. For instance, those people who fall secondary to a syncopal episode or loss of consciousness would be unable to break the fall and therefore result in a higher impact on the ground.[1] Moreover, certain medical problems may lead to sensory impairment which is also a risk factor for falls. In fact, a portion of patients had a hospital visit related to ophthalmic (17%) and ENT (1.9%) pathology at 90 days before injury. However, not all people who have risk factors will necessarily sustain a fall or fracture, but any acute event may lead to an increased risk especially in frailer elderly people with an already reduced baseline physiological reserve.[3]

SUMMARY BOX

- Proximal femoral fractures are associated with high morbidity and mortality in older adults[11] and increase the risk of institutionalization.[12]
- Falls with resultant proximal femoral fractures, may arise from the inability to cope with acute medical problems. [16]
- The incidence of proximal femoral fractures worldwide is known to be greater with increasing age[8] and more common in women compared to men [11]
- The incidence of proximal femoral fractures in Malta in those aged over 70 years old was found to be 7.29 per 1000 persons per year in females and 4.66 per 1000 persons per year in males in this study.
- The local trend of proximal femoral fractures in Malta matched the worldwide trend of increased incidence with older age and female gender.
- In this study, 18% of patients with proximal femoral fractures living at home were admitted to a care home within 6 months of the event.
- Over one quarter of patients aged 70 and over who sustained a proximal femoral fracture had a significant hospital visit within the 90 days preceding the event.

LIMITATIONS

A main study limitation includes a degree of selection bias. For instance, patients with a proximal femoral fracture were identified from online databases which include in-patients only and the orthogeriatric service at Mater Dei hospital which includes patients who are receiving care at two specific orthopedic wards only. As a result, those patients who received care in a private hospital or died before reaching the orthogeriatric services might have been missed thereby underestimating the incidence rate. In addition, those patients who sustained a proximal femoral fracture in Gozo were more likely to be misrepresented since cases were obtained from the Gozo online databases only so those proximal femoral fractures who were treated conservatively and not admitted to hospital may have also been missed.

Moreover, Bugeja et al.[5] showed a seasonal variation in proximal femoral fracture incidence in Malta, with summer months having the lowest number of proximal femoral fractures and mortality. The incidence and mortality of proximal femoral fractures in this study, was recorded from data that was collected over 6 months from May till October 2019. The seasonal variation may therefore have affected the results presented.

Six out of 195 patients were lost to follow up being foreign nationals visiting Malta who returned to their country of origin as soon as it was fit for them to travel post proximal femoral fracture surgery. As a result, these were lost to follow-up so data on their longer postoperative outcomes could not be included. These represent 3% of the study population.

CONCLUSION

This study highlights the profound medical and social impact of proximal femoral fractures in the elderly in Malta, having a high mortality rate and a high rate of admission to care homes. Incidence rate in Malta matched incidence rates in central Europe [7] Moreover, multiple risk factors for proximal femoral fractures have been identified in the literature. These risk factors can be used for screening strategies for primary and/or secondary fracture prevention. This study showed that the majority of patients sustained a proximal femoral fracture following a fall. As a result, we recommend that those patients who present with a fall should have an in-patient comprehensive geriatric assessment including a falls risk and fracture risk assessment. In addition, many elderly patients made use of emergency services, ophthalmic services, and elective surgery within 3 months prior to a proximal femoral fracture. As a result, we would suggest that elderly patients admitted with acute medical problems, have sensory impairment or undergo elective surgeries, should be screened for falls and fracture risk and be referred to falls prevention clinics.

REFERENCES

1. Aizen E, Dranker N, Swartman R and Michalak R. (2003), 'Risk Factors and Characteristics of Falls Resulting in Proximal femoral Fracture in the Elderly' IMAJ; 5:333-336. Available from https://pubmed.ncbi.nlm.nih.gov/12811949/.
2. Ambrose AF, Gee P and Hausdorff JM. (2013), 'Risk factors for falls among older adults: A review of the literature' Maturitas; 75:51-61.
3. Berry SD, & Miller RR. (2008), 'Falls: epidemiology, pathophysiology, and relationsproximal femoral to fracture' Current osteoporosis reports; 6:(4)149–154.
4. Bugeja M, Aquilina S, Farrugia C, Esposito I(2018), 'Demographic Study of Proximal femoral Fractures in the Maltese Islands' Geriatr Orthop Surg Rehabil.; 23;9.
5. Burke-Doe A, Hudson A, Werth HR. (2008), 'Knowledge of Osteoporosis Risk Factors and Prevalence of Risk Factors for Osteoporosis, Falls and Fracture in Functionally Independent Older Adults', Journal of Geriatric Physical Therapy; 31:(1)11-17.
6. Dhanwal DK, Dennison EM, Harvey NC, Cooper C. (2011), 'Epidemiology of proximal femoral fracture: Worldwide geographic variation' Indian J Orthop.; 45:(1)15-22.
7. Kenkre JS & Bassett JHD. (2018), 'The bone remodeling cycle' Ann Clin Biochem.; 55:(3)308-327.
8. Pillai A, Eranki V, Shenoy R, Hadidi M(2011), 'Age related incidence and early outcomes of proximal femoral fractures: a prospective cohort study of 1177 patients' J Orthop Surg Res.; 6:5.
9. Rapp K, Büchele G, Dreinhöfer K, Bücking B, Becker C, Benzinger P. (2019), 'Epidemiology of proximal femoral fractures: Systematic literature review of German data and an overview of the international literature' Z Gerontol Geriatr.; 52:(1)10-16.
10. Rey-Rodriguez MM, Vazquez-Gamez MA, Giner M, Garrachón-Vallo F, Fernández-López L, Colmenero MA, Montoya-García MJ. (2020), 'Incidence, morbidity and mortality of proximal femoral fractures over a period of 20 years in a health area of Southern Spain' BMJ Open.; 10:(9) e037101.
11. Sterling RS. (2011), 'Gender and race/ethnicity differences in proximal femoral fracture incidence, morbidity, mortality, and function' Clin Orthop Relat Res.; 469:(7)1913-1918.
12. Uriz-Otano F, Pla-Vidal J, Tiberio-López G, Malafarina V(. 2016), 'Factors associated to institutionalization and mortality over three years, in elderly people with a proximal femoral fracture-An observational study' Maturitas.; 89: 9-15.
13. World Health Organization(2018), 'Falls' [online]. Accessed on 27th April 2020. Available from: https://www.who.int/news-room/fact-sheets/detail/falls
14. Yoo J, Lee JS, Kim S, Kim BS, Choi H, Song DY, Kim WB, Won CW. (2019), 'Length of hospital stay after proximal femoral fracture surgery and 1-year mortality' Osteoporos Int.; 30:(1)145-153.
15. Zammit P, Ferry P, Cordina J, Vassallo M, Dalli S, Vella A, Bugeja V, Muscat J, Zammit K. (2016), 'Orthogeriatrics in Malta: a 3-year experience' Malta Medical Journal.; 28:(1) 38-40. Available from https://www.um.edu.mt/library/oar/handle/123456789/9710.
16. Zapatero A, Barba R, Canora J, Losa JE, Plaza S, San Roman J, Marco J. (2013), 'Proximal femoral fracture in hospitalized medical patients' BMC Musculoskeletal Disord.; 14:15.

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ORIGINAL ARTICLE

Barriers to Staff Attendance at the Basics in Medical Education (BiME) Course organized by the Faculty of Medicine and Surgery, University of Malta

a case study approach

Petramay Attard Cortis, Fiona Muir

Background

The Basics in Medical Education (BiME) course aims to promote faculty development within the Faculty of Medicine and Surgery, University of Malta. Despite being offered free of charge the turnout has been underwhelming. This research aimed to identify barriers to staff attendance.

Methods

A qualitative, explanatory, single-case study was performed in 2020 after obtaining Ethics Committee permission. Data was collected via semi-structured interviews with faculty members who self-selected to participate after receiving an invitation email; and through documentation analysis of anonymised participant feedback forms collected from previous iterations of the course held in 2018 and 2019. Data analysis was performed using Pattern Matching.

Results

Individual and institutional barriers to attendance were identified. The main barrier was an individual's personal characteristics, particularly a lack of appreciation of the importance of faculty development. Other barriers included a lack of time; a reduced awareness of the concept of separate professional and educator identities; a lack of information about the course; a feeling of isolation from the faculty community; and a possible insufficiency of institutional governance and recognition. Funding, and the interprofessional aspect of the course, were found not to be barriers to attendance.

Conclusions

An understanding of the specific barriers to attendance at the BiME course may allow the Faculty to mitigate these, encouraging staff attendance, and thus promote faculty development in medical education at the University of Malta.

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The role of the medical educator has evolved over time - from a deliverer of knowledge to a student-learning facilitator to the twelve well-defined roles of the medical teacher..[1] As such, Steinert[2] argues that faculty development is important to enhance an individual's knowledge, skills, and behaviours.[3]

The Medical Education Unit (MEU) at the University of Malta (UM) was set up in October 2017 as a non-statutory unit,[4] with the aims of Staff Development, Quality Assurance, Medical Education Research, and maintenance of Standards in Medical Education. To address faculty development the MEU offers a Basics in Medical Education (BiME) Course. This full-time in person course which is held over three days has been delivered to Faculty members on three occasions during 2018-2019 at the Medical School, Mater Dei Hospital. The BiME Course is targeted at all Faculty members, including resident academics, members of the visiting teaching stream and casual staff. In July 2019, the Human Resources office confirmed that the Faculty had six hundred and fifty-five faculty members (personal correspondence), divided into sixty-nine resident academics; three hundred and sixty-five members of the visiting teaching stream; and two hundred and twenty-one casual staff members. The BiME course covers topics: Medical Education Theory; Curriculum Development, Delivery and Evaluation; and Assessment and Feedback. All faculty members are invited to attend free of charge; participation is voluntary.

Interest and attendance at the BiME Course were less than expected by the MEU, therefore the objective was to identify barriers to staff attendance. The evidence-based recommendations from this study may facilitate course attendance, improve faculty development, and enhance the delivery of teaching experiences to students.

Several barriers to continuous professional development (CPD) exist such as time and funding,[5-9] but these have not been studied in relation to the Faculty of Medicine and Surgery's BiME course. Thus, this explanatory single-case study set out to identify barriers to CPD attendance at the BiME course compared to those reported in the literature.

MATERIALS AND METHODS

A qualitative, explanatory, holistic, single-case study was performed in 2020. Ethical approval was obtained from the Faculty Research Ethics Committee, Faculty of Medicine and Surgery, UM (FRECMDS_1819_114, 4th December 2019) and from the School of Medicine, University of Dundee (SMED REC Number 19/ 202, 20th December 2019.)

Research was carried out using the theoretical lens of post-positivism,[10] the ontology of critical realism and the epistemology of objectivism. When using a post-positivist theoretical perspective, it is recommended that the methodology should include the collection of multiple data sources to allow data triangulation.[10] This led to the choice of a case study methodology for investigation of the research question: Why are staff members at the Faculty of Medicine and Surgery, University of Malta not attending the Basics in Medical Education Course? Additionally, the research question fulfils the criteria posed by Yin,[11] Bassey,[12] and Stake[13] for the use of case study research.

Interviews and documentation were chosen as the data sources. Thirteen individual, face-to-face, semi-structured interviews were held at a place of the interviewee's choosing. Documentation analysis of forty-four anonymised BIME course feedback forms (2018-2019) were examined for barriers to attendance, as informed by the Theoretical Propositions developed through the first part of the Pattern Matching (PM) process.

Pattern Matching (PM) is a method of data analysis used in qualitative research which firstly involves the identification of predicted patterns (called Theoretical Propositions) from the literature and from author experience on the topic in question. Later, these are compared with observed data to look for congruence, thus strengthening the research's internal validity. A step-by-step description of the PM data analysis process used for this case study has been published by Attard Cortis and Muir.[14]A visual representation of the process followed is presented in Figure 1.

