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EDITORIAL

# Editorial

## Lessons from COVID 19

Simon Attard Montalto

For the past nine months, the world has been taken over by the COVID 19 pandemic with almost all of the repercussions being negative, both to the individual, society, health services, economies and life in general. But have there been any lessons to be learnt from this worldwide crisis and, more importantly, have these been addressed?

### COVID AND THE WORLD STAGE

How did this pandemic arise in the first place, and can a similar event be avoided in the future? All evidence points to the transmission of a β coronavirus from animals, probably pangolins or bats,[1] to humans essentially due to close contact and poor hygiene practices in 'live' markets and illegal trade in wildlife. Clearly a massive rethink and overhaul of these practices (and how mankind relates to wild animals in general) is a must, starting with the question whether they should be permitted in the first place.[2] Almost without exception, once mankind interferes with nature, disaster follows – unusually, on this occasion, it is not just nature that has lost out!

Although the WHO mobilised relatively quickly, declaring a Public Health Emergency on 30.1.20 and, later, a Global Pandemic,[3] could their response have been improved? Once it was known that a new virus with credentials to create a pandemic had crossed over to man, could a better, internationally-coordinated effort with immediate early warning and drastic lockdown measures have helped to contain the infection 'locally' and limit the infection to epidemic rather than pandemic proportions? Could the disaster that afflicted the north of Italy, for example, have been averted? In this regard, an effective pan-global early-warning and more effective alarm system needs to be established that, amongst others, would ensure that there is no place for withholding or delaying dissemination of data.

**Cover Picture:**

'drawing of Dawn, a sculpture by Michelangelo for the Cappella Medici'

*Pencil*

**By** Alexander Manché

Alexander Manché founded the Cardiothoracic Unit in Malta in 1995, having trained in the UK and the US for almost 20 years.

He also pioneered the transplant programme, mitral valve repair and minimally invasive aortic valve surgery. He was responsible for training the new generation of surgeons.

His interests include art, music, travel and medical history.

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## Pandemic management

At country level, the management of a health crisis on this scale must be led by the Health Authorities, with early and aggressive measures that will, inevitably, impact society, daily life and the economy. Ultimately, this pandemic has shown very clearly that a 'gentle' approach, for example by allowing for natural herd immunity to develop and similar measures,[4] do not work. Indeed, countries that embraced this option, even with the best of intentions, invariably fared worse in terms of absolute numbers of COVID 19 infections and mortality.[5] This bitter lesson was highlighted further by those countries led by self-acclaimed 'champions' who belittled the pandemic and adopted a 'gung-ho' attitude, that promptly condemned their countries to the worst statistics on the entire planet.[5] Politicians are simply not trained to manage a pandemic and should (humbly) seek and take the advice of those who are.

## The lessons from Malta

The Malta experience, uniquely, provides two clear lessons: firstly, how to manage a pandemic well and, subsequently, how to unmanage the very same pandemic! Malta's approach was hailed as the 'best model' in pandemic management,[6] with a strict policy of track, trace and isolate cases. This was only made possible as Malta's well-informed Health Authority was ably supported by the Ministry and Division of Health, efficiently and effectively mobilised front-liners including the police, and a frightened but compliant population. This formula worked, bringing the local pandemic under tight control within a two-month period. Although a second wave was expected (and was probably inevitable), particularly after the relaxation of lockdown measures, this was ensured by 'over-eager' winding down, over-optimistic sound bites ensuring a false sense of security, compounded by downright irresponsible actions allowing and even encouraging 'uncontrolled' mass events. Although the economic argument was (and remains) valid, the problem posed by the health issue was (and remains) greater and should have swayed the decision makers. The fear of a second tsunami after opening the national airport did not materialise, since this was (and remains) reasonably well 'controlled'. Similarly, although the influx of COVID 19-positive migrants has increased absolute case numbers, this has had no impact on the subsequent dispersal of the virus as all these individuals have been corralled immediately on arrival. Unquestionably, it has been mass gatherings ranging from family parties to day-long events that have ensured that the virus has been released into the general population.[7] This, in turn, has ensured that the R factor remains steadily above 1 and the second wave is now considerably greater both in absolute numbers and duration than the first.[5] As a consequence, Malta has plummeted towards the bottom of Europe's pandemic activity status, and is on most countries 'with caution' list for travel purposes. Of greater concern, there is presently little evidence of the situation easing, and the increasing mean age of infected persons including the spread of the virus into care homes with access to the extremely vulnerable, will result in a steady escalation in COVID-related deaths.[8]

Presently, the restrictive measures in State hospitals, the Medical School, University, Churches, shops, etc., etc., are more likely to increase rather than diminish.[9,10] The reopening of schools and revitalisation of the economy look to be in jeopardy, whist return to normality remains ever less likely. Once pandemic control

is lost, it is very difficult to retrieve the situation and this can only be achieved through stringent Public Health measures,[11] backed up with an effective and safe vaccine. Ultimately, all other initiatives and drivers (political, societal, economic, business interests, etc.), however valid, are dependent on the health of the nation's population and, alone or with an ailing population, cannot effect a turnaround.

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ORIGINAL ARTICLE

# CPR performance in lay people with telephone assisted CPR instructions – A prospective manikin-based observational study

Mark A. Attard Biancardi, Peter Spiteri, Jason Attard, Marika Debono, Joanne Mifsud, Alexander Borg Farrugia, Maria Borg Curmi

## Background

Emergency Medical Services (EMS) in Europe, annually encounter about 275,000 out-of-hospital cardiac arrests (OHCA), whilst in the United States this number rises to 420,000. The chance of survival from an OHCA is dependent on the recognition of cardiac arrest by Emergency Medical Dispatchers' (EMDs), early bystander cardiopulmonary resuscitation (CPR), and early defibrillation. Telephone assisted CPR (TCPR) by EMDs (also known as dispatcher assisted CPR – DA-CPR) has been shown to double the frequency of bystander CPR so much so that it has now included as a key parameter in the 2015 European Resuscitation Council guidelines.

## Method

A prospective, manikin-based observational study was conducted in Malta between July 2018 and July 2019. The aim of this study was to test a set of TCPR instructions in Maltese on lay people with no previous knowledge of CPR. The primary endpoint was to check for understanding and correct execution of such instructions vis-à-vis hand positioning during chest compression, compressions depth and rate. Participants were recruited from 10 localities around Malta. Data was collected using Laerdal's Resus Annie® QCPR manikin and SkillReporterTM (PC) software.

## Results

One hundred fifty-five participants were included in the study. Approximately 7 out of 10 participants performed compressions with the correct hand position, 6 out of 10 participants achieved a compression rate between 100 – 120/min, and 2 out of 10 rescuers achieved the recommended 50-60mm compression depth.

## Conclusion

Laypeople with no previous CPR training can understand and execute a set of chest compression-only TCPR instructions in Maltese. The introduction of a standard operating procedure and training of EMDs on policy, expectations and performance is vital if bystander CPR and survival rates are to improve locally. Training, coupled with quality improvement projects such as call collection for review, analysis and feedback is the way forward.

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## Introduction

It has been reported that Emergency Medical Services (EMS) in Europe, annually encounter about 275,000 out-of-hospital cardiac arrests (OHCA), whilst in the United States (US) this number rises to 420,000.[1] Sixty-five to 70 percent of all sudden cardiac deaths (SCDs) are attributable to coronary heart disease (CHD), however, the frequency of CHD is much lower in SCDs occurring under the age of 40.[2-3] Ten percent of SCDs are due to other types of structural heart disease including congenital coronary artery anomalies, myocarditis, hypertrophic cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy.[2-4] Structural heart disease is much higher in subjects under the age of 30. Five to 10 percent of SCDs are arrhythmic, occurring in the absence of structural heart disease such as long QT syndrome, Brugada syndrome, Wolff-Parkinson-White syndrome and catecholaminergic polymorphic ventricular tachycardia (VT).[3-4] In the absence of any structural abnormality or electrophysiologic abnormality on the ECG, these entities are often termed primary electrical disease.[5-7] Fifteen to 25 percent of cardiac arrests are noncardiac in origin. These include trauma, bleeding, drug intoxication, intracranial haemorrhage, pulmonary embolism, near-drowning, and central airway obstruction.[5-8] Survival rates have been reported to be poor with a survival to hospital discharge of less than 10%.[9] According to our local cardiac arrest registry, in Malta survival to hospital discharge is around 3%.[10]

The chance of survival from an OHCA is dependent on the recognition of cardiac arrest by Emergency Medical Dispatchers' (EMDs), early bystander cardiopulmonary resuscitation (CPR), and early defibrillation.[11] To-date, in order to increase bystander intervention, millions of laypeople (non-specialists within the general public) have undergone CPR training, and AEDs have been widely disseminated in the community.[12] Despite these efforts, many OHCA patients still fail to receive bystander intervention,[11,13] and it is estimated that 65% of CPR-trained bystanders will fail to provide CPR.[14] In Malta the rate of bystander CPR is around 38%.[10] Similarly, in the United Kingdom (UK) the rate of bystander CPR is around 40%.[15] Impediments to initiating CPR include panic, fear of causing harm, not performing CPR adequately (even for those who have received CPR training or have performed CPR in the past),[14,16-18] and a reluctance to perform mouth-to-mouth ventilation.[19-20] Telephone assisted CPR (TCPR) by EMDs, is proven to be an effective and reasonable method to improve the rate of bystander-performed CPR.[21] Furthermore, TCPR by EMDs (also known as dispatcher assisted CPR – DA-CPR) has been shown to double the frequency of bystander CPR,[22] so much so that it has now obtained a key position in the 2015 ERC guidelines.[23]

According to the 2015 European Resuscitation Guidelines (ERC), OHCA has occurred if a patient is unconscious and not breathing normally.[23] However, the ability to recognize OHCA over the phone can be challenging especially if agonal breathing occurs.[24-25] Despite this, recognition of OHCA by EMDs in certain European countries such as Finland, has been reported to be as high as 70–83%.[26-28] In Malta, EMDs do not yet have a standard protocol on TCPR but, nevertheless, provide TCPR in approximately 58% of OHCA victims.[29]

The aim of this study was to test a set of TCPR instructions in Maltese on lay people with no previous knowledge of CPR, and assess the effectiveness and quality of the CPR provided.

## Methods and Materials

A prospective, manikin-based observational study was conducted in Malta between July 2018 and July 2019. A set of TCPR instructions in Maltese was drawn up and tested on lay people with no previous knowledge of CPR. The primary endpoint was to check for understanding and correct execution of such instructions vis-à-vis hand positioning during chest compression, compressions depth and rate. Ethical approval was granted from the Faculty Research Ethics Committee (Ref no. FRECMDS_1718_061).

TCPR instructions in Maltese were created using commonly used language *(figure 1)*. These included instructions on the recognition of cardiac arrest and compression-only CPR. English TCPR instructions from the resuscitation academy were also used with permission as guidance *(figure 2)*.[30] Given that this study was manikin-based, instructions about the recognition of cardiac arrest were not tested, and only instructions relating to compressions-only CPR were assessed. Six experienced EMD's were recruited and underwent training on how to deliver TCPR instructions.

**Figure 1** All caller interview – Cardiac arrest recognition and TCPR instructions in Maltese.

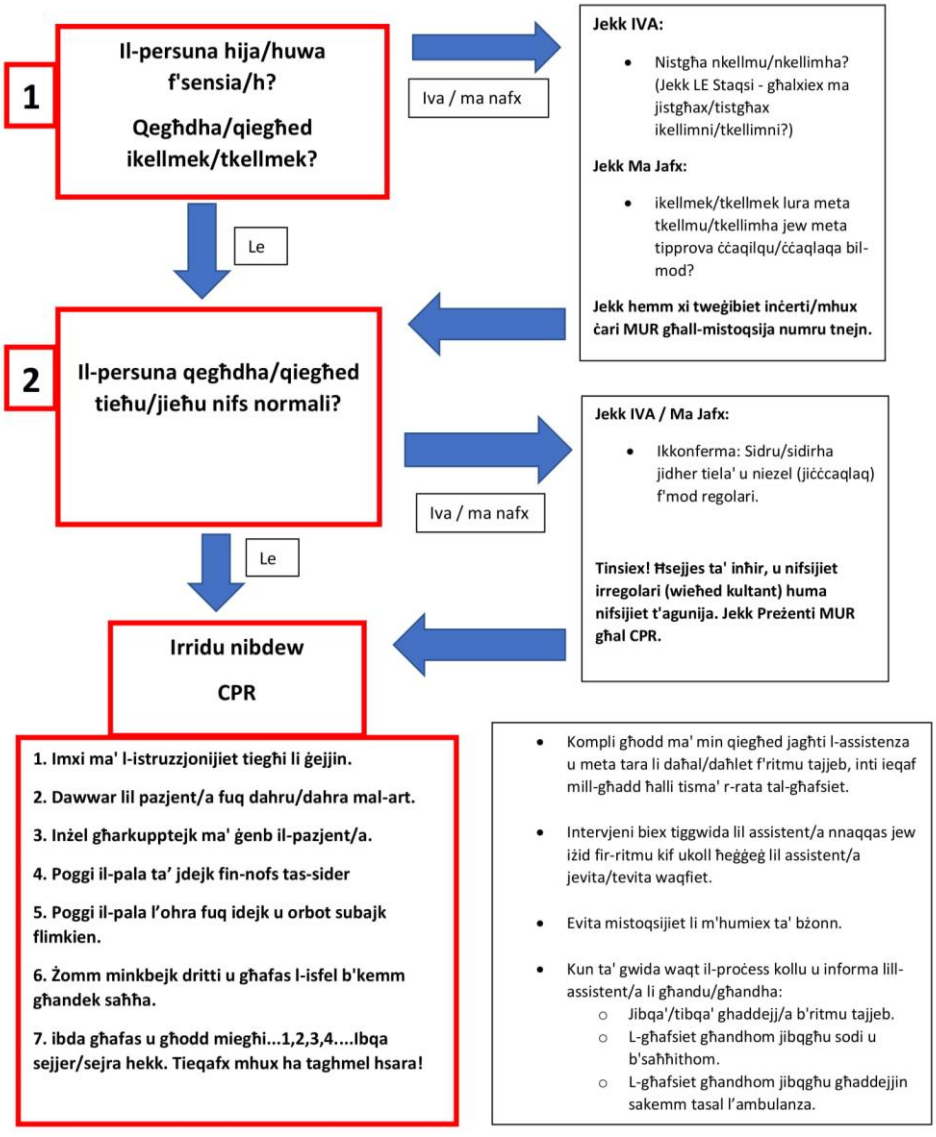
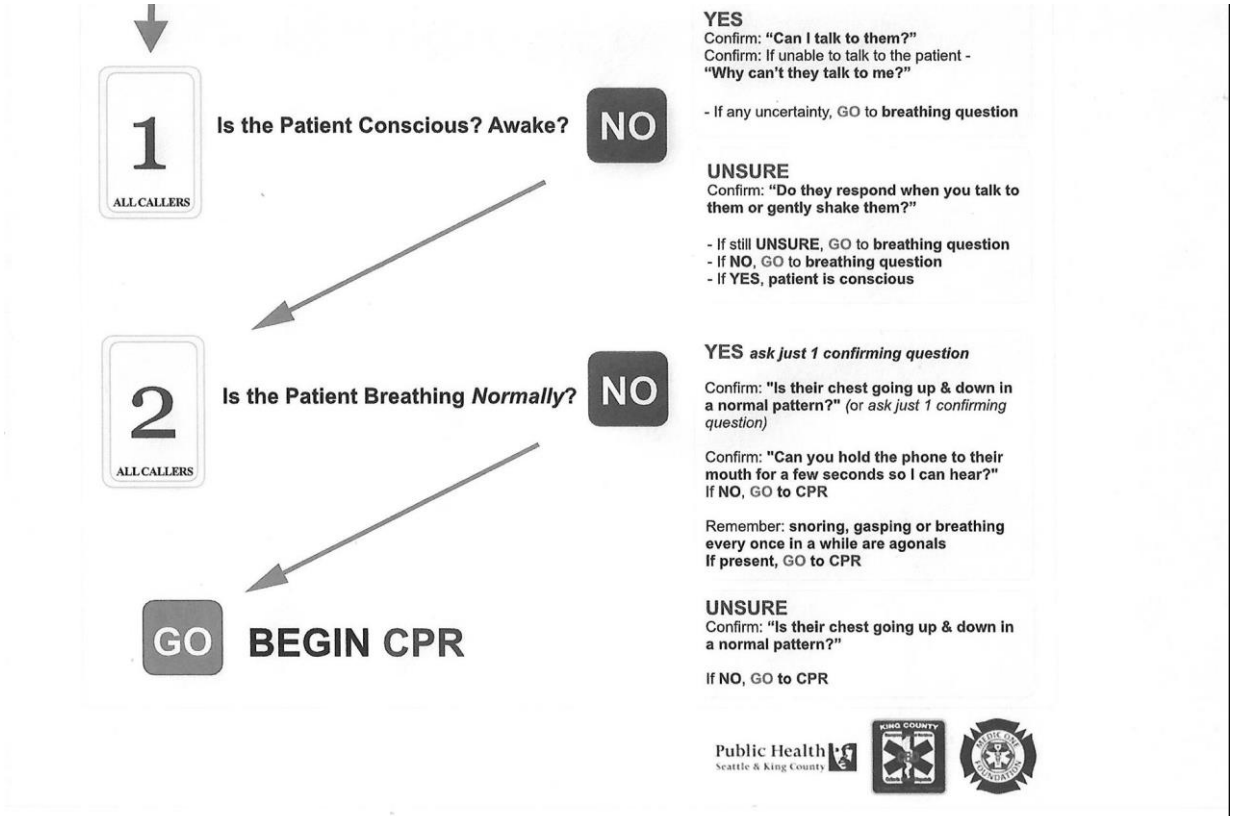
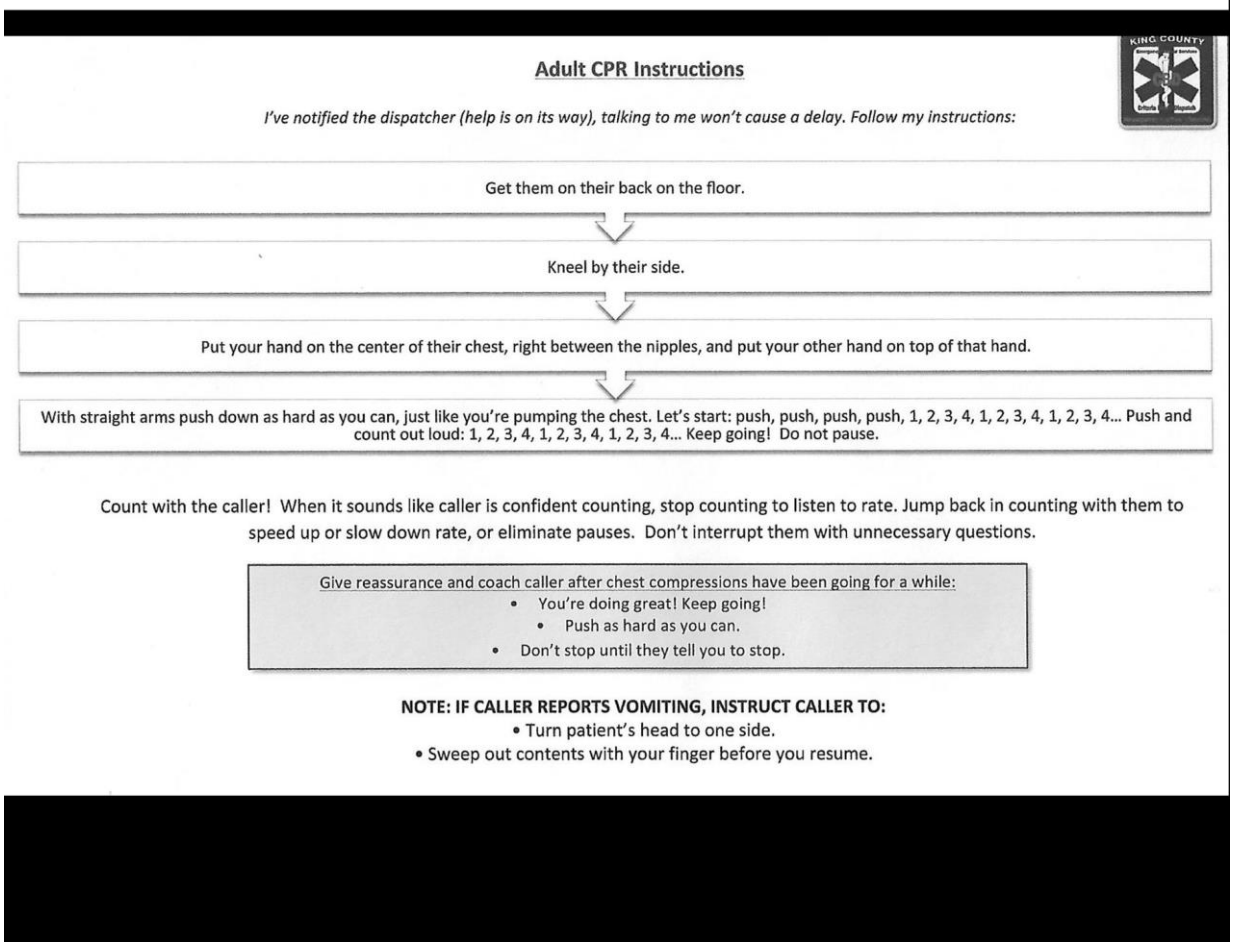


**Figure 2** TCPR instructions in English used with permission from the Resuscitation Academy



Participants were recruited from 10 localities around Malta. With a population of around 441,000 people,[31] Malta is subdivided into five districts *(figure 3)*, each consisting of a number of localities. These include the Northern Harbour District, the Western District, the Northern District, the South Eastern District and the Southern Harbour District.[32] Localities were invited to participate in the study via their respective local councils. Ten localities accepted to participate, two from each district *(figure 4)*. The inclusion criteria included age over 18 years of age and no previous CPR training. Each Local Council issued an open public invitation to its residents in the form of a poster, stating clearly the eligibility criteria *(Figure 5)*. Attendance was voluntary and the authors had no part in the selection process of participants. Consent was obtained from all participants before data collection.

Data was collected using Laerdal's Resus Annie® QCPR manikin and SkillReporterTM (PC) software. Participants were asked to follow a set of compression-only CPR instructions in Maltese simulating a telephone call. Data was collected over one minute of compression-only CPR. Information about the correct hand position, depth of compressions, fully released compressions and mean rate of compressions were recorded and stored. Study investigators also noted the correct hand, elbow and shoulder positioning during the simulation. A depth of 50-60mm and a rate of 100-120/min was taken as the 'correct' standard reference.[23] For correct hand positioning, an arbitrary performance target of 90% or better was set. After data collection, all participants in each locality were trained in Basic Life Support and AED use by certified instructors.

**Figure 3** Districts of Malta and Gozo

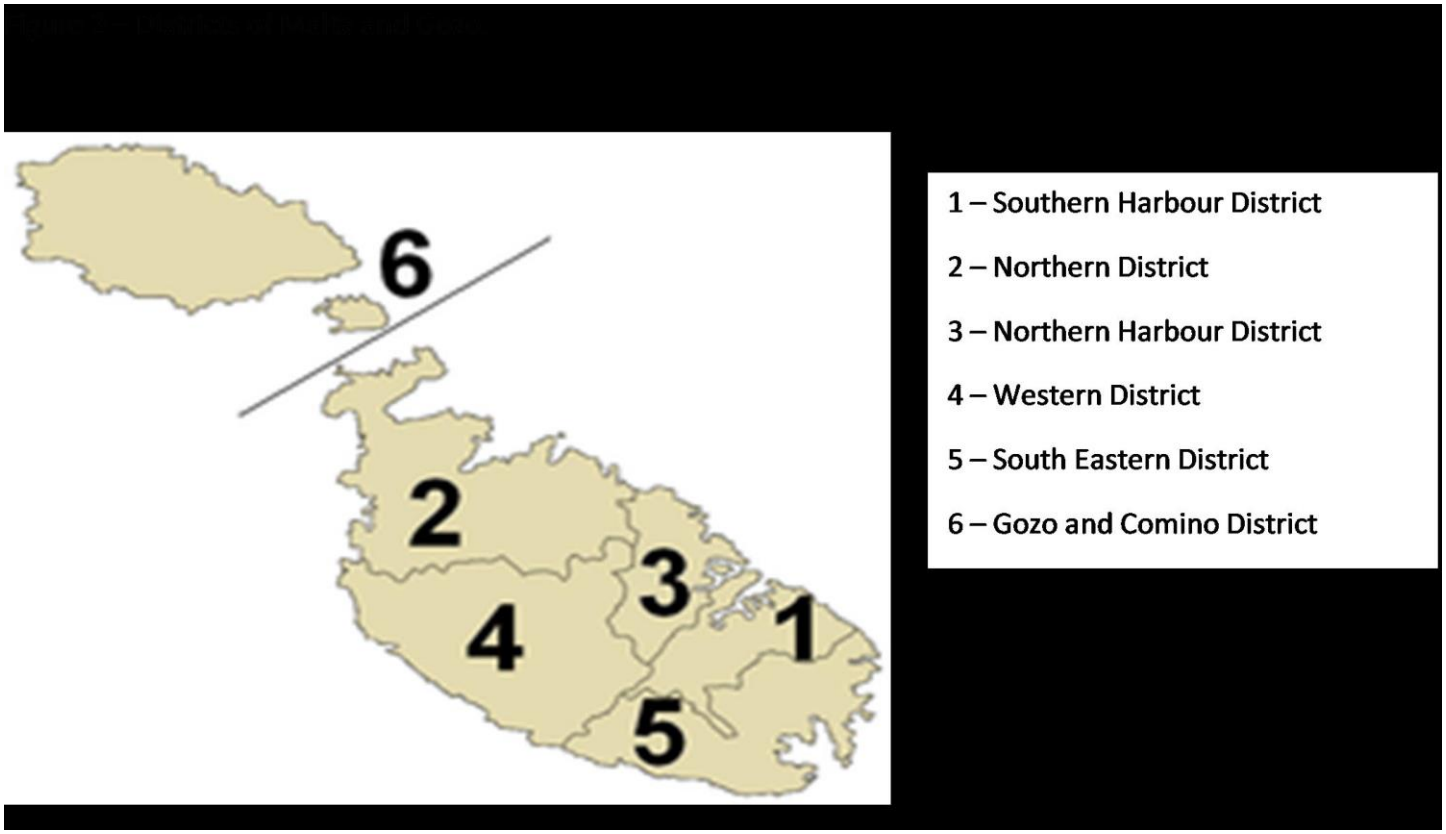


**Figure 4** Localities taking part in study

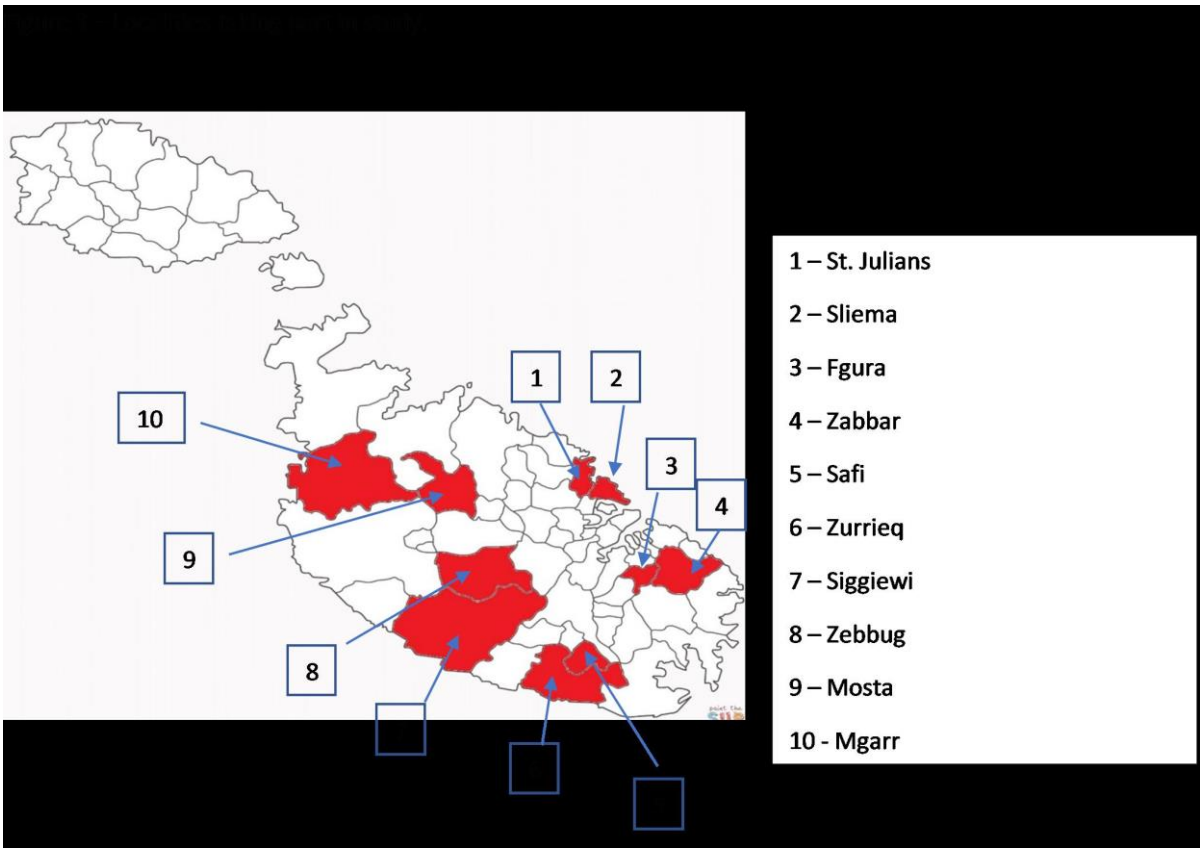
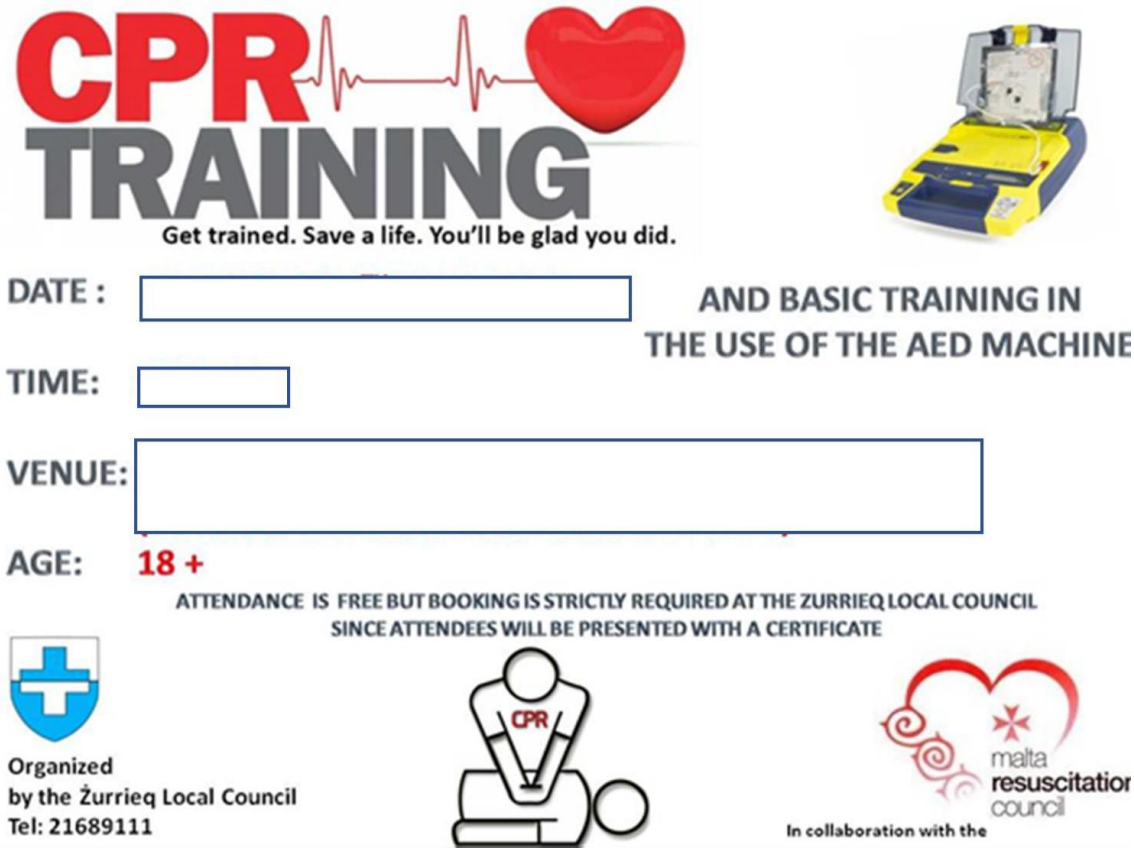



**Figure 5** Invitation poster used for recruitment of participants.



## STATISTICAL ANALYSIS

Descriptive and inferential analyses were performed through a combination of Microsoft Office Professional Plus 2010 Excel and IBM SPSS Statistics version 22. Details on how the variables were modelled are shown in *Table 1*.

**Table 1** Sociodemographic and CPR variables

| **Sociodemographic variables** | | |
|---|---|---|
| **Variable** | Grouping | Variable type |
| **Age** | <25 | Ordinal |
| | 25-34 | |
| | 35-44 | |
| | 45-54 | |
| | 55-64 | |
| | 65+ | |
| **Gender** | Male | Binary |
| | Female | |
| **Education** | Primary/Secondary | Binary |
| | Tertiary | |
| **District of Residence** | Northern Harbour (Sliema, St. Julians) | Nominal |
| | Southern Harbour (Fgura, Zabbar) | |
| | South Eastern (Safi, Zurrieq) | |
| | Western (Siggiewi, Zebbug) | |
| | Northern (Mgarr, Mosta) | |
| **CPR performance variables** | | |
| Compressions with correct hand position (%) | | Continuous |
| Compressions fully released (%) | | Continuous |
| Deep enough compressions (%) | | Continuous |
| Mean depth (mm) | | Continuous |
| Mean rate (per minute) | | Continuous |

A Kolmogorov-Smirnov test was performed to test the normality of the distribution for dependent continuous variables. Kruskal-Wallis test was used to identify if there were any statistically significant differences between the independent variables, age groups and district of residence, and the dependent variables, proportion of compressions with correct hand position, compressions fully released, deep enough compressions and mean rate of compressions. Mann-Whitney U test was used to identify if there were any statistically significant differences between the independent variables, gender and education, and the dependent variables, proportion of compressions with correct hand position, compressions fully released, deep enough compressions and mean rate of compressions. One-way analysis of variance (ANOVA) was used to identify if there were any statistically significant differences between the independent variables, age groups and district of residence, and the dependent variable, mean depth of compressions. Independent-samples t-test was used to identify if there were any statistically significant differences between the independent variables, gender and education, and the dependent variable, mean depth of compressions.

## RESULTS

The distribution of participants by age group, gender, highest educational attainment, and district of residence (based on Local Administrative Units Level 1) are shown in Table 2. Assuming a performance target of 90% or more, 64.5% (*n*=100) of the cohort performed compressions with the correct hand position and 73.6% (*n*=114) fully released their compressions appropriately. Only 12.9% (*n*=20) of participants performed deep-enough compressions. The distribution of the overall performance of the recruited sample with regards to compressions with correct hand position, compressions fully released and deep-enough compressions are shown in Table 3. The distribution of the overall performance of the recruited sample for mean depth (mm) and mean rate (per minute) are shown in Tables 4 and 5, respectively. With regards to mean depth of compressions, only 18.1 % (*n*=28) of the cohort achieved the recommended 50-60mm depth of compressions (Table 4). Just over half of the participants (53.5%, *n*=83) performed the compressions at the recommended rate of 100 – 120/min (Table 5).

The variable distribution of mean depth followed a normal distribution (Kolmogorov-Smirnov D test, D(155) = 0.064, *p*=0.200). In contrast, the variable distribution of compressions with correct hand position (D(155) = 0.360, *p*=<0.001), compressions fully released (D(155) = 0.300, *p*=<0.001), deep-enough compressions (D(155) = 0.323, *p*=<0.001) and mean rate (D(155) = 0.100, *p*=0.001) did not follow a normal distribution.

The distribution and univariate analyses between the sociodemographic variables and the various dependent continuous variables are shown in Tables 6-10. There were no statistically significant differences between age groups, gender, education and district of residence in relation to compressions with the correct hand position (Table 6). Females were statistically significantly more likely to perform compressions which were fully released when compared to males (Mann-Whitney U test, U=2343.500, *p*=0.017). No statistically significant differences were found however, between age groups, education and district of residence in relation to compressions which were fully released (Table

7). Males were statistically significantly more likely to perform deep enough compressions when compared to females (Mann-Whitney U test, U=2446.000, *p*=0.037) (Table 8). Similarly, participants with tertiary education (Mann-Whitney U test, U=2388.500, p=0.016) and from the Western district (Kruskal-Wallis H test, $x^2$=15.468, p=0.004) were statistically significantly more likely to perform deep-enough compressions when compared to the rest (Table 8). No statistically significant difference was found however between age groups, and the proportion of deep-enough compressions. With regards to the mean depth of compressions, participants with tertiary education were statistically significantly more likely to have a higher average mean depth of compressions (Independent-samples t-test, t(153)=1.860, p=0.004). There were no statistically significant differences between age groups, gender and district of residence, in relation to mean depth of compressions (Table 9). Table 10 shows that participants with primary or secondary education were statistically significantly less likely to have a higher mean rate of compressions when compared to participants with tertiary education (Mann-Whitney U test, U = 2209.500, *p*=0.004). There were no statistically significant differences between age groups, gender and district of residence, in relation to mean rate of compressions (Table 10).

**Table 2** Sociodemographic variables of the recruited sample

| Age Groups | Frequency | Percent |
|---|---|---|
| <25 | 24 | 15.5% |
| 25-34 | 27 | 17.4% |
| 35-44 | 29 | 18.7% |
| 45-54 | 21 | 13.5% |
| 55-64 | 24 | 15.5% |
| 65+ | 30 | 19.4% |
| **Gender** | **Frequency** | **Percent** |
| Male | 70 | 45.2% |
| Female | 85 | 54.8% |
| **Education** | **Frequency** | **Percent** |
| Primary | 1 | 0.6% |
| Secondary | 76 | 49.0% |
| Tertiary | 78 | 50.3% |
| **District of Residence** | **Frequency** | **Percent** |
| Northern Harbour | 25 | 16.1% |
| Southern Harbour | 25 | 16.1% |
| South Eastern | 55 | 35.5% |
| Western | 23 | 14.8% |
| Northern | 27 | 17.4% |
| **Total** | **155** | **100.0%** |

**Table 3** Frequency and proportion of compressions with correct hand position, compressions fully released and deep enough compressions

| | Compressions with correct hand position | | Compressions fully released | | Deep enough compressions | |
|---|---|---|---|---|---|---|
| Performance (%) | Frequency | Percent | Frequency | Percent | Frequency | Percent |
| 0-89 | 55 | 35.5% | 41 | 26.5% | 135 | 87.1% |
| 90-99 | 15 | 9.7% | 42 | 27.1% | 15 | 9.7% |
| 100 | 85 | 54.8% | 72 | 46.5% | 5 | 3.2% |

**Table 4** Frequency and proportion of mean depth of compressions

| Mean Depth (mm) | Frequency | Percent |
|---|---|---|
| <50 | 126 | 81.3% |
| 50-60* | 28 | 18.1% |
| >60 | 1 | 0.6% |

*Gold standard

**Table 5** Frequency and proportion of mean rate of compressions

| Mean Rate (per minute) | Frequency | Percent |
|---|---|---|
| <100 | 40 | 25.8% |
| 100-120* | 83 | 53.5% |
| >120 | 32 | 20.6% |

*Gold standard

**Table 6** Distribution and univariate analyses between the sociodemographic variables and the proportion of compressions with correct hand position

| | Compressions with correct hand position (%) | | | | | |
|---|---|---|---|---|---|---|
| **Age Groups** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| <25 | 24 | 79.6 | 100.0 | 74.0 | 100.0 | 0.558* |
| 25-34 | 27 | 77.2 | 100.0 | 80.0 | 100.0 | |
| 35-44 | 29 | 61.8 | 98.0 | 3.0 | 100.0 | |
| 45-54 | 21 | 60.8 | 98.0 | 4.0 | 100.0 | |
| 55-64 | 24 | 77.1 | 100.0 | 69.3 | 100.0 | |
| 65+ | 30 | 67.1 | 100.0 | 2.3 | 100.0 | |
| **Gender** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| Male | 70 | 64.7 | 100.0 | 2.0 | 100.0 | 0.157† |
| Female | 85 | 75.2 | 100.0 | 56.0 | 100.0 | |
| **Education** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| Primary/Secondary | 77 | 66.6 | 99.0 | 6.0 | 100.0 | 0.124† |
| Tertiary | 78 | 74.4 | 100.0 | 47.3 | 100.0 | |
| **District of Residence** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| Northern Harbour | 25 | 76.1 | 100.0 | 100.0 | 100.0 | 0.147* |
| Southern Harbour | 25 | 61.0 | 99.0 | 2.0 | 100.0 | |
| South Eastern | 55 | 70.3 | 99.0 | 37.5 | 100.0 | |
| Western | 23 | 81.7 | 100.0 | 87.5 | 100.0 | |
| Northern | 27 | 64.8 | 99.0 | 4.0 | 100.0 | |
| **Overall** | **155** | **70.5** | **100.0** | **16.0** | **100.0** | |

*Kruskal-Wallis Test

† Mann-Whitney U Test

**Table 7** Distribution and univariate analyses between the sociodemographic variables and the proportion of compressions which were fully released

| | Compressions fully released (%) | | | | | |
|---|---|---|---|---|---|---|
| **Age Groups** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| <25 | 24 | 83.7 | 98.0 | 87.0 | 100.0 | 0.806* |
| 25-34 | 27 | 85.9 | 100.0 | 81.0 | 100.0 | |
| 35-44 | 29 | 89.7 | 99.0 | 94.0 | 100.0 | |
| 45-54 | 21 | 87.1 | 99.0 | 97.0 | 100.0 | |
| 55-64 | 24 | 92.0 | 99.5 | 95.0 | 100.0 | |
| 65+ | 30 | 87.4 | 95.0 | 82.3 | 100.0 | |
| **Gender** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| Male | 70 | 83.1 | 97.5 | 81.3 | 100.0 | 0.017† |
| Female | 85 | 91.4 | 100.0 | 93.0 | 100.0 | |
| **Education** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| Primary/Secondary | 77 | 89.8 | 99.0 | 84.0 | 100.0 | 0.469† |
| Tertiary | 78 | 85.5 | 99.0 | 90.0 | 100.0 | |
| **District of Residence** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| Northern Harbour | 25 | 92.3 | 95.0 | 83.0 | 100.0 | 0.054* |
| Southern Harbour | 25 | 87.7 | 100.0 | 93.0 | 100.0 | |
| South Eastern | 55 | 86.0 | 99.0 | 89.5 | 100.0 | |
| Western | 23 | 77.3 | 91.0 | 68.5 | 99.5 | |
| Northern | 27 | 95.5 | 100.0 | 98.0 | 100.0 | |
| **Overall** | **155** | **87.7** | **99.0** | **86.0** | **100.0** | |

*Kruskal-Wallis Test

† Mann-Whitney U Test

**Table 8** Distribution and univariate analyses between the sociodemographic variables and the proportion of deep enough compressions

| | Deep enough compressions (%) | | | | | |
|---|---|---|---|---|---|---|
| **Age Groups** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| <25 | 24 | 26.3 | 0.0 | 0.0 | 48.3 | 0.219* |
| 25-34 | 27 | 22.9 | 0.0 | 0.0 | 24.5 | |
| 35-44 | 29 | 31.7 | 4.0 | 0.0 | 66.0 | |
| 45-54 | 21 | 26.1 | 1.0 | 0.0 | 44.0 | |
| 55-64 | 24 | 12.3 | 0.0 | 0.0 | 5.8 | |
| 65+ | 30 | 8.7 | 0.0 | 0.0 | 3.0 | |
| **Gender** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| Male | 70 | 30.6 | 0.5 | 0.0 | 68.8 | 0.037† |
| Female | 85 | 13.3 | 0.0 | 0.0 | 8.0 | |
| **Education** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| Primary/Secondary | 77 | 14.1 | 0.0 | 0.0 | 6.0 | 0.016† |
| Tertiary | 78 | 28.1 | 1.5 | 0.0 | 56.8 | |
| **District of Residence** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| Northern Harbour | 25 | 1.3 | 0.0 | 0.0 | 0.0 | 0.004* |
| Southern Harbour | 25 | 8.8 | 0.0 | 0.0 | 1.0 | |
| South Eastern | 55 | 27.8 | 0.0 | 0.0 | 62.5 | |
| Western | 23 | 31.3 | 13.0 | 0.0 | 56.0 | |
| Northern | 27 | 28.6 | 2.0 | 0.0 | 47.5 | |
| **Overall** | **155** | **21.1** | **0.0** | **0.0** | **24.5** | |

*Kruskal-Wallis Test
† Mann-Whitney U Test

**Table 9** Distribution and univariate analyses between the sociodemographic variables and the mean depth of compressions (mm)

| | Mean depth (mm) | | | | | |
|---|---|---|---|---|---|---|
| **Age Groups** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| <25 | 24 | 40.3 | 40.5 | 33.3 | 49.3 | 0.514* |
| 25-34 | 27 | 42.0 | 40.0 | 36.0 | 46.0 | |
| 35-44 | 29 | 43.4 | 42.0 | 37.0 | 51.0 | |
| 45-54 | 21 | 42.6 | 43.0 | 35.0 | 49.0 | |
| 55-64 | 24 | 38.2 | 34.0 | 32.0 | 45.3 | |
| 65+ | 30 | 34.0 | 33.0 | 29.0 | 41.3 | |
| **Gender** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| Male | 70 | 41.6 | 42.0 | 32.0 | 50.8 | 0.920† |
| Female | 85 | 38.6 | 39.0 | 32.0 | 45.0 | |
| **Education** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| Primary/Secondary | 77 | 38.1 | 37.0 | 32.0 | 45.0 | 0.004† |
| Tertiary | 78 | 41.8 | 42.0 | 34.3 | 49.8 | |
| **District of Residence** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| Northern Harbour | 25 | 33.0 | 32.0 | 29.0 | 37.0 | 0.269* |
| Southern Harbour | 25 | 34.0 | 32.0 | 28.0 | 42.0 | |
| South Eastern | 55 | 42.4 | 41.0 | 35.0 | 50.0 | |
| Western | 23 | 44.4 | 46.0 | 37.0 | 50.0 | |
| Northern | 27 | 43.1 | 44.0 | 36.5 | 49.5 | |
| **Overall** | **155** | **40.0** | **39.0** | **32.0** | **46.5** | |

* Analysis of Variance
† Independent-samples t-test

**Table 10** Distribution and univariate analyses between the sociodemographic variables and the mean rate of compressions (per minute)

| | Mean rate (per minute) | | | | | |
|---|---|---|---|---|---|---|
| **Age Groups** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| <25 | 24 | 115.9 | 113.5 | 102.0 | 121.8 | 0.514* |
| 25-34 | 27 | 106.3 | 110.0 | 101.5 | 115.0 | |
| 35-44 | 29 | 115.4 | 107.0 | 98.0 | 123.0 | |
| 45-54 | 21 | 103.5 | 105.0 | 93.0 | 115.0 | |
| 55-64 | 24 | 106.8 | 107.0 | 98.0 | 116.3 | |
| 65+ | 30 | 108.6 | 108.0 | 102.0 | 110.8 | |
| **Gender** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| Male | 70 | 110.3 | 109.0 | 99.0 | 119.0 | 0.920† |
| Female | 85 | 109.1 | 110.0 | 99.0 | 117.0 | |
| **Education** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| Primary/Secondary | 77 | 105.2 | 105.0 | 95.0 | 116.0 | 0.004† |
| Tertiary | 78 | 114.0 | 110.0 | 104.3 | 119.0 | |
| **District of Residence** | **Frequency** | **Mean** | **Median** | **1st Quartile** | **3rd Quartile** | ***p* value** |
| Northern Harbour | 25 | 111.4 | 109.0 | 105.0 | 123.0 | 0.269* |
| Southern Harbour | 25 | 109.7 | 110.0 | 103.0 | 117.0 | |
| South Eastern | 55 | 110.2 | 109.0 | 98.0 | 116.0 | |
| Western | 23 | 114.4 | 113.0 | 103.0 | 127.0 | |
| Northern | 27 | 102.7 | 105.0 | 91.5 | 115.0 | |
| **Overall** | **155** | **109.6** | **109.0** | **99.0** | **119.0** | |

*Kruskal-Wallis Test

† Mann-Whitney U Test

## Discussion

The decision to use compression-only CPR instructions on lay people rather than the standard compressions with ventilations, was based on evidence from randomized controlled trials.[33-34] In a systematic review and meta-analysis by Cabrini *et al.,* (2010), it was shown that compression-only CPR is superior to standard CPR at least when performed by untrained bystanders.[34] Other observational studies of bystander-initiated CPR comparing standard and compressions-only CPR reported similar survival rates.[35-37] Apart from survival rates, compression-only CPR instructions are easier to teach to lay persons during BLS courses and easily communicated by dispatchers under real conditions during TCPR.[20,34] Moreover, bystanders are more likely to accept and perform compressions-only CPR rather than standard CPR, since this avoids mouth-to-mouth contact.[19-20]

The choice of words used during TCPR has been shown to be important in order to engage with the caller. Phrases like:

*"Irridu nibdew CPR"*

*(we need to start CPR)*

Has been associated with higher caller agreement. According to *Riou et al.,* (2018), talking about bystander-CPR in terms of willingness *("want", "be willing", "would like",*

*"be happy to")* was associated with low caller agreement (43%).[38] On the other hand, talking about it in terms of futurity *("going to", "will")* and/or obligation *("need", "have to")* was associated with high caller agreement (97% and 84% respectively).[38]

In this study, we showed that the phrases used for hand positioning during CPR:

*"Poggi il-pala ta' jdejk fin-nofs tas-sider"*

*(Put your hand on the centre of their chest)*

Was understood and executed accurately by approximately 7 out of 10 rescuers with no previous background of CPR training. No statistical significance between age, gender, level of education and district of residence was found vis a vis correct hand positioning in our study. With regards to phrases about locking of fingers and elbow positioning:

*"Poggi il-pala l'ohra fuq idejk u orbot subajk flimkien"*

*(Put your other hand on top of that hand and clasp your fingers together)*

and

*"Żomm minkbejk dritti"*

*(Keep your elbows straight)*

This study found that all participants understood and executed these instructions accurately. Similarly, phrases about the rate of compressions:

*"ibda għafas u għodd miegħi...1,2,3,4....Ibqa sejjer/sejra hekk. Tieqafx mhux ha taghmel hsara!"*

*(Keep pushing and count out loud…1,2,3,4…keep going, do not pause, you won't cause any harm)*

Was understood and accurately executed in 6 out of 10 rescuers adhering to the recommended 100-120/min compression rate. No statistical significance between age, gender and district of residence was found on rate of compressions. We opted not to use metronomes to help rescuers with their compression rate but counting repeatedly with them from 1 to 4 throughout the whole minute of CPR. In two separate studies, Park *et al.,* (2013) and Scott *et al.,* (2018), showed that rescuers receiving instructions with metronome assistance although performing better with correct compression rate had consistently shallower compression depth than those receiving instructions without metronome assistance.[39-40]

When it came to phrases about depth:

*"għafas l-isfel b'kemm għandek saħħa"*

*(Push down as hard as you can)*

Only 2 out of 10 rescuers achieved the recommended 50-60mm depth, and the vast majority of participants achieved a depth less than 50mm. Overall males performed deeper compressions when compared to females, whilst rescuers with tertiary education and those living in the western district (Siġġiewi and *Ż*ebbug) had a significantly higher compression depth when compared to the rest. No statistical significance was found between age and depth of compressions. It is well documented in the literature that even with correct knowledge and feedback, rescuers often do not achieve adequate depth.[41-43] Moreover, physical fatigue,[44-45] overall rescuer's physical fitness, height and weight [46-47] all impact on the quality of depth of chest compressions. These variables might partly explain our findings that males were better than females at deeper compressions. The amount of power required to depress a sternum by 5 cm is about 500 N,[48] and it can be difficult to judge how much force is required to achieve 5cm of compression even for trained

professionals. Data from two RCTs by Mirza *et al.,* (2008), suggest that instructions to "push down as hard as you can" ("*għafas l-isfel b'kemm għandek saħħa")* are superior to instructions to "push down firmly 2 inches (50mm)" in achieving improvement in chest compression depth.[49]

## Limitations

Manikin simulation cannot replicate the complexity, urgency and constraints of a real life scenario. Although participants were taken from the five main districts of Malta, the sample size was still small and Gożo, a separate district, was not included in this study. CPR efficiency by rescuers was not tested in this study since the main aim was to test understanding and execution of TCPR instructions in Maltese.

## Conclusion

This study showed that, in Malta, laypeople with no previous CPR training can understand and execute a set of chest compression-only TCPR instructions in Maltese. The introduction of a standard operating procedure and training of EMDs on policy, expectations and performance is vital if bystander CPR and survival rates are to improve locally. Training coupled with quality improvement projects such as call collection for review, analysis and feedback is the way forward.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ORIGINAL ARTICLE

# Dry needling reduces pain in Sanglah General Hospital Denpasar workers with myofascial pain syndrome in the upper trapezius muscle

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## BACKGROUND

Myalgia is a common complaint in the general population, but it is underappreciated and often undertreated. Myofascial pain syndrome is a form of myalgia that is characterized by local regions of muscle hardness. The main components of this syndrome are the trigger points that are composed of taut bands. Various invasive and non-invasive procedures are available to inactivate myofascial trigger points. Dry needling involves inserting a filiform needle directly into a trigger point without injection of material. Dry needling is a treatment modality that is minimally invasive, cheap, easy to learn, and carries a low risk for reducing pain.

## OBJECTIVE

The aim of this study was to test the hypothesis that dry needling could reduce pain in subjects with myofascial pain syndrome in the upper trapezius muscle on Sanglah Hospital's workers.

## METHOD

Twenty-six subjects with myofascial pain syndrome in the upper trapezius muscle were randomly divided into two groups: 13 subjects in the control group received acetaminophen, and 13 subjects in the dry needling group received dry needling and acetaminophen. The numeric rating scale was assessed before, 1 hour, 24 hours, and 7 days after the treatment. Side effects of dry needling were evaluated every day for 7 days follow-up. The total amount of acetaminophen was assessed at last day follow up.

## RESULTS

At baseline, the numeric rating scale was same in control versus dry needling group. Reduction in all numeric rating scale at 1 hour, 24 hours, and 7 days after dry needling was significant ($p$<0.05).

## CONCLUSION

Dry needling could reduce pain and oral analgesic consumption in subjects with myofascial pain syndrome in the upper trapezius muscle. There were no side effects of dry needling reported on this study.

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## BACKGROUND

Myalgia is a common widespread problem, but is often ignored and therapy,when applied is often inadequate. Myofascial Pain Syndrome (MPS) is a form of myalgia with local muscle stiffness. The main component in MPS is the presence of trigger points that cause pain and the appearance of band links. In addition to medical therapy, MPS therapy is focused on inactivating trigger points. Inactivation of trigger points can be in the form of non-invasive mechanical stimulation and invasive actions. Dry needling (DN) is one way to inactivate trigger points. DN is an invasive procedure using filiform needles without using drugs.[1-7]

MPS often causes acute and chronic muscle pain with diverse manifestations such as tension-type headache, shoulder pain, low back pain, and other symptoms. Pain in MPS is usually blunt and difficult to localize.[1-2]

Trigger points are hyper-irritative points within the band link of skeletal muscle fibers, that produce local ischemia and hypoxia with central and peripheral sensitization. There are two types of trigger points, active trigger points that cause pain even though the muscles are resting and latent trigger points which are not spontaneous triggers of pain.[2-3,6]

Epidemiological studies of MPS are still difficult because there is no consensus which regulates the diagnostic criteria of this syndrome by default. The highest prevalence of musculoskeletal pain in the neck area in workers is 60-76% with the highest intensity of 77.3% occurring in the upper trapezius muscle. This is due to the high involvement of the hands (e.g. typing, raising arms, transporting goods), thus increasing muscle demands in the surrounding anatomical area. In Indonesia, MPS is more prevalent in women at 58.8%, work as employees ranks highest at 41.2%, with the highest average age of 20-40 years.[4,9-11]

The mechanism for the formation of band links is due to muscle trauma as a result of excessive use. This triggers the production and release of acetylcholine from the motor terminal of the neuron, even at rest. Persistent release of acetylcholine generates postjunctional membrane depolarization of muscle fibers. Increased muscle work and demand maintains the muscle in a prolonged contraction state. This in turn may compromise the vascular supply of oxygen and nutrients due to a compression effect. This condition, when inadequately treated will lead to hypoxia and subsequent impairment of the calcium channel pump responsible for returning calcium ion into the sarcoplasmic reticulum.

This mechanism then continually triggers both the release of Calcium and causes its inadequate intake from the sarcoplasmic reticulum. This results in shortening of the sarcomere. If this phenomenon is prolonged, muscle tissue hypoxia will occur followed by the release of vasoactive and allogeneic substances such as CGRP, Substance P, bradykinin, cytokines, and protons. Local pain, peripheral and central sensitization will occur as a consequence of the release of these substances. This cycle will continue if not corrected.[1,2,12-15]

The principle of managing MPS is to deactivate trigger points and maintain normal body biomechanics. Therapy modalities focus on trigger points, both through pharmacological and non-pharmacological therapy aimed at reducing inflammation and sensitization which are the sources of the onset of pain. Giving analgesics can reduce pain significantly, but does not restore function. Trigger point

manipulation is needed. This can be in the form of both invasive and non-invasive action. Examples of the latter are massage, electrical stimulation, and magnetic therapy. Invasive therapy is often done as an injection of local trigger points with certain substances; it can also be done using DN. [2-4,6,7]

DN is an attempt to activate trigger points using thin filiform needles to penetrate the skin and stimulate the areas that underlie the trigger points, viz., muscles, and connective tissue. It is done for the management of pain and the disruption of muscle spasm. Other advantages of DN are that it is cheap and easy to carry out with minimal side effects.

## METHODS

This study used an experimental pre-test and post-test control group design with research subjects divided into two groups, namely the treatment group (analgesic and DN) and the control group (analgesic). The study was conducted on workers in the Sanglah General Hospital in Denpasar from September to October 2018. This study was declared ethically feasible by the Research Ethics Commission of the Faculty of Medicine, Udayana University/Sanglah Hospital Denpasar with no: 1602/UN14.2.2/PD/KEP/2018

The inclusion criteria in this study were workers aged 20-50 years who experienced pain in the upper trapezius muscle with a numeric rating scale (NRS) ≥ 4 together with trigger points located on examination in the upper trapezius muscle. The subjects were cooperative and willing to be included in the study and signed a document confirming informed consent. Exclusion criteria in this study were subjects with a history of immunodeficiency (malignancy, HIV infection, and diabetes mellitus), a history of blood clotting disorders, the use of drugs that interfere with blood hemostasis, infection and insertion wounds, needle phobia, allergy to acetaminophen and the ingestion of analgesics and muscle relaxants in the previous 24 hours. Subjects who met the eligibility criteria were divided into two groups using a coin toss as a simple randomization technique. The drop out criteria in this study were subjects who did not collect the questionnaires, consumed analgesics other than acetaminophen and muscle relaxants during the observation period, underwent non-invasive and other invasive therapies, together with those who were unwilling to continue therapy.

Calculation of sample size used the Pocock formula with an alpha of 0.05 obtained by the 18 total samples needed. To avoid a dropout of 15%, a sample size of at least 22 subjects was necessary.

Trigger points were obtained by palpation of the upper trapezius muscle and the location of a band link and pain response from the subject. DN procedures were carried out by one person who was competent in carrying them out. This study used a Huanqiu brand needle with a diameter of 0.25 mm and a length of 40 mm, the needle was inserted into the trigger point of the upper trapezius muscle until a local twitch response appeared. It was then withdrawn when there were no more visible twitch responses from the muscle. The procedure was repeated on any other existing trigger points. The DN procedure was stopped when there was a reduction in the frequency of appearance of a local twitch response and reduced resistance on palpation. The DN procedure was only performed once, i.e. at the beginning of the study period for each patient. Subjects in both groups were given an analgesic (1g of acetaminophen) at the start of

the procedure and were then were allowed to take it again with a maximum dose of 4 grams/day. The pain scale was assessed using NRS. NRS is a pain measuring system using numbers 0-10. NRS was assessed before DN was performed, then reassessed 1 hour, 24 hours, and 7 days after the DN. Subjects were followed for 7 days and during the observation period were evaluated for the presence of DN side effects in the form of bruising, swelling and bleeding, together with an assessment of the use of acetaminophen. If during the observation period, the subjects consumed other analgesics and muscle relaxants, underwent other non-invasive or invasive therapies, or refused to continue therapy, they were excluded from the study.

Data was analyzed using SPSS version 20.0. Descriptive data analysis was performed to study the distribution of age, gender, type of work, and initial NRS value. Normality test was based on numerical data using the Shapiro-Wilk test. Comparison of the mean reduction in NRS values before and after treatment in both groups was done using the ANOVA test if the data was spread normally or the Mann-Whitney test if the data was spread abnormally with a significance level of $p<0.05$. If drop out >15%, the intention to treat analysis was done.

## Results

There were 26 subjects who met the eligibility criteria in this study. The subjects of the study were randomized by simple randomization and divided into 13 subjects as the treatment group (acetaminophen and DN therapy) and 13 subjects as the control group (acetaminophen therapy). The basic criteria of the research subject and statistical analysis in the form of age, sex, and type of work are presented in table 1. Statistically, no variable results were found for age, sex, and type of work.

The effect of acetaminophen and DN administration on NRS improvement in labor in Sanglah Hospital Denpasar was assessed by comparing the difference in NRS reduction between the control group and the treatment group at 1 hour, 24 hours, and 7 days after treatment. The normality test of NRS reduction difference data using the Shapiro Wilk test showed that the distribution of data was not normal, the hypothesis test used was the Mann-Whitney test, the level of significance was measured by the value $p<0.05$. The difference in NRS at 1 hour, 24 hours, and 7 days was found to be statistically significant. The analysis results are presented in table 2.

There were significant differences in the total and duration of analgesic use during the 7-day observation period in both groups. The results of the total analysis and duration of analgesic use are presented in table 3.

In the treatment group, evaluation of DN side effects, viz., bruising, swelling and bleeding was carried out over a 7-day period. No side effects were found in any subject in the treatment group.

**Table 1** Basic characteristics

| Variables | Treatment (*n*=13) | Control (*n*=13) | *P* |
|---|---|---|---|
| Age (year) | 48 (23-50) | 35 (23-50) | 0.054 |
| Sex | | | |
| Men | 5 (38.5%) | 4 (30.8%) | 0.500 |
| Women | 8 (61.5%) | 9 (69.2%) | |
| Occupation | | | |
| Nurse | 6 (46.2%) | 4 (30.8%) | |
| Student | 4 (30.8%) | 6 (46.2%) | 0.670 |
| Others | 3 (23.1%) | 3 (23.1%) | |

**Table 2** Analysis of NRS reduction differences at 1 hour, 24 hours, and 7 days after treatment

| | **Treatment (*n*=13)** | **Control (*n*=13)** | ***P*** |
|---|---|---|---|
| 1 hour | 2 (0-4) | 0 (0-1) | 0.003* |
| 24 hour | 3 (0-5) | 1 (0-4) | 0.014* |
| 7 days | 4 (3-7) | 3 (1-7) | 0.001* |

*statistically significant

**Table 3** Total and duration of analgesic use

| | Treatment (*n*=13) | Control (*n*=13) | *P* |
|---|---|---|---|
| Total analgesic (gram) | 2 (0-3) | 4 (1.5-21) | 0.008* |
| Duration (days) | 2 (0-5) | 5 (2-7) | 0.004* |

*statistically significant

## Discussion

The median age of this study is 48 (23-50) in the treatment group and 35 (23-50) in the control group. This result is not much different from the study conducted by Tsai et al. who quote an average age of 41.5±10.4 in the control group and 46.4±12.2 in the treatment group. [17] Research conducted by Tekin et al (2013) also found similar results regarding the mean ages of that study's participants; these were 42±12 and 42.9±10.9 years in the control and treatment groups, respectively.[18] Research conducted by Cerezo-Tellez et al. obtained a mean age of 46±16.2 in the control group and 40.1±13.1 in the treatment group.[19] This result is in accordance with previous studies which stated that the productive age range contains the highest percentage of those who experience MPS. This is due to individuals who are more active in using their muscles being in the productive age.

Based on the gender category, this study contains 17 female subjects and 9 male subjects. This is similar to the research conducted by Gerber et al (2015) who quotes 10 female subjects more than male subjects.[20]

Research conducted by Tekin et al (2013) with a total sample of 39 subjects also quotes 31 more female than male subjects.[18] Research conducted by Tsai et al (2010) also found that there were 21 more female than male subjects.[17] The results of this study support the view that women make more use their hands and shoulders in doing work and have lower pain thresholds when compared to men.

The subjects of this study were 10 nurses, 10 students, and 6 employees in other occupations (3 cleaning service employees, 2 administrative employees, 1 nutrition officer). Until this study there have been no studies that specify the types of work carried out by the subjects. Research conducted by Cerezo-Tellez et al. looking at the prevalence of MPS, divided occupations based on job characteristics. Their results showed that most MPS sufferers were subjects who worked by hand and often raised their hands higher than their shoulders by 76.6 %, followed by 72.3% of subjects who did repetitive work.[9] Research conducted by Meulemeester et al. also states that someone with long repetitive and static work such as employees who work at a computer can trigger MPS.[21] This is caused by a motor unit that works excessively and causes changes in muscle morphology, muscle pain, and fatigue.

The effect of DN administration on NRS improvement was assessed by comparing the median difference in NRS reduction between the control and treatment groups at 1 hour, 24 hours, and 7 days after treatment. In this study, the effectiveness of DN addition to NRS reduction was statistically significant ($p$<0.05) compared to the use of acetaminophen alone at 1 hour, 24 hours, and 7 days after treatment. A similar study carried out by Tsai et al. compared NRS decrease before and immediately after DN and obtained significant results.[17] Abbaszadeh-Amirdehi et al. also conducted a similar study and obtained significantly different results when compared to the control group (subjects without MPS).[22] Gerber et al. assessed the scale of pain using VAS before DN performed 3 times in 3 weeks in subjects with bilateral or unilateral upper trapezius chronic MPS. There was a significant decrease in VAS ($p$<0.01) after 3 weeks both in subjects with bilateral and unilateral MPS. [20] Longer observations were carried out by Cerezo-Tellez et al. by assessing VAS at 30 and 45 days after DN with results that were significant in both observations ($p$<0.01) compared to the control group (which only underwent muscle stretching therapy.[19]

During the observation period, there were no subjects in the treatment group who reported any side effects of DN actions in the form of bruising, swelling and bleeding. Very little data was obtained regarding the side effects of DN actions in similar studies. Research conducted by Martin-Pintado-Zugasti et al. reported a side effect of bleeding in 4 of the total 26 subjects studied. The absence of side effects in this study was due to the fact that the operators who carried out DN actions were properly trained and competent in their field.[23] This proves that DN is a minimally invasive procedure that is easy to perform and has minimal side effects.

The total amount and duration of use of analgesic drugs (acetaminophen) during the 7-day observation period were found to be statistically significant ($p$<0.05). Until now, researchers have not found any studies that directly compare the addition of DN with the use of analgesic drugs. The results of this study support that DN actions can reduce the total and duration of analgesic use.

## Conclusion

The results of this study prove that DN is effective in reducing the scale of pain in upper trapezius muscle MPS; these results are consistent with previous similar studies. The analgesic effect caused by DN is related to the modulation of central and peripheral pain. This includes segmental inhibition and release of biochemical cascades such as endogenous opioids. In addition, this study also shows that DN can reduce the use of analgesic drugs in upper trapezius muscle MPS without significant side effects.

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ORIGINAL ARTICLE

# A prospective audit of requests for CT Pulmonary Angiography (CTPA) in haemodynamically stable non-pregnant medical patients with suspected PE

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## Introduction

Pulmonary embolism (PE) is a common and occasionally fatal disease, therefore investigation must be targeted and accurate. Unnecessary investigation presents an increased risk of harm to the patient. On occasion, CT Pulmonary Angiography (CTPA) is not requested according to established guidelines.

## Aim

This study aimed to address the criteria by which CTPAs were being requested. Approval was obtained from data protection and ethics committees. Anonymous data was collected from hospital software and patients' case notes between Aug-Sept 2017.

## Methods

106 patients were recruited. Hospital notes were examined for demographics, reason for presentation, documentation of pre-test probability (PTP) testing, arterial blood gases (ABGs), electrocardiogram (ECG), indication for CTPA, and any complications. Hospital software provided data on blood investigations including D-dimer, CXR, time of CTPA order, and department ordering CTPA.

## Results

Dyspnoea, followed by a raised D-dimer, was the most common trigger for ordering CTPA (45.3%). A large majority (60.4%) of patients undergoing CTPA did not have ABGs taken. One fifth (21.7%) of CTPAs were positive. A PTP score was only documented in 10.4% of patients and was equally divided between Wells and Geneva scores. The Wells score was retrospectively calculated, with only 9.4% having a score >4 indicating likely PE. 1 patient had anaphylaxis to contrast and 5 developed contrast-induced nephropathy.

## Conclusions

A basis for requesting a CTPA needs to be established, utilising the well-validated Wells Score, and D-dimer where indicated. A suspicion of PE should trigger a request for an ABG. CTPA is not without morbidity, and therefore should only be requested according to evidence-base.

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## Introduction

Pulmonary embolism (PE) is a common and occasionally fatal disease, therefore investigation must be targeted and accurate. It can manifest in a variety of ways, ranging from no symptoms or seemingly innocuous ones, to sudden death. The gold standard for investigation of PE is CT Pulmonary Angiogram (CTPA), albeit this is not without its risks, namely radiation exposure, risk of contrast nephropathy and anaphylaxis. Hence, unnecessary investigation presents an increased risk of harm to the patient. On occasion, CTPAs are requested arbitrarily rather than according to established guidelines.

A high clinical suspicion is required to diagnose PE. Furthermore, effective scoring systems and algorithms have been developed to help guide physicians along the most appropriate management path. Once recognised, PE remains a highly treatable condition.

## Aims

This study aimed to address the criteria by which CTPAs were being requested by medical or emergency doctors in a local hospital, and whether these were in accordance with the European Society of Cardiology (ESC) guidelines.[1] The primary aim of the audit was to assess whether CTPAs were being ordered appropriately. Secondary aims included whether scoring systems to stratify risk of PE were being used (Geneva or Wells Scores), whether supplementary investigations such as electrocardiogram (ECG), chest x-ray (CXR), arterial blood gases (ABGs) and D-Dimer were being requested and to identify any CTPA-related complications.

## Methodology

### *Patient Population*

All patients admitted from the Emergency Department to the Medical Department who underwent CTPA, within a 5-week period (between August and September 2017), were recruited prospectively, bringing the total to 106 subjects.

### *Questionnaire Design*

An extensive literature review was carried out, so as to create a template by which data would be scrutinised. Criteria which should be met for every patient suspected of having PE were documented in a tick-the-box fashion. Pre-test probability testing was given its due importance in the questionnaire, as was the D-dimer result. The performing department was clearly documented, together with demographic data on each patient.

### *Data Collection*

Approval was obtained from the data protection and University of Malta Research Ethics Committee. Data was collected prospectively from hospital software and case notes. Case notes were examined for demographics, reason for presentation, patient assessment, documentation of pre-test probability (PTP) testing, ABGs, ECG, indication for CTPA, any complications, and further management. Hospital software provided data on blood investigations including serum chemistries, troponin, D-dimer and pro-BNP; CXR; time of CTPA order; and department ordering CTPA.