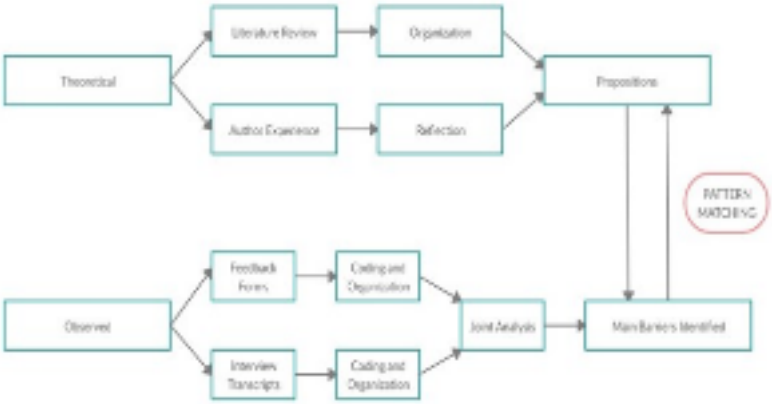

Figure 1 A flow chart of the Pattern Matching process used for this research. Attard Cortis, P. (2020). Barriers to Staff Attendance at the Basics in Medical Education (BiME) Course organized by the Faculty of Medicine and Surgery, University of Malta: a case study approach. MMEd Thesis. University of Dundee.

The Theoretical Propositions developed for this research were:

- Time is a significant barrier to attendance[5-9]
- Individual personal characteristics influence attendance irrespective of external motivators or barriers[5]
- The idea of separate professional and teaching identities[7] is poorly developed locally and this lack of awareness acts as a barrier to attendance (author experience)
- Positive or Negative Incentives, or lack thereof, influence attendance[7]
- The lack of a sense of belonging to the Faculty community acts as a barrier to attendance[5,6]
- A lack of awareness of the existence of the BiME course is a barrier to attendance (author experience)
- Funding[8,9] is not a barrier to attendance (author experience)
- Interprofessional education[6] is not a barrier to attendance (author experience)

The strengths of this case study include clear alignment of the theoretical lens, ontology, epistemology, methodology, methods and analysis choices; a well-defined bounded system of study i.e., the three previously organized BiME courses; addressed a "why" question with significant utility to the Faculty; and addressed a contemporary phenomenon. Furthermore, the data collected provided rich descriptions of the barriers to attendance as experienced by the faculty members who volunteered and who were forthcoming with their thoughts and opinions, allowing data saturation to be reached. A reflexive stance was useful to establish rigour and trustworthiness in this qualitative research.[15]

Generalisability was limited to the well-defined case of the BiME courses held in 2018 and 2019. Therefore, the findings may not be generalizable to other courses organized by the UM or to other faculty development courses. However, the research methodology is explained in detail and with the small pool of medical educators in Malta, it is possible for medical educators who work in similar contexts to decide whether the findings could be applicable to their situation.

As an insider researcher an inherent culture bias was present.[16] However, the cultural context of the case study was important to situate and analyse the research findings. The risk of confirmation bias was reduced by transcribing interviews and feedback form data, and transcripts were member checked. Coding and analysis followed a PM technique (Figure 1) and the theoretical propositions to increase dependability.

Figure 2 A graphical representation showing the research findings in relation to barriers to attendance at the BiME course Attard Cortis, P. (2020). Barriers to Staff Attendance at the Basics in Medical Education (BiME) Course organized by the Faculty of Medicine and Surgery, University of Malta: a case study approach. MMEd Thesis. University of Dundee.

Faculty member participants who volunteered for interview may have been subject to acquiescence, social desirability, or sponsor biases.[16] Additionally, it is not possible to know if participants were significantly different from non-participants, or if they experienced significantly different barriers to attendance from non-participants. Furthermore, no casual members of staff participated and thus the barriers experienced relate only to resident academic and visiting teaching faculty members.

RESULTS

The results are presented as the "Main Barriers Identified" (Figure 1) as matched to the theoretical "Propositions" (Figure 1) extracted from the literature and author experience prior to the start of data collection. In Figure 2, eight themes as barriers were considered as per the theoretical propositions. Within these, sixteen sub-themes were identified.

Time

Nine interviewees stated that time was a barrier. Three stated that time was not a barrier although they showed an appreciation that time may be a barrier to visiting faculty members. Six mentioned that an increasing number of medical students may be a possible barrier due to the additional time commitment. The need to keep abreast with CPD in medical education as well as in the participant's primary specialty, for example clinical practice or research, was seen as a possible challenge by six participants.

Individual Characteristics

The individual's general attitude was seen as a determining factor and many faculty members were unable to identify personal barriers to attendance on open questioning, possibly as a reflection of their positive attitude and internal motivation.

"… ideally the people who are selected to teach, are only those people who are extremely strongly motivated to teach… I think the selection process is extremely important." (Visiting Teaching Participant 6)

Nine interviewees highlighted that, if faculty members believe attending faculty development is not important, then they would not turn up. Also, an individual's resistance to change was considered a barrier by four interviewees.

A person's comfort with, and approach to, technology was related to barriers to attendance. While one interviewee mentioned that online faculty development programmes may be preferred to face-to-face courses, and another mentioned that online learning may be more efficient in terms of learning time required, the majority preferred attending courses in person. Despite this, forms of blended learning were viewed positively.

Four participants emphasized that a lack of continuity and follow up may be a barrier to attendance and may have a domino effect on their peers i.e. make it less likely that other faculty members will attend. Continuity was also deemed important by course participants, as demonstrated by feedback form analysis in reply to the question for wishes for future CPD in medical education.

Personal commitments were cited by five interviewees and logistical barriers were also considered. While travel to the course was not a problem for the majority, issues including parking facilities for those not based at Mater Dei Hospital or University were. The venue received positive comments through the feedback forms. Access to study leave or vacation leave for course attendance was considered a barrier by five participants.

Three faculty members stated that the course tutors could be a barrier to attendance, as they review the course based on the tutors' credentials which would form part of their decision-making process. The fact that an international medical education expert with an excellent reputation was a tutor on this course helped to mitigate this barrier. From the feedback form analysis, it was clear that the tutor input was well received; sixteen course participants praised tutors for their work. Only one participant commented, "some deliveries were a bit rushed as they assumed prior knowledge".

Regarding the programme, five faculty members said that content would be a determining factor when deciding to attend. Particularly, they would consider if it was like previous faculty development courses which they may have attended; whether the topics would be of personal interest; and that having increased clarity about the course aims as well as a programme with specific learning outcomes would encourage attendance.

Separate professional and teaching identities

The proposition from the literature and author experience was that separate professional and teaching identities are poorly developed locally and this lack of awareness could act as a barrier to attendance. Nine interviewees agreed with this.

"I think it is still a bit muddled… when we graduated, we were expected to teach your peers or teach medical students… and I don't think that was fair... because although you just graduated, you graduated as a doctor not as a teacher." (Visiting Teaching Participant 5)

The idea of separate professional and educator identities was perceived as not having a strong local foothold, though the concept seems to be gaining traction. Additionally, lack of institutional feedback was perceived by three participants as being a barrier.

"… on what basis are people basing their own self-judgement? …Does the University provide these people with formal assessment… Do they get proper feedback?" (Visiting Teaching Participant 6)

Positive and negative incentives or lack thereof

Positive and negative incentives, or their absence, could possibly influence attendance. This was observed not only from an individual's perspective, but also from the institution. The role of the

institution in rewarding good medical education practices and disincentivizing poor practice was deemed relevant in relation to BiME course attendance.

When asked about the role of positive incentives, interviewees presented contrasting views. Five expressed the idea that the lack of positive incentives may be a barrier. Positive incentives that were lacking included promotion; adequate financial remuneration for visiting teaching staff; formal teaching awards; and evidence of attainment of CPD points. However, others stated that learning from the course was a positive incentive in itself. Concern was expressed about the effectiveness of faculty development initiatives that motivated attendance using positive incentives and the difficulty of implementing these in a fair and transparent manner.

Faculty members were divided regarding the role of negative incentives. Five agreed that a lack of negative consequences for course non-attendance acted as a barrier, although concerns were raised that this may not be appropriate for adult learners or even if this would be a realistic local possibility.

"... I don't think anyone was ever stopped from lecturing… because they underperformed." (Visiting Teaching Participant 3)

The rest of the faculty members expressed the idea that negative incentives should not be adopted. They stated that these could possibly be considered in a formative manner; or even introduced gradually, making BiME course attendance mandatory for new recruits. Finally, using such negative incentives may be counterintuitive.

Since 2016 Faculty increased its work on faculty development through the creation of the MEU which was seen as a positive step forward, despite the need for more continuity between initiatives and a focused strategy. In both the feedback forms and the interviews, there is repeated reference to making the BiME course compulsory for faculty members.

"… in my opinion, had it been made compulsory, it would have been better." (Resident Academic Participant 5)

Furthermore, it was stated that the UM gives priority to research and publications when considering promotions, and less so to education and teaching excellence. This lack of recognition and structure in relation to educational governance may be a barrier to attendance.

"…a need to ensure that the people… who progress within the Faculty, are people who have a commitment to teaching… research and publications often are given a lot of weight… look at what the major focus of our University is… an institution that prepares our students to deliver their role… as doctors…" (Visiting Teaching Participant 6)

Isolation

Seven participants agreed that a sense of isolation from Faculty community could act as a barrier to attendance. A further three admitted that this could be a challenge for some, although they did not personally relate to this position. In contrast it could be one of the mitigating factors of this barrier, helping to enhance community. This was supported by comments in the feedback forms, where the opportunity for networking and meeting other staff was seen as a positive course facet.

Awareness of the Course

Five interviewees had not heard of the BiME course prior to the study participation email, and all stated that they would have attended had they been aware. A sixth participant who had attended the course was concerned that for most faculty members this lack of awareness was a significant barrier.

Funding

The BiME course is provided to participants free of charge and therefore the study proposition is that funding would not be a barrier to attendance, and most faculty members did not mention this barrier. However, two interviewees considered that this could be an issue because attendance to the course outside working hours could lead to loss of earnings from private practice.

Interprofessional education

Nine faculty members agreed that the interprofessional aspect of the BiME course was not a barrier to attendance. They emphasized that this was a positive aspect in view of networking and community-building. This was echoed by findings in the feedback forms from all sessions. On the other hand, two participants expressed reservations in this regard in view of potential differences between the outlook of pre-clinical and clinical faculty members; as well as in view of possible limited benefits of the course if delivered to very junior staff.

In summary, the barriers to attendance at the BiME course in Malta are multifactorial, with both individual and institutional barriers reported. The strongest barrier was found to be an individual's personal characteristics, particularly a lack of appreciation of the importance of faculty development. Other barriers include a lack of time; a

reduced awareness of the concept of separate professional and teaching identities; a lack of information about the course; a feeling of isolation from the faculty community; and a possible insufficiency of institutional governance and recognition.

DISCUSSION

Time, and Promoting the Educator Identity

Time is a significant barrier to BiME course attendance, as reported in the literature.[6,7,9] Importantly, more than half the staff members at the Faculty of Medicine and Surgery, UM are part of the visiting teaching group and thus, their medical education role is held in addition to a considerable commitment to clinical practice. Subsequently, time was found to be more of a barrier for visiting staff than for resident academic staff which is similar to the findings of Aziz et al[8]This is sometimes compounded by difficulty in obtaining study leave to attend faculty development programmes which concurs with Wearne et al[17] The main hospital in Malta - Mater Dei Hospital - is the teaching hospital affiliated with the Faculty of Medicine and Surgery, UM therefore discussion between the two institutions may help to streamline clinical and educational commitments for clinicians who are also faculty members.