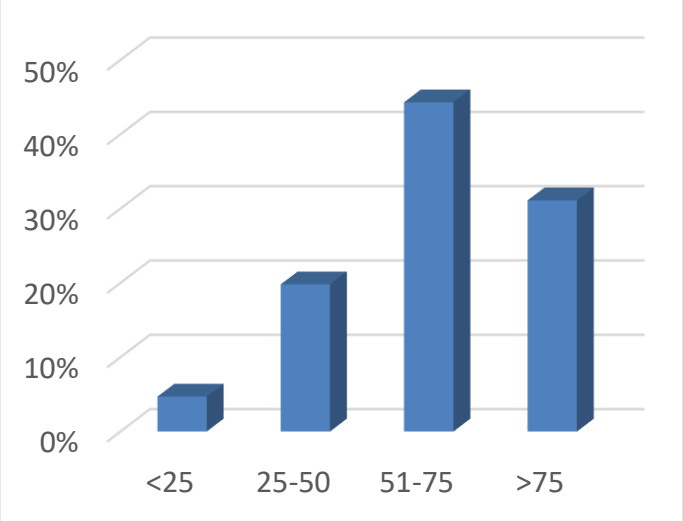
## Results

### *Demographics*

106 patients were recruited, of which 60.4% were female. A good proportion were over 50

years of age (*Figure 1*). The mean age of the study population was 63.8 years, with a median age of 68 years.

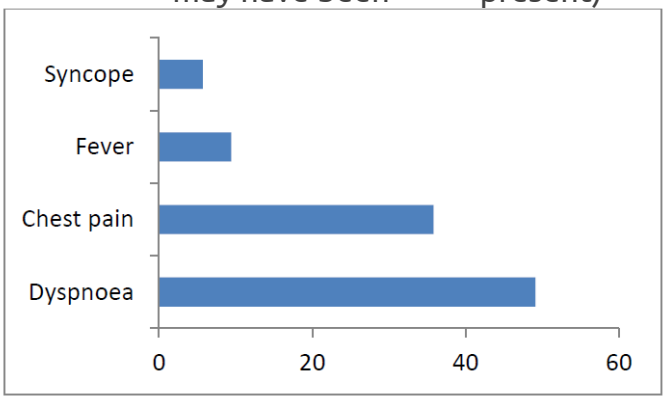
**Figure 1** Percentage distribution of age groups of subject population




### *Presentation to Accident & Emergency (A+E)*

Dyspnoea was the most common reason for presentation to A+E, being present in almost half (49.1%) of patients (*Figure 2*). Other reasons for presentation to hospital included cough, lethargy, palpitations and lower limb swelling.

**Figure 2** Presenting symptoms of subjects undergoing CTPA (>1 symptom may have been present)




### *Performing department and overview of CTPA outcome*

The CTPA scans taken into consideration were all those requested from A+E or medical specialities. *Figure 3* shows that the majority were requested by the A+E department. Just over a fifth (21.7%) of CTPAs were positive for PE. Analysis of CTPA results requested by the individual department revealed that just under a third (29.0%) of scans ordered from A+E were positive, while only over one tenth (11.4%) ordered from the medical wards were positive (*Figure 4*).

**Figure 3** Department requesting CTPA

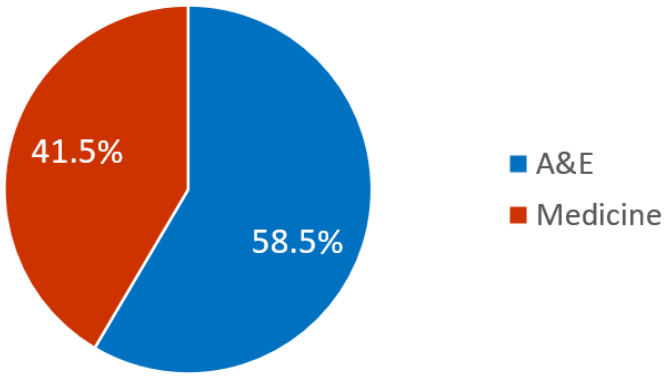
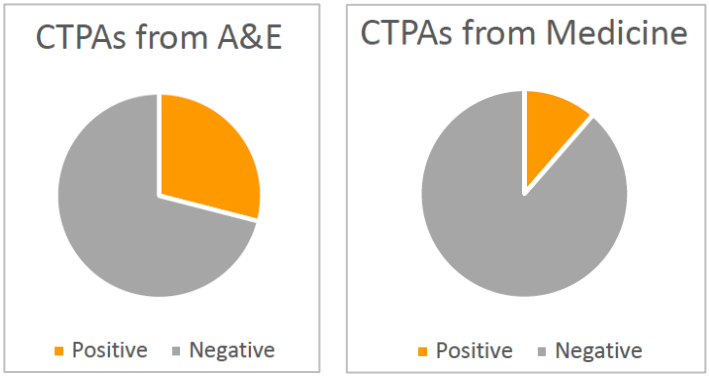



**Figure 4** Proportion of CTPAs positive for PE by requesting department



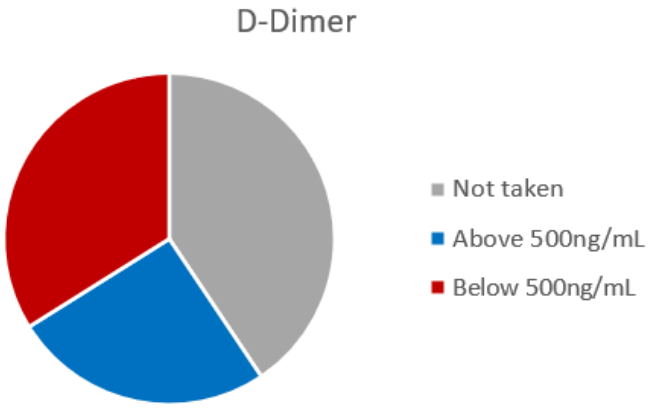
### *CTPA – date, timing and primary indication*

The majority of patients had 2 or more symptoms that raised the suspicion for PE. The most common primary indication for CTPA was tachypnoea or sudden onset dyspnoea, present in almost two thirds (62.3%) of patients. Raised D-dimer was the second most common indication for CTPA, present in just under half of patients (45.3%). In a third (33.0%) the primary indication was pleuritic chest pain while 19.8% of patients demonstrated oxygen desaturation. Haemoptysis was an indication in only 3.8% of patients. Other reasons for performing CTPA included tachycardia, syncope and new RBBB.

### *Serum investigations*

Complete blood count was measured in all subjects, and renal function in 99%. D-Dimer was considered in only 59.4% of patients. The cut-off for a normal D-Dimer was taken to be 500ng/mL. It was elevated in 42.9% of patients in whom it was checked, implying that a good majority of those undergoing CTPA had a normal D-Dimer. Furthermore, 43.5% of patients with confirmed PE did not have a D-Dimer taken (*Figure 5*).

**Figure 5** Proportion of those undergoing CTPA having a raised D-dimer, normal D-dimer, or not having had a D-dimer taken.




Of those subjects with an elevated D-Dimer, 40.7% were found to have a PE on CTPA. A positive CTPA was reported in only 5.6% of subjects with a normal D-Dimer, applauding the sensitivity of D-Dimer.

ABG analysis was found to be grossly underutilised in the study population, being drawn in only 39.6%. The majority (83.3%) were found to have resting hypoxaemia (PaO2 <80mmHg). The correlation of hypoxic patients also having a confirmed PE was of 76.9%. This is to be expected as PE tends to cause Type 1 Respiratory Failure.

### *ECG*

The most frequently encountered ECG changes in patients with PE are tachycardia, non-specific ST and T waves changes, right heart strain and right bundle branch block (RBBB).

Every patient in the study had an ECG taken during the in-patient stay, and this was normal in half of subjects (50.9%). Sinus tachycardia was the most common abnormality, present in 21.7%, while a bundle branch block was evident in 7.5%. Other ECG changes included ST changes, atrial fibrillation and heart strain pattern.

### *CXR*

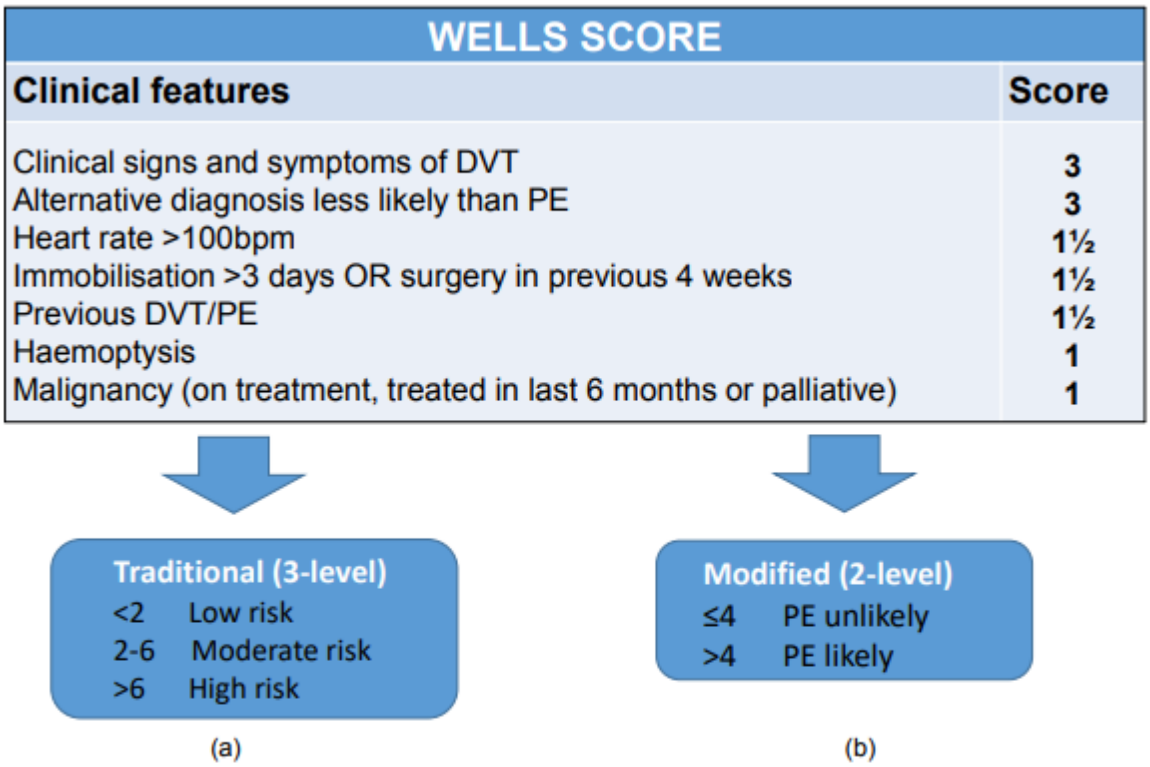
Every subject recruited in the study underwent a chest x-ray. The large majority (70.8%) were normal, while a small proportion revealed consolidation (7.5%), pleural effusion (6.6%) or pulmonary venous congestion (5.7%). Other changes included lung metastases, pleural plaques and interstitial lung disease.

### *Scoring system*

The Wells [2-3] and Geneva[4] scores are the two most widely accepted scoring systems for PE. The modified (2-tier) Wells Score was selected for this audit (*Figure 6*). A score was only documented in 10.4% of patients. Of these, the Wells score was documented in 54.5%, and the Geneva score in 45.5%.

The data collectors retrospectively calculated a Wells Score on each individual in the study. The score was agreed upon by 2 data collectors separately. The majority of patients (34%) had a Wells score of zero (*Table 1*).

**Figure 6** Traditional vs Modified Wells Score




*(a) Traditional 3-level Wells' score stratification for risk of PE*
*(b) Modified 2-level Wells' score stratification system utilised in this study*

According to the ESC Guidelines[1], a Wells Score of ≤4 implies that PE is unlikely and therefore a D-dimer should be taken. 90.6% of the study population had a Wells Score of ≤4. Of these, just under a quarter (22.6%) had a positive D-dimer and therefore correctly underwent CTPA, with a pick-up rate for PE of 41.7%. In the sub-group where PE was unlikely (Wells ≤4) and a D-dimer of <500ng/ml which excludes PE, unfortunately all 36 patients nonetheless underwent CTPA, of which only 2 CTPAs were positive. Another third (34%) of patients in the 'unlikely PE' subgroup did not have D-dimer levels checked. In the small proportion of patients (9.4%) where PE was likely (Wells Score >4), 40% had a positive CTPA (*Figure 7*).

### *Outcome of CTPA*

More than a fifth (21.7%) of CTPA scans were positive for PE. A number of patients had more

than one embolus. The vast majority were segmental (52.2%) while a sub-segmental PE was present in 21.7%. In 30.4% a main artery was involved while in 47.8% it was the interlobar artery which contained thrombus. Bilateral PE was present in 8.7%.

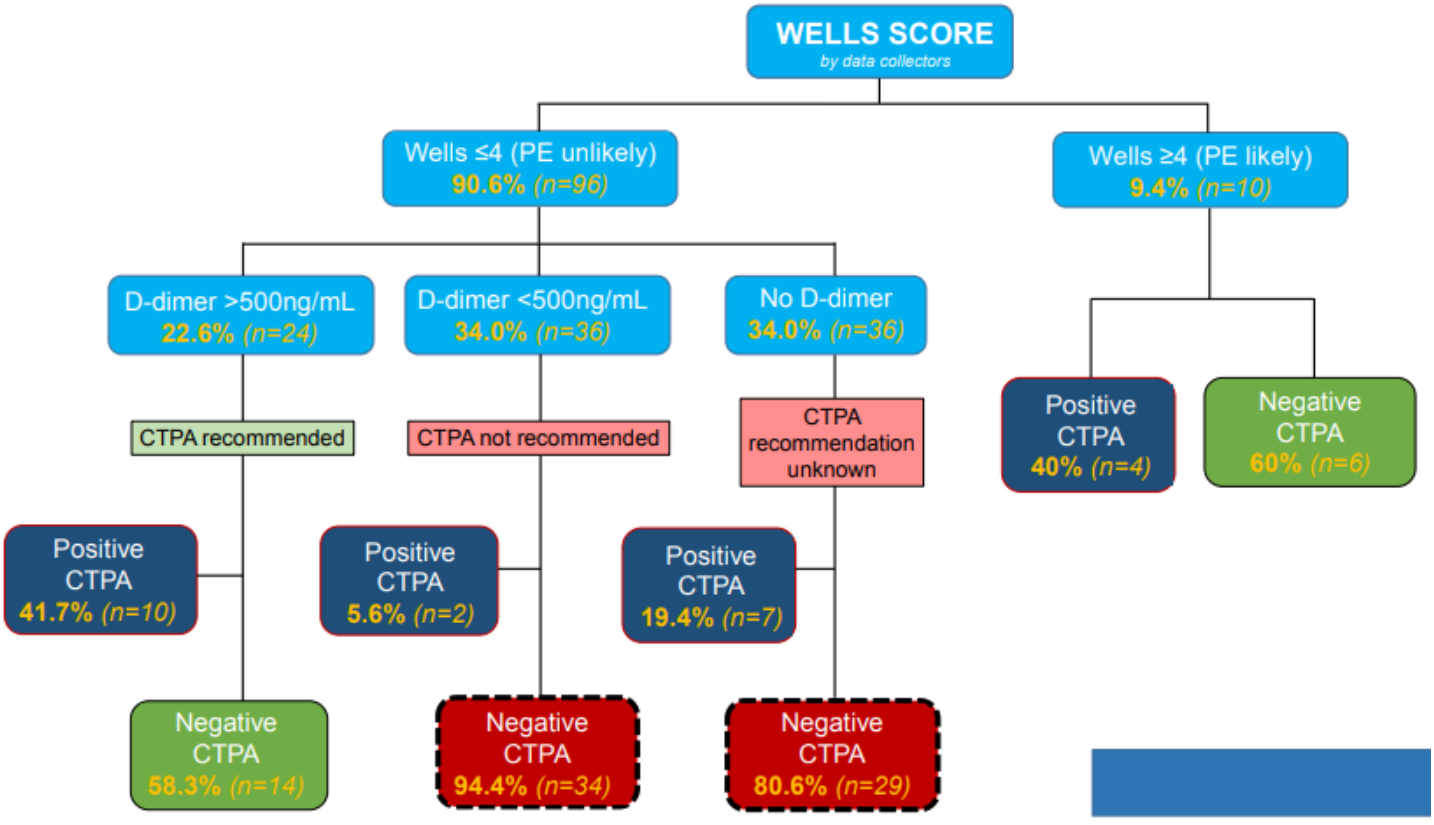
32.1% of the patient population were unnecessarily exposed to ionizing radiation from a CTPA which was not indicated according to the ESC guidelines, while another 27.4% were possibly unnecessarily exposed, as the D-dimer was not checked.

One patient suffered contrast-induced anaphylaxis as a major complication from CTPA. A deterioration in eGFR was noted in 5 patients (4.7%). All-cause mortality was 10.4% during the study period.

**Table 1** Distribution of Wells score (as calculated by the investigators)

| Wells Score | Percentage of subjects |
|---|---|
| 0 | 34 |
| 1 | 10.4 |
| 1.5 | 20.8 |
| 2.5 | 7.5 |
| 3 | 13.2 |
| 3.5 | 0.9 |
| 4 | 3.8 |
| 4.5 | 1.9 |
| 5.5 | 2.8 |
| 6 | 0.9 |
| 6.5 | 0.9 |
| 7 | 0.9 |

**Figure 7** Summary of results: risk for PE, based upon the Modified Wells Score, and subsequent investigation with CTPA and/or D-dimer



## Discussion

PE can present in a number of ways, the most commonly reported symptoms in this audit being acute shortness of breath, and pleuritic chest pain. These two symptoms were the main documented reasons for ordering a CTPA in patients making up the subject population. Other conditions may present similarly to PE, and thus a high index of clinical suspicion is necessary. History-taking should be geared towards specific factors that increase thrombotic tendency, thus precipitating PE. These risk factors are incorporated into the Wells Score, a validated scoring system used to grade the probability of PE. These include symptoms of DVT, prior history of DVT and PE, recent immobilisation and presence of malignancy. Haemoptysis and tachycardia are also features that are associated with PE. If no alternative diagnosis better explains symptoms, this adds to the Wells Score and increases the probability of PE. Although the Wells and Geneva scores which are clearly delineated in the ESC Guidelines on Acute Pulmonary Embolism are referred to locally as a guide to stratify risk for PE and thus refer patients for CTPA accordingly, there was no established local guideline at time of data collection.

A scoring system (Wells or Geneva) was only calculated in 10.4% of study patients prior to ordering a CTPA. When the Wells Score was calculated retrospectively, PE was ruled out in at least one third, yet these still underwent CTPA, placing a not insignificant burden on radiology time and costs, whilst also exposing patients to unnecessary risks. These include ionizing radiation, contrast nephropathy and anaphylaxis. 1 patient sustained contrast-induced anaphylaxis following scanning while 5 patients (4.7%) experienced a deterioration in their eGFR. 10.4% of patients passed away during the study period however further mortality data was not looked into.

Arterial blood gas analysis is a recommended investigation in patients presenting with symptoms suggestive of pulmonary pathology. These were only taken in a minority (39.6%) of the study population. A sizeable proportion (43.5%) of patients with a positive CTPA did not have ABGs taken. Type 1 Respiratory Failure was present in 76.9% of patients with PE in whom ABGs were taken. These findings are very relevant as ABG analysis is a convenient bedside test which allows a rapid reflection of the physiological status of a patient and is valuable in prioritising an acutely unwell patient.

A D-Dimer assay is recommended in those patients in whom PE is unlikely, thus a Modified Wells Score of ≤4. It is a highly sensitive but non-specific test for PE. D-dimer was only checked in 62.5% of those in whom it was indicated, and ruled out PE in 34% of those with a low Wells Score (≤4). In only 2 patients was a positive CTPA (non-guideline request) associated with a negative D-dimer.

A limitation to the study was the relatively short period of recruitment. However, in this short period, it already became clear that guidelines were not being adhered to, with unnecessary risks to the patient and uncalled for costs to the hospital system. Furthermore, the Modified Wells Score was calculated retrospectively by the investigators, as PTP testing was only done in a minority of patients, and its absence would have precluded further evaluation. This may have been inaccurate by either under- or over-estimating the Wells score, since it was obtained from the patient's case notes rather than from first-hand history-taking and physical examination. Lastly D-

dimer values were taken at face value rather than adjusting for age[5]. Thus, the number of CTPAs correctly requested may have been even lower.

## Conclusions

A basis for requesting a CTPA needs to be established, utilising the well-validated Wells Score[1], and D-dimer where indicated. A suspicion of PE should trigger a request for an arterial blood gas (ABG). CTPA is not without morbidity, and therefore should only be requested according to evidence-base. In the light of this audit's overwhelming evidence that CTPAs are often requested without adherence to guidelines, there is currently liaison with the IT department to render a Well score compulsory, as well as a D-dimer level if indicated, when digitally requesting a CTPA. The authors, together with major stake holders, agree that employment of such measures when ordering CTPAs should decrease unnecessary requests, hence diminishing risks to patients, such as contrast-induced nephropathy, anaphylaxis and radiation exposure, as well as limiting health-care costs.

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ORIGINAL ARTICLE

# Psychiatric admissions in Malta: demographics and diagnoses

Bertha Grech, Beppe Micallef Trigona

## Background

The decision to hospitalize a patient exhibiting signs of psychiatric distress is made after outpatient management resources have been exhausted or if a patient cannot receive optimal care outside of hospital. The rising number of admissions also has an effect on costs burden within the national health system. This audit is set to determine the main psychiatric reasons for admission to hospital in Malta and analyse demographics, source of referrals and mental health act status whilst comparing such result to those abroad.

## Methods

Data from admissions between the 15th October 2018 till the 1st March 2019 was collected, using a recently established electronic database system. Details including; age, sex, nationality, type of admission (new case versus readmission), mental health act status and reason for admission were collected.

## Results

300 patients admitted to Mount Carmel hospital during the stated period. Roughly 2 male patients were admitted for every female. 75.3% of the cohort were of Maltese nationality. The majority of foreign patient were European, 14%, followed by African, 8.3%, Asian and American. The most common sources of referrals were casualty at 40%, followed by those from general practitioners at 26.7%.

## Conclusion

Reasons for admission were most commonly, substance abuse (15.3%), depression (15%) and acute psychosis (13.3%), following similar trends across Europe. Methods to decrease unnecessary referrals include better training of emergency doctors and general practitioners. Additionally, recent implementation of a 24 hour on call crisis service should provide better acute management of patients and help to prevent saturation of inpatients with cases that can handled in the community.

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## Introduction

Admission to hospital for inpatient treatment of psychiatric cases is the most restrictive and clinically disruptive form of management. The need for hospital admission most commonly indicates that presenting symptoms cannot be managed outside an institutional setting. Increasing number of admissions also has an effect on costs burden within the national health system.[1]

In Malta the admission process to the main psychiatric facility occurs provided that the patient presents a ticket of referral with details leading up the admission. In cases where the patient does not want to be admitted voluntarily, admission under the mental health act is undertaken. Patients can be referred by any physician, most commonly from the emergency department or through general practitioners.

This audit is set to determine the main psychiatric reasons for admission to hospital in Malta and to analyse similar factors in these patients including demographics, source of referrals and mental health act status whilst comparing such results to a similar study in Scotland.

## Materials and Methods

The study was conducted at Mount Carmel Hospital, Malta and approved by both the local audit committee and by the data protection management. Data from admissions between the 15th October 2018 till the 1st March 2019 was collected. A total of 18 weeks were thus analysed. Data was collected from a recently established electronic database system denoting details about all acute admission to hospital. Each patient case was studied and the following details were noted; age, sex, nationality, type of admission (new case versus readmission), mental health act status (voluntary versus involuntary) and reason for admission/ diagnosis.

In cases were information was absent from the electronic database, online electronic case summaries were opened or physical files were reviewed accordingly. No patient contact was necessary for this audit.

## Results

Over a time, span of 18 weeks, 300 patients were referred and admitted to Mount Carmel hospital. The age range of these admission was that between 17 and 90 years of age. Most patients fall between the ages of 20 and 39, these amounting to 140 cases, 46.7% of the total number of admissions. The second most common age group,40-59 years, included 32.3% of 300 admissions studied (table 1).

**Table 1** Patient age

| Age group | Number of patients | % from total admissions |
|---|---|---|
| 0-19 | 15 | 5 |
| 20-39 | 140 | 46.7 |
| 40-59 | 97 | 32.3 |
| 60-79 | 39 | 13 |
| 80+ | 9 | 3 |

Male admissions were more common when compared to the opposite gender. 65.7% of patients,197 case were in fact male (table 2). Roughly 2 male patients were admitted for every female.

75.3% of the cohort were of Maltese nationality. The majority of foreign patient were European, 14%, followed by African, 8.3%, Asian and American (table 3).

**Table 2** Admission gender

| Gender | Number of patients | % from total admissions |
|---|---|---|
| Male | 197 | 65.7 |
| Female | 103 | 34.3 |

**Table 3** Nationality of patients

| Nationality | Number of patients | % from total admissions |
|---|---|---|
| Maltese | 226 | 75.3 |
| European (excluding Maltese) | 42 | 14 |
| African | 25 | 8.3 |
| Asian | 6 | 2 |
| American | 1 | 0.3 |

Most referrals came from accident and emergency department in Mater dei Hospital, the main hospital in Malta. A total of 40% of admissions were referred from the aforementioned. Another 23.7% of cases were transferred from wards within this hospital. The second most common source of referral was from general practitioners who referred 26.7% of the 300 subjects. Other referrals came from geriatric hospitals, detox centre and private clinics (table 4).

New cases, meaning first time admission to the psychiatric facility amounted to 64.3% whereas the remaining amount were patients having previous admissions at hospital (table 5).

205 inpatients, 68.3% of the cohort, were inpatients on a voluntary basis whereas 30.7% were sectioned under the mental health act for assessment and observation (schedule 2) The remaining 1% present for involuntary assessment for observation and treatment (schedule 3) (table 6).

Reasons for admission were most commonly, substance abuse (15.3%), depression (15%) and acute psychosis (13.3%) (table 7).

**Table 4** Source of admission

| Referred from | Number of patients | % from total admissions |
|---|---|---|
| A&E | 120 | 40 |
| HC/GP | 80 | 26.7 |
| MDH (wards) | 71 | 23.7 |
| Private clinic | 11 | 3.6 |
| POP | 7 | 2.3 |
| Detox | 4 | 1.3 |
| GGH | 2 | 0.6 |
| KGH | 2 | 0.6 |
| SVPR | 2 | 0.6 |
| CYPS | 1 | 0.3 |

**Table 5** Admission type

| Type of admission | Number of patients | % from total admissions |
|---|---|---|
| New admission | 193 | 64.3 |
| Readmission | 107 | 35.7 |

**Table 6** MHA status of patient

| MHA status | Number of patients | % from total admissions |
|---|---|---|
| voluntary | 205 | 68.3 |
| IAO inpatient assessment | 92 | 30.7 |
| IATO inpatient assessment /treatment | 3 | 1 |

**Table 7** Reason for admission

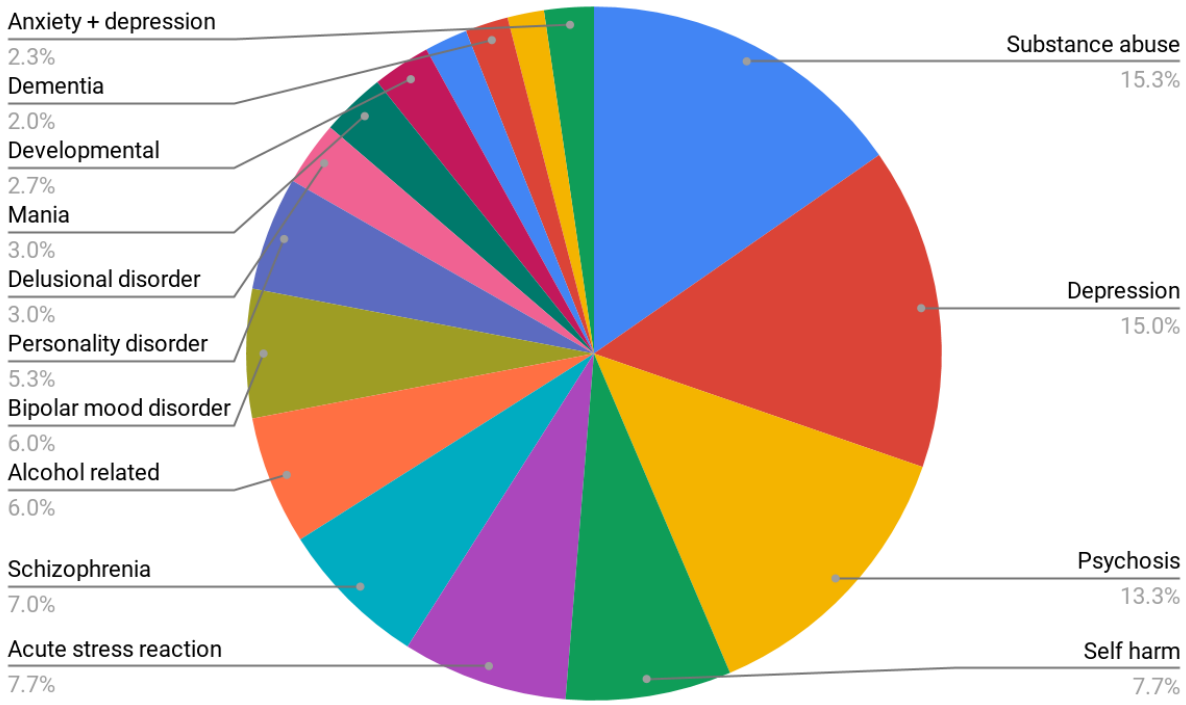
| Reason for admission | Number of patients | % from total admissions |
|---|---|---|
| Substance abuse | 46 | 15.3 |
| Depression | 45 | 15 |
| Psychosis | 40 | 13.3 |
| Self harm | 23 | 7.7 |
| Acute stress reaction | 23 | 7.7 |
| Schizophrenia | 21 | 7 |
| Alcohol related disorders | 18 | 6 |
| Bipolar mood disorder | 18 | 6 |
| Personality disorder | 16 | 5.3 |
| Delusional disorder | 9 | 3 |
| Mania | 9 | 3 |
| Developmental disorder | 8 | 2.7 |
| Alcohol + substance misuse | 6 | 2 |
| Dementia | 6 | 2 |
| PTSD | 5 | 1.7 |
| Anxiety + depression | 4 | 1.3 |
| Anxiety | 3 | 1 |

## Discussion

Several specific patient characteristics, especially early onset of disease, hospital admission in the past year, comorbid substance use disorder, global illness severity, and poor social function, were previously found to contribute to risk of hospital admission.[1]

Reasons for inpatient stay at the main psychiatric hospital on the island revealed that substance abuse (15.3%) and depressive mood disorder (15%) are the most common causes for admission figure 1). This is also seen in Scotland however the rates are 35% for depressive mood disorder and 25.2% for substance abuse. The difference in rates could be due to presence of categories such as bipolar disorder (6%) and self-harm (7.7%) which could be caused by depressive disorder. These subgroups were not listed in the Scottish study used for comparison. The same can be said about the alcohol abuse category (6%) and mixed substance use (2%) that can be included with substance abuse disorder. Other reasons for admission abroad accumulate up to 18.3% for schizophrenia and related psychoses, 17.2% for anxiety and stress related disorders with the remainder associated with eating and personality disorders.[2] In the United Kingdom schizophrenia and related psychoses accounted for 26.0% of admissions and substance misuse 19.1%.[3] Similar trends can be seen across the European Union likewise.[4] In Malta psychotic episodes lead to 13.3% of the total admission. Such episodes are mostly substance induced thus also adding to the total amount of patients needing admission due to a substance related disorder.

**Figure 1** Reason for admission




In general, depressive disorders are more common in females whilst men were more likely to present with psychotic disorders, alcohol use, and substance use disorders and to be assessed as aggressive toward others.[5-6]

Males admissions represent 65.7% of the total when compared to 34.3% of females (figure 2). Other studies show that females have a higher number of hospitalisations although men have a higher risk of a first hospitalisation and their stays prove to be longer.[6] Female gender is thought to be one of the risk factor for hospitalisation, others include suicidality, drug treatment administered at casualty, restraining measures applied, dementia, number of consultations, referral to hospital by a physician, or the patient presenting at the emergency department unaccompanied.[7]

With regards to most common age group requiring admission in Malta, patient were found to be between the ages of 20 and 39 (figure 3). This can be related to the fact that age of onset for the most common diagnosis are as follows; substance use disorders (age 20 years) and mood disorders (age 30 years)[5]. In the United Kingdom the most common age category for admission is between the ages of 25 and 44, thus a great overlap of age can be seen with that found locally.

31.7% of patients were brought to hospital involuntarily using the mental health act (figure 4). Compared to foreign tendencies, the total frequencies of admission and compulsory admission rates vary remarkably across the European Union, from 30% in Sweden to 3.2% in Portugal. Variation hints at the influence of differences in legal frameworks or procedures despite the tendency for harmonisation of strategies for mental health care delivery, rules and regulations for involuntary placement or treatment of mentally ill persons.[8]

**Figure 2** Admission gender

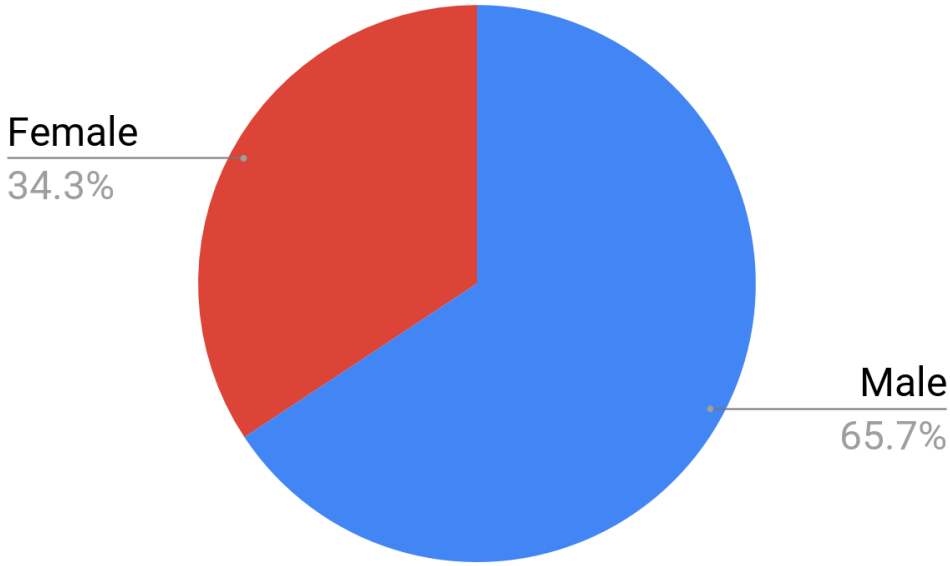



**Figure 3** Patient age

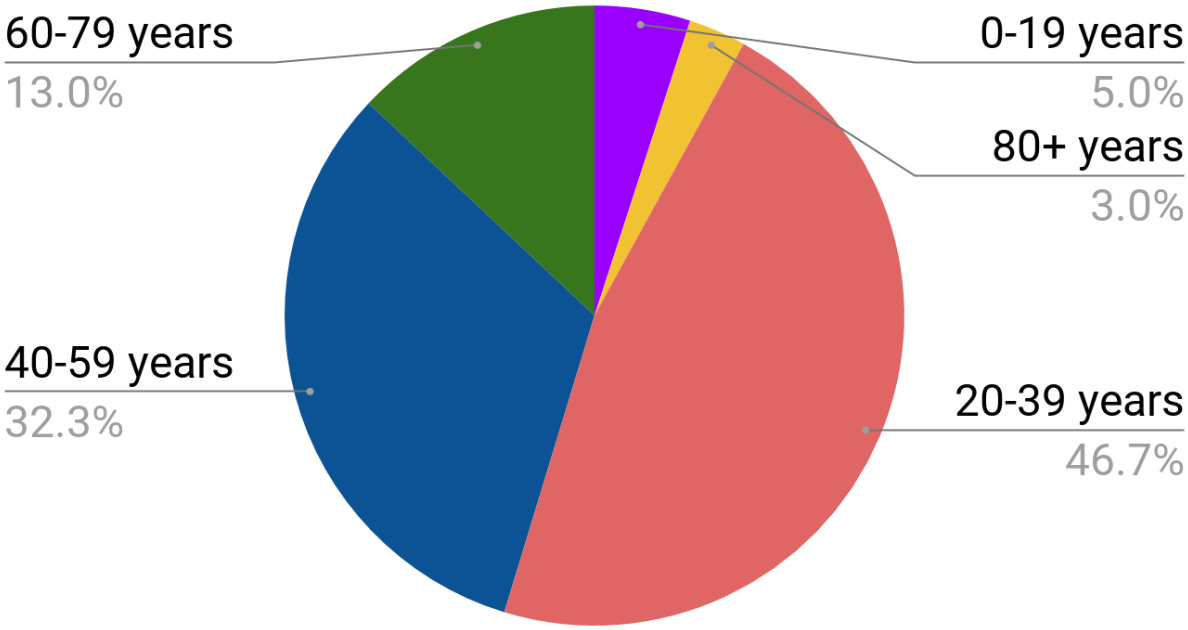


**Figure 4** Admission type

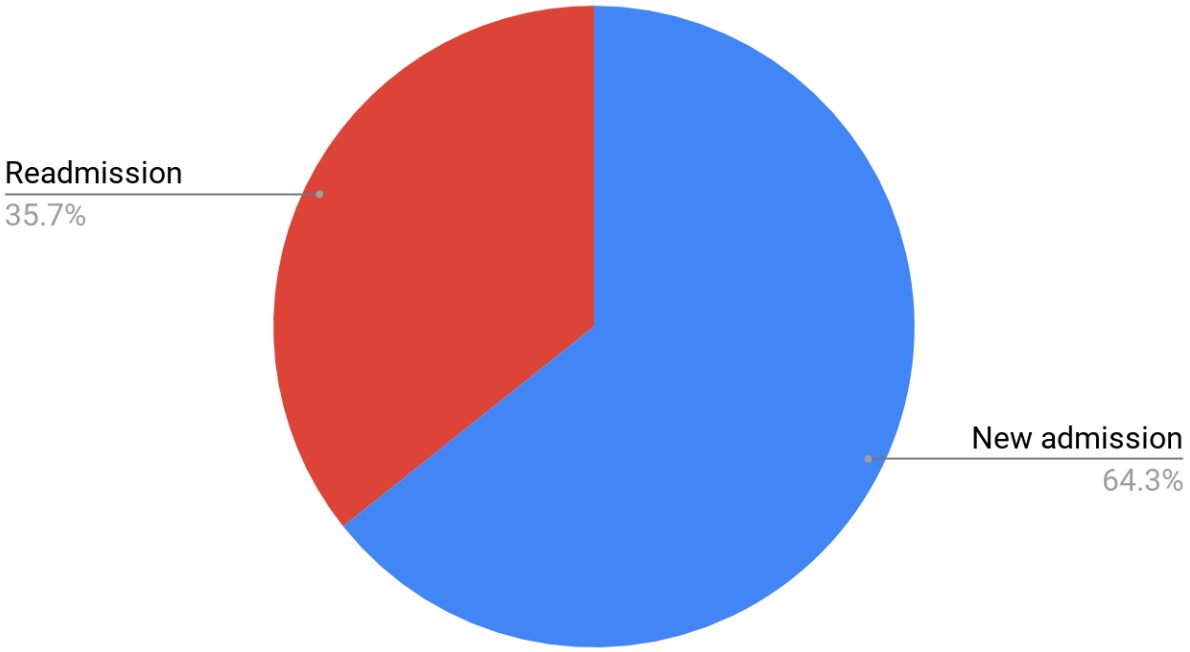
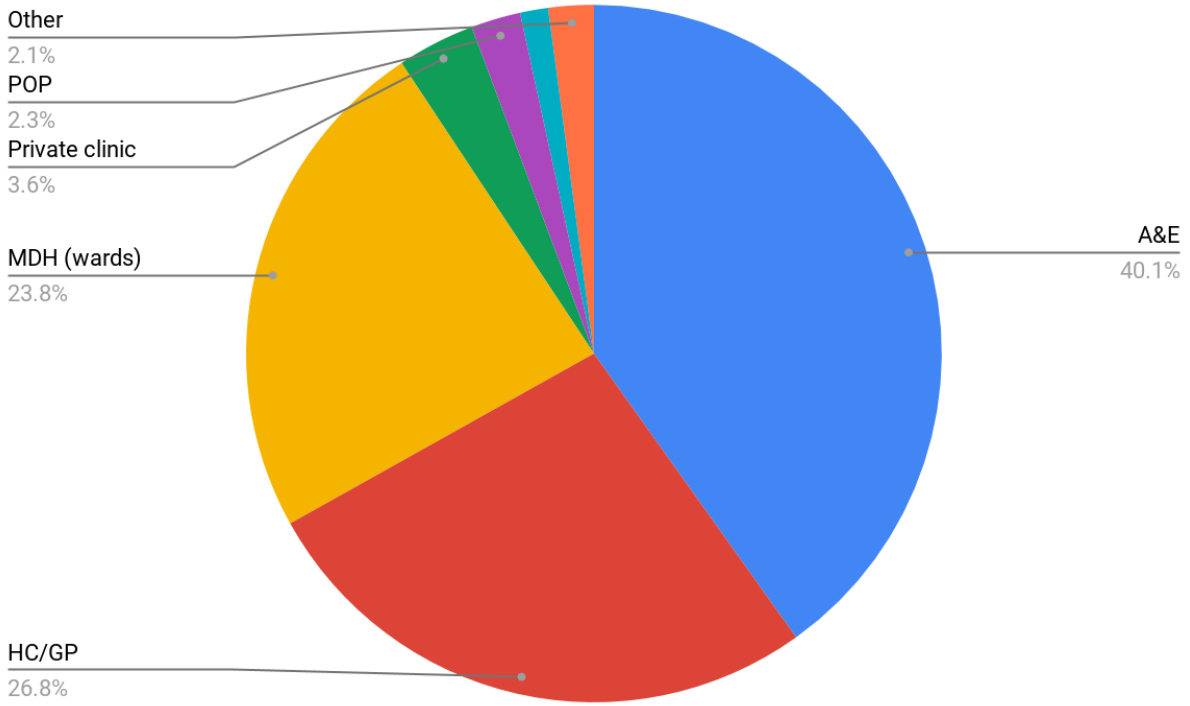



**Figure 5** Source of admission



There are many paths that lead to inpatient psychiatric treatment: referral by a specialist including general practitioners, walk ins directly attending emergency department, referral by community psychiatric services, patients brought in by the police, as well as transfers from other hospital departments. For many patients with psychiatric problems, the first port of call is casualty, in fact the majority, 40% of referrals, are sent from accident and emergency. Following casualty, the most common source is that *via* general practitioners at health centres, 26.7%, followed by transfer from wards within the general hospital,23.7% (figure 5).

These above factors should help guide clinical and programmatic efforts to focus outpatient care on psychiatric patients at high risk for hospital admission. Furthermore, evaluation of sources of referral can result in more effective management by providing more resources and better training to attending physicians. Seeing how the number of prescriptions of antidepressant drugs issued to patients with a diagnosis of depression in primary care in the United Kingdom has increased[9] by 33% goes to show how general practitioners are dealing with more psychiatric consultations. Providing adequate and updated training to family doctors could lead to better community management and divert admission to hospital whenever possible. Once a patient is referred or walks into casualty, it is the assessment done by emergency physicians that determines a dischargeable case versus an admission, also bearing in mind that some patients will request the admission themselves.

As of March 2019, crisis psychiatric services at casualty have extended their on-call hours from 8am till 5pm to a 24 hour service. Having a psychiatric specialist on site leads to review by a trained psychiatric physician allowing for better assessment of each case and cutting down on unnecessary admissions. Overall, there is also a need to assess the role of relevant community services, together with evaluation of the quality and continuity of outpatient care, family and social support to possibly reduce the risk of hospital admission.[1] As with every developing specialty, patient education and especially in the case of psychiatry, family education is essential in promoting better timing for admissions based on warning signs together with public knowledge of the available resources such as non-governmental organisations and support helplines.

Suggestions for re-audit include analysing admissions occurring after the introduction of extended 24 hour crisis service recently introduced and to see how this affected the number and type of admissions to the hospital.

The limitations of this audit include the limited number of patients analysed and the fact that some patients were not yet discharged with a formal diagnosis thus an impression of the diagnosis was used. In other cases, updates of the working diagnosis may have not been uploaded accordingly.

## Conclusion

The decision to hospitalise a patient is taken to be the last resort after outpatient management has failed, if risk is too high or if community support is not sufficient to mitigate this risk. Evaluation of services has shown that admission to hospital is more common in males locally. The most common reasons for admission are substance abuse and depressive disorder with local rates comparable to those in the UK and Scotland. 68.3% of all patients are admitted voluntarily with the remaining 31.7% needing sectioning

by applying the mental health act. The vast majority of referrals are done through the emergency department. The goal of an acute psychiatry specialist is to optimally assess the clinical presentation and use all available community resources. Implementation of a 24 hour on call crisis service should provide better acute management of patients and help to prevent saturation of inpatients with cases that can handled in the community. This may also help prevent patients from future institutionalisation, cuts down on costs yet ensuring that inpatient hospitalisation is reserved for situations with high imminence of danger to the patient or others.

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ORIGINAL ARTICLE

# Factors that influence tobacco use in Georgian youth

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## Objective

Social environment, especially education, levels of awareness, friends and parental behavior greatly affects the use of tobacco among teenagers. The research aims to identify various factors that promote tobacco use in youth.

## Method

Qualitative and analytic cross-sectional descriptive research method was carried in among students from Tbilisi State University.

## Results

Most respondents have started tobacco consumption at juvenile age. The community played a decisive role in starting tobacco use. Respondents started using tobacco with their classmates and close friends. The survey has shown that tobacco consumption was perceived as a positive social behavior among teenagers. Introducing the tobacco control laws that prohibit tobacco consumption and advertising in public places, particularly near schools are of paramount importance.

## Conclusion

Interventions that focus particularly on multiple risk factors may have an impact on the use of tobacco by adolescents. Where possible, such programs should be personalized to ensure that they address the specific set of risk factors that has a bearing on each individual's tobacco use.

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## Introduction

Tobacco consumption is one of the leading causes of death in the world.[1-4] According to World Health Organization (WHO), globally, 7 million people die each year as a result of tobacco consumption.[5] Nearly 80% of 1 billion smokers worldwide live in low- and middle-income countries, where the burden of tobacco related illness and death is heaviest.[6-7] The use of tobacco is particularly popular among men, adolescents, people having low social-economic status and education.[8] Tobacco consumption by adolescents is a major concern. According to the World Bank, between 82,000 to 99,000 adolescents and young adults aged up to 18 years become regular consumers of tobacco.[9]

Tobacco consumption is the actual problem in Georgia as well.[10-11] Over 40% of the population, including children and pregnant women, are being exposed to tobacco smoke.[12] According to the research conducted in Georgia in 2016,[13] 40% of respondents aged from 14 to 25 have tasted tobacco. The age at which the respondents have started smoking varied from 12 to 24, and the average age was 15. According to the research conducted in 2016 by the National Center for Disease Control and Public Health,[14] tobacco consumption in Georgian students is 43%. Tobacco dependence is induced both by routinely exhibited behavior and social factors.[15-17]

Public health measures are most effective for reducing tobacco consumption: public education, increasing taxes on cigarettes and restricting tobacco consumption in public areas.[18-19] WHO has developed a Framework Convention on Tobacco Control (WHO FCTC) that entered into force on 27 February 2005.[20] To date, 180 countries, including Georgia, have ratified the WHO FCTC, and thus undertook a commitment to implement full-scale measures in the field of tobacco control in the country. On May 17, 2017, Georgia adopted the Law on Tobacco Control under which from May 1, 2018, the tobacco consumption was prohibited at closed public and work places, as well as in some open areas and public transport, in order to promote tobacco, use restrictions.[21]

The research aims to identify properties and factors that promote tobacco consumption among teenagers.

## Materials and Methods

The present study combined qualitative and quantitative methods. The basic premise of this mixed methodology is that such integration permits a more complete and synergistic utilization of data.[22-23]

Qualitative research method of direct interviews was carried out among 4 students. A nonprobability sampling method and its most convenient type – a snowball sampling was used for the respondent selection. Respondents were the students of Tbilisi State University (Georgia). Participation was voluntary. Primary data was used, where we have collected data our self, using the interviews. Units of data analyses were words and phrases, where we recorded the interview, and created a transcript afterwards. Interviews have been conducted in June, 2019.

An analytic cross-sectional descriptive study was conducted. Participants were 350 students from Tbilisi State University, who at the time of the survey were at the Bachelor's level of teaching. Students were chosen at the Tbilisi State University on the survey day. The questionnaires were administered randomly to respondents that consented after carefully

explaining the objectives of the study. Out of the 350 respondents, a questionnaire was filled out by 321 (91.7%), while 29 (8.3%) of them refused to participate in the survey (Table 1).

**Table 1** Demographic characteristics of respondents

| Variable | Frequency | % |
|---|---|---|
| Gender | | |
| Male | 205 | 63.9% |
| Female | 116 | 36.1% |
| Age | | |
| 18-20 | 128 | 39.9% |
| 21-23 | 107 | 33.3% |
| 24-26 | 86 | 26.8% |
| Have you ever smoke cigarette? | | |
| Yes | 243 | 75.7% |
| No | 78 | 24.3% |
| If yes, at what age did you start smoking? (n=243) | | |
| 10-17 | 87 | 36% |
| After 18 | 156 | 64% |
| Do you still smoke? (n=243) | | |
| Yes | 203 | 84% |
| No | 40 | 16% |

The survey instrument was a semi-structured questionnaire. The questionnaire was modified from the relevant studies.[24] In order to access the difficulty of the questionnaire, 15 pilot interviews were initially conducted.

The data collected from the subjects using the questionnaire contained questions on use of tobacco, knowledge & attitude towards tobacco, exposure to other people smoking, attitude towards stopping smoking, knowledge about media messages about smoking, discussion of smoking in school, etc. The questionnaire contained multiple response questions with only one option to be selected. The response sheet did not have any name on it and it was confidentially collected in a box kept. The field works took place between January and March 2019. Each interview lasted for 35-45 minutes on average.

*Data Collection and Analysis.* After the questionnaire had been built, the information of 321 students were collected by a convenient sampling method. Data entry and analysis were done using Microsoft Excel and SPSS version 20. The analysis is performed at the sig. of 5%.

The main limitation of the study was the fact that it was conducted only in one university due to time and budget allocated for the research.

*Ethics.* The study was approved by the Ethics Committee of the Health Policy Institute. An informed consent was taken from each participant. Only those who voluntarily agreed and gave the verbal consent was included in the study.

## RESULTS

Male and female that participated in the study was 63.9% and 36.1% respectively. Respondents were mostly in the age of 18-20 years (39.9%, *n*=128); 75.7% (*n*=243) was recorded as the smoking prevalence in the community. Current smokers were 84% (*n*=203) respectively. The most prevalent age of initiation was after 18 years (48%, *n*=118). The legal age to buy tobacco in Georgia is 18 years, but 36% (*n*=87) of smokers reported starting smoking before they reached that age (Table 1).

Regarding reasons for smoking, 60% (*n*=146) sometimes smoked so as to cool off; over 51% (123) sometimes smoked in order relieve stress whereas, 54% (*n*=131) always smoked to feel relaxed. For increase of sexual performance, 45.0% (109) of respondents sometimes smoked to enhance their work output. 53% (*n*=129) always smoked as family members smoked, 52% (*n*=127) always smoked to enjoy with friends. 58% (*n*=141) of respondents sometimes smoked to be sociable, 49% (*n*=118) of respondents sometimes don't think its harmful (Table 2). Gender and Age group were associated with past ($p<0.05$) but not with present ($p>0.05$) smoking history (Table 3).

**Table 2** Reasons for smoking

| Variable | Reasons for smoking (*n*=243) | | |
|---|---|---|---|
| | **Always** | **Sometimes** | **Never** |
| **To relieve stress** | 86 (35%) | 123 (51%) | 34 (14%) |
| **To feel relaxed** | 93 (38%) | 131 (54%) | 19 (8%) |
| **To increase work output** | 37 (15%) | 109 (45%) | 97 (40%) |
| **Family members smoke** | 129 (53) | 68 (28%) | 46 (19%) |
| **Friends smoke** | 127 (52%) | 101 (42%) | 15 (6%) |
| **In order to be sociable** | 37 (15%) | 141 (58%) | 65 (27%) |
| **I don't think its harmful** | 58 (24%) | 118 (49%) | 87 (36%) |
| **It is cool** | 67 (28%) | 146 (60%) | 30 (12%) |

Table 3 Cross-tabulation of history of cigarette smoking and demographic data (*n*=321)

| Variable | Have you ever smoked cigarette? | | Total | p-value | Do you still smoke? | | Total | p-value |
|---|---|---|---|---|---|---|---|---|
| | **Yes** | **No** | | | **Yes** | **No** | | |
| **Gender** | | | | | | | | |
| Male | 157 | 48 | 205 | | 134 | 23 | 157 | |
| | 49% | 15% | 63.9% | 0.0001 | 55% | 10% | 65% | 0.776 |
| Female | 86 | 30 | 116 | | 69 | 17 | 86 | |
| | 27% | 9% | 36.1% | | 28% | 7% | 35% | |
| **Age group** | | | | | | | | |
| 18-20 | 77 | 51 | 128 | | 50 | 27 | 77 | |
| | 24% | 16% | 39.9% | | 21% | 11% | 32% | |
| 21-23 | 94 | 13 | 107 | 0.029 | 86 | 8 | 94 | 0.155 |
| | 29% | 4% | 33.3% | | 35% | 3% | 39% | |
| 24-26 | 72 | 14 | 86 | | 67 | 5 | 72 | |
| | 23% | 4% | 26.8% | | 28% | 2% | 29% | |

### *Qualitative method*

**Interview 17 years old males.** When asked why young people have started consuming tobacco, the respondent answered that the major motivation was a curiosity to taste it. From the course of the interview, it became clear that the interest was directly related to his close social environment and friends:

*"In the 6th grade, I started to collect stamps, which were made from cigarette boxes. A group was formed, who did such activities. Those who were collecting the marks were two years older, i.e. 14 years old, and already smokers. They looked-like grown-ups for me then. After that me and my friend decided to start smoking, but we did not know how to take puffs and after tasting it we gave it up".*

Despite the fact that he did not enjoy tobacco the first time, he still continued smoking, which makes the hypothesis of the orientation on others more representative.

*"I was training myself from childhood and my organism could not accept it. After smoking one or two cigarettes, I felt sick and nauseated".*

This respondent began to smoke cigarettes again at the age of 15, in the 9$^{th}$ grade. It should be emphasized that the repeated consumption of cigarettes resulted from social relations:

*"The environment has affected. Our class went on hiking for two days and I smoked one cigarette. One boy was smoking actively in that period and he offered it to the rest of the boys".*

The interview has shown that the consumption of tobacco was considered to be manifestation of their adulthood, maturity and their behavior, primarily or not, was largely influenced by others.

*"They used to light cigarettes before girls and act like adult men, thus demonstrating themselves as being stronger than others".*

The parents of the respondents were also tobacco consumers.

When asked if tobacco consumption was perceived in young people more positively than negatively, the respondent noted that this behavior was more positively perceived in young people. To the question why he considered it so important, he referred to age-related experience:

*"Some people develop mentally at a later age, others from a younger age, but most of them do not realize. If I were this smart back in my school days, I would not have tasted any cigarettes, but some people could not realize this even at my age".*

The respondent was also asked in which situations he enjoyed smoking tobacco and whether or not he considered this more as an obsessive behavior or experience of having physiological pleasure.

*"Cigarettes make a man relaxed they say, but I think that it's more psychological moment, you only think that it relaxes you, but in fact it does not have any effect on the nerves".*

In addition to the main hypotheses of the research, one more factor, the role of stress, was revealed in the process of interview.

*"When I finished 9$^{th}$ grade, I sustained a trauma and I wanted to do something and I used to smoke one box of cigarettes every day".*

**Interview 21 years old females.** The respondent started to consume tobacco when she became a university student, namely, when she moved from her hometown to Tbilisi as a result of which the composition of her close social environment was upgraded to a greater extent. Perhaps it is a behavior that is caused by stress resulting from a change of environment, but from a respondent's interview it was found out that the main role, the main impact was the fact that smoking is perceived as a positive behavior by a social group.

*"I perceived this behavior as a manifestation of freedom"* - this quotation emphasizes the fact that a subject considered this behavior as an act of adulthood and maturity, which she demonstrated to the individuals, who were important members of her social environment.

To a question how she perceived consumption of tobacco by her peers initially, before she started smoking herself, the respondent noted that she considered it positive.

Nowadays she has quitted smoking and notes:

*"Nowadays, I rarely see those people, whom I used to meet every day and with whom I started smoking."*

**Interview 19 years old males.** In this interview with the respondent the direct confirmation of hypothesis was made:

*"I was actively involved in sports and when I quitted it, I was forced to take this bad step because of the classmates' influence".*

The person interviewed in the first interview, noted the role of stress, and in the subsequent interview the stress and pleasure factors were not neglected either, and the respondent was asked relevant questions in order to reveal the importance of these variables, in his case.

*"- What do you think, why people consume tobacco?*

*- To get pleasure or relieve stressful environment.*

*- Do you think it is the reason for starting the consumption of tobacco?*

*- I do not think so. Some are interested in smoking at an early age and are becoming imitators of this malicious habit."*

Thus, this answer emphasizes the correct formulation of research that the reasons for starting the consumption of tobacco in young people are

perceived as socially reputable behavior that causes their interest in tobacco consumption.

When asked which other factors generating his interest in cigarettes, he outlined arousing, besides the immediate social environment, also pointed out the role of cinema, which made this behavior even more aesthetic.

*"I used to smoke more for "aesthetic" purposes; the influence of movie culture was present as well."*

The interviewed person also believed that tobacco consumption by famous movie characters also encouraged teenagers to smoke. To a more insistent question why he considered it this way, the respondent answered:

*"When you are young, you do not pay attention to those bad factors that tobacco consumption may cause. I did not even think about these bad results before the hair loss became more intense and I realized that it was terrible to use tobacco".*

The frequency and the circumstance under which the tobacco was consumed were revealed as well.

*"I used to smoke about 2 boxes every week, in the surrounding of my friends or classmates."*

In regard to the physiological pleasure, he noted that he felt it the least.

*"That was the least; I felt a great discomfort because I was engaged in active sports. My organism and particularly my endocrine system, could not easily adopt those harmful substances."*

The more the purpose of orientation on other is pointed out in the hypothesis, the more diverse are the dimensions of demonstrating its positive reputation to others. There are several aspects of behavior that can be described – one manifests no only his own maturity, but light forms of "narcissism". In Fromm's viewpoint [17] it is not necessary that narcissistic person make the whole person into the subject of his narcissism: sometimes any aspect of his personality - physical skills, sharp-wittedness, behavioral capability, etc. may acquires narcissistic hint. In this case, when describing the behavior of tobacco consumption, the respondent noted the following:

*"I used to demonstrate my beautiful and long fingers to friends as I smoked. You feel as if you are more self-confident."*

**Interview 18 years old females.** The respondent started to smoke in the ninth grade when she moved from the old school to a new one. To the question whether or not the most part of her new classmates smoked tobacco, she gave positive answer. In addition, a sympathy to a boy who himself used to smoke a tobacco proved to be decisive.

When asked why she started to consume a tobacco, she said:

*"Everyone starts for one reason, just to show off herself ".*

Her family members - father and brother also consume tobacco.

In the interview she said that she tried to give up smoking several times, however, she often found herself in a situation where most of the people were smokers and she started smoking again. In addition, the girl used to consume tobacco to express her identity to a specific group.

The role of stress was also obvious in her case as well. I would like to note that coping with stress by means of smoking tobacco, as the responses show, results from the fact that the given behavior is perceived as a norm that expresses the person's maturity, self-confidence and independence.

## Discussion

This study evaluated the smoking prevalence among students and the reasons for and factors that influenced smoking. The prevalence of ever smoked was 75.7% which is very high. Most similar studies in Georgia have reported the opposite with lower prevalence rates.[25] However, other studies have

reported higher prevalence of smoking.[26] The most prevalent age of initiation was after 18 years (48%, *n*=118). The legal age to buy tobacco in Georgia is 18 years, but 36% (*n*=87) of smokers reported starting smoking before they reached that age. The similar results were observed in other studies as well.[27-28] The debuting age is of serious concern, that the younger the age at which experimentation occurs, the more health risk to the users.[29] The rate of youngsters smoking in this study calls for more concern and intervention, this age group being most vulnerable.

Several reasons were given by the respondents for smoking such as relieving stress, "to cool off", to feel relaxed and to increase work output. The similar results were observed in other studies.[30]

However, increased work out put, and to cool off, to relieve stress and to feel relaxed were not major reasons for smoking as far less than 50% gave them as reasons for smoking. Whereas, friends smoke, Family members smoke and being social was implicated as major reasons for smoking. People smoke with different motives, some associate smoking with feeling less stressed and relaxed.

In this population, smoking was correlated with Gender and Age. Male to female prevalence of smoking put male rate of smoking higher than females. This is in line with other surveys that showed that the frequency of tobacco use differs significantly between the sexes.[31] However, this study provided a distinction between gender association with past (correlated) and present (un-correlated) history of smoking. This means that in this population, there was no gender-mediated influence on current smoking habit. Similarly, Age were correlated only with past, but not with present smoking history in this population. Current smokers were not differentiated according to Age, whereas there were more past smokers among 18-20 age group. These differentials have implications for policy development and appropriate strategy formulation to deal with the scourge.

## Conclusion

Most of the respondents start smoking tobacco as a juvenile. In this regard, the influence of the circle of friends and family is also very important. The youth's organism has responded negatively to tobacco consumption; however, they continued this behavior. The respondent pointed out that tobacco consumption is perceived more positive than negatively in youth. In their particular case, a close social environment played a decisive role in starting tobacco consumption.

The results support policies and legislation which restrict the availability of tobacco to minors. Introducing the tobacco control laws that prohibit tobacco consumption and advertising in public places, particularly near schools are of paramount importance. Interventions that focus particularly on multiple (i.e. personal attributes, family, and contextual/school) risk factors may have an impact on the use of tobacco by adolescents. Where possible, such programs should be personalized to ensure that they address the specific set of risk factors that has a bearing on each individual's tobacco use.

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ORIGINAL ARTICLE

# High levels of sugar and salt in commercial baby foods in Malta: results from a pilot study using the World Health Organization draft nutrient profile model

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## Background

A major determinant of healthy growth and development is good nutrition during infancy and early childhood. The high level of marketing and wide-spread availability of commercially available complementary foods (baby foods) have led to various concerns about the nutritional content and potentially problematic marketing strategies used to promote these products, since this may adversely affect the parents' practices and the health status of young children. The aim of this pilot study was to assess the nutritional characteristics of commercially available foods for infants and young children under the age of 36 months in Malta, and to identify if these foods met the nutritional standards outlined in the WHO draft nutrient profile model (NPM) for this age group.

## Methods

A pilot study was carried out in two supermarkets and one large pharmacy that consented the photographing of over 243 food labels of foods marketed for infants and young children under 36 months in Malta. The nutritional quality of these foods was analysed using a validated World Health Organization NPM.

## Results and Conclusion

Only 88 (36%) out of the 243 food products tested according to a draft of the WHO NPM met the appropriate nutritional standards criteria used by this model. Tested products were found to contain high amounts of sugar and salt. The findings suggest that the quality of most of the food and beverages marketed for infants and young children currently available on the local market are not suitable for infants and young children in this age group.

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## Introduction

The World Health Organization (WHO) recommends exclusively breastfeeding until 6 months of age (meaning that the infant receives no other food or liquid aside from breastmilk), with continued breastfeeding along with appropriate complementary foods up to two years of age or beyond.[1] Despite this recommendation and a growing body of evidence which corroborates the beneficial effects of following the recommendations, nearly two thirds of infants under 6 months are not exclusively breastfed.[2]

The introduction of solid food is an important transition in the life of an infant and young child.[3] It is a time where infants are exposed to different foods, varying in texture, taste, smell, and sight, as well as to the surrounding adults and siblings that, in turn, will affect their food preferences and their eating behaviour.[4-5] This phenomenon is well documented and known as the first 1,000 days (from conception to age two years) where a child's eating pattern is programmed[6] and this is relevant since the behaviours and preferences established in early childhood tend to carry over into later years.[4] Breastfed infants, who are exposed to varying flavours in breast milk, normally show better food acceptance to a wider variety of foods later in life.[7-9]

Incorrect eating patterns, inadequate nutrition and unhealthy behaviours are known to contribute to the development of childhood obesity.[10] In Malta around 35% of girls and 37% of boys are overweight or obese, and this has drawn attention as an important public health issue.[11] Prevention of overweight and obesity requires a life-course approach, and actions must be taken to promote healthy nutrition at all stages of life, including infancy.[12]

Young children and babies have an innate preference for sweet tastes and dislike of bitter and sour flavours.[13] Therefore, early and repeated exposure to sweet complementary foods is particularly worrying as it may further reinforce sweet preferences.[14] Furthermore, premature introduction of complementary foods may displace breastfeeding, which brings a host of benefits including reduced risk of obesity and diabetes later in life.[15]

As the use of commercial baby foods has increased, there have been concerns about their poor nutritional content (and potential negative health consequences) and the marketing strategies used to promote these products.[16] More specifically, the nutrition-related concerns include: their sweet-taste profile, the lack of diverse ingredients, the limited food texture, as well as their poor nutritional quality; both in nutrition composition as well as in micronutrient bioavailability, quantities do not reach the recommended levels that may pose long term effects.[17-20] Another concern is that many baby food products have marketing statements which indicate suitability for children at 4 months of age, a marketing strategy which does not align with WHO recommendations, and which may encourage premature introduction of complementary foods.

Previous work has been done to assess the sugar and sodium levels in packaged baby and toddler foods (n=240 foods from nine retail stores), where it was found that 58% of the products assessed either had a high level of sodium or more than 20% of calories from sugar.[21] WHO also recently conducted research on foods for infant and young children in four cities of four European countries in the WHO European Region and found that baby foods were too high in sugar

and often contained marketing messages that did not align with WHO recommendations.[22]

To further understand the situation, this pilot study aimed to obtain a snap-shot of commercially available complementary foods, its quality and its level of appropriate promotion for infants and young children in Malta at common points of sale, examining its composition according to the draft Nutrient Profile Model (NPM), developed by the WHO for infants and young children under 36 months. Nutrient profiling models offer a reliable method to assess the nutritional quality of food products and can be defined as 'the science of categorising foods according to their nutritional composition'.[23] Nutrient profile models can help countries to identify products which can and cannot be promoted for infants and young children up to 36 months. This is a crucial step in developing effective legal and policy measures to promote health, which ultimately benefits consumers and, consequently, improves public health.[24]

The WHO Regional Office for Europe recently published a report which proposed criteria for identifying products appropriate for promotion for infants and young children.[16] The criteria together referred to as a 'nutrient profile model' (NPM) were developed using an established WHO approach, including an extensive literature review. The model establishes compositional thresholds and provides guidance on product-labelling and promotions. The compositional thresholds of an early version of the NPM was validated using 1,328 products on the market in Denmark, Spain and the UK in 2016/2017, amended and pilot tested in seven additional countries (Estonia, Hungary, Italy, Malta, Norway, Portugal and Slovenia) in 2018 with a further 1314 products. Details of pilot testing with products sold in Malta is provided here. The proposed NPM was updated following the pilot test and feedback from the countries involved; this involved amendments to some of the thresholds (notably protein was lowered to the European Commission threshold) and simplification of some categories. The published version can be adapted by governments, to restrict inappropriate promotion of foods for infants and young children in their own countries.[16]

## Materials and Methods

The Health Promotion and Disease Prevention Directorate (Malta) participated in a pilot testing study for WHO to provide nutrition and market data on commercially prepared baby food products.

### Data Collection

Data were collected in August of 2018 from three local retailers in Malta, two local main supermarkets and one pharmacy outlet. Retailers were invited to participate and consented to allow the photographing of the baby foods products. The 243 baby food products found in these retailers were photographed and data were collected, including information about ingredient list and nutrition information (Figure 1). The main manufacturers from which collected information in Malta were: Cuore di Natura, Ella's Kitchen, Good Gout, Heinz, Hipp, Kiddylicious, Maltova, Milupa, Nestle, Organix, Organu, Piccolo, Plasmon and Tesco.

The foods marketed as suitable for infants and young children 6-36 months of age were classified as follows (Supplementary Table 1):

- Dry powdered and instant cereal/starchy food

- Soft–wet spoonable, ready-to-eat foods, typically smooth or semi-puréed packaged in jars or pouches and can be spoon-fed
- Meals with chunky pieces, often sold in trays or pots
- Dry finger foods and snacks
- Juices and other drinks

## Testing the compositional thresholds of the WHO Nutrient Profile Model

The nutrition information, mainly calories, protein, sugar and the type of sugar, total fat, saturated fat and salt, were evaluated according to the compositional thresholds of the WHO NPM, as detailed below.

The data were entered into a pre-designed spreadsheet which determined the number of products that passed the nutrient requirements of the NPM, after selecting an appropriate food category. This was sent to WHO and the WHO Collaborating Centre at University of Leeds for final cleaning and analysis.

## NPM requirements for foods and nutritional composition

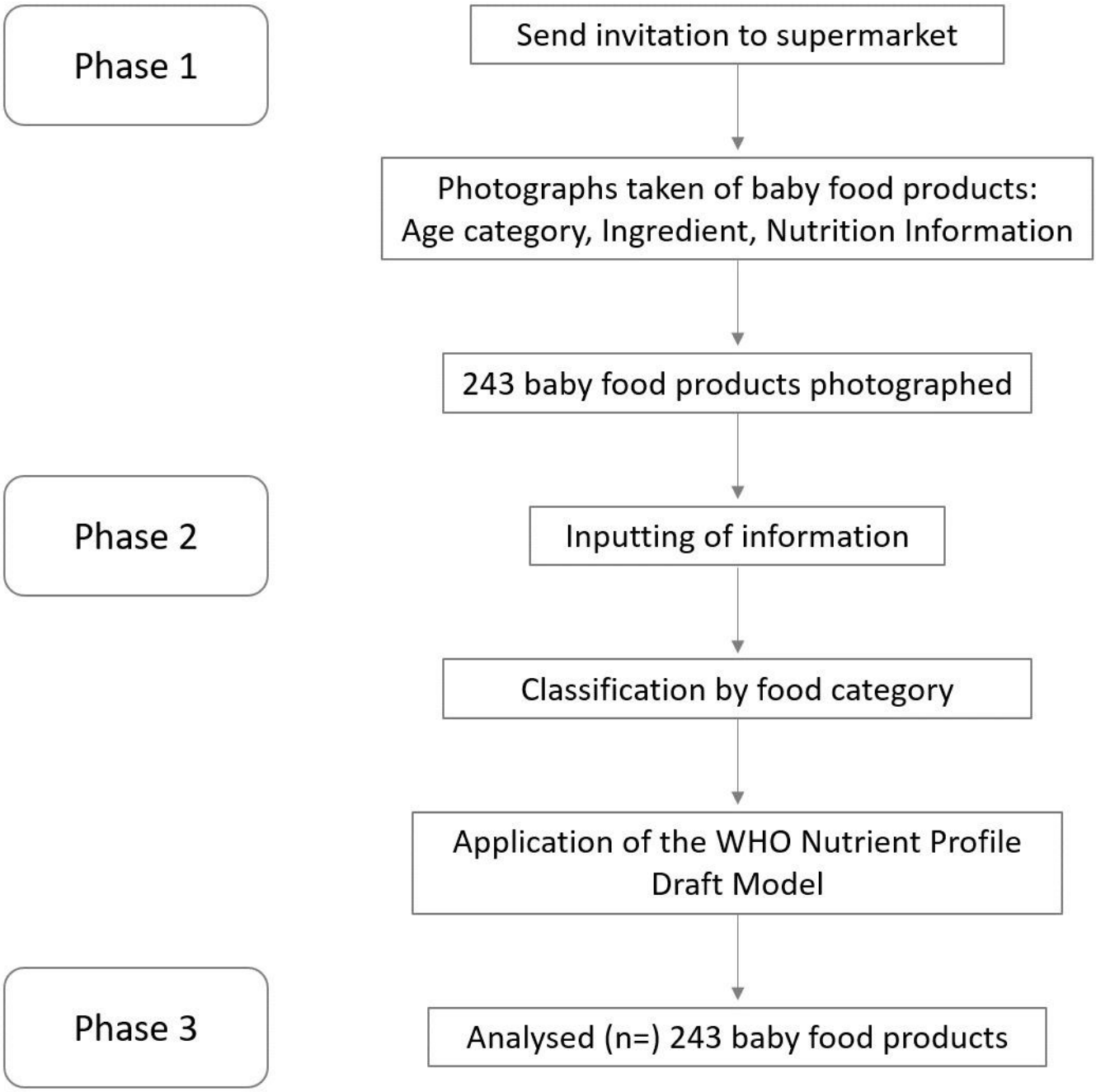
Six main compositional criteria of the draft NPM, relating to commercially available complementary foods (CACF) for infants and young children up to 36 months, could be assessed. The nutritional information for each product was compared with these requirements and specifications of the draft NPM version pilot tested, which were as follows:

1. Products marketed as suitable for this age group should not contain any added sugars or other sweetening agents. The following listed ingredients were classed as added sugars and sweeteners for this analysis: sugar, (any) syrup, juice (but lemon or lime juice are not), molasses, malt extract, barley malt, malted barley extract, maltose, dextrose, fructose, glucose, sucrose and honey (Added lactose was not classed as an added sugar as it is a component of milk, neither galacto-oligosaccharides, fructo-oligosaccharides, inulin, maltodextrose, maltodextrin and glycerol, which are often found in breast-milk substitutes). Based on the criteria above, fruit drinks did not meet the requirements of the piloted NPM;
2. Savoury snacks and finger foods should contain less than 15% energy from total sugars;
3. A minimum energy density threshold of 60 kcal/100 g was set for some soft–wet spoonable puréed foods intended for infants being weaned off breast milk.
4. The maximum permitted sodium content was set to be 50 mg/100 kcal and 50 mg/100 g for all foods (or only < 50 mg/100 kcal if dry cereal) except cheese purées and cheese meals (where cheese was listed in the front-of-pack product name and the protein content from dairy was 2.2 g/100 kcal), where the suggested limit was 100 mg/100 kcal and 100 mg/100 g of product.
5. Protein was considered sufficient in puréed meals that had the word ‘cheese’ in its name if total protein was ≥ 3 g/kcal in initial pilot tests. In foods where the first word contained “fish” or “meat” in the product title, protein was considered sufficient if ≥ 15% of total weight of the product and total protein was > 6g/kcal. Protein was considered sufficient in other puréed meals if named protein was ≥ 10% of total weight of the product and total protein was ≥ 3.75g/kcal.