However, an additional barrier identified is the concept of separate professional and teaching identities which may not be widely accepted in Malta. This is congruent with the findings of Brownell & Tanner.[7] Some faculty members stated that ignorance in this respect could be attributed to individual and institutional failings. By increasing local awareness of these separate identities, Faculty may encourage BiME course attendance. Furthermore, if this is supported by a structure that rewards faculty members for investing their time in CPD activities, attendance can be promoted.[7]

In the pursuit of excellence in medical education in Malta, the BiME course is the first step. This could be advanced by the development of an Intermediate Medical Education Course and an Advanced Medical Education Course, possibly progressing to formally recognized post-graduate qualifications in medical education. Liaising with other Faculties at the UM or partnering with international Universities with a proven track record in medical education faculty development, could create successful collaborations. Such faculty programme development could create a trained educator workforce, and as part of the course programme could encourage research as well as evidence-based quality improvement and educational governance initiatives with high local utility. This would create continuity and a follow up path to the BiME course, addressing the institutional hurdle identified by Nadeem & Yasmin[18] as well as the research findings.

Identifying and Motivating the Individual Educator

The most frequently mentioned barrier to attendance by faculty members was the individual's personal characteristics, particularly in relation to a lack of interest regarding the importance of faculty development in medical education, similar to Caffarella & Zinn.[5] This hurdle could be overcome if internally motivated individuals are identified, recruited, and rewarded. Others lacking these qualities could be given feedback and encouraged to improve, possibly through the creation of communities of practice of motivated medical educators.[19-21]

The lack of negative incentives was seen to act as a barrier to attendance by some interviewees. Faculty would need to consider the benefits of retaining untrained staff versus the risk of demotivating other faculty members and possibly failing to improve institutional standards and governance in medical education. This is particularly relevant because Malta has a small and limited number of medical educators, and other Universities are establishing a local presence in medical education.

Reward Structures

A lack of recognition and reward for course attendance was mentioned as a barrier, akin to the literature.[22-24] Tangible reward structures could include the establishment of awards in medical education[25,26] and the development of a formative feedback framework for faculty members including input from senior Faculty staff, peers, and students, such as collaboration with the Malta Medical Students Association (MMSA)'s Standing Committee on Medical Education (SCOME). The BiME course should remain a free resource.

Increasing BIME Course Awareness and Reducing Isolation

Providing clear and detailed information about the BiME course to faculty members would address the lack of awareness. A carefully designed and ergonomic introductory manual should be developed with messages from the Faculty's Dean and MEU's

Head, while highlighting the institution's position on the importance of faculty development. Additionally, it could launch some of the reward structures and outline the Faculty's strategy to address the institutional recognition and governance barriers. The positioning of the BiME course in relation to faculty members' progression in pursuing a medical education career within the Faculty would situate its relevance within the local context and could encourage faculty members to attend.

Details of the course tutors, with photographs and biographies, outlining their credibility in medical education as well as an outline of the BiME course programme with its aims, learning objectives and long-term outcomes clearly formulated might help, too. These would address the identified barriers regarding course tutors and the course programme, which are similar to barriers reported in the literature.[8,27-28] The inclusive nature of the course could be emphasized by including testimonials from faculty members who attended previous iterations. The BiME course manual could be hand-delivered to individual faculty members by appointing 'medical education champions', or even through the organization of a course re-launch event associated with an opportunity for community building.

The findings of this study may be used as a foundation for future research wherein a quantitative questionnaire could be distributed to all faculty members at the Faculty of Medicine and Surgery, UM. Also, in-depth research into the barriers experienced by different faculty member cohorts - namely resident academics, visiting teaching staff and casual staff - would be important as no casual staff members participated in this study. Additionally, different barriers may be experienced to different extents by the different cohorts.

To conclude, recommendations as informed by this study include increased consideration of the individual's characteristics, possibly at the faculty member recruitment stage as internal motivation seem to be key;[29] promotion of the idea of separate professional and educator identities;[7] development of reward strategies for excellence in medical education;[25-26] encourage the development of communities of practice;[19-21] re-branding and re-launching of the BiME course.

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REFERENCES

1. Harden R, Crosby J. (2000) AMEE Guide No 20: The good teacher is more than a lecturer - the twelve roles of the teacher. Medical Teacher, 22,(4) 334-347.
2. Steinert Y. (2014) Faculty development in the health professions: a focus on research and practice. Springer.
3. Phuong TT, Cole SC, Zarestky J. (2018) A systematic literature review of faculty development for teacher educators. Higher Education Research & Development, 37,(2) 373-389.
4. University of Malta. (2018) Faculty of Medicine and Surgery - Faculty Committees. https://www.um.edu.mt/ms/facultycommittees
5. Caffarella RS, Zinn LF. (1999) Professional development for faculty: A conceptual framework of barriers and supports. Innovative Higher Education, 23,(4) 241-254.
6. Swanwick T, McKimm J. (2010) Professional development of medical educators. British Journal of Hospital Medicine(2005), 71,(3) 164-168.
7. Brownell SE , Tanner KD. (2012) Barriers to faculty pedagogical change: Lack of training, time, incentives, and… tensions with professional identity? CBE—Life Sciences Education, 11,(4) 339-346.

8. Aziz Z, Jet CN, Rahman SSA. (2013) Continuing professional development: views and barriers toward participation among Malaysian pharmacists. The European Journal of Social , Behavioural Sciences, 4,(1) 713.
9. Ikenwilo D, Skåtun D. (2014) Perceived need and barriers to continuing professional development among doctors. Health Policy, 117,(2) 195-202.
10. Illing J. (2014) Thinking about research: Theoretical perspectives, ethics and scholarship. In T Swanwick (Ed.), Understanding Medical Education: Evidence, Theory and Practice (Second ed pp. 331-347). Wiley Online Library.
11. Yin RK. (2018) Case study research and applications: Design and methods. Sage publications.
12. Bassey M. (2003) Case study research. In J Swann J, Pratt (Eds.), Educational Research in Practice - Making Sense of Methodology (1st ed pp. 113--123). Continuum.
13. Stake RE. (1995) The art of case study research. Sage.
14. Attard Cortis P , Muir M. (2021) Twelve tips for using Pattern Matching in data analysis for qualitative medical education research. Medical Teacher,(2021): 1-5.
15. Rettke H, Pretto M, Spichiger E, Frei IA , Spirig R. (2018) Using reflexive thinking to establish rigor in qualitative research. Nursing Research, 67,(6) 490-497.
16. Sarniak R. (2015) 9 types of research bias and how to avoid them. https://www.quirks.com/articles/9-types-of-research-bias-and-how-to-avoid-them
17. Wearne S, Greenhill J, Berryman C, Sweet L, Tietz L. (2011) An online course in clinical education: Experiences of Australian clinicians. Australian Family Physician, 40,(12) 1000.
18. Nadeem N, Yasmin R. (2018) Faculty Development Practices in Medical Colleges of Lahore, Pakistan. Pakistan Journal of Medical , Health Sciences, 12,(1) 66-72.
19. Joy JA, Garbely JM, Shack JG, Kurien M, Lamdan RM. (2008) Supervising the supervisors: a case-based group forum for faculty development. Academic Psychiatry, 32,(6) 521-524.
20. Nora LM. (2010) The 21st century faculty member in the educational process: what should be on the horizon? Academic Medicine, 85,(9) S45-S55.
21. Mennin S, Kalishman S, Eklund MA, Friedman S, Morahan PS, Burdick W. (2013) Project-based faculty development by international health professions educators: practical strategies. Medical Teacher, 35,(2) e971-e977.
22. Steinert Y, McLeod PJ, Boillat M, Meterissian S, Elizov M, Macdonald ME. (2009) Faculty development: a "field of dreams"? Medical Education, 43,(1) 42-49.
23. Huwendiek S, Mennin S, Dern P, Ben-David MF, Van Der Vleuten C, Tönshoff B, Nikendei C. (2010) Expertise, needs and challenges of medical educators: Results of an international web survey. Medical Teacher, 32,(11) 912-918.
24. O'Sullivan E. (2010) A national study on the attitudes of Irish dental faculty members to faculty development. European Journal of Dental Education, 14,(1) 43-49.
25. Pessar LF, Levine RE, Bernstein CA, Cabaniss DS, Dickstein LJ, Graff SV, Hales DJ, Nadelson C, Robinowitz CB, Scheiber SC. (2006) Recruiting and rewarding faculty for medical student teaching. Academic Psychiatry, 30,(2) 126-129.
26. Irby DM, O'Sullivan PS. (2018) Developing and rewarding teachers as educators and scholars: remarkable progress and daunting challenges. Medical Education, 52,(1) 58-67.
27. Lindsay E, Wooltorton E, Hendry P, Williams K, Wells G. (2016) Family physicians' continuing professional development activities: current practices and potential for new options. Canadian Medical Education Journal, 7,(1) e38-46.
28. Cook DA, Price DW, Wittich CM, West CP, Blachman MJ. (2017) Factors Influencing Physicians' Selection of Continuous Professional Development Activities: A Cross-Specialty National Survey. The Journal of Continuing Education in the Health Professions, 37,(3) 154-160.
29. Steinert Y, Macdonald ME, Boillat M, Elizov M, Meterissian S, Razack S, Ouellet M, McLeod PJ. (2010) Faculty development: if you build it, they will come. Medical Education, 44,(9) 900-907.

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ORIGINAL ARTICLE

Paediatric Triage Practice and Emergency Severity Index in the Maltese Islands

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Background

In the paediatric emergency department (PED) triage is a keystone service designed specifically for the recognition of severely ill patients. In this study, the local paediatric triage practice was assessed.

Methods

Data was collected retrospectively for children under 16 years of age presenting to the PED during the first seven days of August 2018, September 2018, January 2019 and February 2019. A triage priority category was assigned according to the Emergency Severity Index (ESI) algorithm (version 4) and compared to that assigned by the triage nurse.

Results

The kappa coefficient for inter-rater reliability (triage nurse vs investigator) was 0.360 (95% CI 0.329, 0.390). Weighted kappa was calculated to be 0.424 (95% CI 0.395, 0.454). Concordance between nurse triage and investigator triage was present for 51.32% of cases, whilst Chi-squared test showed significant differences between raters for the categories ESI-2, ESI-3, and ESI-5.

Conclusion

This study has highlighted some concerns with our local paediatric triage practices, with fair to moderate agreement for inter-rater reliability, and the possibility of significant over-triage. The main recommendation is that paediatric triage is carried out by healthcare professionals who are experienced in dealing with sick children.

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A reliable paediatric triage system classifies patients into different categories of varying urgency, identifying patients who need immediate care and those who can wait.[1]It is necessary when demand exceeds supply of the limited resources available; be it time, physical space, staff numbers or training.[2,3] Correctly classifying high priority patients avoids a delay in diagnosis and management of seriously ill children, whilst correctly identifying low urgency cases avoids prolonged waiting times for high urgency cases and improves the efficiency and flow of an emergency department (ED).

The local Paediatric Emergency Department (PED) is a relatively recently established department, having opened in 2015, and thus, the setting up of services is still ongoing, including proficiency in paediatric triage. The aim of this study was to assess local paediatric triage practice.

MATERIALS AND METHODS

Study Setting

In Malta, there is one general hospital with an ED, that provides care for a population of around 0.5 million. Around 22,000 paediatric patients attend the ED every year. At the time of the study (2018-2019), adult and paediatric patients were triaged by a common cohort of nurses who usually work with adults. Paediatric patients (patients under 16 years of age) were then seen in a separate section of the ED, staffed by a separate cohort of nurses working only with children, and a combination of emergency and paediatric physicians. The PED section at the time housed six cubicles which were for use by paediatric patients only, and was staffed at any one time by two to four nurses and one to two doctors. The triage system used for both adults and children is that of Emergency Severity Index (ESI) (version 4).