6. Total fat requirement was set at < 4.5 g/100 kcal for all products except dry cereals (< 3.3 g/100 kcal, no added high protein) and cheese, fish or meat meals (6 g/100 kcal). Industrially produced trans fatty acids should not be included in CACFs.

Additionally, the packaging of the products was assessed for messages related to age at which the product would be suitable for consumption and any nutritional composition or health claims.

**Figure 1** Steps of the pilot study



## RESULTS

In August 2018, a total of 243 CACF products were sampled in Malta.

The number of CACF products in the pilot test and the percentages of products meeting the Nutrient Profiling Model (NPM) requirements from the Maltese data by different composition criteria are represented in Figure 2 and Table 1.

The food categories that were least likely to meet the NPM requirements were the soft-wet spoonable, ready to eat foods (33%) and the dry finger foods and snacks (18%). Of this latter category, only 37% had no added sugars and only around half of these products (47%) had less than 15% of total energy from sugar. The confectionery and bars, as well as the rusks and teething biscuits *did not meet any* NPM requirements relating to sugar content.

Regarding the sodium content, the one tray/pot meal examined with chunky meat or fish exceeded the recommended levels for salt and did not meet any of the NPM requirements. Also, only 66% of the dry finger foods and snacks fell below the recommended sodium levels.

Another concern was related to the low quantity of protein in these products, namely in the soft-wet spoonable and ready to eat foods, with only 25% meeting the protein requirements.

82 products out of a total 243 products (34%) were found to be promoted as suitable for infants under 6 months. 182 products were classed as having a nutrition, compositional or health claim – no information given for 2 products – so we could say that about 75% of products had a nutrition, compositional or health claim.

**Figure 2** Summary of CACF products meeting proposed NPM requirements by compositional criteria for Malta (%)

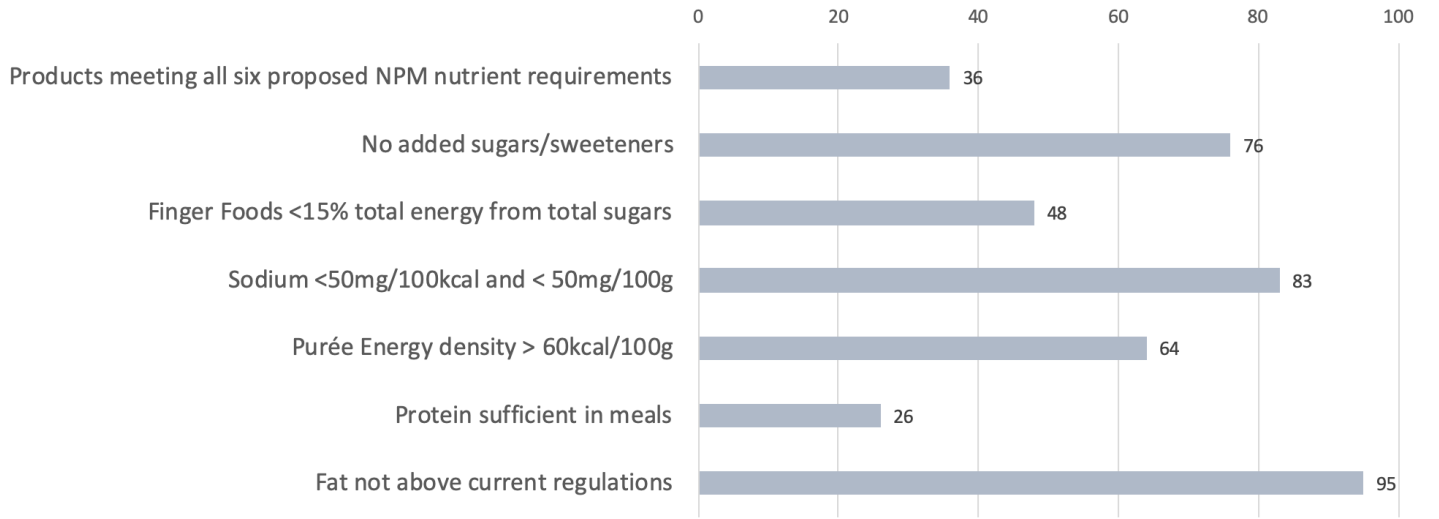


**Table 1** Percentage of products meeting NPM requirements by subcategories

| Food category | Total number of products | Meet all six proposed NPM nutrient requirement (%) | No added sugar/ sweeteners (%) | Finger Foods ≤15% total energy from total sugar | Sodium ≤50mg/100kcal and ≤50mg/100g[b] (%) | Energy density >60 kcal/100g[c] (%) | Protein sufficient in meals[d] (%) | Fat not current regulation[e] (%) |
|---|---|---|---|---|---|---|---|---|
| **1. Dry powdered and instant cereal/starchy food** | **38** | **71** | **76** | **n/a** | **95** | **n/a** | **n/a** | **100** |
| 1a Dry instant cereal | 18 | 100 | 100 | n/a | 100 | n/a | n/a | 100 |
| 1b Dry cereal (with high protein foods) | 20 | 45 | 55 | n/a | 90 | n/a | n/a | 100 |
| **2. Soft-wet spoonable, ready-to-eat foods** | **159** | **33** | **87** | **n/a** | **85** | **64** | **25** | **96** |
| 2a Fruit purée (with or without vegetables) | 53 | 42 | 89 | n/a | 100 | 51 | n/a | 100 |
| 2b Vegetable purées | 17 | 47 | 100 | n/a | 47 | n/a | n/a | 94 |
| 2c Fruit purée with cereal or milk | 12 | 67 | 83 | n/a | 92 | 92 | n/a | 92 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 2d Vegetables with cereal, soft-wet spoonable | 8 | 13 | 88 | n/a | 63 | 25 | n/a | 100 |
| 2e Cheese meal, soft–wet spoonable | 3 | 67 | 100 | n/a | 67 | 100 | 100 | 100 |
| 2f Fish meal, soft-wet spoonable | 5 | 0 | 100 | n/a | 60 | 100 | 0 | 100 |
| 2g Meat/poultry meal, soft-wet spoonable | 8 | 25 | 100 | n/a | 100 | 38 | 25 | 100 |
| 2h Meal/other, soft-wet spoonable | 28 | 4 | 96 | n/a | 79 | 64 | 21 | 86 |
| 2i Dairy, soft-wet spoonable | 17 | 35 | 41 | n/a | 88 | 100 | n/a | 100 |
| 2j Meat only purée | 8 | 25 | 100 | n/a | 100 | n/a | 25 | 100 |
| 2k Fish only purée | 0 | - | - | n/a | - | n/a | - | - |
| **3. Meals with chunky pieces** | **2** | **50** | **50** | **n/a** | **50** | **n/a** | **100** | **100** |
| 3a Tray/pot chunky meat or fish meal | 1 | 0 | 0 | n/a | 0 | n/a | 100 | 100 |
| 3b Tray/pot chunky vegetable meal | 1 | 100 | 100 | n/a | 100 | n/a | n/a | 100 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **4. Dry finger foods and snacks** | **44** | **18** | **37** | **47** | **66** | **n/a** | **n/a** | **88** |
| 4a Confectionery and bars | 1 | 0 | 0 | 0 | 0 | n/a | n/a | 100 |
| 4b Sweet snacks | 31 | 16 | 23 | 35 | 77 | n/a | n/a | 90 |
| 4c Rusks and teething biscuits | 1 | 0 | 0 | 0 | 100 | n/a | n/a | 100 |
| 4d Savoury snacks | 10 | 30 | 80 | 100 | 40 | n/a | n/a | 80 |
| 4e Fruit (fresh or dry whole fruit or pieces) snacks | 1 | 0 | 100 | 0 | 0 | n/a | n/a | 100 |
| **5. Juices and other drinks** | **0** | **-** | **-** | **n/a** | **-** | **n/a** | **n/a** | **-** |
| 5a Fruit juices and drink | 0 | - | - | n/a | - | n/a | n/a | - |
| 5b Vegetable juices | 0 | - | - | n/a | - | n/a | n/a | - |
| 5c Other drinks non-milk/non-formula | 0 | - | - | n/a | - | n/a | n/a | - |
| **Total percentage of applicable product passing** | **243** | **36** | **76** | **48** | **83** | **64** | **26** | **95** |

n/a = the criteria were not applicable to that category.

[a]The following listed ingredients have been classed as added sugars and sweeteners for this analysis: sugar, (any) syrup, juice (but lemon or lime juice are not), molasses, malt extract, barley malt, malted barley extract, maltose, dextrose, fructose, glucose, sucrose and honey. Added lactose was not classed as an added sugar as it is a component of milk. Additionally, galacto-oligosaccharides, fructo-oligosaccharides, inulin, maltodextrose, maltodextrin and glycerol, which are often found in breast-milk substitutes, were not classed as sweeteners.

[b] Or < 100 mg sodium/100 kcal and 100 mg sodium/100 g if cheese meal; or only < 50 mg/100 kcal if dry cereal.

[c] Energy density requirements were not set for the dry foods.

[d] Protein was sufficient in puréed meals with cheese in name if total protein was ≥ 3 g/kcal. Protein was sufficient in puréed meals with a fish or meat first-named food if these were ≥ 15% of total weight of product and total protein was > 6 g/kcal. Protein was sufficient in other puréed meals if named protein was ≥ 10% of total weight of product and total protein was ≥ 3.75 g/kcal.

[e]Total fat requirement was < 4.5 g/100 kcal for all products except dry cereals (< 3.3 g/100 kcal, no added high protein) and cheese, fish or meat meals (6 g/100 kcal).

## Discussion

The current study was conducted to investigate the situation of the commercially available complementary foods in Malta suitable to be marketed for infants and young children up to 36 months. This study has provided a snapshot of the nutritional characteristics of baby food, indicating that these food products are high in sugar quantities and high in salt. As mentioned, infants are born with a preference for sweet and salty tastes[8], so it is important that measures are taken to diversify exposure to other flavours and to ensure the acceptability of a wider range of nutritious foods later in life.[25]

From 243 food products tested, only 36% were suitable and complied with the composition requirements of the nutrient profile model pilot tested. These results are broadly comparable with the results from the other countries that participated in the pilot test, and also with the validation undertaken for Danish, Spanish and United Kingdom products marketed in 2016/2017.[16] Between countries, there is a gap in food regulation and each country applies different legislation[17], which in this study was confirmed through the wide range and form of products tested.

The WHO recommends exclusively breastfeeding until 6 months of age (meaning that the infant receives no other food or liquid aside from breastmilk), with continued breastfeeding along with appropriate complementary foods up to two years of age or beyond.[1] However, the evidence from this study demonstrates that parents and carers of infants and young children are likely to encounter marketing which conflicts with the WHO recommendations, where 34% of the marketed products were found to be promoted as suitable for infants under 6 months. A study conducted in the UK also verified that many products available were targeted at infants from age 4 months and that such products were sweet.[26]

Updated guidelines, regulations and legislation are needed to ensure that product promotions and labelling do not undermine important public health recommendations. The draft NPM model published by the WHO provides guidance on product-labelling and promotions to end all forms of inappropriate promotion of these products.[16] First, baby foods should not be marketed as suitable for children under 6 months. Front-of-package age restrictions for heavily puréed and very smooth products intended as weaning foods (e.g. suitable for age 6-12 months) should be added, as well as a ban on misleading labels and claims related to sugar and product healthiness and all types of marketing of fruit drinks and juices, confectionary and sweet snacks. Additionally, and according to evidence, the consumption of commercial complementary feeding is, in some cases, higher than homemade baby foods, what can be associated, among others, with higher intakes of added sugar.[25, 28-30] In fact, the global market for commercially available complementary foods is growing rapidly.[31]

A potential limitation of this study is the small sample and low number of retailers that were surveyed (two supermarkets, one pharmacy). Only the stores who agreed to participate were included, and this was likely to result in sampling bias. Furthermore, this paper used labels to assess the nutritional content of baby food, but previous work comparing laboratory determined sugar content against nutrition labels indicated that labels may be inaccurate, and often they may underestimate the actual amount of sugar found in baby foods.[27] Future

work may be needed to assess the nutrient content of baby foods in Malta using laboratory analysis and companies must be held accountable for the accuracy of their food labels.

Following the pilot test and feedback from the countries involved, the draft NPM was updated with amendments to some of the thresholds and simplification of some categories. The main amendments to thresholds were as follows:

- Notably protein was lowered back in line with the current European Commission threshold.[32] In the published NPM, for soft-wet spoonable meals total protein ≥ 3g/10 kcal from all protein sources, or ≥4g/10 kcal if protein source is named as first food (of which ≥ 2.2g/100 kcal protein from dairy if cheese mentioned in front-of-pack name). Each named protein not less than 25% by weight of total named protein. Protein source mentioned in the product name must be ≥ 8% by weight of the total product, or ≥ 10% If protein named as the first food(s) in front-of-pack name.
- Additionally a limit was set on the amount (≤ 5% by weight) of processed or concentrated 100% fruit (whole fruit that is puréed or dried) to be used as ingredients (for instance, powder of dried apple and purée of dried strawberries) in certain categories such as meals, with a maximum of 2% from dried fruit.

More research on this topic is needed. Besides the assessment of products available, there is a need to examine other marketing strategies employed by the companies which sell CACFs, such as their approach on social media and their digital marketing strategies.

The results of this study provide a valuable insight of the available food products in the Maltese islands. The poor nutritional quality of baby foods may have a negative impact on the growth and development of infants in the short and long term if no action is taken. In addition to developing a NPM, the WHO discussion paper also highlights requirements for labelling, marketing and promotion that are needed alongside the NPM to ensure that consumers are not misled, and that appropriate infant feeding is protected.[16] It is important that a multisectoral approach be adopted to implement updated guidelines, regulations and legislation to protect the health of young people.

## Summary Box

- Exclusively breastfeeding until 6 months of age (meaning that the infant receives no other food or liquid aside from breastmilk), with continued breastfeeding along with appropriate complementary foods up to two years of age or beyond is recommended by the WHO;
- Commercially available complementary foods are widely used by parents, and the global market for these products is growing rapidly;
- In Malta, 82 products out of the total 243 products (34%) were found to be promoted as suitable for infants under 6 months;
- Only 36% of the CACFs analysed in Malta were in accordance with the requirements of a draft version of the WHO Nutrient Profile Model;
- The results of this pilot study have offered a baseline for future work.

## Acknowledgements

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**Supplementary Table 1** Food categories used in pilot testing the nutrient profile model for all foods marketed as suitable for infants and young children 6–36 months of age used in sugar analyses.

| | Food category | Definition and examples |
|---|---|---|
| 1 | Dry, powdered and instant cereal/starchy food | |
| 1a | Dry or instant cereals/starch with or without naturally sweet foods | Dry rice, cereal, pulverized rusks or starchy root (at least 25% cereal and/or starch root content) with or without naturally sweet foods (e.g., dry fruit)<br>To be prepared for consumption with milk or other appropriate nutritious liquid (e.g., formula)<br>Includes dry instant-type porridges and dry breakfast cereals (e.g., puffed rice or cereal hoops), if marketed as suitable for infants and young children<br>Excludes wet ready-to-eat cereals |
| 1b | Dry or instant cereals/starch with an added high-protein food | Dry rice, cereal, pulverized rusks or starchy root (at least 25% cereal and/or starchy root content) with an added high-protein food (e.g., milk or whey powder) to be prepared for consumption with water or other appropriate protein-free liquid |
| 2 | Soft–wet spoonable, ready-to-eat foods | |
| 2a | Fruit purée with or without vegetables | ≥ 95% single or mixed fruit (or mixed with vegetables)<br>Includes fruit-only smoothie purée/drinks and any spoonable fruit-only or fruit-and-vegetable purée |
| 2b | Vegetable purée | ≥ 95% single or mixed vegetables or legumes<br>Excludes products containing any fruit |
| 2c | Fruit with cereal or milk products | Largest ingredient is single or total fruit, plus cereals or dairy<br>Includes foods such as smoothies with > 5% dairy or cereal, high-fruit breakfast foods (e.g., fruit-based breakfast rice/ porridge) and desserts (e.g., apple crumble or fruit-based baby rice)<br>Excludes fruit/vegetable-based purées with < 5% cereal or dairy, which are categorized as 2a or 2b |
| 2d | Vegetables with cereals or milk products | Puréed or semi-puréed vegetables/legumes with > 5% cooked weight in cereal (e.g., pasta, rice, barley), or a pseudocereal (e.g., quinoa, chia, buckwheat)<br>Includes savoury-type meals with cereals (e.g., pasta with tomato and courgette) or pseudocereal (e.g., butternut squash, carrot and quinoa) or with milk products (e.g., cauliflower cheese/ macaroni cheese)<br>Includes vegetable-based foods containing cheese, where cheese is not mentioned in the product name |

| | Food category | Definition and examples |
|---|---|---|
| 2e | Meal with cheese mentioned in the name | A puréed or semi-puréed meal containing vegetables, other carbohydrates and cheese (e.g., cheesy pasta with tomato and vegetables) |
| 2f | Meal with fish mentioned first (as food) in name of product | A puréed or semi-puréed meal containing vegetables, other carbohydrates and fish<br>Fish is mentioned as first food in product name (e.g., "Tasty fish pie" or "Salmon and pea risotto") |
| 2g | Meal with meat or poultry or other traditional source of protein mentioned first (as food) in name of product | A puréed or semi-puréed meal containing vegetables, other carbohydrates and meat, poultry or other traditional source of protein, where the source of protein is mentioned as first food in product name (e.g., "Hearty beef hotpot" or "Chicken and potato pie") |
| 2h | Meals with meat, poultry, fish, offal or other traditional source of protein (but not named as the first food in product name) | A puréed or semi-puréed meal containing vegetables, other carbohydrates and traditional source of protein, where the meat/protein is not listed as first food in product name (e.g., "Hearty shepherd's pie", "Cottage pie" or "Carrot, potato and lamb hotpot") |
| 2i | Dairy with or without fruit or other naturally sweet foods | Foods with dairy as the largest main ingredient by weight (i.e., greater than the sum of total fruit or total grain ingredients) such as yogurt, fromage frais, custard, porridge or rice pudding, made with or without other naturally sweet foods such as fresh fruit, fruit juice or dried fruit (excluding honey and other added sugars) |
| 2j | Only meat or poultry in name of product | Puréed or semi-puréed poultry, where poultry is the only food listed in product name and constitutes the single largest ingredient (except water) |
| 2k | Only fish or other traditional source of protein in name of product | Puréed or semi-puréed fish or other traditional source of protein, where this is the only food listed in product name and constitutes the single largest ingredient (except water) |
| 3 | Meals with chunky pieces | |
| 3a | Meat, fish or other traditional source of protein-based tray or pot meal | Non-puréed soft meals containing chunky pieces of vegetables, legumes or other carbohydrates and meat, fish or other traditional source of protein (often sold in trays) |
| 3b | Vegetable-based tray or pot meal | Non-puréed soft meals containing chunky pieces of vegetables, legumes or other carbohydrates (often sold in trays) |
| 4 | Dry finger foods and snacks | |
| 4a | Sweet confectionery, sweet spreads and fruit chews | Confectionery includes: chocolate and other products containing cocoa; white chocolate; jelly sweets and boiled sweets; chewing gum and bubble gum; caramels; liquorice sweets; marzipan; sweetened or "yogurt"-coated fruit etc.<br>Sweet spreads: spreadable chocolate and any other sweet sandwich/toast topping such as jam, marmalade or honey and sweet nut spreads etc. |

| | Food category | Definition and examples |
|---|---|---|
| | | Fruit chews include any dried and processed fruit products such as fruit gums, bars or fruit strips/leathers/roll-ups (i.e., a dense chewy food made from pulped and dehydrated/dried fruit) |
| 4b | Sweet snacks and finger foods | Any sweet baked, fried, dried or dehydrated food intended to be eaten between meals with ≥ 15% energy from total sugar (≥ 2.5 g/100 kcal) is classed as a sweet snack or finger food<br>Any starchy food, fruit-based or vegetable-based product where the sugar content is < 15% of total energy may be classed as a savoury snack (category 4d)<br>Including foods such as: sweet pastries; croissants; cookies/biscuits; sponge cakes; wafers; fruit pies; sweet buns; chocolate-covered biscuits; cake mixes and batters; cereal or energy bars (i.e., cereal/ granola or muesli bars); and crisps/puff products made from fruit, vegetables or starchy foods (which may be coated in fat/oil) |
| 4c | Rusks and teething biscuits | Light, crumbly or twice-baked dry sweet biscuit or bread to be chewed for teething or softened with liquid |
| 4d | Savoury snacks and finger foods | Foods consisting of ≥ 95% single or mixed grains, rice, potato, nuts, seeds, fruits or vegetables, including popcorn and maize corn with total sugar content < 15% energy from total sugar (< 2.5 g/100 kcal)<br>Any product with ≥ 15% energy from total sugar is classed as a sweet snack (category 4b)<br>Includes foods such as savoury biscuits and pretzels, baked chips/crisps (e.g., potato, grain or other starchy food etc.), rice cakes coated in powdered fruit or vegetables, cereal bars and rusks made without added sugars |
| 4e | Fruit (fresh or dry whole fruit or pieces) | Includes fresh whole or peeled fruit (e.g., apple) and dried fruit (e.g., dry slices of plain apple, freeze-dried strawberries, raisins, dry apricots, prunes)<br>Excludes fruit pieces coated in sugar or oils/fats (e.g., banana chips, sweetened cranberries or yogurt raisins) |
| 5 | Juices and other non-formula drinks | |
| 5a | Single or mixed fruit juices | Drinks made using anything other than ≥ 95% whole fruit (or fruit and vegetables) including fruit/vegetable cell walls (i.e., not ≥ 95% blended fresh fruit (or fruit and vegetable) pulp (which are classified in category 2a))<br>Includes drinks made using concentrated or strained/sieved fruit (e.g., apple juice, orange juice)<br>Excludes smoothies/purées which are ≥ 95% whole fruit (or fruit and vegetables) (see category 2a) |
| 5b | Single or mixed vegetable juices | Drinks made using "modified" vegetable pulp (i.e., not ≥ 95% blended fresh vegetables)<br>Includes drinks made using concentrated or strained/sieved vegetables<br>Excludes vegetable purées made using ≥ 95% vegetables (see category 2b) |

| | Food category | Definition and examples |
|---|---|---|
| 5c | Other non-milk-based drinks | Includes ready made from cordials, energy drinks, ices, cola, lemonade, orangeade, other soft drinks, and mineral and/or flavoured waters (including aerated) with added sugars or sweetener |

a Exclusions to the food categories:

- products not specifically marketed for children younger than 3 years of age;
- vitamin and mineral food supplements, whether to be consumed as tablets/drops or added to foods at home (e.g., home fortification products such as micronutrient powders, lipid nutrient powders);
- products that function as breast-milk substitutes (i.e., formula milk, follow-on formula milk);
- products whose labels state that they are intended only for pregnant women, mothers or children older than 3 years.

b Products considered to be marketed as foods complementary to breast milk or breast-milk substitutes as being suitable for this age group if they:

- are labelled with the words “baby”, “infant,” “toddler” or “young child”;
- are recommended for introduction at an age of less than 3 years;
- have a label with an image of a child who appears to be younger than 3 years of age or feeding with a bottle; or
- are in any other way presented as being suitable for children under the age of 3 years.

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REVIEW ARTICLE

# Sodium-glucose co-transporter 2 (SGLT2) inhibitors

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Type 2 diabetes mellitus is a progressive metabolic disorder. Marked hyperglycaemia leads to serious vascular complications. Hence, addressing this modifiable risk factor is of paramount importance. Sodium-glucose co-transporter 2 (SGLT2) inhibitors represent a relatively new class of antidiabetic agents. They offer an intermediate glucose-lowering effect and through other pleiotropic effects provide cardiac and renal benefits. This review focuses on the mechanism of action, benefits and adverse effects of SGLT2 inhibitors. The authors also delineate the ideal type 2 diabetic candidate to receive SGLT2 inhibitors. This is critical as SGLT2 inhibitors should not be used in a 'one-size-fits-all approach' but their use should be individualized based on certain patient characteristics. This patient-centred approach aims at maximizing the benefits and reduce the risks associated with SGLT2 inhibitors.

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## Introduction

Type 2 diabetes mellitus is a complex metabolic disorder in which hyperglycaemia occurs as a result of a number of pathophysiological disturbances. DeFronzo refers to these pathophysiological processes as the ominous octet. These are summarized in Table 1.[1] Marked hyperglycaemia is associated with long term end organ damage due to microvascular and macrovascular complications.[2] Good glycaemic control reduces the risk of onset and progression of such complications.[3] However, achieving optimal glycaemic control remains a challenge. Sodium-glucose co-transporter 2 (SGLT2) inhibitors are a relatively new class of oral antidiabetic agents.[4] They offer a new strategy for achieving glycaemic control and have been associated with cardiovascular and renal-outcome benefits.[5] Despite their effectiveness in the treatment of type 2 diabetes, a number of adverse effects have been linked to SGLT2 inhibitors.[6] Hence, SGLT2 inhibitor therapy re-enforces the importance of personalized patient-centred management. The latter approach reduces the risks of adverse effects by the analysis of patient's characteristics prior to the prescription of such agents.[7]

## The physiological actions of SGLT2 inhibitors

The kidneys play a pivotal role in glucose handling. In healthy adults, they filter 160-180g of glucose per day.[8] This filtered glucose is then reabsorbed and returned to the systemic circulation via the proximal convoluted tubule. 90% of renal glucose reabsorption is mediated through SGLT2 activity.[9] SGLT2 is a high capacity, low affinity transporter distributed over the luminal surface of the S1 and S2 segment of the proximal convoluted tubule.[10] The residual filtered glucose is reabsorbed by the low capacity, high affinity sodium-glucose co-transporter 1 (SGLT1).[11]

Hyperglycaemia increases the filtered and reabsorbed glucose up to two-fold.[8] Furthermore, in type 2 diabetes, SGLT2 activity seems to be upregulated due to increased expression of the SGLT2 transporter genes. This leads to increased glucose reabsorption with resultant hyperglycaemia.[4, 12]

SGLT2 inhibitors block the reabsorption of the filtered glucose through the SGLT2 in the proximal convoluted tubule, hence inducing glycosuria and osmotic diuresis. This leads to decreased glycated haemoglobin levels, body weight and systolic and diastolic blood pressure.[13-14]

SGLT2 has recently also been discovered on pancreatic α-cells.[15] Inhibition of these transporters by SGLT2 inhibitors, blocks glucose influx into the pancreatic α-cells, leading to increased glucagon secretion.[15] This process blunts the SGLT2 inhibitors' hypoglycaemic effect, as glucagon promotes endogenous glucose production (via glycogenolysis and gluconeogenesis).[16] Another postulated mechanism behind glucagon secretion is the compensatory glucagon release that occurs in response to the acute decline in serum glucose concentration due to the induced glycosuria secondary to SGLT2 inhibition.[17] Overall SGLT2 inhibition results in a reduced insulin: glucagon ratio. This reduced insulin: glucagon ratio meets two of the pathophysiological mechanisms making up the ominous octet leading to hyperglycaemia (Table 1) and hence one would expect SGLT2 inhibitors to increase glucose levels. However, there are two mechanisms by which this ratio may actually

benefit type 2 diabetes patients utilising SGLT2 inhibitors.

**Table 1** Pathophysiological Mechanisms making up the Ominous Octet (Adapted from DeFronzo).[1]

| | |
|---|---|
| 1. | Decreased insulin secretion |
| 2. | Decreased incretin effect |
| 3. | Increased lipolysis |
| 4. | Increased renal glucose re-absorption |
| 5. | Decreased glucose uptake |
| 6. | Increased hepatic glucose production |
| 7. | Increased glucagon secretion |
| 8. | Neurotransmitter dysfunction |

In fact this reduced insulin: glucagon ratio has been termed as the 'Robin-Hood effect' by one review paper.[18] SGLT2 inhibition lowers insulin secretion, hence preventing unnecessary glucose utilization by peripheral tissues creating a 'pseudo-fasting' state and thus encourages lipolysis to generate free fatty acids.[18] Through β-oxidation and the citric acid cycle, energy is released from fatty acid metabolism. In addition, when the processing capacity of the citric acid cycle is overwhelmed, free fatty acid metabolism leads to the biosynthesis of ketone bodies. Ketone bodies are another alternative energy substrate. Hence, SGLT2 inhibition favours the switch from carbohydrate to lipid metabolism. This also contributes to weight loss in the long term.[18]

Furthermore, the increased glucagon secretion, results in increased endogenous glucose production. Additionally, the reduced insulin secretion prevents unnecessary glucose uptake by peripheral tissues, allowing more glucose to be filtered through the glomerulus. Glucose reabsorption *via* the SGLT2 in the proximal convoluted tubule is however inhibited by SGLT2 inhibitors. The energetic costs of gluconeogenesis and caloric loss of glycosuria promote further weight loss.[19]

As aforementioned, the hyperglycaemia in type 2 diabetes leads to an increase in the concentration of filtered glucose in the proximal convoluted tubules. This results in overactivity of the SGLT2 and SGLT1 transporters with resultant increased glucose and sodium reabsorption. The tubular fluid at the macula densa in the distal convoluted tubule will thus have a reduced sodium concentration. As a response, the tubulo-glomerular feedback system leads to renin-angiotensin-aldosterone system (RAAS) activation and afferent arteriole vasodilatation, with glomerular hyperfiltration being the end result.[20]

The vasodilatory effect on the afferent arteriole is predominantly responsible for the glomerular hyperfiltration observed in diabetes.[12] Glomerular hyperfiltration accompanied by glomerular capillary hypertension is responsible for the initiation and progression of renal disease in diabetes.[12] SGLT2 activity is an important factor in diabetic renal disease pathophysiology, as SGLT2 transporters are upregulated due to enhanced SGLT2 gene expression and due to increased activation of the angiotensin II type 1 receptor generating increased SGLT2 transporters.[12,21] These actions worsen glomerular hyperfiltration and hypertension generating a

vicious cycle that propagates diabetic nephropathy.[12]

By blocking the SGLT2 in the proximal tubule, SGLT2 inhibitors reverse the detrimental mechanisms that lead to glomerular hyperfiltration and hypertension. In fact, treatment with SGLT2 inhibitors is associated with a minimal, reversible decrease in the estimated glomerular filtration rate (eGFR) as a result of afferent arteriole vasoconstriction.[12] This reduction in eGFR with SGLT2 inhibitors mimics that of angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARB).[12]

## Clinical Benefits

SGLT2 inhibitors have a unique mechanism of action independent of insulin secretion and action. In addition, they provide a number of metabolic and haemodynamic effects that reduce the risk of cardiovascular and renal disease.

### Glycaemic Control

SGLT2 inhibitors are intermediate glucose-lowering agents, with mean HbA1c reductions of 0.6-1.1% when compared to placebo. A meta-analysis by Monami et al reported a reduction in HbA1c over 24 weeks that was more pronounced in patients who were younger, had a short history of diabetes duration and had a higher body mass index, HbA1c and fasting blood glucose level.[5, 22]

Several studies have demonstrated that SGLT2 inhibitors are non-inferior when compared to other anti-diabetic agents.[4]

In a 78 week double-blind, placebo-controlled trial by Rosenstock et al, type 2 diabetic patients controlled solely on basal insulin who were prescribed empagliflozin required a reduced dose of insulin whereas the placebo group were observed to need an increased insulin dose.[23]

In another 52 week, double-blind trial by Schernthaner et al, type 2 diabetics inadequately controlled on metformin and a sulfonylurea were randomly assigned to canagliflozin or sitagliptin. The HbA1c reduction was significantly greater with canagliflozin (-1.03%, -11.3mmol/mol) when compared to sitagliptin (-0.66%, -7.2mmol/mol). Furthermore, participants on canagliflozin lost weight and had better systolic blood pressure readings when compared to sitagliptin treated patients (p value <0.001). Despite the better glycaemic control, subjects on canagliflozin suffered from increased genital tract infections. However, the overall results of this study have to be reviewed with caution since 38.5% of participants did not complete the study.[24]

Hence, SGLT2 inhibitors provide additional glycaemic control in combination with both oral antidiabetic agents and insulin.

### Weight Loss

Glycosuria leads to a negative caloric balance, resulting in a weight loss of circa 2-3kg. This has been demonstrated in 12-week trials of empagliflozin, canagliflozin and dapagliflozin.[25]

This weight loss is usually apparent after 6 weeks from the initiation of SGLT2 inhibitor therapy and the rate of weight loss gradually decreases until it stabilizes between weeks 26-34.[26] Most of the early decline in body weight with SGLT2 inhibition is due to the depletion of hepatic glycogen and the associated water loss. In the long term, mesenteric and subcutaneous adipose tissue loss contributes to further weight loss.[16]

Furthermore, in patients on insulin therapy, SGLT2 inhibitors reduce insulin dose requirements and may mitigate insulin-induced weight gain.

## Decrease in Systolic and Diastolic Blood Pressure

Decreases in systolic and diastolic blood pressure by 1.6-6.9mmHg and 0.88-3.5mmHg respectively were demonstrated with SGLT2 inhibitor treatment.[27] SGLT2 inhibitors lead to osmotic diuresis and mild natriuresis. This creates a reduced intravascular volume and an initial reduction in blood pressure readings. In the long term, weight loss and inhibition of the RAAS contributes to decreased blood pressure readings.[27]

## Cardiovascular Benefits

Empagliflozin, canagliflozin and dapagliflozin have been associated with reduced cardiovascular morbidity and mortality in type 2 diabetic patients with cardiovascular disease.

The EMPA-REG OUTCOME study showed that empagliflozin reduces the risk of cardiovascular events. Although there were no significant between-group differences in the rates of myocardial infarction or non-fatal stroke, in the empagliflozin group there was a significantly lower death rate from cardiovascular causes (3.7% *vs* 5.9%), hospitalisation for heart failure (2.7% *vs* 4.1%) and death from any cause (5.7% *vs* 8.3%) when compared to the placebo group.[28] Furthermore, the divergence between the empagliflozin and placebo primary outcome curves was evident after only 3 months, suggesting the rapid effect of empagliflozin.[29] On the other hand, in the CANVAS trial it took 1 year for canagliflozin treatment to show separation in the survival curve for major adverse cardiac events (MACE).[29] However one should note that empagliflozin's postulated rapid effect is a matter of debate and further studies are required to ascertain whether pharmacological intra-class effects exist.

The CANVAS trial reported that canagliflozin decreased the rate of death from cardiovascular causes, non-fatal myocardial infarction or non-fatal stroke when compared with placebo occurring in 26.9 *vs.* 31.5 participants per 1000 patient-years respectively with a p value of <0.001 for non-inferiority and a p value of <0.02 for superiority. Like the EMPA-REG OUTCOME study, the reduction in occurrence of the individual components of the composite outcome in those subjects treated with canagliflozin were not statistically significant.[30]

The results of the DECLARE-TIMI 58 trial are similar to the aforementioned studies. Dapagliflozin treatment did not result in a lower rate of MACE (p value of 0.17) but resulted in a lower death rate from cardiovascular causes and hospitalisation rates from heart failure when compared to placebo (p value of 0.005).[31]

These studies demonstrated the significant cardiovascular benefit of empagliflozin, canagliflozin and dapagliflozin in a high risk population with established cardiovascular disease. Further studies are required to assess whether SGLT2 inhibitors will have such a beneficial effect on type 2 diabetics who do not have overt cardiovascular disease.

## Heart Failure

As aforementioned, the EMPA-REG outcome and the DECLARE-TIMI 58 trial demonstrated reduced hospitalisation rates for heart failure.[28, 31] In addition, a sub-analysis of the CANVAS trial revealed that canagliflozin

reduced the overall risk of heart failure events in patients with type 2 diabetes mellitus and high cardiovascular risk with no clear difference in effects on heart failure with reduced ejection fraction versus heart failure with preserved ejection fraction.[32]

The natriuretic, glycosuric and metabolic effects of SGLT2 inhibitors benefit patients with heart failure. Furthermore, the above physiological effects have also been demonstrated in patients without diabetes mellitus.[33] In fact, the U.S. Food and Drug Administration (FDA) has approved dapagliflozin as a treatment for heart failure with reduced ejection fraction in patients with or without type 2 diabetes.[34]

### Renal Benefits

Empagliflozin and canagliflozin appear to reduce the progression of nephropathy. The secondary analysis of the EMPA-REG outcome revealed that patients on empagliflozin had a reduced risk of incident or worsening nephropathy when compared to the placebo group (12.7% vs 18.8% respectively).[35]

Canagliflozin reduced the progression of albuminuria when compared to placebo in the CANVAS trial (89.4 *vs.* 128.7 participants per 1000 patient years respectively). Additionally, the need for renal replacement therapy and death from renal causes occurred less frequently in the canagliflozin group when compared to placebo (5.5 *vs.* 9 patients per 1000 patient-years).[30]

## Risks associated with SGLT2 inhibitors

### Genital Tract Infections

The most frequent adverse event of SGLT2 inhibitors are genito-urinary tract infections.[14]

There are several studies that concluded that SGLT2 inhibitor treatment in type 2 diabetics was linked with an increased incidence of urinary tract infections and genital mycotic infections.[36-38]

Nicolle et al, (2015) showed that despite the increased risk of urinary tract infections in type 2 diabetics treated with canagliflozin, there was no risk of serious or upper urinary tract infections.[38]

However, this has been recently challenged and the U.S. FDA has issued warnings about cases of necrotizing fasciitis of the perineum in patients taking SGLT2 inhibitors. The FDA has received 12 reports of Fournier's gangrene between March 2013 and May 2018.[39] Patients with previous genital mycotic infections are at higher risk of developing such infections with dapagliflozin according to Thong et al (2018).[40]

Patients should be informed of the risks of urinary and genital tract infections and advised to seek medical help early on if they develop any symptoms indicative of a urinary tract infection.

### Euglycaemic diabetic ketoacidosis

In 2015, the FDA issued a safety warning regarding the risk of diabetic ketoacidosis in people with type 2 diabetes being managed with SGLT2 inhibitors.[41] Fadini et al, (2017) analysed the diabetic ketoacidosis reports from the FDA adverse drug reporting (ADR) system and concluded that SGLT2 inhibitors are associated with diabetic ketoacidosis.[42] They also suggested that this is not limited to any particular demographic or co-morbid population and can occur after any duration of SGLT2 inhibitor use.[42]

One possible pathophysiological event contributing to diabetic ketoacidosis in patients using SGLT2 inhibitors is due to their 'Robin-Hood effect' (kindly refer to section 2.0 The physiological actions of SGLT2 inhibitors).

Despite this, the European Medicines Agency (EMA) states that the benefits of SGLT2 inhibitors continue to outweigh the risks in the treatment of type 2 diabetes.[43] Physicians need to be made aware of the possible risk factors for diabetic ketoacidosis in patients treated with SGLT2 inhibitors. These include:

- Insulin deficiency as in latent auto-immune diabetes of adults[14]
- Type 2 diabetics with evidence of low insulin secretory capability (labile diabetes control, lean body build or episodes of ketosis)[14]
- Sudden reduction in the insulin dose[44]
- Increased insulin requirements such as in post-operative cases and patients with an acute illness[44]
- Alcoholism[44]
- Starvation[44]
- Dehydration

If diabetic ketoacidosis is suspected, blood or urine ketone levels should be checked, even if the patient is normoglycaemic. If diabetic ketoacidosis is confirmed in a patient on SGLT2 inhibitors, these should be stopped immediately. [44]

## Lower limb amputations

The FDA and EMA have issued warnings as there was an increased risk of leg and foot amputations with the use of canagliflozin in type 2 diabetics.[6] This cautionary advice is mostly based on the CANVAS trial where 7 cases of lower limb amputations out of 1000 patients resulted in the 100mg canagliflozin group, compared to 3 cases of lower limb amputations out of 1000 patients in the placebo group.[30]

Hence, with such evidence, it might be appropriate to avoid SGLT2 inhibitors in patients with peripheral vascular disease, neuropathy, active foot ulceration or a previous amputation.[14]

## Malignancy

The potential carcinogenic effect of any drug cannot be assessed in short term trials.[45] Initial data on dapagliflozin by HW Lin et al, suggested an association with male bladder cancers and female breast cancers.[46] However, Wiviott et al, concluded that dapagliflozin therapy was not associated with increased bladder cancer risk.[31]

A recent meta-analysis by Tang et al, demonstrated that SGLT2 inhibitors were not significantly associated with an overall increased risk of malignancy. However, it was noted that there was an increased risk of bladder cancer with empagliflozin.[45]

## Skeletal Fractures

SGLT2 inhibitors may affect bone metabolism.[13] They can lead to increased renal reabsorption of phosphate resulting in an increased serum phosphate concentration. This hyperphosphataemia may promote parathyroid hormone secretion which in turn stimulates bone resorption in order to maintain serum calcium levels.[6] In addition, SGLT2 inhibitors increase the serum concentration of fibroblast growth factor 23 leading to bone disease and decreased 1,25 dihydroxyvitamin D levels. The overall effects are reduced calcium absorption from the gut and impaired bone calcification, hence increasing the overall risk of bone fractures.[6]

There is conflicting evidence on the effect of SGLT2 inhibitors on bone metabolism. A meta-analysis by Tang et al, does not support the harmful effects of SGLT2 inhibitors on bone

fractures.[47] The fracture event rate was 1.59% in the SGLT2 inhibitors group and 1.56% in the control group.[47] Watts et al, reported that the risk of fractures was increased with canagliflozin therapy.[48] A small but statistically significant decrease in total hip bone mineral density was reported with canagliflozin when compared to placebo over a 2 year period (-0.9% and -1.2% reduction in BMD in canagliflozin 100mg and 300mg respectively when compared to placebo).[49] There were no statistically significant changes in BMD at other sites (femoral neck, lumbar spine, distal forearm).[49] Watts et al, concluded that the cause of the increased fracture risk with canagliflozin is unknown and extrinsic factors i.e.: the increased risk of falls due to orthostatic hypotension from the SGTL2 inhibitor induced volume depletion is a more likely explanation.[48] This risk is exacerbated in patients receiving diuretics.[48]

With regards to this issue, further future safety monitoring from randomised controlled trials and studies on SGLT2 inhibitors on bone health and interaction with anti-resorptive therapy are still required.

**Table 2** Renal adjusted dosing of canagliflozin, dapagliflozin, empagliflozin and ertugliflozin

| | Canagliflozin | Dapagliflozin | Empagliflozin | Ertugliflozin |
|---|---|---|---|---|
| Starting Dose | 100mg daily | 5mg daily | 10mg daily | 5mg daily |
| Maximum Dose | 300mg daily | 10mg daily | 25mg daily | 15mg daily |
| Renal Adjustment | eGFR >45-60: patients should not be initiated on canagliflozin but if they are already tolerating canagliflozin, use a maximum dose of 100mg daily | eGFR <60: use is not recommended | eGFR >45-60: patients should not be initiated on empagliflozin but if they are already tolerating empagliflozin, use a maximum dose of 10mg daily | eGFR <60: use is not recommended |
| | eGFR <45: use is contraindicated | eGFR <45: use is contraindicated | eGFR <45: use is contraindicated | eGFR <45: use is contraindicated |
| | ESRD and Haemodialysis: use is contraindicated | ESRD and Haemodialysis: use is contraindicated | ESRD and Haemodialysis: use is contraindicated | ESRD and Haemodialysis: use is contraindicated |

### Acute kidney injury

The FDA had issued warnings about the risk of acute kidney injury for canagliflozin and dapagliflozin.[14] However an analysis by Nadkarni et al, revealed that there was no evidence for an increased risk of acute kidney injury (AKI) associated with SGLT2 inhibitor use in patients with type 2 diabetes when compared to non-users over a 1 year follow-up in two large health systems.[50] Nevertheless, renal function should be monitored prior to and during treatment with SGLT2 inhibitors.[51] Table 2 demonstrates the renal adjusted dosing of canagliflozin, dapagliflozin, empagliflozin and ertugliflozin.[52]

## Indications for SGLT2 inhibitors

In the past, pharmacological management of diabetes has revolved around improving blood glucose and HbA1c levels. However, nowadays management is shifting towards prescribing antidiabetic agents that also provide cardiovascular benefits and reduce mortality.

The 2019 update to the consensus report "Management of hyperglycaemia in type 2 diabetes" by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) recommends prescribing SGLT2 inhibitors with proven cardiovascular benefit, after initiation of metformin and lifestyle changes in patients with established atherosclerotic cardiovascular disease (ASCVD). Moreover, the consensus report also recommends SGLT2 inhibitor use among type 2 diabetics with ASCVD and heart failure. Another consensus recommendation regarding SGLT2 inhibitors is their use in type 2 diabetics with chronic kidney disease irrespective of cardiovascular disease if the eGFR permits, since they have been shown to provide renal outcome benefits.[7]

Based on the benefits and adverse effects of SGLT2 inhibitors, the ideal type 2 diabetic candidate to receive SGLT2 inhibitor therapy requires the following characteristics:

- young age[22]
- eGFR >45 in empagliflozin and canagliflozin
- eGFR >60 in dapagliflozin and ertugliflozin
- heart failure
- established atherosclerotic cardiovascular disease
- obese/overweight[22]
- hypertensive
- no past/present history of frequent mycotic infections/urosepsis/pyelonephritis and indwelling urinary catheters[14]
- no past history of peripheral vascular disease/neuropathy/active ulceration/gangrene[14]
- no past history of diabetic ketoacidosis or unprovoked ketosis[14]

Dapagliflozin was recently approved for the management of type 1 diabetes mellitus as an add on therapy with insulin, when the latter fails to achieve control in over-weight patients. Despite its significant improvement in glycaemic control and weight loss, there was a higher risk of DKA in patients with type 1 diabetes.[53]

## SGLT2 inhibitors and other pharmacological therapies

Before prescribing an SGLT2 inhibitor, physicians should discuss the benefits and adverse events related to these new therapeutic agents. The patient's renal function and overall fluid status must be checked (by assessing blood pressure, jugular

venous pressure, skin turgor, chest auscultation for pulmonary oedema and lower limb oedema). A detailed history should be taken with a focus on any previous urinary tract infections or any features of peripheral vascular disease, while specifically looking for any active ulcerations. A urinalysis is commendable to screen against asymptomatic UTI and ketonuria. Renal function should be monitored pre- and post-treatment initiation.[51] A moderate drop in eGFR is expected when starting an SGLT2 inhibitor.[12] Elderly individuals and other patients who are at risk of falls (e.g.: those suffering from orthostatic hypotension) would benefit from a bone mineral density test prior to SGLT2 inhibitor therapy. Canagliflozin should be avoided in patients with osteoporosis as it was associated with a greater loss of bone mineral density over time.[49]

Current diabetes treatment, anti-hypertensive treatment and diuretic therapy need to be specifically analysed, as treatment adjustment may be necessary.[13]

### Diabetic Treatment

In patients receiving a biguanide or an incretin based therapy (DPP4-inhibitors or GLP-1 receptor agonist), an SGLT2 inhibitor can be started without any adjustments. However, these patients should be advised to watch for possible loose stools or vomiting and ensure regular fluid intake. If such gastrointestinal effects occur, the biguanide or incretin based therapy's dose should be lowered and vigorous fluid intake encouraged to reduce the risk of diabetic ketoacidosis. Ideally, treatment with SGLT2 inhibitors should be interrupted or postponed until there is correction of the fluid loss.

In those patients on insulin or insulin secretagogues (sulfonylurea or glinides), treatment adjustment depends on the HbA1c level. If patients have an elevated HbA1c (>8.5%), then no dose adjustment is usually required. Patients with an HbA1c level of <8.5% may need to reduce their insulin/insulin secretagogue dose when initiating an SGLT2 inhibitor.

In all of the above settings, glucose monitoring is essential so that the diabetic treatment is titrated accordingly.[13]

### Diuretics

Patients on diuretics may need diuretic dose adjustments. This decision should ideally be taken in conjunction with a cardiologist, especially in cases of chronic heart failure.[13]

### Anti-hypertensive Treatment

Patients who are >65 years of age, suffer from atrial fibrillation or frequent syncopal events or orthostatic hypotension or who have a blood pressure <140/80mmHg, may require a lower anti-hypertensive dose if an SGLT2 inhibitor is prescribed. In these patients, blood pressure should be monitored on a weekly basis initially and the dose of anti-hypertensive treatment adjusted as necessary.[13]

In addition, since SGLT2 inhibitors cause a moderate drop in eGFR, patients taking nephrotoxic agents (ACE-i, ARB, NSAIDs, diuretics, digoxin and aminoglycosides) should be closely monitored so as to avoid acute kidney injury.

## Conclusion

SGLT2 inhibitors represent a new class of oral antidiabetic medications that not only target glucose homeostasis but through other pleiotropic effects offer cardiac and renal protection. The 2019 update to the consensus report "Management of hyperglycaemia in type 2 diabetes" by the ADA and EASD

recommends SGLT2 inhibitor use with proven cardiovascular benefit, after first line therapy with metformin and lifestyle changes. In addition, SGLT2 inhibitor use is recommended in patients with atherosclerotic cardiovascular disease with co-existent heart failure and in patients with type 2 diabetes and chronic kidney disease (CKD) (irrespective of their cardiovascular disease status) as they reduce CKD progression.[7] Empagliflozin has demonstrated a wide spectrum of beneficial effects ranging from reducing kidney disease progression, hospitalisation for heart failure and cardiovascular and all-cause mortality.[28] Although the trials offer promising data, SGLT2 inhibitor use requires careful patient selection, so that those that will benefit from such therapy will be prescribed these medications. Patients on this treatment need regular monitoring to avoid or pick up adverse effects early on.

## Key Points

- SGLT2 inhibitors are a relatively new class of oral antidiabetic agents with a unique mechanism of action, independent of insulin secretion and action.
- SGLT2 inhibitors provide an intermediate glucose-lowering effect by inducing glycosuria and in addition offer cardiac and renal outcome benefits through other pleiotropic effects.
- SGLT2 inhibitors are associated with a number of risks including: genital tract infections, euglycaemic diabetic ketoacidosis, lower limb amputations, skeletal fractures, risk of malignancy and acute kidney injury.
- Empagliflozin has demonstrated a wide spectrum of beneficial effects including the following: a reduction in progression of kidney disease, a decrease in hospital admissions for heart failure and also a reduction in cardiovascular and all-cause mortality.
- When it comes to SGLT2 inhibitors, physicians need to move away from a one-size-fits-all approach towards a more personalized patient-centred management. Despite the multiple benefits SGLT2 inhibitors offer, their prescription requires careful assessment by the prescribing physician to identify those patients who would benefit from such drugs so as to ensure a reduced risk of adverse events.

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CASE REPORT

# Leptospirosis – the unsuspecting culprit a case report and literature review

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Leptospirosis is caused by spirochete bacteria in the genus Leptospira and can present with a vast range of clinical symptoms. We report a case of leptospirosis in a 47-year-old gentleman who presented with sepsis and ended up with multi-organ failure. He was treated with piperacillin/tazobactam and doxycycline was added at a later stage. The patient recovered well with no complications. A literature review follows

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## Introduction

Leptospirosis is a worldwide public health problem with 1.03 million annual cases worldwide per year.[1] Patients with leptospirosis may present with predominant pulmonary symptoms, ranging from cough, chest pain, breathlessness and mild to severe haemoptysis to acute respiratory distress syndrome (ARDS). The pulmonary symptoms usually appear between the fourth and sixth day of illness. The evolution of the disease may be very rapid and may result in death in less than 72 hours.[2] The patient can also present with kidney and liver failure. Leptospira bacteria are excreted in bodily fluids including urine and then penetrate their host through abrasions in the skin or via the mucosal membrane. There are a lot of peridomestic animals (rats, horses, cows, dogs, and pigs) and feral animals (bats, coyotes, sea lions, and even frogs) that can carry *Leptospira* bacteria in their kidneys. These animals are then presumed to excrete *Leptospira* in the environment.[1] Occupations that have direct (including veterinarian and farmer) or indirect (such as plumbing or sewer worker) contact with animal excrete are at risk of contacting *Leptospira*.[2]

## Case report

A 47-year-old, Gozitan man suffering from diabetes mellitus presented to the Accident and Emergency Department with sepsis. He complained of a three-day history of lethargy, nausea, vomiting, loose stools, 24 hours of fever, decreasing appetite and oral intake. He also had myalgia, especially over his right shoulder and chest. He denied any recent travel. However, on further questioning, he claimed to work in the fields daily and was noted to have several abrasions. The patient was a non-smoker and only drank alcohol socially.

Vital signs in the emergency department were notable for a blood pressure of 106/63mmHg which decreased to 85/46mmHg within an hour and tachycardia at 130bpm. The patient was alert and orientated. The ocular examination was notable for scleral icterus. The skin appeared jaundiced, however, an examination of the heart, lungs, abdomen and lower limbs were unremarkable.

## Initial laboratory study results

The initial blood test results are shown in Table 1. Chest radiography was normal and electrocardiography showed sinus tachycardia at 134 beats/min.

The patient was admitted to the intensive care unit for sepsis shock and multiorgan dysfunction. Intravenous piperacillin/tazobactam was initiated with aggressive fluid resuscitation together with noradrenaline as inotropic support.

The following day, he was still dehydrated. Chest auscultation revealed few sparse basal crackles, the abdomen was slightly tender in the epigastric area but there was no guarding/rebound. Serologic test results for acute hepatitis A, B and C infections were negative. An abdominal ultrasound showed hepatosplenomegaly. Doxycycline was added to piperacillin/tazobactam.

Day 2 post-admission, there was bronchial breathing on the right base and CXR confirmed a mild consolidation in the right lung middle field. His CRP increased from 200mg/L to 423mg/L and platelets decreased from 118 x109/L to 96 x109/L. Results also came back positive for the legionella urinary antigen.

Day 3 post-admission, his general condition improved. His CRP decreased from 300mg/L to 197mg/L. Serum Leptospira IgM came back as positive so leptospirosis was confirmed.

Day 4 post-admission, his oxygen saturation dropped to 88% on air. He was given 7L/min oxygen via a normal mask which kept his oxygen saturations at 96%. Bronchial breathing in the right base persisted. He was restarted on metformin which was stopped during admission.

**Table 1** Initial blood test results

| Investigation | | Normal range |
|---|---|---|
| White blood cell count | 7.3 x $10^9$/L | 4.3 - 9.43 x$10^9$/L |
| Haemoglobin | 15.4g/dL | 14.1 - 17.2g/dL |
| Platelets | 115 x $10^9$/L | 146 - 302 x $10^9$/L |
| CRP | 200mg/L | 0 - 5 mg/L |
| Sodium | 125mmol/L | 135 - 145mmol/L |
| Creatinine | 117umol/L | 62 - 106umol/L |
| Bilirubin | 66.5umol/L | 0 - 17.1umol/L |
| Alkaline phosphotase (ALP) | 72U/L | 40 - 129U/L |
| Aspartate aminotransferase (AST) | 118U/L | 10 - 50U/L |

Day 5 post-admission, he maintained his blood pressure and inotropic support could be stopped. A chest X-ray showed deterioration in the right lung. The consolidation had increased in size involving almost the whole right lung. There was a mild right pleural effusion and there was also a new consolidation in the left lung (Figure 1).

Day 6 post-admission, he was clinically stable but developed respiratory distress. A diagnosis of acute respiratory distress syndrome was made and non-invasive ventilation was started. CRP continued to decrease from 50mg/L to 39mg/L. Computed tomography of the thorax showed the presence of many consolidations commencing from upper lobes and involving both lower lobes bilaterally associated with bilateral pleural effusions (right more than left). There were bulky mediastinal and enlarged hilar lymph nodes. There was some oedema of the right axilla and right chest wall. The spleen was seen to be enlarged (16x10cm). The CT imaging was very suggestive of leptospirosis (Figure 2.)

The clinical picture demonstrated that he was responding to treatment. He was continued on piperacillin/tazobactam 4.5g TDS for a total of 10 days and doxycycline 100mg BD for a total of 7 days. Despite the deterioration after an initial improvement, he did well and recovered fully with no complications on discharge.

**Figure 1** Chest X-ray on Day 5

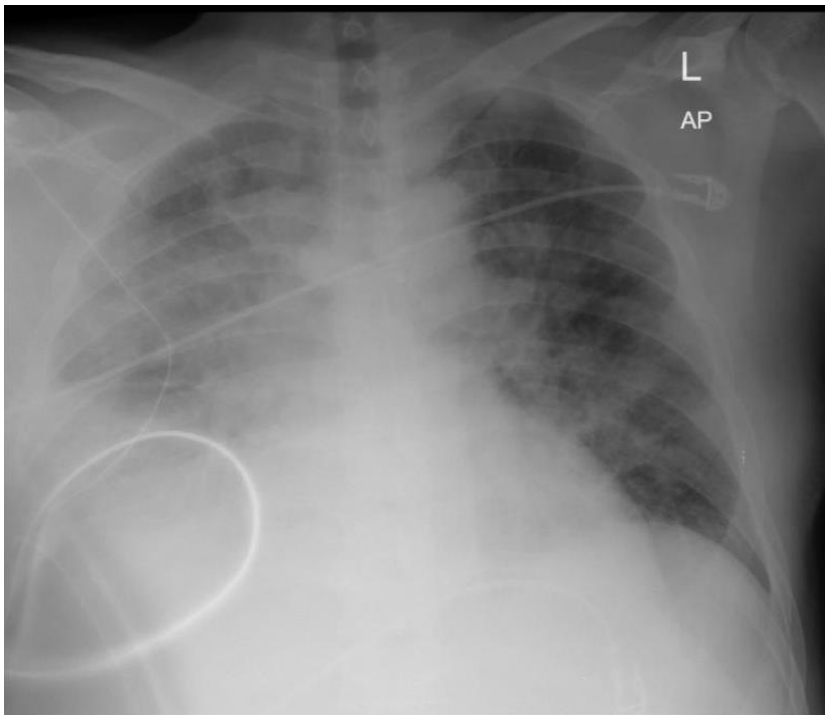
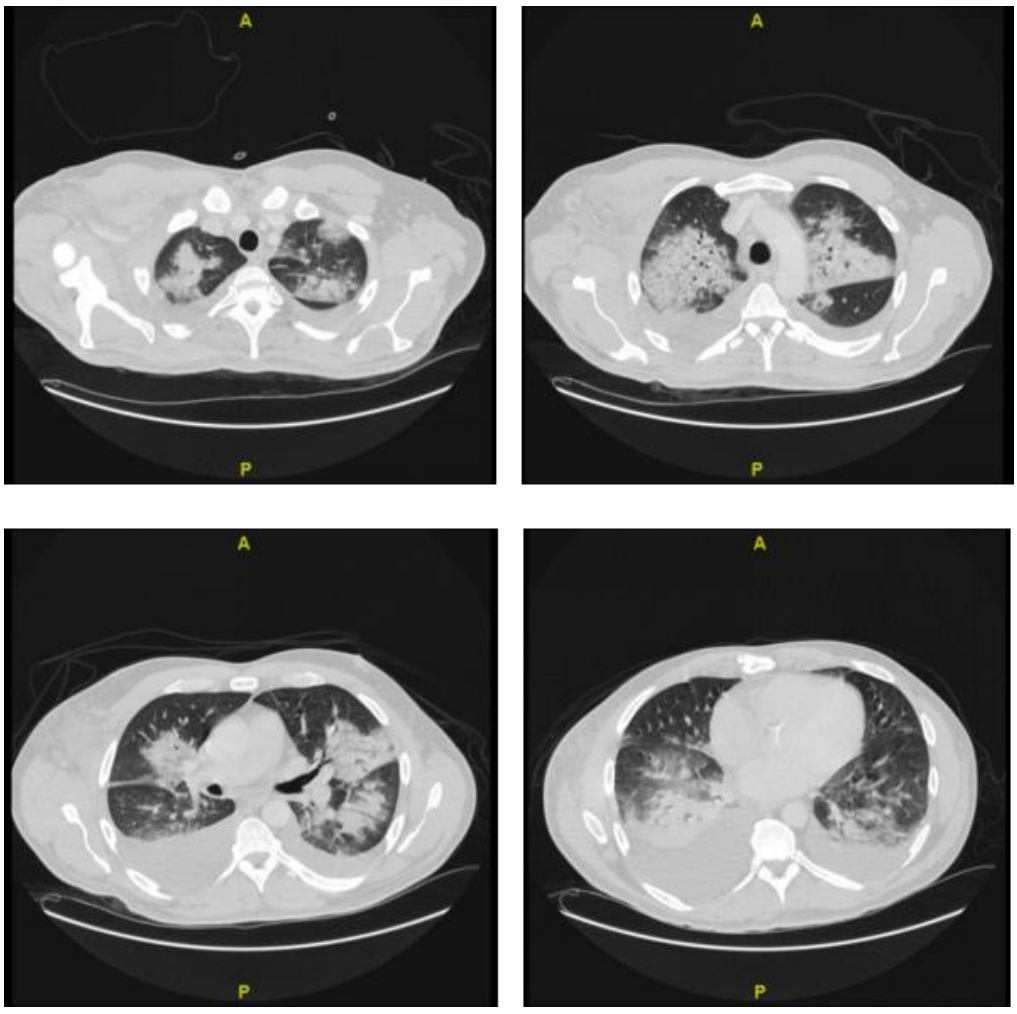



**Figure 2** CT thorax on Day 6 suggestive of Acute Respiratory Distress Syndrome



## Discussion

### *Clinical Manifestation and Differential Diagnosis*

Leptospirosis usually presents itself as an acute febrile illness and mimics several other diseases.[3] The illness can range from a mild infection with symptoms like influenza to severe disease. Leptospirosis follows a biphasic pattern with an acute septicaemia phase which lasts for 1 week.[4] Then the symptoms resolve when antibodies are produced, and the spirochete is excreted in the urine. Three to four days after remission, fever may recur which is the second phase of the illness. Usually, the illness cannot be clinically distinguished from other febrile illness syndromes. In the second phase of the disease, a severe form of infection, called Weil's syndrome, can happen and is characterised by renal failure, bleeding, and jaundice.[5]

In the acute phase, symptoms vary from fever, headache, severe myalgia, anorexia, nausea, vomiting and conjunctival suffusion without purulent discharge. The headache in leptospirosis is similar to that of dengue fever which is characterised by retro-orbital pain and photophobia.[5] Myalgia is usually in the calf or lumbar areas.[3] In the second phase of the disease, Leptospirosis can affect any organ including the brain, liver, kidney, lungs, heart, and eyes.

The differential diagnosis of Leptospirosis is vast and must take into consideration all local diseases which might present as fever. Infections like influenza, malaria, rickettsioses, arboviral infections (dengue fever, yellow fever, amongst others), Hantavirus, scrub typhus and HIV seroconversion must be considered.[5-6] Severe fever and haemorrhage may make leptospirosis clinically identical to viral haemorrhagic fevers.[7]

### *Investigations*

Early diagnosis of leptospirosis is essential. General laboratory results are very non-specific. One usually finds an increased ESR and liver function tests can be slightly increased. Renal function can be impaired. Leucocytosis can happen when the infection is severe, and platelets have been noted to decrease. Urinalysis can show proteinuria, pyuria, and haematuria.[5] However, these investigations can only give a possible diagnosis of leptospirosis.

### *Microscopy and culture*

Leptospirosis can be detected by microscopic observation of the organism and by isolation of the spirochete in cultures. Body fluids like urine, blood, and cerebrospinal fluid (CSF) can be seen under dark field microscopy to visualise the organism. The timing of the sample is crucial. This method has low sensitivity as $1x10^4$ leptospires/ml must be present, for leptospires to be seen.[3]

*Leptospira* can be isolated in the acute phase of infection. Cultures from various body fluids and tissues can isolate *Leptospira*. As with direct visualisation, blood cultures can only help in the early phase of the illness, meaning from before the onset of symptoms to the end of the first week, during which leptospiraemia happens. These should be taken before the patient takes antibiotics. Urine cultures can also be taken but should be used during the leptospirosis phase which is one week after onset of symptoms. Other fluids like CSF and peritoneal dialysate can be used to culture *Leptospira* during the first week of infection. After, serological methods and molecular methods can be used to identify the isolated leptospires.[4]

### *Serological diagnosis*

Detection of specific antibodies and antigens can be used to confirm leptospirosis. Serological methods can be genus-specific or serogroup specific. The microscopic agglutination test (MAT) remains the definite serological investigation of choice. Antibodies can be detected in the blood after 5 to 7 days after onset of the infection.[8] In MAT, the patient serum is mixed with leptospiral cultures. These are then examined by dark field microscopy for agglutination. MAT detects IgG and IgM which are serogroup specific. Therefore, all serogroups should be tested. A high titre for a specific serovar signifies that it is the cause of the infection. For a definite diagnosis, paired sera are required. Some disadvantages of MAT are that it is complex, requires maintenance of *Leptospira* cultures and that in the acute phase, sensitivity is low.[4]

Due to the limitations of MAT, other rapid screening tests for the diagnosis of leptospirosis in the acute phase have been developed. IgM antibodies can be identified during the first week of illness.[9] This can be done using techniques like ELISA, dipstick, lateral flow, indirect hemagglutination assay, and latex agglutination.[3] However, there are still limitations of any serological test in the acute phase. Furthermore, rapid diagnostic tests should be confirmed with a reference test.[10]

### *Molecular Diagnosis*

DNA detection by polymerase chain reaction (PCR) has been applied for the detection of Leptospira in the acute setting. DNA has been amplified in several media including blood, CSF, urine, aqueous humour, and tissues.[11] PCR has been demonstrated to be useful in the detection of *Leptospira* when antibody production has not yet begun. On the other hand, the sensitivity of DNA detection by PCR decreases throughout the disease. A limitation of PCR is that it currently cannot distinguish between different serovars.[12] Real-time PCR has also been used to quantify bacterial load in leptospirosis.[13]

In a recent study, investigating the cost-effectiveness of different management concluded that management based on the clinical judgement was most efficient.[14]

### *Treatment and Prevention*

Empirical treatment for leptospirosis usually consists of penicillin or doxycycline. Treatment should be tailored according to how severe the infection is, with oral antibiotics for a simple febrile illness to IV penicillin in severe life-threatening infections.[15]

Treatment should be started during the early stages of diagnosis of leptospirosis and during this period oral doxycycline is advised. In late or severe infections (including Weil's disease), intravenous penicillin has been shown to reduce the length of hospital stay. Treatment should be started as suspicion of leptospirosis is made and should be given for a total of 7 days. In another study comparing IV penicillin G and ceftriaxone, it was shown that there was no difference in mortality, therefore, they are both equally effective.[16] Ciprofloxacin should also be given to patients with associated uveitis.[15]

*Leptospira* species has a bacterial cell wall. Theoretically, this would make it susceptible to many different antibiotics. A study in 2003, showed that the *Leptospira* species is susceptible in vitro to penicillin, cephalosporins, aminoglycosides, macrolides, quinolones and tetracyclines amongst others. However, leptospira spp. was not shown to be

susceptible to metronidazole, glycopeptides, sulfamides, and rifampicin.[17]

Severe leptospirosis infections can be associated with damage to any organ and even with multi-organ failure. Jarisch-Herxheimer reactions have also been reported. Cases with acute kidney injury or pulmonary haemorrhage (with associated ARDs) sometimes would need further treatment with adjunctive therapies like haemodialysis and mechanical intubation respectively. Pulmonary leptospirosis is usually due to an inflammatory response to the leptospires toxin which damages the host.[15] Corticosteroids can inhibit this response but this is still controversial. A review in 2014 noted that a randomised control study has shown that these are ineffective in pulmonary leptospirosis and can even increase the risk for other nosocomial infections. On the other hand, other studies showed that pulse dose steroids successfully treated leptospiral pulmonary involvement and even renal involvement.[18-19]

Prophylaxis against leptospirosis with doxycycline does not significantly affect the incidence of infection but has been shown to decrease morbidity and mortality during outbreaks of the disease.[20] The prevention of leptospirosis usually entails better sanitation. Leptospirosis is usually carried around by rodents, therefore eradication of rodents in endemic areas is essential. Using personal protective gear can also prevent infections.

Vaccinations are also currently available against leptospirosis. The current vaccinations are killed, whole-cell suspensions (bacterins). These have multiple side effects and have low efficacy. Therefore, better vaccines are needed. In these last two decades, new DNA vaccines have been promising and are an important strategy of minimising leptospirosis infection.[21]

## Conclusion

Leptospirosis is an infectious disease present not only in developing countries but also in industrialized nations. Diagnosing leptospirosis may be a challenge in view that it can mimic several other diseases. A high index of suspicion is needed to make the diagnosis based on the history and clinical manifestation since laboratory investigations will take days to confirm leptospirosis.

The disease has a biphasic pattern. Thus, after an initial improvement, deterioration in the clinical picture with multi-organ failure is not uncommon. Early antibiotic therapy should be started in every case of suspected leptospirosis since in most cases, early treatment prevents morbidity and mortality.

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CASE REPORT

# Complicated diverticular disease: case report

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Recently, diverticular disease of colon, especially of its left half, has become one of the most acute issues of abdominal urgent surgery. Increased proportion of the elderly population and progressing incidence of diverticulosis as well as its severe complications due to perforation and diverticular abscess formation encourages focused attention to this problem especially given the fact that this condition is characterised by usually asymptomatic early stage that makes its diagnostics even more challenging.[1-7] This article covers a clinical case of complicated diverticular disease of sigmoid colon with perforated diverticulitis entering the right inguinal canal through dilated internal inguinal ring. The patient had a history of surgery, namely, bilateral herniotomy due to bilateral inguinal hernia. The final diagnosis was set upon diagnostic laparoscopy followed by conversion to laparotomy, herniotomy due to relapsing right-sided inguinal interstitial hernia with removal of diverticulum incarcerated and locked in hernial sac, and resection of sigmoid colon with formation of sigmostoma. Our findings indicate that in special cases when the inflamed diverticulum location is anatomically atypical, the only method of complicated diverticulitis diagnostics and treatment is laparotomy with abdominoscopy and removal of the infection source.