Definition of ESI

ESI is a triage system that is based on acuity and resource needs.[4] A patient classified as an ESI-1 is a patient that is dying or at immediate risk of dying and thus needs immediate resuscitative care. An ESI-2 is a patient that should not wait, thus a patient in a high risk situation, who is in severe pain or distress, or confused, lethargic, or disoriented. ESI-3, ESI-4, and ESI-5 patients are respectively less urgent patients, that are classified according to the number of resources that might be required to reach a disposition decision.[4]

Objectives

The primary objective was to determine inter-rater reliability, that is, whether different healthcare providers (namely triage nurses and investigators) agree on their classification of case urgency.[4] The secondary objective was to then describe ways in which triage classification varied between the healthcare providers.

Inclusion and Exclusion Criteria

The population targeted was children under 16 years of age presenting to the PED during the first seven days of the months of August 2018, September 2018, January 2019, and February 2019. These months were chosen in order to obtain representative data for both summer and winter months. ENT, gynaecology and ophthalmic cases were excluded as these cases are managed by separate departments.

Data Collection And Study Design

Permissions to carry out the study and to access online electronic triage records were obtained from the hospital Data Protection Office and ED management. Ethics approval was obtained from the Faculty Research Ethics Committee of the University of Malta.

Prior to conducting the study, the investigators (three paediatric physicians) underwent training in ESI system triaging using the ESI Implementation Handbook 2012 Edition, online training tools available through the Agency for Healthcare Research and Quality,[4] as well as discussion and practice at triaging with senior nurses officially trained in ESI triage.

Data was retrospectively collected from triage sheets obtained via the hospital electronic patient system which were immediately anonymised. Using the information available on the triage sheets (age, the presenting complaint statement, and any documented parameters), the investigators then assigned an ESI according to the algorithm outlined in the ESI handbook (Figure 1).

Statistical Analysis

Data was interpreted using data analysis functions in Microsoft Excel. The kappa coefficient (calculated using QuickCalcs GraphPad software) was used to assess inter-rater reliability. Chi-squared test was used to assess for any significant differences in the number of cases in each ESI category between when

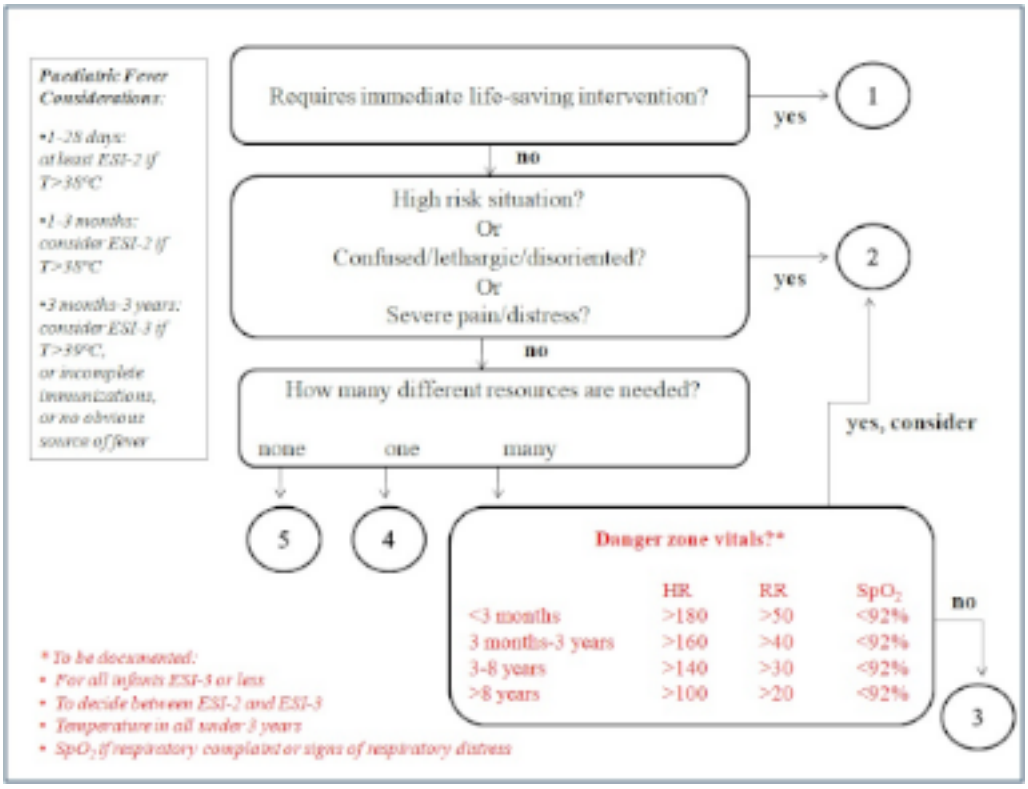

Figure 1 ESI Triage Algorithm, version 4 (adapted from ESI implementation handbook).4 (T: Temperature, HR: Heart rate, RR: Respiratory rate, SpO2: oxygen saturation)

triage was performed by nurses and when the investigators assigned an ESI category.

RESULTS

A total of 1582 cases were reviewed over the time period described, with a slight male predominance (53.22% males, 46.78% females). The mean age was 4.63 years (95% CI 4.42, 4.84), median 2.87 years. The mean door-to-triage time was 21.16 minutes (95% CI 20.35, 21.97), with a median of 17 minutes and a range of 0 to 110 minutes. The three most common presenting complaints were fever (27.24%), trauma (10.37%), and vomiting (10.30%). 19.41% of patients were admitted and 78.38% were discharged, with the rest either failing to attend when called for physician review or discharged against medical advice.

Figure 2 shows the distribution of ESI assigned to the cases reviewed by nurses, as well as the ESI given by the investigators after cases were assessed as per ESI guidelines and algorithm. It was not possible for the investigators to assign an ESI in 25 cases (1.58%) due to there being insufficient documented information available on the triage sheet.

The kappa coefficient for inter-rater reliability (triage nurse vs investigators) was 0.360 (fair agreement) (95% CI 0.329, 0.390). Linear weighted kappa was calculated to be 0.424 (moderate agreement) (95% CI 0.395, 0.454).

Investigators agreed with the ESI category assigned by the nurse at time of triage in 51.32% of cases. Table 1 compares the different ESI categories assigned by nurses when reviewing the patients and those assigned by the investigators when reviewing triage sheets during the study. In the nurses' triage, for ESI-2 and ESI-3 there was a significantly higher number of cases ($p < 0.001$), whilst for ESI-5 there was a significantly smaller number ($p < 0.001$).

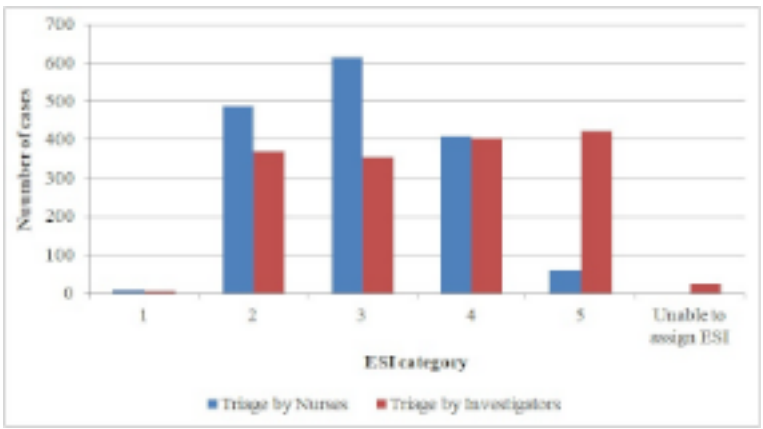

Figure 2 Distribution of ESI categories assigned to the cases by nurses and investigators

Table 1 Comparing proportion of cases in each ESI category for when triage was performed by nurses and when triage was performed by investigators

ESI Category	Number of cases when triaged by nurses	Number of cases when triaged by investigators	Observed Chi-squared	p value
1	8	5	0.695	0.404
2	487	370	21.907	*< 0.001*
3	616	355	101.218	*< 0.001*
4	409	405	0.026	0.871
5	62	422	316.127	*< 0.001*

DISCUSSION

Inter-Rater Reliability

In this study the weighted kappa score was 0.424 (95% CI 0.395, 0.454), indicating moderate agreement. Previous studies have however found good inter-rater reliability for the ESI triage algorithm.[5,6,7,8] The findings in this study could be explained by the fact that analysis was retrospective. In the study by Baumann, although excellent inter-rater reliability was concluded, it was noted that when triage categories were assigned retrospectively, inter-rater agreement was poor to good.[6]

Furthermore, the ESI assigned by the investigators was solely based on the description given in the triage statement and parameters recorded by the nurse during the triage process, without having the opportunity to physically assess the child, which is a more realistic representation and which ultimately also affects triage decisions. Such retrospective assessment lacks cues which are available when the patient is present in front of the healthcare professional,[3] as well as the stressful environment of an ED in which triage takes place.[9]

On the other hand, this mirrors the situation at the receiving end of the process, when nurses and doctors inside the PED receive the triage sheet and rely on the ESI assigned and description given at triage in order to prioritise cases especially during busy periods, whilst the patient waits in a separate waiting area. This further emphasizes the importance of communicating and conveying an accurate description of the child's general condition, including parameters as applicable, in order to minimise the chances of a possibly critically ill child not being seen within a safe time frame.

Triage Accuracy

As described in the ESI handbook, a frequently selected threshold for accuracy of triage categorisation is 90%.[4] In this study however, there was concordance in ESI categories between nurses and investigators for only 51.32% of cases. Determining which was the more accurate between the nurses' triage and the investigators' triage is equivocal. Due to the retrospective nature of the study and the lack of clinical cues, it can arguably be said that the nurses' triage performed at the time of reviewing the patient was more reflective of patient condition. However, a counter argument could be that since the investigators strictly followed the ESI algorithm, their assigned ESI category was more true to the ESI triage system described in the handbook. For the purpose of this study, the latter was taken to be the standard to compare to. As a result, this study highlights significant mis-triage of 48.68%, with the majority being over-triaged, thus implying that a significant number of cases would have required less urgent attention. Although this may be seen to be due to the triaging team attempting to err on the side of caution, one also has to consider that such over categorisation ends up putting an extra strain on the PED staff especially during busy periods, making it difficult to keep up with such a number of high priority cases at the same time. As a result, over-triaging leads to truly high priority cases ending up being attended to with delay and this might have devastating consequences for the child in question. Thus, both over-triage and under-triage require further investigation, as they can both affect patient care.[10,11,12]

A possible explanation for such results might be that the local triage team consists of nurses mainly trained in adult care and triage, with minimal exposure to paediatrics. One has to appreciate that the needs of children in an ED differ from those of adults. Children respond differently to physiological and psychological stressors, they are more susceptible to a range of conditions such as viral infections and dehydration, and they have a limited ability to communicate their needs.[4,5,13] The paediatric population also varies in itself according to

the specific child's age and development.[1] Additionally, in a mixed adult and paediatric ED, there is a tendency to compare acuity of paediatric patients to that of adults.[6] Thus, this makes it harder to quickly and accurately assess a sick child when compared to an adult,[14] especially if one has only received basic paediatric training or has limited experience working with children. Furthermore, not working within the PED might mean that one is not aware of certain departmental specific practices or policies, and thus not being able to predict the number of resources required.[1] It has been shown that paediatric nurses perform more accurate and consistent paediatric triage when compared to general ED nurses, since they have more experience with children.[15,16]To confirm this hypothesis in the local setting, further studies assessing triage specifically performed by paediatric nurses (vs other ED nurses) would need to be conducted.