Recently, diverticular disease of colon, especially of its left half, has become one of the most acute issues of abdominal urgent surgery. Progressing incidence of diverticulosis as well as its severe complications due to perforation and diverticular abscess formation encourages focused attention to this problem. This article covers an interesting case of complicated diverticulitis of sigmoid colon with perforated diverticulitis entering the right inguinal canal through dilated internal inguinal ring.

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## Case Report

On October 14, 2018, a self-referred 73-years-old patient admitted the outpatient unit of the State Budgetary Healthcare Institution of the Arkhangelsk Oblast 'Severodvinsk Municipal Clinical Emergency Hospital No. 2' with complaints on pain in the iliac region on the right 3 days after the disease onset.

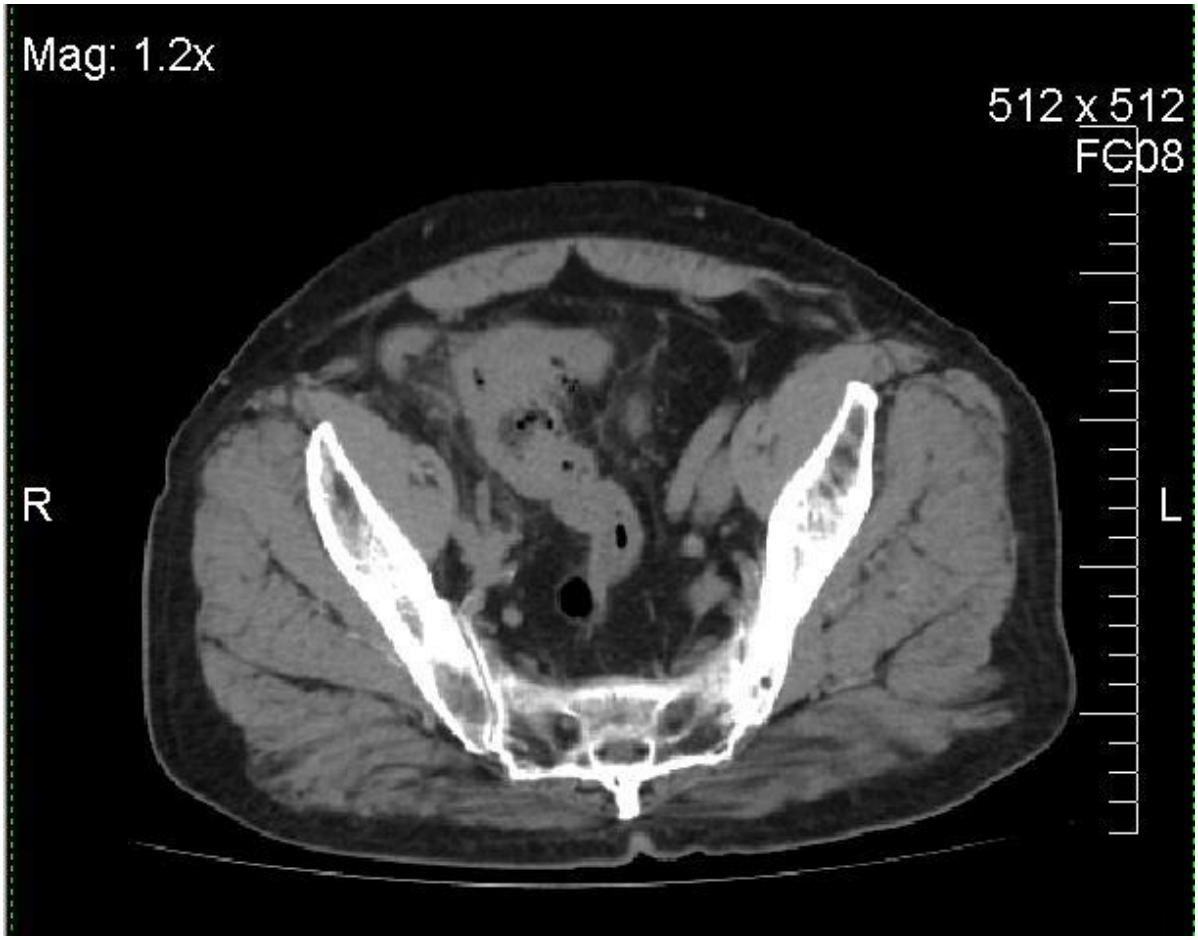
Upon examination, the patient's state was satisfactory with heart rate of 75 bpm and stable haemodinamics. Vesicular breathing, no rales, respiratory rate of 16 bpm. Clear, wet tongue. Abdomen not bloated, involved in breathing, soft, tender in the iliac region on the right with positive peritoneal signs (Mendel signs, Voskresenskiy signs) with negative Blumberg's sign. The patient has a history of surgery, namely, bilateral herniotomy due to bilateral inguinal hernia

The blood test showed the following parameters: leukocytes - 10.1× $10^9$/l, C-reactive protein – 183 mg/l.

CT of the abdominal cavity and retroperitoneal space [Figure 1]. Sigmoid colon in the iliac region on the right had signs of marked inflammatory changes such as unevenly thickened wall up to 6 mm, multiple gas bubbles parietally, infiltrated surrounded subcutaneous tissue (gas bubbles in it cannot be excluded).

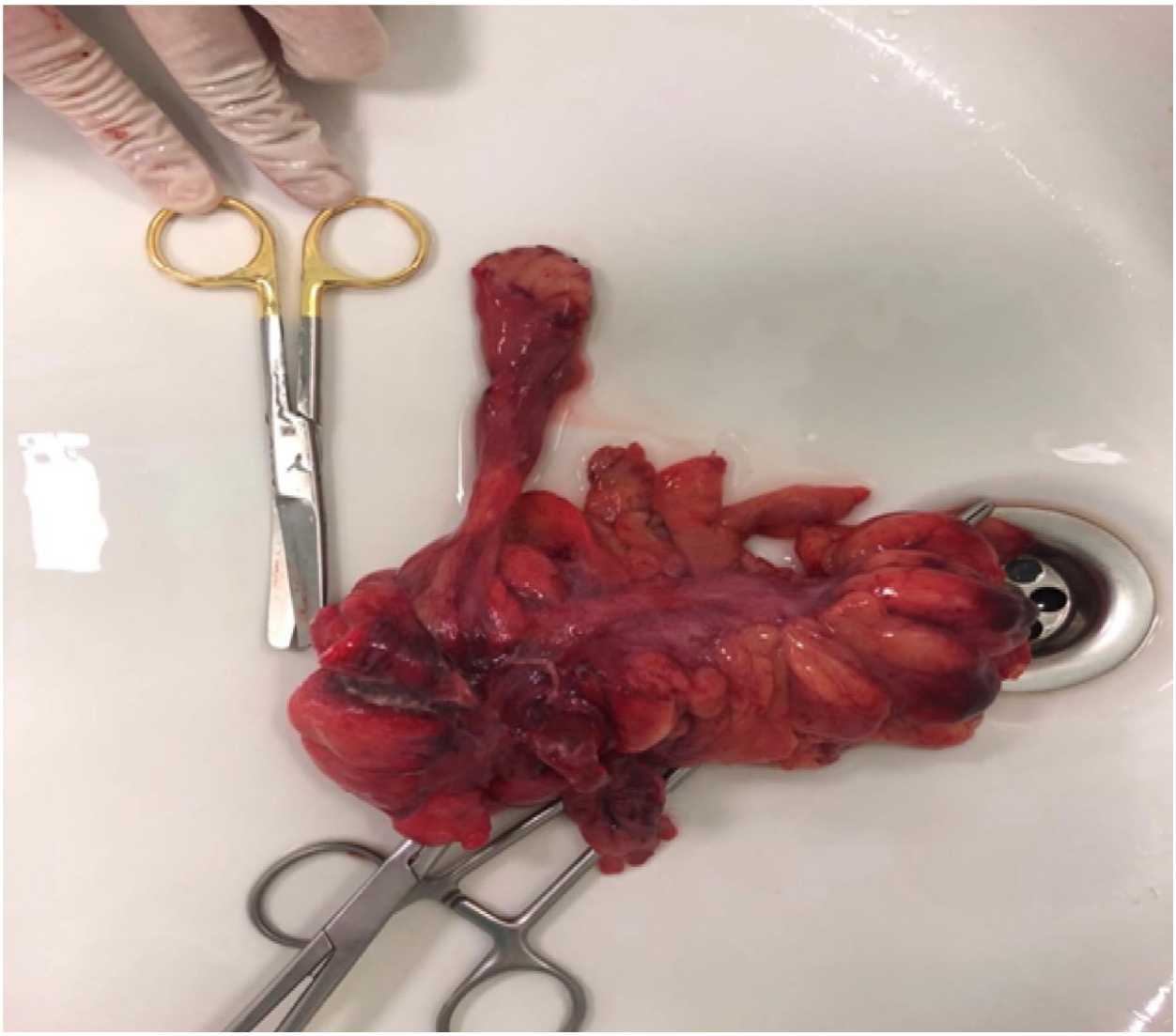
Conclusion: Acute sigmoiditis, perforation is not excluded.

**Figure 1** Abdominal CT: sigmoid colon in the iliac region on the right



Diagnostic laparoscopy was carried out which the following findings: sigmoid colon elongated, located in the iliac region on the right, immobilised, fixed within this region with the area of necrosis on its wall. Conversion to midline laparotomy: sigmoid colon loop located in the iliac region on the right; a diverticulum branched from it entering the right inguinal canal through dilated internal inguinal ring along with the adjacent sigmoid colon wall with the signs of necrosis. Removing of diverticulum from the inguinal canal was not feasible. Conversion to the right inguinal region was carried out, the hernia sac was isolated from adhesions in the initial part of the inguinal canal and opened. In the sac, a top of the diverticulum was found among adhesions fused with the inguinal sac walls. Adheolysis and herniotomy were carried out followed by plastic repair of the inguinal canal with local tissues. Then resection of the pathological part of sigmoid colon with diverticulum was performed through the abdominal cavity [Figure 2].

**Figure 2** Photo of the resected part of sigmoid colon with diverticulum



## Conclusion

Recently, diverticular disease of colon, especially of its left half, has become one of the most acute issues of abdominal urgent surgery. Increased proportion of the elderly population and progressing incidence of diverticulosis as well as its severe complications due to perforation and diverticular abscess formation encourages more focused attention to this problem. At present, a number of approaches to complicated diverticulitis diagnostics and treatment have become irrelevant and require reconsideration. Today, the leading role in diagnostics of diverticulitis complications belongs to CT. The management is based on the imaging data and minimally invasive procedures, including laparoscopic and endoscopic surgeries are becoming increasingly popular. However, in special cases when the inflamed diverticulum location is anatomically atypical, the only method of complicated diverticulitis diagnostics and treatment is laparotomy with abdominoscopy and removal of the infection source as demonstrated by our findings.

## Informed Consent

Written informed consent was obtained from patients who participated in this study.

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/CASE REPORT

# Extrinsic compression of an anomalous left main coronary artery in a patient with pulmonary arterial hypertension presenting with myocardial injury

Maria Bonello, John Bonello, Tiziana Felice, Maryanne Caruana

Extrinsic compression of the left main coronary artery (LMCA) caused by severe pulmonary arterial dilatation in the setting of pulmonary arterial hypertension (PAH) is a recognised entity.[1] This can present with angina, cardiogenic shock, malignant arrhythmias or sudden cardiac death.[2] We report the case of a 17-year-old female with a history of primary PAH who presented with acute chest discomfort, elevated biomarkers and ECG changes. Invasive and non-invasive imaging confirmed her diagnosis and identified an anomalous origin of the left main coronary artery and significant LMCA extrinsic compression by an enlarged main pulmonary artery (MPA). The abnormal anatomical location of the LMCA resulting from its anomalous origin could have further contributed to the risk of compression.[3]

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## Introduction

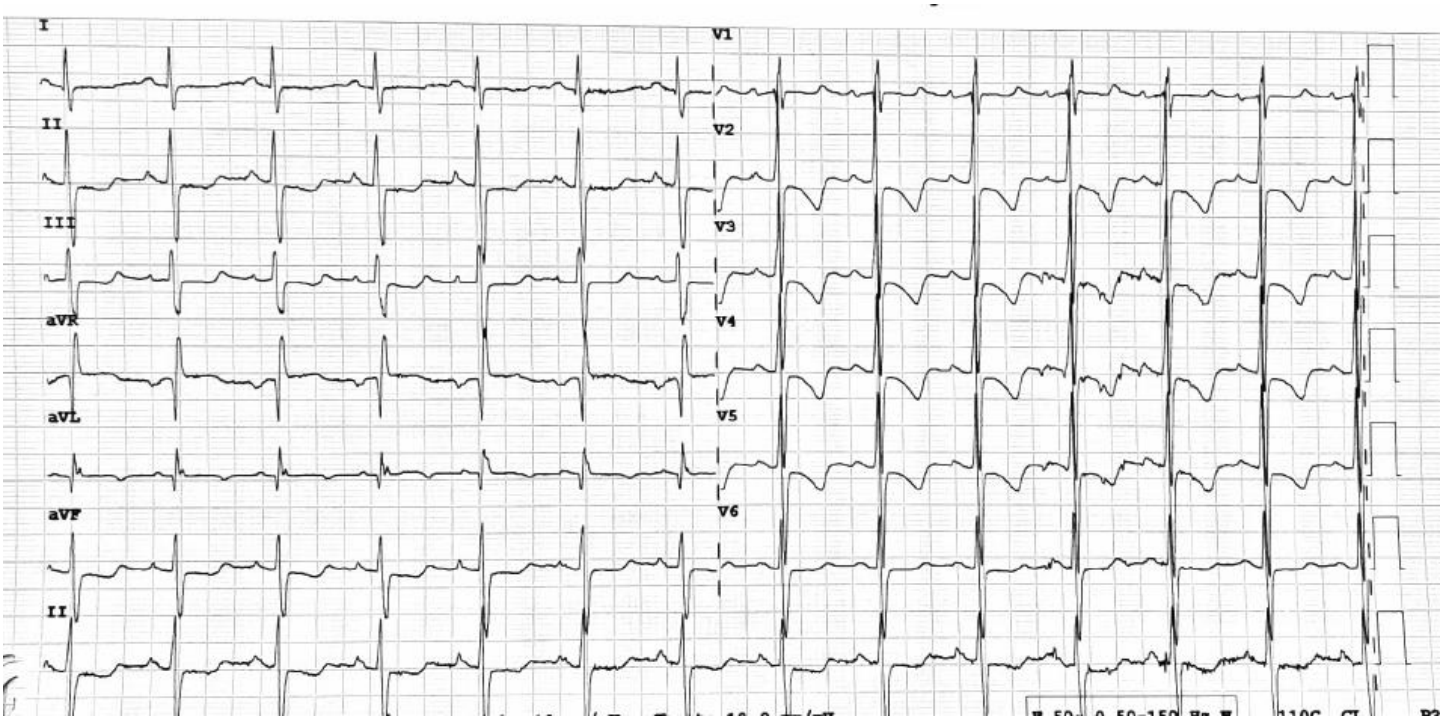
Extrinsic compression of coronary arteries by severely dilated pulmonary arteries in severe PAH is a recognised phenomenon.[1,3] This can lead to angina with/without myocardial injury, cardiogenic shock, arrhythmias and even sudden cardiac death.[2]

## Case Report

A 17-year-old female with severe primary PAH diagnosed at the age of 13 years and established on sildenafil since, presented to the Accident and Emergency Department of our institution with compressive chest pain and presyncope. She was also being followed up by an inherited cardiomyopathy specialist in view of suspected biventricular non-compaction cardiomyopathy. She had an implantable loop recorder (ILR) *in situ* for several months in view of a history of presyncope and syncope.

On clinical examination, she had a split second heart sound with a loud pulmonary component and an end diastolic murmur at the left upper sternal border all in keeping with her known PAH. A high sensitivity troponin T of 1087ng/L (UL 14ng/L) was recorded upon admission which peaked at 1446ng/L within a few hours. A 12-leadECG upon admission showed wide spread downsloping ST-segment depressions and deep T wave inversions as well as subtle ST segment elevations in lead aVR (Figure 1). No arrhythmias were detected on ILR check.

**Figure 1** Twelve-lead electrocardiogram (ECG) at time of admission showing widespread downsloping ST segment depressions and deep T wave inversions as well as subtle ST segment elevations in lead aVR.



An invasive right and left heart catheter study confirmed severe PAH with near-systemic pulmonary artery pressures (PAP) (systolic PAP = 75mmHg vs. systolic aortic pressure = 80mmHg) and a mean PAP of 52mmHg under general anaesthesia. Aortography revealed the LMCA to be originated anomalously from the aorta at the level of the sinotubular junction. A tight long stenosis of its proximal segment was also clearly evident (Figure 2) which is the likely cause of the documented myocardial injury. Retrospective review of a recent cardiac computed tomography (CT) scan confirmed the anomalous coronary origin with extrinsic compression by an adjacent severely dilated MPA with the latter measuring 45 x 48mm (Figure 3).

**Figure 2** Aortographic image of the anomalous origin of the left main coronary artery and a tight stenosis on a long proximal segment.

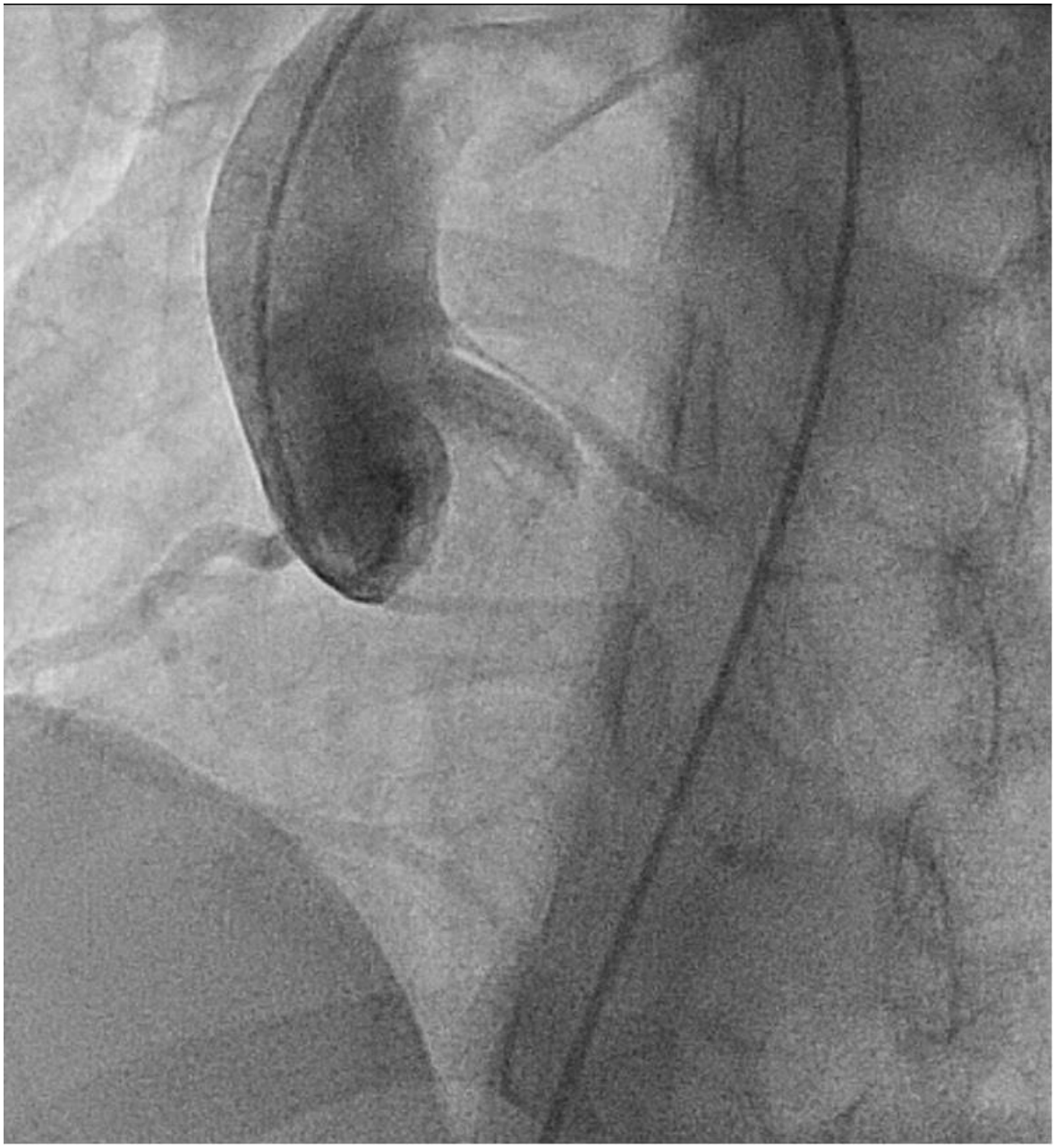
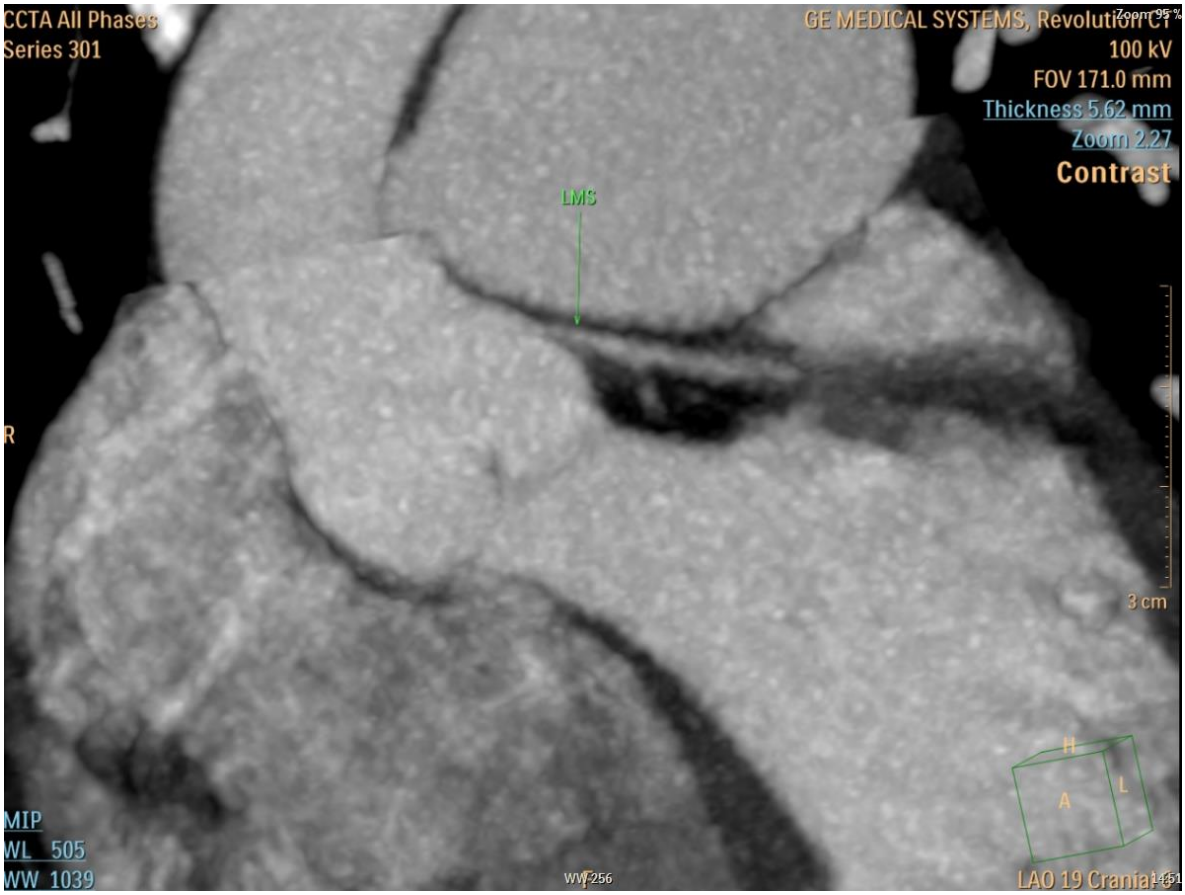


**Figure 3** Extrinsic left main coronary artery compression by the enlarged pulmonary arteries. Cardiac CT also shows the anomalous origin of the left main artery above the sinus of valsalva.




Following extensive discussion about a high-risk LMCA stenting, it was decided to uptitrate advance pulmonary vasodilator treatment in the first instance. She responded well to the addition of macitentan and has reported improvement in her breathlessness and chest discomfort and no further syncopal episodes.

## Discussion

We report the case of a patient that sustained myocardial injury as a result of severe extrinsic compression of the LMCA by a severely dilated main PA in the setting of primary PAH. Myocardial injury identified by elevated cardiac troponin markers has been documented in patients with PAH and is associated with an adverse prognosis. LMCA compression in the setting of PAH is probably an underestimated cause of anginal chest pain.[5] Nonetheless, the prevalence of LMCA compression in patients with pulmonary hypertension and angina is high and various imaging modalities including CTCA have indentified significant LMCA compression in patients with chest pain.[1] A number of risk factors have been associated with LMCA compression in raised pulmonary pressures. These include young age, pulmonary trunk dilation of more than 40mm and a PA trunk / aorta ratio of >1.2.[6] In keeping with our case, Albadri et al highlighted the high anomalous of origin the LMCA is possibly another risk factor for LMCA compression.[3] Percutaneous coronary intervention of the compressed

coronary artery segment in addition to pulmonary hypertension treatment appears to offer an effective and favourable outcome.[1,3,5]

Our case is rather unique in that the compressed coronary artery had an anomalous origin. To the best of our knowledge, there has been only one similar case of an anomalous LMCA extrinsic compression reported in the literature. [4]

In conclusion, chest pains in patients with severe PAH should always alert clinicians to the possibility of coronary compression, especially if accompanied by ischaemic ECG changes and/or cardiac biomarker elevation.

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ORIGINAL ARTICLE

# Abdominal X-ray use in Mater Dei hospital, Malta

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## Aim

To examine a sample of patients who underwent Plain Abdominal X-Rays (AXR) in Mater Dei Hospital (MDH) Emergency Department, Malta and assess if indications for AXR requests met current Hospital Guidelines, relevance of findings in clinical management and if further imaging was required to confirm diagnosis.

## Method

Retrospective review of 550 plain AXR taken between January 2016 till June 2016.The data collected from the MDH PACS System included patient age, gender, AXR indication and findings, follow-up CT abdomen. Guidelines from the Royal College of Radiology were used to confirm if an AXR was indicated or not. Data was then analysed using Microsoft Excel formulas.

## Results

Of 550 plain AXR reviewed, 62.6% were inappropriately requested with indications which did not meet the guidelines. Only 204 requests had a valid indication for plain abdominal x-ray as the initial modality of choice.

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## Introduction

Multiple literature reviews on the use of abdominal x-rays (AXR) in emergency departments1 and in the evaluation of acute abdominal pain2 have concluded that AXR has a very limited role in the evaluation of patients with acute abdominal pain and exposes patients to significant amounts of radiation3.

No local guidance exists with regards to the use of AXR in the workup of emergency department patients. A local audit carried out in 2011 demonstrated that 137 AXR were carried out in the first week of January 2011, with 62% of these being not indicated according to Royal College of Radiology (UK) guidelines4.

CT imaging of the abdomen has been shown to have a much higher diagnostic yield in the workup of abdominal complaints, with higher sensitivity and specificity for pathology5, even in diagnosing intestinal obstruction6.

Anecdotal evidence seems to suggest that despite growing evidence of the futility of performing AXR and the increasing local availability of CT imaging, many patients are subjected to AXR as the initial imaging modality of choice for the abdomen. This risks exposing patients to unnecessary radiation and in the worst case scenario a missed diagnosis due to a normal AXR.

For this reason we have decided to examine a sample of patients who underwent AXR in Mater Dei Hospital emergency department and whether CT imaging was performed regardless of AXR result.

## Method

A total of 550 plain abdominal x-rays taken at Mater Dei Hospital emergency department were collected using the PACS system. These were taken between 1st January 2016 and 23rd January 2016 as well as 1st June 2016 and 26th June 2016. The data collected was patient age, gender, indication (via online request) for AXR, AXR report and whether they were admitted. Furthermore any patient who also had a CT Abdomen done within one week also had the result of the CT recorded. Data regarding patient admission to hospital was collected via iSoft. All data was collected retrospectively and to our knowledge none of the authors were directly involved in the management of these cases.

This data was recorded using Microsoft Excel. AXR were deemed to be indicated if the online request indicated any of the following:

- Suspected foreign body
- Suspected large or small bowel obstruction
- Acute exacerbation of colonic inflammatory bowel disease

As Mater Dei Hospital emergency department provides ready access to abdominal CT imaging, the following were not considered valid reasons for requesting AXR:

- Undifferentiated abdominal pain
- Acute abdominal pain with guarding
- Palpable mass
- Suspected perforation of hollow viscus
- Abdominal trauma
- Suspected renal colic
- Constipation

Guidelines from the UK Royal College of Radiology were used when deciding whether an AXR was indicated or not7. Negative AXRs were any reported as

either "NAD" or "faecal loading" only. Any other report was deemed positive. Data was then analysed using Microsoft Excel formulas.

## Results

Of 550 plain abdominal x-rays (AXR) taken, 258 (46.9%) were of female patients. 20 AXRs belonged to paediatric patients (under 16 years of age). The average age was 60.1, with ages ranging between 0 and 101 years. The median age was 65(Figure 1).

From the total number of AXRs done, 134 (24.4%) were followed by a CT abdomen within 1 week. The distribution of these CTs is shown in figure 2.

With regards to validity, only 204 (37.1%) had a valid indication for plain abdominal x-ray as the initial modality of choice (Figure 3). It is worth noting that of these, 50 patients went on to have abdominal CT imaging nonetheless.

316 (57.5%) of patients who had AXR were admitted to hospital as inpatients. Of these, 203 had negative AXR findings and 118 went on to have CT imaging of the abdomen (Figure 2).

It is also worth noting that 73 patients had only "abdo pain" as the reason for request for AXR on iSoft.

The number of AXR done in the first two weeks of January and June in the emergency department was also recorded (Table 1).

**Figure 1** Histogram of age

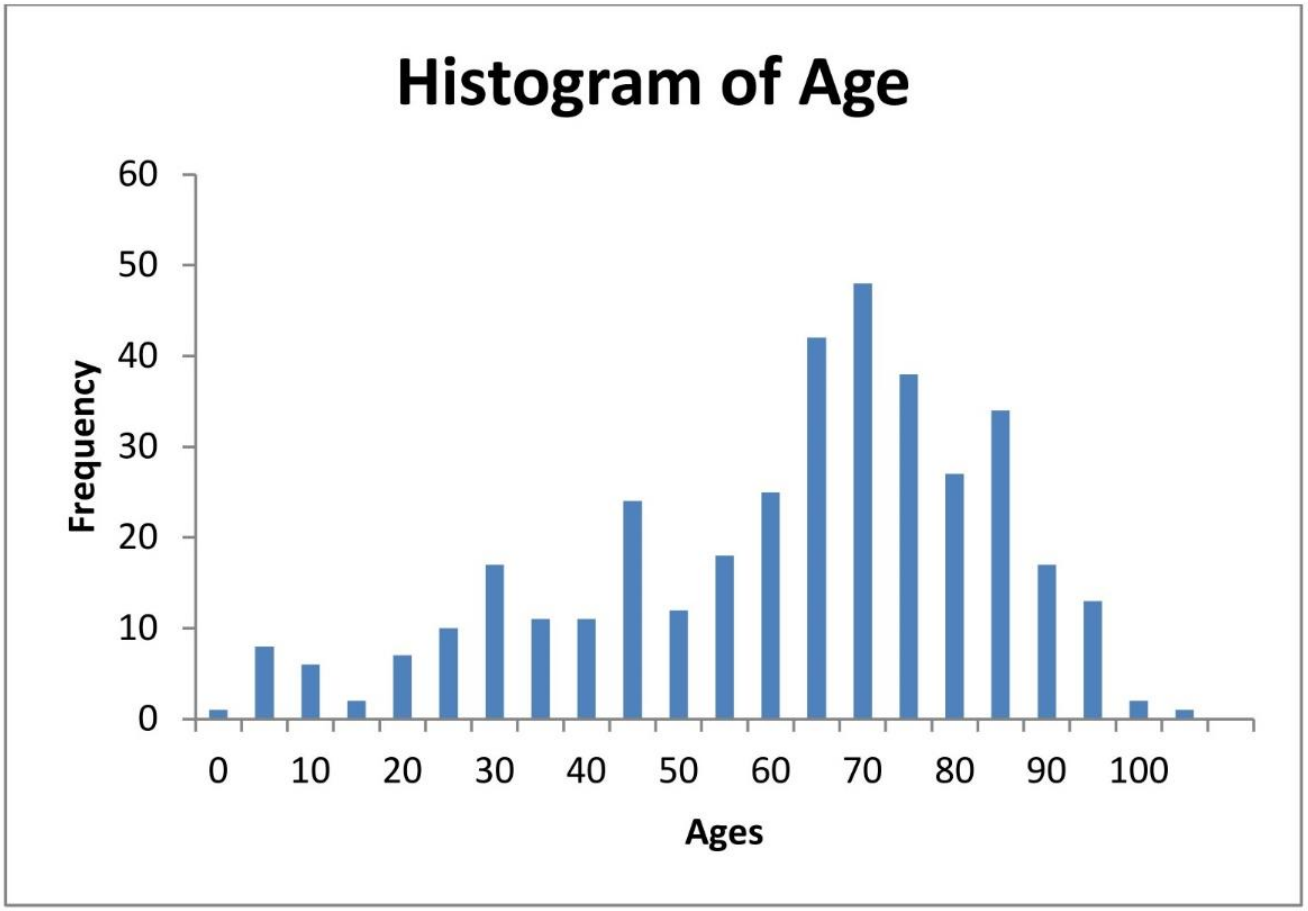

**Figure 2** Distribution of CT imaging

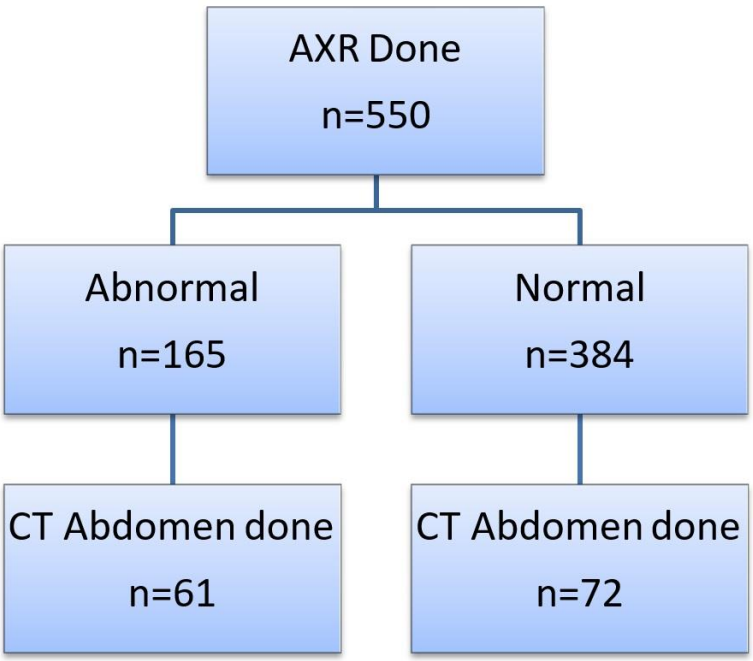


**Figure 3** Validity of AXR request

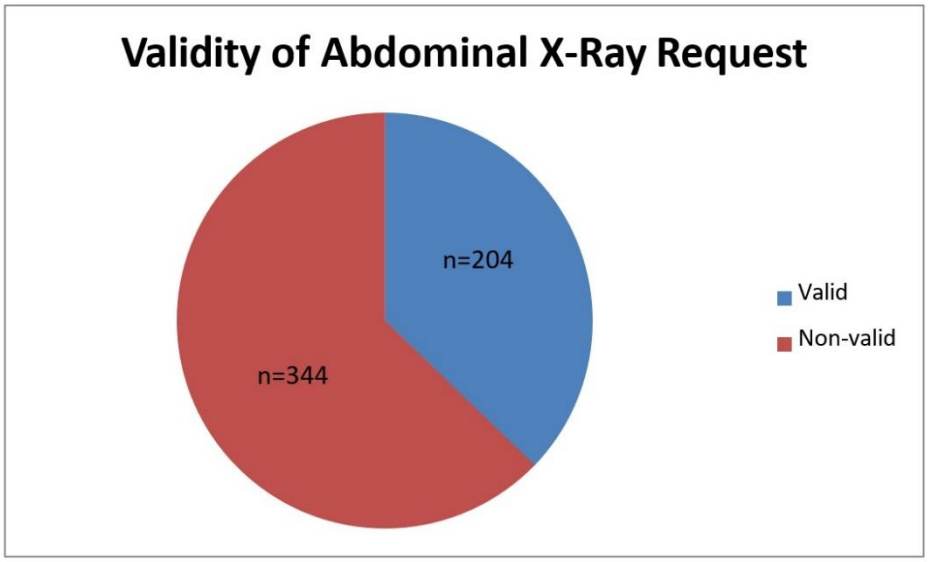


**Table 1** Number of AXR by week

| | |
|---|---|
| 1st week of January 2016 | 90 |
| 2nd week of January 2016 | 86 |
| 1st week of June 2016 | 93 |
| 2nd week of June 2016 | 62 |

## Discussion

Compared to 2011, the number of AXR requested in the emergency department seems to have decreased slightly. However, the number of inappropriately requested AXR remains almost unchanged (62% in 2011 vs 62.6% in 2016).