Specific ESI Measures

A study by Mirhaghi et al, showed that the ESI triage system has a tendency to allocate patients to ESI-2 and in Travers et al, it was found that ESI-5 is under-utilized for paediatric patients.[15,17] The ranges of normal values for parameters suggested by the ESI guidelines are not evidence-based,[15] and certain other modifications to the current ESI system in use might be necessary to account for the differences in the paediatric population described above. Moreover, there are varying local patterns of care which are followed for certain cases in the PED. What constitutes an ESI resource may vary between different centres, and ESI resources may need to be defined differently when caring for children, since a simple procedure in an adult may require more training, time, and staff when performed on a child.[15] It is however important to point out that resources in the context of ESI are not a nursing workload measure, but they are used as a proxy for acuity.[4]

SUMMARY BOX

What is already known about this subject:

- There are several paediatric-specific considerations when it comes to triage.
- The Emergency Severity Index can have limitations with respects to paediatric triage.
- Under- and over-triaging can provide challenges to appropriate emergency service.
- Experience in dealing with children is essential for good quality paediatric triage.
- What are the new findings:
- Fair to moderate agreement for inter-rater reliability was found in our local paediatric triage practice.
- The possibility of significant over-triage in the local setting is brought forward.
- The main recommendation is that paediatric triage is carried out by healthcare professionals who are experienced in dealing with sick children.

RECOMMENDATIONS

Thus, based on the above findings it is our recommendation that paediatric triage is performed by paediatric nurses working regularly with children. Since the onset of the COVID-19 pandemic, pressures on adult ED services have required nurses who work in the PED regularly to take over paediatric triage. A separate study is required to reassess local paediatric triage practices under these conditions. There have been other changes to the PED brought about by the COVID-19 pandemic: relocation of the PED and triage areas, changes in PED attendance rates and patient flow, and new infection control measures. These would be important confounding factors that would need to be considered should this separate study be performed.

Should these COVID-19 pandemic related changes be reversed, our recommendation would be to offer paediatric training and adequate exposure to general ED nurses.[3,5,18] For example, visual aids with normal ranges of parameters according to age could be used. This could be supplemented by having the ESI electronic system alerting the user when parameters are in the danger zone. Computerized software-led triage systems are also available.[3,19] ED nurses could also have a job shadowing period in the PED. Continuous education, such as through regular refresher training courses and competency evaluation for triage nurses, is also recommended.[3,20] Such sessions could also be an opportunity to divulge usual practices at the PED and train triage nurses in recognising rashes (blanching versus non-blanching) and clinical signs to spot the unwell child (signs of respiratory distress, etc.), which they may otherwise not be accustomed to since they usually work with adult patients.

LIMITATIONS

This data was collected from one hospital, making it a single centre study. Although being the sole hospital providing paediatric emergency services in the country ensures a comprehensive and diverse case mix, it may not reflect the care and services in other hospitals or countries and thus generalisations with these results cannot be made. As already highlighted earlier, a significant limitation of this study is its retrospective nature. Thus one also has to consider the unequal settings when the ESI category was assigned by the triage nurse in a real-life stressful scenario versus that assigned by the investigators in a relatively calmer environment with no actual patient present. Furthermore, although the investigators went through ESI triage training, they lacked the experience offered when working daily in the triage room. Incomplete documentation on triage sheets was another limitation in this study.

CONCLUSION

This study has highlighted some concerns with our local paediatric triage practices, with fair to moderate agreement for inter-rater reliability, and the possibility of significant over-triage. The main recommendation is that paediatric triage is carried out by healthcare professionals who are experienced in dealing with sick children. Thus, the key action is to improve the knowledge, skills, and confidence in paediatric triage. This can be achieved by continuous education, encouraging specialisation, and promoting interdisciplinary collaboration.[5,15]

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REFERENCES

1. Wang L, Zhou H, Zhu JF. Application of emergency severity index in pediatric emergency department. World J Emerg Med 2011;2:(4)279-282.
2. Robertson-Steel I. Evolution of triage systems. Emerg Med J 2006;23:(2)154-155.
3. FitzGerald G, Jelinek GA, Scott D, Gerdtz MF. Emergency department triage revisited. Emerg Med J 2010;27:(2)86-92.
4. Gilboy N, Tanabe T, Travers D, Rosenau AM. Emergency Severity Index (ESI): A Triage Tool for Emergency Department Care, Version 4. Implementation Handbook 2012 Edition. AHRQ Publication No. 12-0014. Rockville, MD. Agency for Healthcare Research and Quality. November 2011.
5. Jafari-Rouhi AH, Sardashti S, Taghizadieh A, Soleimanpour H, Barzegar M. The Emergency Severity Index, version 4, for pediatric triage: A reliability study in Tabriz Children's Hospital, Tabriz, Iran. Int J Emerg Med 2013;6:(1)36.
6. Baumann MR, Strout TD. Evaluation of the Emergency Severity Index (version 3) triage algorithm in pediatric patients. Acad Emerg Med 2005;12:(3)219-224. PMID: 15741584
7. Durani Y, Brecher D, Walmsley D, Attia M, Loiselle J. The Emergency Severity Index Version 4: reliability in pediatric patients. Pediatr Emerg Care 2009;25:(11)751-753.
8. Green NA, Durani Y, Brecher D, Depiero A, Loiselle J, Attia M. Emergency Severity Index version 4: a valid and reliable tool in pediatric emergency department triage. Pediatr Emerg Care 2012;28:(8)753-757.
9. Magalhães-Barbosa MC, Robaina JR, Prata-Barbosa A, de Souza Lopes C. Reliability of triage systems for paediatric emergency care: a systematic review. Emerg Med J 2019;36:(4)231–238.
10. Raynaud L, Borne M, Coste S, Daban JL, Tourtier JP. Triage protocol: both undertriage and overtriage need to be evaluated. J Trauma 2010;69:(4)998.
11. Hupert N, Hollingsworth E, Xiong W. Is overtriage associated with increased mortality? Insights from a simulation model of mass casualty trauma care. Disaster Med Public Health Prep 2007;1(1 Suppl):S14-S24.

12. Armstrong JH, Hammond J, Hirshberg A, Frykberg ER. Is Overtriage Associated With Increased Mortality? The Evidence Says "Yes." Disaster Med Public Health Prep 2008;2:(1)4-5.
13. Thomas DO. Special considerations for pediatric triage in the emergency department. Nurs Clin North Am 2002;37:(1)145-viii. doi:10.1016/s0029-64650[03]0090-2
14. Thompson T, Stanford K, Dick R, Graham J. Triage assessment in pediatric emergency departments: a national survey. Pediatr Emerg Care 2010;26:(8)544-548.
15. Travers DA, Waller AE, Katznelson J, Agans R. Reliability and validity of the emergency severity index for pediatric triage. Acad Emerg Med 2009;16:(9)843-849.
16. Durojaiye L, O'Meara M. A study of triage of paediatric patients in Australia. Emerg Med (Fremantle) 2002;14:(1)67-76.
17. Mirhaghi A, Heydari A, Mazlom R, Hasanzadeh F. Reliability of the Emergency Severity Index: Meta-analysis. Sultan Qaboos Univ Med J 2015;15:(1)e71-e77.
18. Chung JY. An exploration of accident and emergency nurse experiences of triage decision making in Hong Kong. Accid Emerg Nurs 2005;13:(4)206-213.
19. Sadeghi S, Barzi A, Sadeghi N, King B. A Bayesian model for triage decision support. Int J Med Inform 2006;75:(5)403-411.
20. Da Silva JA, Santos EA, Ribeiro LE, Barbosa Teixeira Lopes MC, Pinto Okuno MF, Assayag Batista RE. Emergency Severity Index: accuracy in risk classification. Einstein 2017;15:(4)421-427.

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CASE REPORT

Heterotrophic gastric mucosa presenting as indolent lower abdominal pain and masking as ectopic pancreas

the role of digital rectal examination in the management of undifferentiated lower abdominal pain

Jacqueline Eleonora Ek, Marius Caruana

A case of inflamed ileal Heterotropic Gastric Mucosa, presenting in a non-English speaking migrant of African descent, soon after his recovery from COVID-19, with early predominant signs apparent only on digital rectal examination (DRE); masking as ectopic pancreatic tissue on computed tomography images and the nature of which was only confirmed histopathologically. We put forward an argument for non-dismissal of the role DRE can have in the management of undifferentiated lower abdominal pain while revising the nature of ectopic pancreas and why this case was in fact not such.

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This case report of inflamed ileal heterotropic gastric mucosa presenting as indolent lower abdominal pain elicited mainly on digital rectal examination showcases a tie between Covid-19 Community Migrant Care and emergency medicine roping in expert opinions from radiology, surgery and histopathology. The non-dismissal of clinical signs led to one particular patient receiving a rare diagnosis accompanied by a timely laparotomy with a good post operative recovery.

CLINICAL CASE

A migrant who had just recovered from COVID-19 in an appropriate isolation facility started to report abdominal pain and distention. His condition continued to progress complaining of lack of appetite and tenesmus, with localised tenderness developing in the suprapubic area. A digital rectal examination (DRE) was performed with the patient reporting severe pain on palpation of the anterior rectal wall, more severe than any of the abdominal surface

findings. For this reason, the patient was transferred for further investigations at the Emergency Department (ED).

Initial assessment confirmed the findings as per referral with the tenderness elicited by the DRE being noted. The patient was given pain relief with intravenous (IV) paracetamol, kept nil by mouth and started on IV fluids. Plain radiographs of his chest and abdomen were normal. Further radiology of the lumbosacral region showed no fractures, no degenerative changes and no sacroilitis. Blood tests were also grossly normal. Lactate was 1.7, serum amylase 81 U/L and C-reactive protein (CRP) 7 mg/L.

Further evaluation with computed tomography (CT) of the abdomen and pelvis showed a heterogeneous pancreatic head with small foci of necrosis and mild narrowing of the portal vein. It also showed a mass in the pelvis with a large cystic component; located in the lower mesentery, close to the distal third of the ileum. Composed of a solid part measuring 54 x 30 x 45mm resembling pancreatic tissue with enhancing walls, free fluid and stranding around it a cystic component measuring 42 x 30mm. All other intra-abdominal organs were reported normal with no pathology. The radiological report described ectopic pancreatic tissue in the pelvis with signs of inflammation (pancreatitis) and pseudocyst. A differential diagnosis was of an ectopic pancreas in Meckel's diverticulum with pancreatitis.

A surgical review was done and based on radiological findings, the patient was admitted with a diagnosis of pelvic ectopic pancreatic tissue and signs of pancreatitis, with the site potentially being Meckel's diverticulum. He was consented for a diagnostic laparoscopy which was converted to a mini-laparotomy for small bowel diverticulum resection. Recovery was uneventful and he was discharged after seven days.

Histopathological findings showed a diverticulum measuring 75mm x 70mm x 5mm. On sectioning there was a cystic area adjacent to the diverticulum measuring 55mm in maximum diameter and containing cloudy white fluid. Adjacent to this was a fatty area which was indurated and with a necrotic core. Microscopic sections showed small bowel with inflamed, focally eroded, ulcerated, and in places flattened mucosa. A dense mixed inflammatory infiltrate and reactive fibroblastic proliferation were noted in the surrounding mesenteric adipose tissue. The epithelium of the diverticulum was partly replaced by foveolar-type epithelium and there were occasional mucinous glands and small tubular glands (possibly oxyntic-type glands) in the surrounding stroma. There was no evidence of dysplasia or malignancy. The findings were in keeping with inflamed diverticulum with ectopic gastric mucosa.

DISCUSSION

Recent growing body of evidence points towards a limited role of DRE in the diagnosis of acute, undifferentiated abdominal pain.[1] Studies in appendicitis have shown it as being only 49% sensitive and 61% specific in diagnostic accuracy.[2] In this case, the DRE provided significantly earlier findings indicative of need for further investigations. Palpation of the anterior wall of the anal canal resulted in extreme abdominal pain which was not reciprocated in surface findings. Dismissing DRE as a useful examination in this case would have led to later referral, requiring the build-up of enough intra-abdominal inflammation to give surface signs, potentially complicating intervention. It leads us to question whether DRE should be reconsidered as an early pointer to developing pelvic pathology, allowing for earlier investigation and intervention, especially in clinical settings where physical examination is the main stay of decision making.