It is worth noting that of those that had a valid indication for AXR, 50 went on to have a CT abdomen regardless of AXR result (figure 2). This further serves to highlight how limited the yield of AXR is especially with the availability of CT abdomen.

Some might feel justified in using AXR as a form of "screening" for bowel obstruction and then proceeding to CT to identify the level of obstruction. The problem with this logic is that if AXR is negative and a clinical suspicion of bowel obstruction remains, then the patient will likely need CT anyway. For this reason we propose that AXR only be used to identify bowel obstruction in patients who have a history of bowel obstruction with an identified cause on previous CT or surgery.

The fact that of the 316 patients requiring admission after AXR 64% had negative AXR findings seems to suggest that AXR has little to contribute with regards to disposition decisions. This also matches the 2011 findings.

The poor quality of information provided in online requests remains an issue (with 73 of 550 requests having only "abdo pain" as an indication) as has been reported in multiple local audits carried out in the past few years. Whilst it is understood that these orders are often submitted under time constraints, this information is the only information available to the interpreting radiologist and more effort needs to be put into these online requests. Realistically this online information is also the only way to conduct audits and studies with large numbers of patients.

Although paediatric numbers were predictably small (only 20 patients were under 16), the number of valid indications was 12 (60%). This might indicate that more consideration is given before ordering AXR on paediatric patients. Further study with larger numbers is required before reaching any conclusions however.

The main limitation of this audit is that information was gathered only from online sources. No patient notes were reviewed. This might mean that patients with valid indications for AXR were underrepresented in view of poor quality of online request forms. However we feel this is limited as the 2011 audit, which whilst looking at a smaller number of patients reviewed patient notes, showed similar rates of valid vs invalid indications for AXR requests.

Potential exists for further study, for example incorporating the use of abdominal ultrasound in combination with pretest clinical scores to decide on which patients to send for CT abdomen.

## Conclusion

The use of AXR remains disproportionately high, and a large number of AXRs are carried out unnecessarily. A large number of patients would benefit from the use of CT imaging of the abdomen as the first modality of choice, and this would actually decrease the overall amount of radiation that a patient receives by omitting the additional radiation of an AXR.

Our recommendation is that in the emergency department only the following patients have AXR:

- Patients with suspected foreign bodies in the abdomen

- Patients with suspected bowel obstruction who already have a history of bowel obstruction with a known aetiology
- Acute exacerbation of colonic inflammatory bowel disease
- Patients who for whatever reason cannot undergo CT imaging

We further recommend that foundation year doctors discuss with an emergency medicine trainee before requesting AXR. The findings were presented at the Emergency Department Teaching sessions and junior doctors updated on the shortfalls of indiscriminate AXR use.

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CASE REPORT

# Acquired unilateral Brown Syndrome in newly diagnosed Systemic Lupus Erythematosus

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Brown Syndrome is a congenital or acquired ocular movement disorder that is known to be a rare complication of Systemic Lupus Erythematosus (SLE). We report a case of acquired Brown Syndrome in an adolescent girl with newly diagnosed SLE which responded well to oral prednisolone

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## Introduction

Brown Syndrome is caused by abnormalities of the superior oblique tendon-trochlea complex that results in difficulty and diplopia on elevating the affected eye when held in adduction. Acquired causes of Brown Syndrome include rheumatological conditions such as SLE and, although rarely reported in the literature, this association may develop and may require treatment.

## Case Presentation

A 14 year 11-month-old adolescent girl with a history of asthma and heavy menstrual bleeding, initially presented with a two-month history of lethargy, a malar rash, occasional shoulder pains anorexia and weight loss of 6 kg. Initial investigations revealed lymphopenia, anaemia, and a raised erythrocyte sedimentation rate (ESR) of 40 mm in the first hour. During the week following presentation the patient developed central chest pains and shortness of breath and was admitted in view of deteriorating symptomatology.

Further investigations showed a raised rheumatoid factor (29 U/ml), anti-nuclear antibody (ANA) positivity (>1/1000), raised anti-double stranded DNA (>800) with homogenous anti-nuclear (ANF) pattern and low complement levels (C3 589mg/L and C4 58mg/L). A diagnosis of Systemic Lupus Erythematosus (SLE) was made; a dose of 80mg intramuscular methylprednisolone was administered and the patient was started on regular analgesia including paracetamol and ibuprofen.

**Figure 1** This shows an axial T2 weighted MRI image demonstrating a subtle increased signal intensity of the right lateral rectus muscle

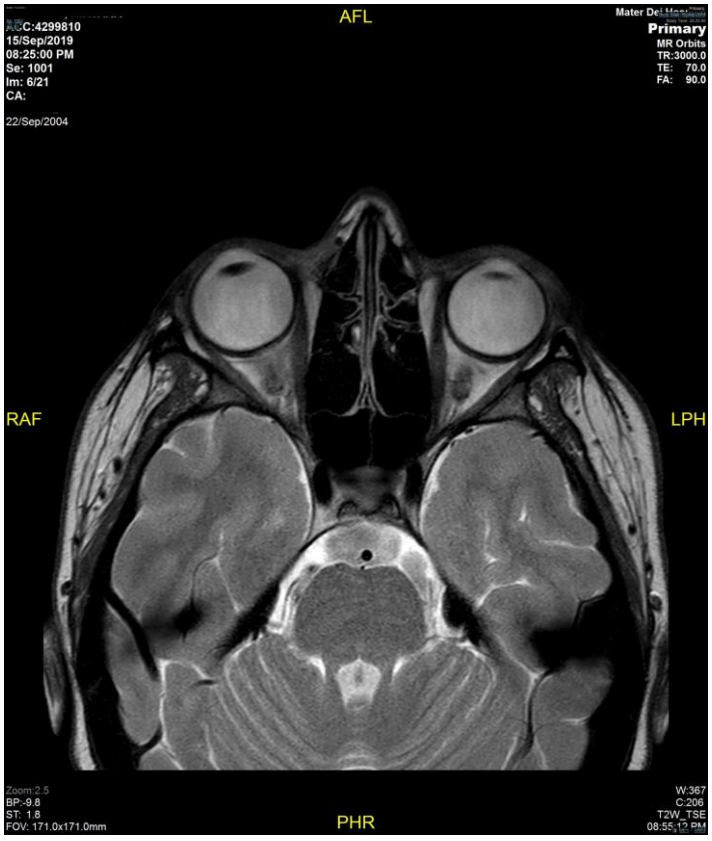
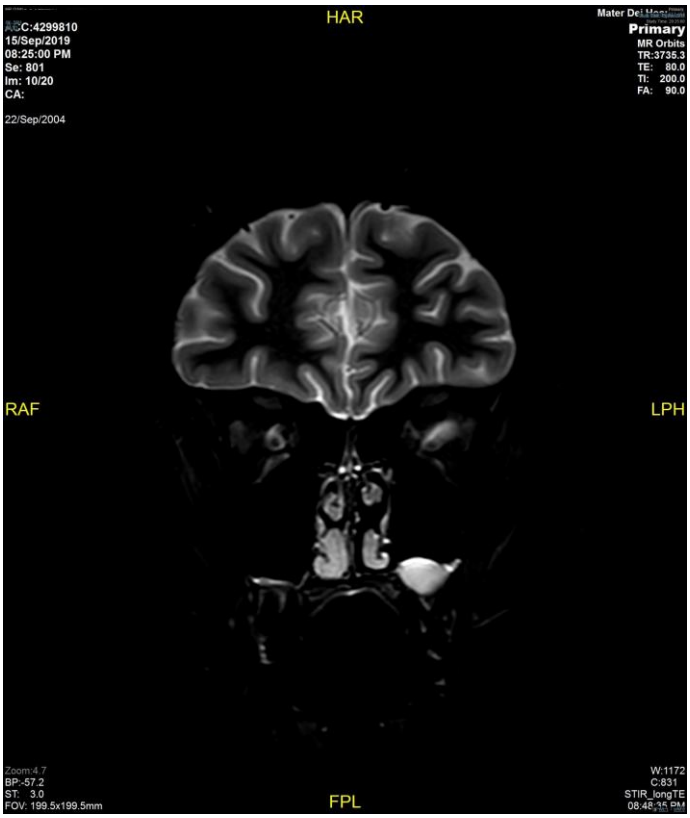


**Figure 2** This shows a coronal STIR MRI image also demonstrating a subtle increased signal intensity of the right lateral rectus muscle




During this admission the patient continued to complain of myalgias, arthralgias and chest pain, and also developed new onset blurred vision on upward gaze. Vertical diplopia of the right eye was reported on upward gaze especially in the superior-nasal direction suggestive of a right-sided acquired Brown's syndrome, confirmed after an urgent ophthalmological assessment. An MRI of the head and orbits confirmed a high intensity signal of the oblique and rectus muscles, affecting the right extraocular muscles more than the left as depicted in Figures 1 and 2. The patient was started on hydroxychloroquine 200mg twice daily and a four-week course of prednisolone by mouth, starting with 20mg daily tailing down by 5mg per week; with close follow up from the multidisciplinary team. The patient remained in good health and, in view of this, further imaging was not deemed to be clinically indicated.

## Discussion

Brown Syndrome is characterized by an upward gaze impairment that occurs when the affected eye is held in adduction and was first described in 1950 by Dr. Harold W. Brown.[1] The pathogenesis of the disease involves congenital or acquired abnormalities of the superior oblique (SO) tendon-trochlea complex that restricts the mobility of the SO muscle.[2] Congenital Brown syndrome is the commonest form, is of unknown aetiology and confers a worse prognosis.[3] Rheumatic and non-rheumatic causes of acquired Brown Syndrome have been described including trauma and a complication of peri-orbital surgery, sinusitis, myopathies, rheumatoid arthritis, juvenile chronic arthritis, and, as in this case report, systemic lupus erythematosus.[4]

A review of the medical literature only discovered three case reports associating the development of Brown Syndrome with the diagnosis of SLE. The first reported case, published in 1990, described a 30-year-old man with a 5-month history of generalised arthralgia and acute alopecia who developed variable diplopia on upward gaze, which was diagnosed as Brown Syndrome; further investigation confirmed an underlying diagnosis of SLE.[5] The other two cases concerned young women who were known to suffer from SLE and who presented with acute diplopia, also diagnosed as Brown Syndrome.[6-7] It is postulated that rheumatic conditions may cause stenosing tenosynovitis of the SO tendon with impingement of the muscle and resultant decreased ocular motility.[8] The increased signal intensity at the level of the SO muscle reported on MRI and the response to oral steroids shown by our patient suggests that this was the most likely underlying pathophysiology. The treatment of acquired Brown Syndrome varied in the literature from conservative management, locally injected steroids and systemic steroids, non-steroidal anti-inflammatories and sometimes even surgery.[3, 8] Among the three case reports of SLE-associated Brown syndrome, one patient responded to oral ibuprofen, one responded to oral prednisolone the third case did not receive any treatment for this complication.

The exact incidence, prognosis and management of acquired Brown Syndrome in cases of SLE is unknown and limited data has been reported and published. Diagnostic difficulties and mild or transient symptomatology of this rare complication have likely resulted in under-reporting.[5]

## Conclusion

This case report describes how a 14-year-old girl, newly diagnosed with SLE, developed concomitant acquired Brown Syndrome which responded well to oral steroids. Although it is a scarcely reported association, Brown Syndrome should be considered as a possible cause of diplopia in patients known to suffer from SLE and its management may involve MRI, ophthalmology input and steroids.[6]

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CASE REPORT

# Iatrogenic sciatic nerve injury: A case report

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Sciatic nerve injury is an uncommon presentation seen in primary care. Detailed history and careful physical examination may sometimes be able to elicit this diagnosis and its possible cause. Sometimes additional imaging modality such as ultrasound or magnetic resonance imaging may be needed to confirm the diagnosis.

This case report will look at a case of 60-years old woman who presented with severe pain and limping over her right lower limb which eventually linked to intramuscular injection given two days earlier for severe knee pain.

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## Introduction

Intramuscular injection is an important way of administering drugs especially in patients who are having severe symptoms such as vomiting, severe pain or severe allergy; if the patient is unable to tolerate orally or for certain oil based or crystallised medication such testosterone or benzylpenicillin. It is usually given over the gluteal region. However, an improperly placed injection on the gluteal region may lead to many unforeseen problems. This includes partial or permanent sciatic nerve injury resulting in transient or permanent mild to severe sensory and motor disturbance including paralytic foot drop.[1] Other complications will include formation of haematoma and infection among others.

This case will look at one such unfortunate incident involving an elderly woman who presented with limping and severe pain over her right lower limb after an intramuscular diclofenac injection.

## Case Report

A 60-years old woman with underlying bilateral severe osteoarthritis had severe exacerbation of right knee pain for two days due to excessive exertion a day earlier. The pain score was 8/10 and the patient was unable to sleep the night before. She noted her pain was exacerbated by walking and relieved by lying down. She therefore sought treatment at her regular general practitioner. She requested for intramuscular injection as oral analgesics was unable to reduce her pain. A 75mg of intramuscular diclofenac sodium injection was given on the right mid-gluteal region under aseptic technique.

Post injection, her knee pain score reduced to 3/10. She was given a short course of oral analgesics which included regular paracetamol and diclofenac sodium. The next day, her pain score reduced further to 1-2/10 and she was able to counter her knee pain with just paracetamol. However, towards the evening, she noted some pain over her injection site causing her to limp. She ignored her symptoms hoping it to get better by the next morning.

The next morning however, she noted the pain over the injection site having increased to give a higher pain score of 10/10. She noted her pain to radiating from the hip to the lower leg. Her right lower leg limp also followed suit, and she had to use a walker to ambulate. The oral analgesics prescribed earlier had minimal effect on her pain. There was no fever.

The severe pain persisted despite taking oral analgesic which lead her to visit to a private hospital rheumatologist. Upon examination, the rheumatologist noted there was small swelling over the injection site at the right mid-gluteal region measuring 3x3 cm. The rheumatologist noted there was also weakness on extending and flexing the right knee with no numbness or foot drop.

An ultrasound of the right gluteal region was performed and it showed a haematoma compressing on the right sciatic nerve. The rheumatologist then proceeded to perform aspiration of the haematoma drawing out about 30mls of blood under aseptic technique. This provided much relief to the patient's symptoms. Her pain score reduce to 5/10 and her limping subsided.

Over the next two days, her pain reduced further and she was able to do her daily activities. She promised herself to be wary of asking for intramuscular injection in the future, reserving it only if she truly needs it. She was very thankful she did not suffer permanent sciatic nerve paralysis.

## Discussion

There is limited data on injuries secondary to intramuscular injections in adults.[2] An older paper reported its incidence as only 0.4% and the injuries included abscess, erythema, wheal and induration formation, persistent local pain, hematoma or bleeding, and subcutaneous fat nodules formation.[3] This case illustrates the caution which must be taken when administering an intramuscular injection over the gluteal region. There is a consensus that upper outer quadrant is the safest site as it avoids many important structures such as gluteal nerves (superior and inferior gluteal nerves, posterior cutaneous nerve and the largest nerve in the body, sciatic nerve (L4-S3), a branch of the sacral plexus which passes under the gluteal maximus muscle and descends into the middle of the posterior thigh, and gluteal arteries such as superior gluteal artery and inferior gluteal artery which lies medial to the sciatic nerve. [1]

The most common mechanism for injury to the sciatic nerve is surprisingly intramuscular injury and not due to direct injury secondary to fall or motor vehicle accident.[4] The most common presentation of a sciatic nerve injury is radicular pain and paraesthesia accompanied by variable sensory and motor component deficit with often poor prognosis for recovery.[4]

In a study done over a period of three years in Iraq, complete recovery was reported in only 30% of patients with sciatic nerve neuropathy following gluteal intramuscular injection with 25% of patient recording no clinical improvement at all.[5] All this points to the importance of giving extra time and caution when administering an intramuscular injection over the gluteal region.

Management of those unfortunate patients with sciatic nerve injection injury should be individualised depending on the severity of the symptoms. This includes oral analgesics, physiotherapy, use of assistive devices and in some severe cases, surgical exploration.[6]

Therefore, intramuscular injection should be avoided if safer option exists. As the authors have notice in their clinical practices, patients tend to request for intramuscular injection, favouring it over oral drugs which they find inconvenient to take or have slower mode of action. Therefore, the ethics principle of "do no harm" certainly flexes its' muscles here reminding physician to only give parental treatment if it's really necessary. Early aspiration of any ensuing haematoma may prevent more serious symptoms and therefore a strong index of suspicion should be maintained in such scenarios.

The main learning points of this article is that intramuscular injection is a common mode of treatment administered, given usually over the gluteal region which stores many important structures including sciatic nerve, which if injured may lead to even permanent paralysis of the nerve if not diagnosed early.[7,8] Therefore, medical personals administering intramuscular injection should be educated to give injection over the safest region in gluteal region i.e. upper outer quadrant and to administer it only if no other safer options exists.[7-8]

With the many risk of administering intramuscular analgesia that include bruising, infection, pain hematoma and lack of evidence for its superior efficacy expect for perhaps a faster mode of action, intramuscular injection should be reserved for those with severe acute pain such as acute gout or are unable to tolerate oral analgesia, among others.[7-8]

## Conclusion

In conclusion, this was an interesting case of incidental right sciatic nerve injury which brought much misery to the unfortunate patient. However quick and decisive action by the physician prevented more dire consequences such as permanent disability and brought an almost instant relieve to the patient's disabling symptoms.


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CASE REPORT

# Management of pregnant women living with type one diabetes mellitus during Ramadan: a theoretical case-presentation discussion

Amy Vella

The Ramadan period is highly significant in the Muslim religion which is characterised by fasting from dawn until dusk. In this case scenario, a 23-year old Muslim woman from Somalia expressed her wishes to fast even though this poses a high risk due to the presence of both type one diabetes mellitus and pregnancy. A management plan was devised to fast safely for optimal wellbeing of her foetus and herself. This consisted of carrying out a thorough assessment and identifying her current needs. Dietary pattern was the major feature of the care plan due to its sudden changes in Ramadan. A modified nutrition plan was advised in this scenario, allowing for a balanced diet in iftar and sahur with adequate caloric intake. No additional plans for physical exercise were sought as physical exertions associated with Tarawih prayers were considered sufficient. Insulin management is important since this accompanies meals and adjustments may need to be made. Therefore, providing education in self-monitoring of blood glucose and injecting insulin is paramount. Follow-up by an obstetric care provider during Ramadan is essential.

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## Case Scenario

A 23-year-old migrant Muslim woman from Somalia with a BMI of 19 kg/m2 was seen in her first pregnancy at the antenatal clinic at 12 weeks of pregnancy. She has a history of Type 1 Diabetes Mellitus of eight years duration and was referred for subsequent management by the specialist diabetes in pregnancy team. She currently lives at the Open Centre for migrants. At 23 weeks gestation, she informs the team that she intends to fast during the coming Ramadan and wishes appropriate advice about how to safely manage her diabetes in the circumstances.

## Introduction

Religious beliefs generally evoke a strong reaction from its followers. Ramadan is the ninth month of the Islamic calendar,[1] and is known as their holy month.[2] Fasting during Ramadan is one of the key pillars of this religion and is highly valued by Muslims.[3] It is believed that this good deed will lead to a multiplication of spiritual rewards, increasing the desire to participate.[4] The fast is observed from dawn to sunset and pregnant women are exempted from fasting. Despite this, some pregnant Muslim women with diabetes decide to fast, as in this case, against the standard medical suggestions.[2] If the patient wishes to fast for Ramadan, she will need adequate monitoring and insulin dose adjustments,[2] as well as responsibility from her side in terms of dieting, adhering to therapy and maintaining contact with the support team.[3] This can only be successful with commitments from healthcare providers and dedication from the patient.[2] Ideally, the patient should be managed in a high-risk clinic by an obsetetrician, diabetologist, nutritionist and a diabetes nurse educator.[5]

## Associated Risks

Diet restriction in pregnancy can be related to adverse maternal and perinatal consequences. According to a previous study, high rates of foetal loss, low birth weight, and increased neonatal admission to the special care baby unit were reported in women following Ramadan.[6] In a study carried out by Alwasel et al,[7] reduced placental weight was observed in mothers who were in their second and third trimester when fasting although birth weight was unaffected, however, this may have an effect on foetal programming leading to long-term health implications. Data from Iraq and Uganda also suggests a link between prenatal exposure to fasting and learning disabilities in adulthood.[4] Contrastingly, several other studies which were conducted on healthy pregnant women during Ramadan have resulted in no complications or detrimental effects on both mother and child.[2] Several profound metabolic alterations are observed in gestation. In pregnancy, women are more vulnerable to elevated ketonemia and hypoglycaemia after a period of fasting. Metabolic adaptation to calorie restriction includes the release of ketoacids, acetoacetic acid and β-hydroxybutyric acid, to replace glucose as the primary substrate. Therefore, transient ketonemia and ketonuria can occur due to energy restriction and hypohydration.[8] In addition to this, fasting in itself leads to alterations in blood glucose, lipid profile, haematological parameters, and body weight.[9] Moreover, a drop in blood pressure is characteristic of the second trimester in pregnancy. This may be provoked during prolonged fasting. Foetal compromise is indicated by reduced foetal movements or maternal signs and symptoms such as vomiting, tachycardia and postural hypotension. Acute onset oligohydramnios

implies foetal stress, and discourages fasting.[10]

## Pre-Ramadan Assessment

The ideal pathway in this scenario should commence with a pre-Ramadan assessment by health care providers, preferably six to eight weeks before the start of Ramadan. This should include the patient's comprehensive medical history, her glycaemic control, self-management capabilities, risk of hypoglycaemia, and her experience during previous Ramadan.[4] Prior causation, recognition, and management of possible diabetic complications such as hyperglycaemia, hypoglycaemia, dehydration, impending diabetic ketoacidosis and hyperosmolar hypgerlycaemic state should also be explored.[11] According to the International Diabetes Federation (IDF) and the Diabetes and Ramadan (DAR) International Alliance, The patient is considered a very high risk patient as she is pregnant and probably makes use of insulin as she lives with type one diabetes.[12] The primary objective of healthcare providers is to advise the patient not to fast, explaining the possible risks as described above. However, if she still decides to fast, she should be given appropriate support and knowledge to reduce the possible risks.[13] Moreover, it is crucial that she self-monitors her blood glucose several times daily.[4] If possible, the healthcare provider can check urine for ketones, as well as temperature, pulse, and breathing rate.[11] Healthcare providers also have a significant role in close monitoring of the patient since she is at high risk.[14] A care plan should be designed to accommodate the patient. There is no one-plan-fits-all, as each individual will have specific factors that will influence the treatment strategy.[4] Patient empowerment is significant to increase motivation and active participation, ensuring total compliance not only during the Ramadan period but for as long as possible.[11] The patient's family, if present, are encouraged to attend to educative sessions so that they also can be aware of hypoglycaemia and hyperglycemic symptoms, meal planning, blood glucose monitoring, insulin administration, exercise and management of acute complications.[15]

The six Cs in nursing care are vital when delivering patient care and should be followed. These consist of: care, compassion, competence, communication, courage, and commitment. The right care defines healthcare providers and it helps the individual personally. Compassion is care emitted through relationships based on respect, empathy, and dignity. Competence means being able to understand the individual's health and social needs. It involves clinical, expertise and technical knowledge. Communication is central to success and listening is as important as what healthcare providers must deliver. Courage enables healthcare providers to do the right deed for the individual, having the personal strength and vision to establish new methods of working. Commitment improves the care and experience of individuals continually to make this vision a reality.[16] Furthermore, it is crucial to assess access to food of choice and links with others in the Somali community or family. This is because barriers faced by patients in this period include long distances to facilities including their monthly appointments and prescribed medication.[17]

## Diet

The patient's nutrition should be assessed in the pre-Ramadan visit, if possible. This will provide an opportunity for healthcare

providers to give out a modified nutrition plan which will improve blood glucose control during fasting, medical nutrition therapy that can help if the patient is overweight so as to safely and successfully lose weight, education regarding recognition of symptoms such as dehydration, hypoglycaemia and other possible acute complications.[18] The latter can be facilitated by attending a session with a dietitian.[19] Adequate glycaemic control can be achieved by individuals with diabetes by maintaining appropriate nutrition,[20] as will be discussed below. The latter should involve meal planning and dietary advice, with a balanced diet of low glycaemic index, low intake of fats, and more intake of fresh fruit, vegetables, and high fibres.[11] Individuals are more prone to consuming foods high in carbohydrates during Ramadan, therefore, portion control should be included. Healthcare providers can follow the Ramadan Nutrition Plan, developed by the DAR International Alliance, which is a web-based tool used to deliver patient-specific nutrition education for Ramadan. Eid is a regularly ignored aspect in diabetes, which is a three-day festival after Ramadan consisting of high intake of calories and carbohydrates with family and friends, hence, this should also be addressed.[21]

As indicated above, exposure to a sub-optimal or limited diet during pregnancy can impact foetal development and has life-long health effects on the offspring.[22] Instead of the usual intake of three meals daily, the Ramadan period limits individuals to only one main meal in a day.[6] It is recommended to spread out three balanced meals during non-fasting hours which helps to prevent excessive rise in post-prandial glucose.[20] In Ramadan, Muslims' eating pattern usually includes iftar, which is the sunset meal and sahur, the dawn meal.[2] However, in Hossain and Zehra,[20] a meal plan of a total of 1200 to 1400 kilocalories consisted of sahur, iftar, dinner and a bedtime snack. The patient should be allowed to choose her frequency of meals according to her own preferences in the non-fasting period, with sufficient caloric balance. Nonetheless, in pregnancy, it is best not to skip a bedtime snack due to change in dietary schedule and prolonged starvation. Sahur should be taken as late as possible before starting to fast again. Moreover, general dietary guidelines for Ramadan remain the same in pregnancy.[20]

Iftar should commence with drinking plenty of water in order to overcome dehydration from fasting, and one or two dried fresh dates to raise blood glucose levels.[18] Ingestion of water, sugar free drinks or fruit juices should be continued to compensate for water and electrolyte deficits.[23] Examples of iftar meals usually contain around 200 kilocalories and include the following: one date and half cup of kidney beans with vegetable, or one date and a cup of dahibarey with chickpeas, or a pinch of salt and one cup fruit chat. The latter plan should be followed only if the patient is also planning to eat dinner afterwards of approximately 500 kilocalories and may consist of: once cup tossed salad, kofta curry and one a half chapati.[20] Other plans may involve iftar as the main meal which contains food similar to the ones described but reaches a total of around 700-900 kilocalories.[18] It is crucial to avoid ingesting large amounts of foods rich in fats and carbohydrates, especially during iftar.[23] The patient should be advised to have dinner as early as possible at iftar. Following this meal, it is suggested to take a late night snack consisting of either a glass of milk or a portion of fruit to maintain normoglycaemia until the sahur meal.[20] Furthermore, some individuals make use of a

snack to break fasting during the day and then take iftar later in the evening.[18]

Sahur is an important meal as omission of this meal can lead to depletion of glycogen stores and ketosis earlier when fasting.[24] It is advised to proportionally distribute the caloric intake between sahur and iftar. For example, iftar should comprise 40 to 50 percent, sahur 30 to 40 percent, and snack 10 to 20 percent, of the total caloric intake. At sahur it is advisable to consume a balanced amount of fat and protein as these have a lower glycaemic index and induce satiety better than carbohydrate-rich foods. Plans should be given according to the nutritional needs of the patient and her body weight should be considered. Example of a typical sahur meal, as suggested by the DAR International Alliance, with 540 to 720 kilocalories includes: two wholegrain bread slices with one large egg, four tablespoons of milk with 3 tablespoons of oats and one handful of almonds, half tub of yoghurt, one small apple and water.[18] Sugary food items should be limited especially during this meal.[11]

Basically, low glycaemic index carbohydrates which are high in fibre are preferred comprising around 45 to 50 percent, protein comprising 20 to 30 percent, and fat, preferably mono and polyunsaturated comprising less than 35 percent, of the whole meal.[18] Inclusion of fresh, steam cooked or boiled vegetable salads without oily dressings, fruit, yoghurt, lentils, whole serial made food items and non-vegetarian items which are grilled or steam cooked represent an ideal diet. Oil rich food items like pakodas, puris, parothas and samosas should be avoided as well as over-eating.[11] Keeping records of time of meal and snacks, together with portion sizes may be useful throughout this period.[25] When breaking the fast due to hypoglycaemia, the patient should consume a small amount of a fast-acting carbohydrate such as a small carton of juice.[13] In this scenario, The patient should avoid high phosphorous and potassium diets such as dates, fried foods, cheese, and tea. Additionally, she should drink up to one to 2.5 litres of water to rehydrate.[20]

## Physical Exercise

Rigorous exercise is not advised during fasting due to the higher risk of hypoglycaemia and dehydration. Regular light-to-moderate exercise can be encouraged, however, the patient should be informed that physical exertions involved in Tarawih prayers are considered part of daily exercise.[13] These usually take place after the Iftar meal and consist of kneeling, rising and bowing.[21] Seen from a physical point of view, this targets both isotonic and isometric muscular activity which covers most of the muscle groups in the body.[26] Additionally, people often walk to the mosque for these prayers, which is also considered part of the exercise regime.[27] If the patient wishes to partake in exercise, it is suggested that the ideal time to carry this out is two hours after sunset, which is in the non-fasting time. Exercise should be avoided in the final few hours of fasting as the risk of hypoglycaemia is maximal, especially since The patient likely makes use of insulin.[20] It is important to monitor blood glucose before, during and postexercise, if possible. If hypoglycaemia can be predicted, the fast should be broken. Moreover, benefits associated with physical activity include improvements in glycaemic values, lipid profile, body weight and mobility.[28]

## Insulin Management

Strict medical supervision is essential in pharmacological management and there should be focused education on how to

manage glycaemic levels.[29] As a general overview, the regularly used option is once or twice daily injections of intermediate or long-acting insulin, together with premeal rapid-acting insulin. It is unlikely that regimens such as one or two injections of long-acting, intermediate, or premixed insulin would provide optimum insulin management. Continuous subcutaneous insulin infusion is another appealing option; however, this is costly and the patient's affordability should be taken into account.[5] Access to appropriate treatment and testing should be assessed, as well as storage of insulin and supplies.[30]

Dose adjustments need to be made by the physician since there is a long fasting period. The long-acting insulin should be reduced by 10 to 30 percent and taken at the sunset meal, iftar. If the patient is on twice daily mixed insulin, the sunset meal dose should be kept the same and the second dose decreased by 20 to 30 percent and taken with the pre-dawn meal, sahur. The rapid-acting insulin can be started with the same dose but may need to be increased at the sunset meal by 10 to 20 percent to avoid hyperlycaemia. The dose at Sahur meal should be kept the same, however, if morning hypoglycaemia occurs, this dose should be decreased by 10 to 20 percent or to omit completely if needed.[31] If the patient was previously on a midday rapid-acting insulin regime, this should be omitted whilst fasting.[27] Another option could be using a basal-bolus insulin regime, although this can be safely achieved in people who are already in good health and have sufficient control.[11]

Furthermore, a more flexible approach includes counting carbohydrates in each meal and adjusting the meal-related insulin doses using a simple algorithm.[32] Principles of carbohydrate counting including correction doses are more significant during Ramadan as type and quality of food differs from standard days. It could enable patients to control their hyperglycaemia without breaking their fast.[33] This could be included in the education session.[32]

## Blood Glucose Monitoring

As mentioned previously, blood glucose monitoring is a cornerstone of Ramadan diabetes management.[4] In some Muslim communities, there is a misconception that pricking the skin invalidates the Ramadan fast. Diabetes educators have a role to strongly emphasise that this is not the case. The patient should be provided with the knowledge and tools to carry out self-monitoring of blood glucose, to effectively self-manage her glucose levels, and identify events of hypoglycaemia and hyperglycaemia. This is particularly significant as the patient probably makes use of insulin, leading to a higher risk of hypoglycaemia.[1]

The ideal monitoring times are outlined as follows: pre-sahur, in the morning, at midday, mid-afternoon, pre-iftar, two hours after iftar, and at any moment when there are symptoms of hypoglycaemia, hyperglycaemia, or feeling unwell.[29] In the latter scenario, the patient is advised to break the fast. The post-meal test decreases the risk of postprandial hyperglycaemia. Additionally, the patient should be encouraged to keep a Ramadan logbook with details of blood glucose measurements. The patient should break the fast if her blood glucose level drops below 3.9 mmol/L, if it rises above 16.7 mmol/L and if symptoms of hypoglycaemia or acute illness are present.[29] Medical help should be sought and any temptation to persevere with the fasting should be resisted.[34] If blood glucose level is between 3.9 to 5.0 mmol/L, the patient should re-check her blood glucose within one hour.[29]

## Obstetric Management

It is crucial that the patient should be followed by an obstetric care provider throughout this period. During the second trimester, at 23 weeks, quickening would have already commenced, and it is important that abdominal circumference and fundal height are checked weekly. If there is less than one centimetre increase in either parameter weekly, prompt detailed investigations should be initiated and safety of fasting reconsidered. In addition, the foetus cannot tolerate periods of fasting for more than eight hours, therefore, the patient might consider to break the fast earlier, or start fasting later in the day. Loss of foetal movement is a definite signal to terminate fasting, as sudden intrauterine death can be precipitated by foetal hypoxia, hypoglycaemia, or hypokalaemia. Other contraindications to fasting include: non-reactive non-stress stress, poor biophysical score, oligohydramnios, intrauterine growth retardation and abnormal colour Doppler indices. Elevated liver enzymes and uric acid should also discourage fasting.[10] Ramadan involves a religious act of fasting from early dawn until sunset. Debatable evidence exists whether this nutritional restriction affects foetuses negatively or if it has a nil effect. A pre-Ramadan assessment will be ideal in the case of the patient in order to assess her experience of living with diabetes. She is considered to be a very high risk patient due to her pregnancy and high probable use of insulin. However, her decision to fast should be respected and a management plan should be outlined in so that she will fast in the safest possible method. A modified nutrition plan can be provided with the help of a dietitian. Dietary recommendations include eating well balanced diets according to the patient's preferences and drinking lots of water to prevent dehydration. If she needs to break the fast, a fast-acting carbohydrate should be ingested. Light exercise is suggested during this period although the Tarawih prayers can be regarded as exercise and deemed sufficient. Modifications in insulin treatment should be made by the physician's consultation and this should be reduced due to an increased risk of hypoglycaemia. In blood glucose monitoring, it is crucial to reassure the patient that this does not invalidate fasting. Since she lives with type one diabetes mellitus, she should self-monitor multiple times a day. Moreover, visiting an obstetric care provider in this period is significant so as to detect any abnormalities throughout the pregnancy.


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