Ectopic pancreas was described as early as 1727 by Jean Schults, as a gland-like tissue at the base of the ileal diverticulum.[3] It was confirmed histologically as pancreatic by Klob in 1859.[4] An ectopic pancreas is defined as pancreatic tissues lacking vascular or anatomic communication with the normal body of the pancreas, possessing histological features of pancreatic acinar formation, duct development, and islets of Langerhans, with its own independent blood supply and ductal system. It can be classified using the Heinrich Classification. It is commonly found in the stomach, duodenum and ileum and less so in the ileus, Meckel's, appendix, mesentery, oesophagus, liver, gallbladder, bile duct, spleen, umbilical cord, retroperitoneal cavity, fallopian tubes, lungs and mediastinum.[3] It is a relatively uncommon congenital abnormality with a range of incidence of 0.55% - 13.7%.[4]

Meckel's diverticulum of its own accord is the commonest congenital anomaly of the gastrointestinal tract[], found at 45 to 90 cm proximal to the ileocaecal valve and is mostly asymptomatic. Ectopic pancreas in Meckel's has only been reported in 2.8-7.5% of cases3. In a study of 10 of these cases, 80% presented with symptomatic abdominal and gastrointestinal bleeding or melena.[3] Differentials for CT findings indicative of an

ectopic pancreas include leiomyomas and gastrointestinal stromal tumors (GIST).[5]

This particular case presented with no signs of GI bleeding. Moreover the location of the mass on laparotomy was recorded at 230cm from the ileocaecal valve, well outside Meckel's range. Histological findings reported an inflamed diverticulum with ectopic gastric mucosa with "oxynitic-type glands", changing completely the diagnosis from a radiological suggestion of ectopic pancreatic tissue to histological Heterotropic gastric mucosa.[6,7]

CONCLUSION

We put forward a recommendation that DRE should be considered as an early pointer to diagnosing pelvic pathology and should aid decision-making regarding the need for further in-hospital investigations.

REFERENCES

1. Kessler C, Bauer SJ. Utility of the digital rectal examination in the emergency department: a review. J. Emerg. Med. 2012;43:(6)1196–1204.
2. Bhavsar AK, Gelner EJ, Shorma T. Common Questions About the Evaluation of Acute Pelvic Pain. Am Fam Physician. 2016;93:(1)41-48.
3. Xiang S, Zhang F, Xu G. Ectopic pancreas in the ileum. Medicine 2019;98:44.
4. Giordane A, Alemanno G, Bergamini C, Prosperi P, Bruscine A, Valeri A. The role of laparoscopy in the management of a diagnostic dilemma: Jejula ectopic Pancreas Developing into Jejunojejunal Intussuseption. Case Rep Surg. 2017;2017:8452947.
5. Mulholland KC, Wallace WD, Epanomeritakis E, Hall SR. Pseudocyst formation in gastric ectopic pancreas. JOP. 2004;5:(6)498-501.
6. Kopácová M, Vykouril L, Vacek Z, et al Inverted Meckel's diverticulum with ectopic pancreatic tissue as a source of severe gastrointestinal bleeding. J Gastrointest Surg. 2010;14:(3)578-581.
7. Kim JY, Lee JM, Kim KW, et al Ectopic pancreas: CT findings with emphasis on differentiation from small gastrointestinal stromal tumour and leiomyoma. Radiology. 2009;252:(1)92-100.

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CASE REPORT

A rare cause of failure to thrive in infancy

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Primary intestinal lymphangectasia (PIL), also known as Waldmann's disease, is a rare disorder characterized by an exudative enteropathy resulting from morphologic abnormalities of the intestinal lymphatics.

Moderate to severe oedema with pleural effusion, pericarditis, or chylous ascites is the main clinical manifestation but lymphoedema, abdominal pain, weight loss, moderate diarrhoea, vomiting, and fat-soluble vitamin deficiencies may also be present. Patients can also develop hypocalcaemia secondary to failure to absorb fat and fat-soluble vitamins.

We report a nine-month-old male infant with a four-week history of diarrhoea, vomiting, failure to thrive, peripheral oedema and tetany. Hypoalbuminaemia, hypocalcaemia, low vitamin D levels and lymphopaenia were found on initial investigations. A raised stool alpha-1-antitrypsin supported a diagnosis of a protein losing enteropathy. At gastroscopy typical 'cotton ball or frosted appearance' was visible particularly in the second (D2) and third part (D3) of the duodenum. Biopsies from D3 revealed dilated lymphatics suggestive of primary intestinal lymphangectasia. The infant was managed with a high protein, high MCT, low fat diet with improvement in his symptoms and growth pattern.

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Primary intestinal lymphangectasia (PIL) is a rare protein-losing gastroenteropathy caused by congenital malformation or obstruction of the intestinal lymphatic drainage.[1] The condition was first described by Waldmann in 1961. Factors causing elevated pressure of lymph drainage in the intestinal wall can lead to dilatation and even rupture of the lymphatic vessels which, in turn, result in the leakage of lymphatic fluid.[2,3] Leakage of lymph will result in hypoproteinaemia, lymphocytopenia and decreased serum levels of immunoglobulin.[4] The condition usually presents in the first two years of life. Up to 2013 less than 200 cases had been reported in children world-wide.[4]

CASE REPORT

9-month-old, male infant (non-consanguineous parents) presented to the paediatric emergency department with a three-week history of vomiting and a four-week history of diarrhoea. On admission he was found to be poorly perfused and dehydrated. Parents had reported poor urine output. Blood pressure was maintained but in view of the severe dehydration and marked hyponatraemia at presentation he was transferred to the paediatric intensive care unit for further management.

On examination the infant had periorbital oedema and lower limb pitting oedema. His abdomen was distended but there were no clinical signs of ascites. An initial ultrasound of the abdomen confirmed the absence of ascites but showed multiple, fluid filled, small intestinal loops with mural thickening due to oedema. Chest imaging did not reveal any evidence of pleural effusions. Urine analysis was negative for protein, serum albumin was 16 g/l (normal value, 32-52 g/l) with a low total protein of 29 g/l (66-87 g/l). Full blood count showed a normal haemoglobin, mild reactive thrombocytosis and significant lymphopaenia with a lymphocyte count of between 0.7 and 0.7 $x10^9$/l (1.16-3.33 $x10^9$/l). Initial elevation of INR was noted and this normalized following administration of vitamin K. Episodes of intermittent carpopedal spasm were attributed to a low calcium and vitamin D deficiency, and these stopped following replacement therapy.

Following rehydration and repeated albumin infusions the condition of the infant improved. A stool alpha-1-antitrypsin level was elevated at more than 2.25 (normal values <0.3mg/g). With the clinical presentation suggestive of a protein losing enteropathy, documented severe hypoproteinaemia and persistent lymphopaenia, a diagnosis of PIL was considered. Once the patient's condition improved, treatment with medium chain triglyceride (MCT) based Milk, MCT oil and a fat free diet were started. Once the patient's stabilised, an upper gastrointestinal endoscopy was performed. During endoscopy, the oesophagus and stomach appeared normal. There were typical 'cotton wool exudative lesions' or 'frost like' lesions on the duodenal mucosa, more prominent in the second (D2) and third (D3) part of the duodenum (Figure 1). Histological examination showed no abnormalities in the oesophagus, stomach and D1 and D2 Biopsies from D3 which showed dilated lymphatic vessels (Figure 2) were also highlighted on D2-40 immunohistochemistry. These changes were consistent with a diagnosis of PIL. The infant was subsequently discharged on an MCT based milk ('Monogen Nutricia'), fat free diet and vitamin and mineral supplementation. Regular review up to three

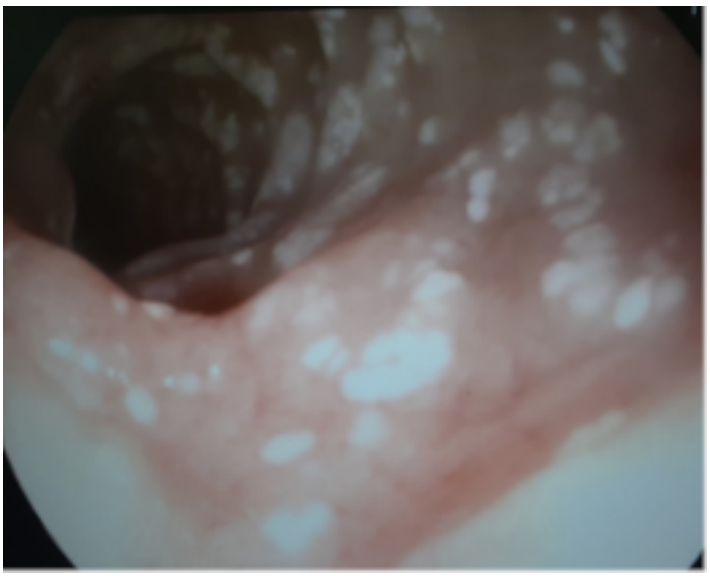

Figure 1 'cotton wool exudative lesions' visible in the duodenum

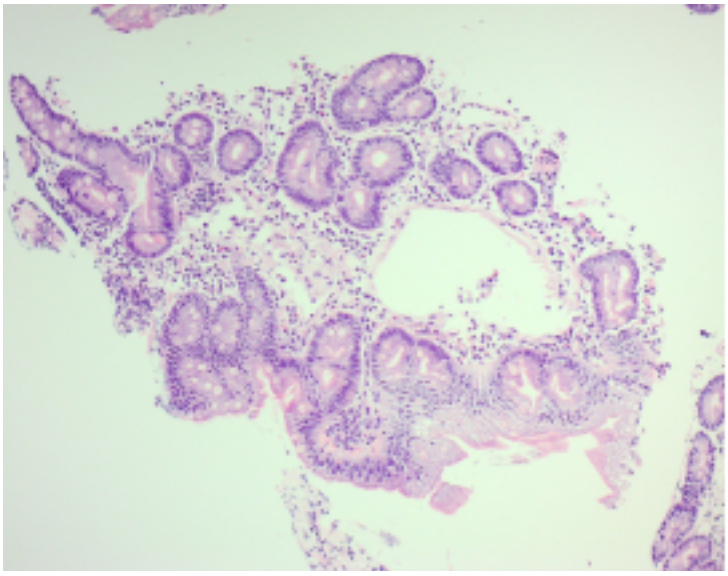

Figure 2 Haematoxylin and Eosin stain of the duodenal biopsy showing a markedly dilated lymphatic within the mucosa. Magnification x100

months post presentation showed a marked improvement in dry weight gain, improvement in abdominal distension, cessation of vomiting and diarrhoea, resolution of tetany and marked improvement in biochemical analysis.

DISCUSSION

PIL is a rare disease characterized by protein-losing enteropathy (PLE).[1] Clinical symptoms are induced by the excessive loss of lymphatic contents including protein, fat, and lymphocytes, resulting in hypoproteinaemia and oedema..[1,5] It is generally diagnosed before the age of three years, and affects boys and girls in equal proportions. The prevalence of the disease is unknown. Patients with PIL often present with oedema, lymphoedema, diarrhoea, ascites that may be complicated by fatigue, abdominal pain, nausea, vomiting, weight loss, inability to gain weight, iron deficiency anaemia and obstructive ileus. Other major features are lymphopenia, hypoalbuminemia, and hypogammaglobulinemia due to lymph leakage from the ruptured lymph vessels.[1,5]

The diagnosis should be considered when young children present with a PLE. An elevated alpha-1-antitrypsin level is highly suggestive of a PLE, and this should warrant further investigation. Secondary intestinal lymphangiectasia can be caused by cardiac causes such as constrictive pericarditis, haematological causes such as lymphoma and other rare causes would include Budd Chiari syndrome, sarcoidosis and scleroderma.[6] Histological confirmation is required but recurrent endoscopies are frequently required to establish a diagnosis. The typical 'snow frost or cotton ball' exudates are not always evident, and biopsies are more likely to show the typical lymphatic dilatation from more distal parts of the small intestine. These are not easily accessible on traditional upper oesophagogastroscopy and may require double balloon interventions.[4,7] Capsule endoscopy provides complete examination of small bowel mucosa thus can evaluate the extent of lymphangiectasia. However, the disadvantage of capsular endoscopy is the inability to obtain biopsies.

Management in the acute stage of presentation may require repeated albumin infusions, management of vitamin D and calcium deficiency resulting in tetany and nutritional support. Immunoglobulin deficiency or concurrent infection due to hypo-gammaglobulinemia may need to be addressed in the acute setting. A high protein, fat free diet and MCT based formula together with vitamin supplementation are required in long term. On occasions, a period of total parenteral nutrition might be required if enteral feeding results in worsening of symptoms. The presence of chylous ascites suggests a more severe form of the disease and is of importance in deciding the management steps in this condition.[8] In refractory cases, the management is guided by the extent of the intestinal lymphangiectasia (IL). MRI lymphangiogram can be used to distinguish between segmental IL or more extensive disease. In the case of segmental IL surgical resection of the area.[9] might be considered in children not improving on the conventional diet. In more extensive disease pharmacological treatment that has been tried with anecdotal evidence of success includes propranolol treatment in infants and use of interleukin inhibitors (tacrolimus or sirolimus) in older children.[10,11] Other therapeutic options described in the literature include octreotide and tranexamic acid but data on these treatments are limited.[8]

CONCLUSION

IL should be suspected when there is a clinical picture of chronic diarrhoea and protein-losing enteropathy accompanied with oedema at any level, as well as hypoalbuminemia, hypocalcaemia, lymphopenia, hypogammaglobulinemia, and hypercholesterolemia. All children presenting with IL should undergo an upper gastrointestinal series with bowel transit time and endoscopy with biopsies taken at the level of the duodenum. Treatment includes diet and the periodic administration of albumin and gamma globulin.

REFERENCES

1. Vignes S, Bellanger J. Primary intestinal lymphangiectasia (Waldmann's disease). Orphanet Journal of Rare Diseases. 2008;3:(1)5.
2. Lee J, Kong M-S. Primary intestinal lymphangiectasia diagnosed by endoscopy following the intake of a high-fat meal. European Journal of Pediatrics. 2008;167:(2)237-239.

3. Liu NF, Lu Q Fau - Wang CG, Wang Cg Fau - Zhou JG, Zhou JG. Magnetic resonance imaging as a new method to diagnose protein losing enteropathy. Lymphology. 2008;41:(3)111-115.
4. Wen J, Tang Q, Wu J, Wang Y, Cai W. Primary Intestinal Lymphangiectasia: Four Case Reports and a Review of the Literature. Digestive Diseases and Sciences. 2010;55:(12)3466-3472.
5. Hauser B, Moreels T, Urbain D, et al Intestinal Lymphangiectasia. Journal of Pediatric Gastroenterology and Nutrition. 2009;48<(2)/li>
6. Lai Y, Yu T, Qiao X-y, Zhao L-n, Chen Q-k. Primary intestinal lymphangiectasia diagnosed by double-balloon enteroscopy and treated by medium-chain triglycerides: a case report. Journal of Medical Case Reports. 2013;7:(1)19.
7. Braamskamp MJAM, Dolman KM, Tabbers MM. Clinical practice. European Journal of Pediatrics. 2010;169:(10)1179-1185.
8. Prasad D, Srivastava A, Tambe A, Yachha SK, Sarma MS, Poddar U. Clinical Profile, Response to Therapy, and Outcome of Children with Primary Intestinal Lymphangiectasia. Digestive Diseases. 2019;37:(6)458-466.
9. Kneist W, Drescher DG, Hansen T, Kreitner KF, Lang H. Die operative Therapie einer segmentalen, primären intestinalen Lymphangiektasie des Jejunums mit ausgeprägtem Chylaskos. Surgical Therapy of Segmental Jejunal, Primary Intestinal Lymphangiectasia. Z Gastroenterol. 2013;51:(06)576-579.
10. Kwon Y, Kim MJ. The Update of Treatment for Primary Intestinal Lymphangiectasia. Pediatr Gastroenterol Hepatol Nutr. 2021;24:(5)413-422.
11. Kwon Y, Kim ES, Choe YH, Kim MJ. Individual approach for treatment of primary intestinal lymphangiectasia in children: single-center experience and review of the literature. BMC Pediatrics. 2021;21:(1)21.

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CASE REPORT

An Unusual case of adult-onset Acute Disseminated Encephalomyelitis

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A 57 year old gentleman presented to our emergency department with a ten day history of progressive loss of balance, left-sided weakness and gait disturbance. CT brain showed bilateral subcortical hypodensities in the parietal lobes with right sided cortical involvement. Subsequent MRI of the neuro-axis showed symmetrical high FLAIR signal in the parietal lobes bilaterally, suggestive of Acute Disseminated EncephaloMyelitis (ADEM), while excluding cord lesions. CSF and serum analysis excluded alternative diagnoses. He was treated with high dose IV methylprednisolone followed by an oral steroid taper, with rapid clinical response aided by physical and occupational therapy.

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CASE PRESENTATION

A 57-year-old gentleman presented to our emergency department with a ten-day history of evolving neurological symptoms. He initially noted numbness of the fourth and fifth fingers of his left hand, but gradually developed worsening left-sided weakness in both his upper and lower limb, together with gait imbalance. There was no history of preceding injury or systemic illness. No recent history of vaccination. His past medical history was notable for hypertension, gastro-oesophageal reflux and benign prostatic hyperplasia. He suffered from chronic osteomyelitis in the right tibia originating from an injury in 1987 that had been managed with multiple courses of antibiotics and hyperbaric therapy over the years. He was taking amlodipine 10mg, omeprazole 20mg and tamsulosin 400mg daily. No known drug allergies. He worked as a carer, did not smoke and drank alcohol moderately. There was no family history of neurological or autoimmune disorders.

On examination, he was apyrexial, parameters were normal, HGT 9.2 mmol/L Systemic examination was normal. ECG and chest X-ray were normal. Patient was alert and orientated to time, place and person. Visual acuity (corrected) and fields were normal. Fundoscopy was normal as was the rest of his cranial nerve assessment. Left sided pronator drift was present. Power was uniformly decreased across all left upper limb muscles and the left hip flexors (MRC 4/5). Tone was increased in his left arm and leg and sustained clonus was present at both ankles (>10

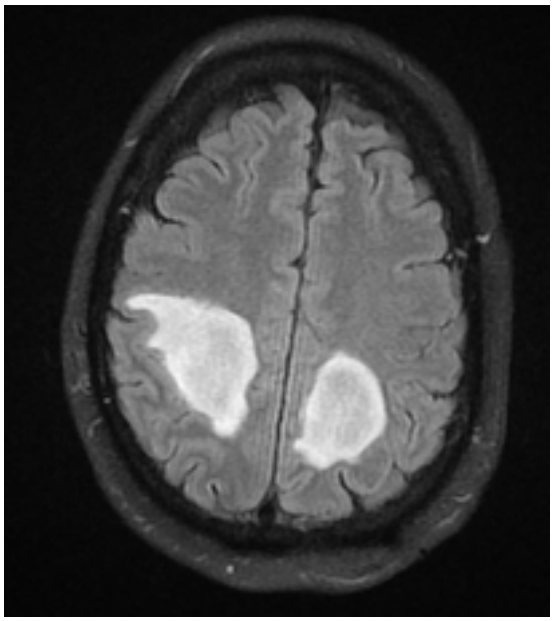

Figure 1 MRI images in T2 Flair sequence taken prior to treatment showing a fairly symmetrical open-ring enhancement pattern in both parietal lobes

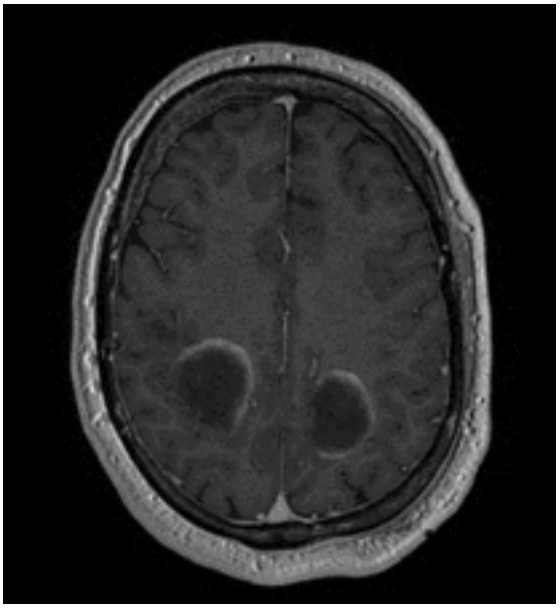

Figure 2 MRI images in T1 post contrast taken prior to treament

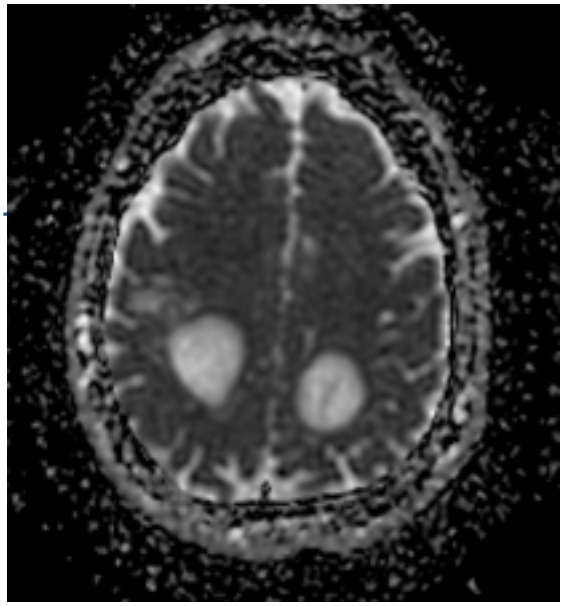

Figure 3 MRI images in DWI showing restricted diffusivity at the edges of the lesions prior to treatment

beats). There was no sensory neglect on examination. Sensory testing revealed reduced light touch perception in the left fourth and fifth fingers. He struggled significantly to stand from a seated position, and when helped up to walk, he had a broad-based gait, his usual gait due to the chronic osteomyelitis.

CT of the neck excluded disc herniation or canal stenosis. CT of the brain identified bilateral subcortical hypodensities in the parietal lobes with cortical involvement on the right. MRI brain showed symmetrical high FLAIR signal in the parietal lobes bilaterally with corresponding subcortical T1 hypointense foci. There was a separate similar lesion posterior to the right sylvian fissure in the right parietal lobe. All three lesions demonstrate an open-ring enhancing pattern and restricted diffusivity at the edges (Figures 1 - 3). Changes were in keeping with actively demyelinating lesions. The symmetrical appearance of the identified changes was highly suggestive of acute disseminated encephalomyelitis (ADEM). A lumbar puncture for CSF analysis and a panel of blood tests were taken to exclude possible differential diagnoses (See Tables 1-5).

Table 1 Cerebrospinal fluid analysis results

Cerebrospinal fluid analysis	
Opening pressure (cm H_2O)	23.5
Colour	Colourless
Turbidity	Clear
Supernatant	Clear
Coaglum	Absent
Protein (mg/L)	536
Globulins	Negative
Glucose (mmol/L)	6.12
Chloride (mmol/L)	121
Erythrocytes ($x10^{12}$/L)	0.000
Nucleated cell count ($x10^{12}$/L)	0.001
Polymorphonuclears ($x10^{12}$/L)	0.000
Lymphocytes/ Mononuclear ($x10^{9}$/L)	0.001
PCR	Negative for enterovirus, herpes simplex, mumps, parechovirus, varicella zoster

**CSF oligoclonal bands was sent but unfortunately sample leaked in transit. It was decided not to repeat lumbar puncture in view of rapid patient improvement.*

Table 2 Serology results

Serology	
White blood cells (x10⁹/L)	9.01
Neutrophils (x10⁹/L)	6.85
Lymphocytes (x10⁹/L)	1.28
Monocytes (x10⁹/L)	0.61
Eosinophils (x10⁹/L)	0.01
Basophils (x10⁹/L)	0.07
Haemoglobin (g/dL)	15.7
Mean cell volume (fL)	86.6
Mean cell Hb (pg)	29.2
Mean cell Hb concentration (g/dL)	33.7
Platelets (x10⁹/L)	302

Table 3 Biochemistry results

Biochemistry	
Urea (mmol/L)	7.0
Creatinine (umol/L)	105
Potassium (mmol/L)	4.10
Sodium (mmol/L)	138
C-reactive protein (mg/L)	15

Table 4 Serology results

Immunology	
EBV IgG	Positive
EBV IgM	Negative
CMV IgG	Negative
CMV IgM	Negative
Syphilis	Negative
ANCA	Negative (<1/10)
ANA	Negative (<1/100)
Complement 3	2090
Complement 4	375
Aquaporin 4 antibodies	<1:10
Myelin oligodendrocytes glycoprotein antibodies	<1:10
COVID-19 PCR	Not Detected

Table 5 Urinalysis results

Urinalysis	
White blood cells	Negative
Nitrites	Negative
Proteins	Negative
Erythrocytes (uL)	25

He was started on intravenous methylprednisolone 1000mg daily for three days followed by an oral steroid taper (prednisolone 50mg daily for 7 days tailing down 10mg each week). Physiotherapists and occupational therapists were involved for rehabilitation. Physiotherapy focused on postural re-education and stepping. Occupation therapist helped with proprioception, motor coordination and stereognosis. He experienced a rapid improvement in his symptoms and signs such that he was discharged after 10 days.

By this time, he had residual left arm drift and left sided incoordination on finger-to-nose testing due to reduced proprioception, tone was normal, no sensory neglect, and power on the left side was normal. He continued to receive physiotherapy and occupational therapy input on an outpatient basis. Follow up MRI brain after 3 months showed that the previously described T2 hyperintense lesions in the parietal lobes were much less conspicuous and had decreased slightly in size in the interim (Figures 4 - 6). When last reviewed after 3 months, his neurological examination was intact, and he had restarted working and driving.

DISCUSSION

Acute disseminated encephalomyelitis is a monophasic demyelinating condition caused by an autoimmune process affecting the central nervous system. This entity is seen more frequently in children rather than adults, mostly preceded by an infection or vaccination. Patients most often present with acutely multifocal neurological deficits progressing rapidly with encephalopathy.

Classically ADEM, due to the acute and rapid progression of motor deficits with encephalopathy, requires admission to hospital. Motor deficits can vary from single limb involvement to quadriparesis.[1,4] Sensory deficits as well oculomotor deficits and dysarthria may be present if brainstem is involved..[1] Other symptoms and signs may include

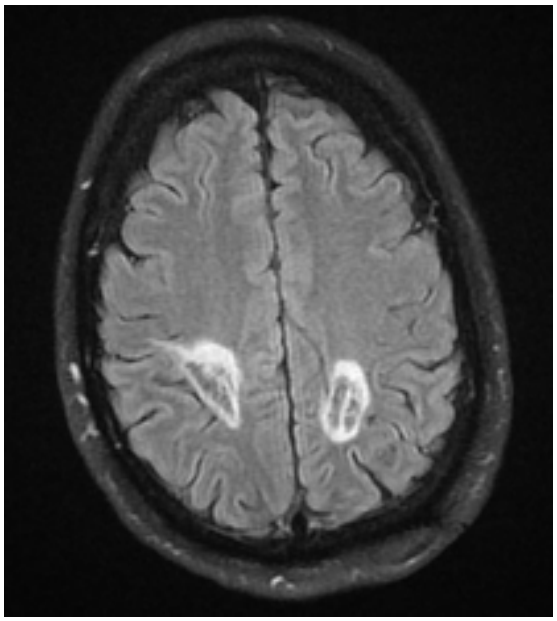

Figure 4 MRI images in T2 Flair sequence taken three months post treatment showing a decrease in size in both parietal lobe lesions

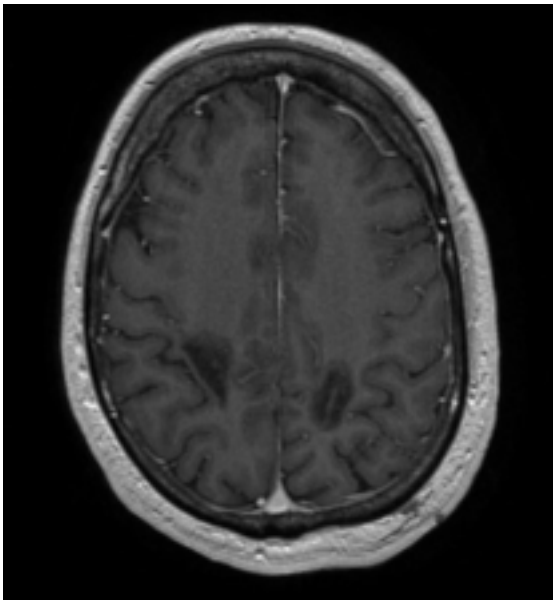

Figure 5 MRI images in T1 post contrast sequence taken three months post treatment

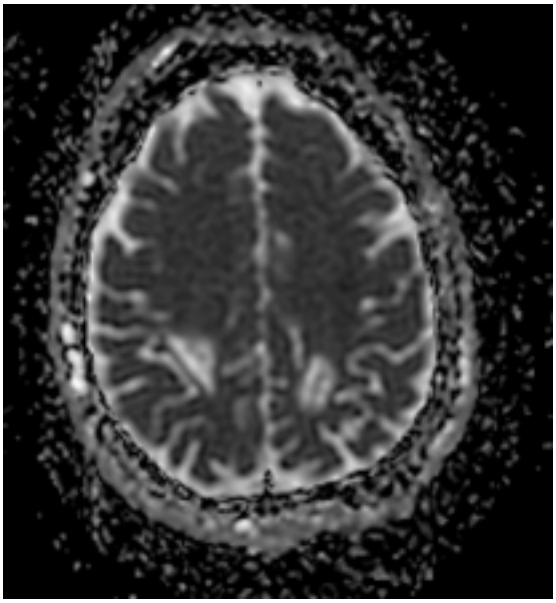

Figure 6 MRI images in DWI taken three months post treatment

ataxia, headache, malaise, meningism, aphasia, optic neuritis, nystagmus and extrapyramidal symptoms.[1,2,4]

Patients with suggestive clinical history and examination need investigation to support the diagnosis of ADEM and eliminate other differential diagnosis (Tables 6,7). MRI of the brain usually shows asymmetric poorly marginated lesions in both hemispheres.[5] Most patients have deep and subcortical white matter involved by demyelination. These usually appear as hyperintense lesions on fluid attenuated inversion recovery (FLAIR) and T2-weighted sequences. Infratentorial lesions involvement may be present as well.[1,4] Lumbar puncture is done for CSF testing. This is done to rule out inflammation and infections. Changes seen in ADEM are non-specific for the condition. These include lymphocytic pleocytosis with a CSF white blood cells of less than 100 cells/mL and mildly elevated CSF protein.

Mainstay treatment for ADEM is immunosuppression. Initial therapy involves high dose glucocorticoids.[6] Methylprednisolone intravenously 1000mg daily for three to five days can be given then switched to oral formulation and tapered over a few weeks.

Table 6 Differential Diagnosis to Acute Disseminated Encephalomyelitis in adults

Differential Diagnosis
Multiple Sclerosis
Chronic autoimmune demyelinating disease
Recurrent attacks separated in time and space
MOG antibody associated disorder
Central nervous system demyelination
IgG serum antibodies directed against MOG
Neuromyelitis optica spectrum disorder
Severe immune mediated demyelination and axonal damage
Positive for aquaporin 4 antibody
Infectious meningoencephalitis
Fever, headaches, meningism
Sarcoidosis
Autoimmune disorder affecting multiple organs
Cranial mononeuropathy, focal or multifocal encephalopathy, myelopathy, myopathy

Table 7 Differences between Acute Disseminated Encephalomyelitis and Multiple Sclerosis

	ADEM	Multiple Sclerosis
Clinical picture	Widespread CNS dysfunction fever headache	Focal signs Motor deficit cranial nerve palsies optic neuritis
Precedent viral infection	Common	No association
Course	Acute, non-progressive	Chronic Mostly relapsing & remitting
MRI	Bilateral lesion Poorly marginated Uniform appearance Diffuse	Predominantly unilateral Well marginated Variable appearance Periventricular white matter involvment
Follow up MRI	Complete/partial resolution of lesions	New lesions
Sequelae	Uncommon	Common

When there is inadequate response to glucocorticoid therapy, intravenous immunoglobulins (IVIg) or plasma exchange may be given to achieve the desired effect. IVIg are usually started after assessing the response of the disease with five-day glucocorticoid therapy. If there is poor response, one might switch to IVIg therapy.[7] Studies have shown that patients with poor response to glucocorticoids fared well with IVIg therapy with regards to clinical improvement with respect to peripheral nervous system involvement.[8] Plasma exchange has been used but data is still limited.

When comparing the clinical course of ADEM in children with that in adults, although the disease is more frequent in children, literature suggests that the clinical course in the adult population is more severe. Adults required admission to intensive care units with longer hospitalization stays. Furthermore, outcome also was worse, fewer adults achieve complete motor recovery and the condition is more frequently fatal.[5]

REFERENCES

1. Schwarz S, Mohr A, Knauth M, et al Acute disseminated encephalomyelitis: a follow-up study of 40 adult patients. Neurology 2001; 56:1313.
2. de Seze J, Debouverie M, Zephir H, et al Acute fulminant demyelinating disease: a descriptive study of 60 patients. Arch Neurol 2007; 64:1426.
3. Van Haren K, Tomooka BH, Kidd BA, Banwell B, Bar-Or A, Chitnis T, et al Serum autoantibodies to myelin peptides distinguish acute disseminated encephalomyelitis from relapsing-remitting multiple sclerosis. Mult Scler. 2013 Nov;19(13): 1726-33.

4. van der Knaap MS, Valk J Acute disseminated encephalomyelitis and acute hemorrhagic encephalomyelitis. In: Magnetic Resonance of Myelination and Myelin Disorders, 3rd edition, Springer, New York 2005. p.604.
5. Ketelslegers IA, Visser IE, Neuteboom RF, et al Disease course and outcome of acute disseminated encephalomyelitis is more severe in adults than in children. Mult Scler 2011; 17:441.
6. Keegan M, Pineda AA, McClelland RL, et al Plasma exchange for severe attacks of CNS demyelination: predictors of response. Neurology 2002; 58:143.
7. Marchioni E, Marinou-Aktipi K, Uggetti C, et al Effectiveness of intravenous immunoglobulin treatment in adult patients with steroid-resistant monophasic or recurrent acute disseminated encephalomyelitis. J Neurol 2002; 249:100.
8. Marchioni E, Ravaglia S, Montomoli C, et al Postinfectious neurologic syndromes: a prospective cohort study. Neurology 2013; 80:882.