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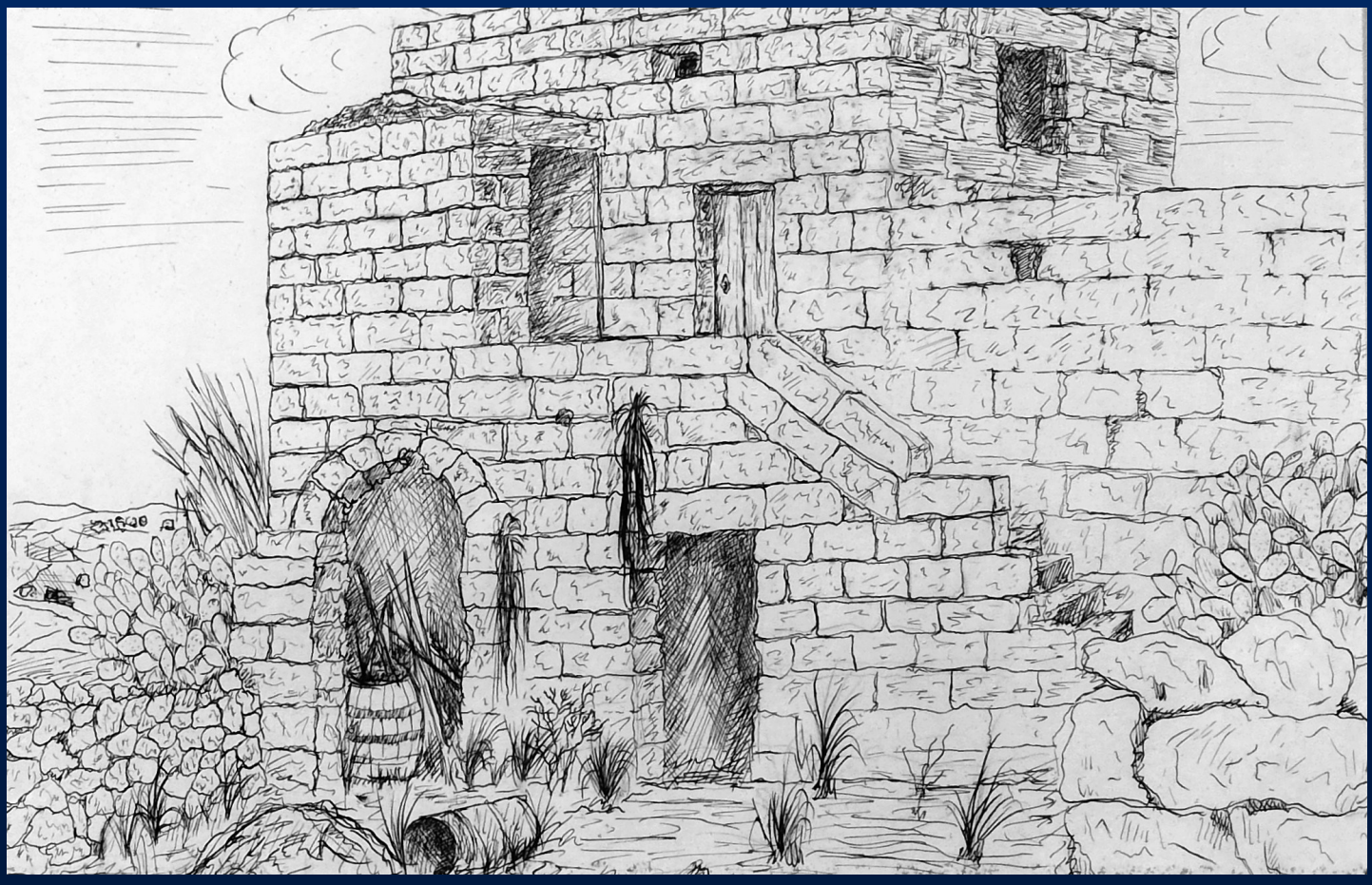

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Zika virus – the 21st century traveller

Karl Camilleri, David Pace

Zika virus (ZIKV) has emerged from the shadows to become one of the hottest topics of public discussion amongst health practitioners and lay people alike, surpassing most of its viral relatives in notoriety. At first, ZIKV infection was a geographically distant problem but has this issue, now, migrated much closer to home?

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ZIKV is an arbovirus of the genus Flavivirus, along with other notable viruses such as dengue, chikungunya, West Nile, Japanese encephalitis and yellow fever viruses. Although only surfacing in the media recently, ZIKV was actually first described in April 1947 in the Zika Forest near Entebbe, Uganda. It was here that during the Rockefeller Foundation's research studies on its relative, the yellow fever virus, ZIKV was isolated from a febrile sentinel Rhesus monkey (*Macaca mulatta*). Like other flaviviruses, ZIKV is mainly transmitted by mosquitoes. Among the various mosquito species, Aedes mosquitoes appear to be the most important vector for ZIKV transmission, with the main vectors in humans being *Ae. aegypti* and *Ae. albopictus*. Aedes species present special difficulty to vector control agencies, mainly because they can reproduce in extremely small amounts of water and their eggs are extremely hardy. Furthermore, both these species are known to thrive in proximity to people and are thus considered to be important vectors in the urban transmission cycle of ZIKV of the recent large-scale epidemics. Moreover, from places with established autochthonous transmission, viraemic travellers have the capacity to introduce ZIKV into new countries, where Aedes mosquitoes may become infected and perpetuate local transmission cycles. Therefore, the potential for autochthonous transmission in countries where Aedes vectors are present is real and is causing major concern given the speed at which the disease has recently spread. Non-vector-borne transmission routes of ZIKV have also been confirmed, including via blood transfusion as well as through sexual contact.

The first human cases of ZIKV were first described in 1952 in Uganda and Tanzania. Subsequently, only isolated cases in Africa and Asia were reported, with a total of less than 20 cases reported in humans in the first 60 years after discovery. This could have been partly because most patients with ZIKV infection are asymptomatic and unnoticeable. The exact ratio of symptomatic to asymptomatic infection is unknown, but about an estimated 20-25% of people

infected with ZIKV develop symptoms of "Zika Fever". These symptoms include a low-grade fever; an erythematous, maculopapular down-spreading rash; retro-orbital headache; bilateral non-purulent conjunctivitis; myalgia and arthritis/arthralgia with periarticular oedema of the small joints of hands and feet.

It was only in 2007, in Yap Island, Federated States of Micronesia, that the first major outbreak of ZIKV outside Africa occurred. This resulted in an estimated 73% of the population above 3 years being infected within 4 months. Several explanations have since been suggested for the outbreak. The lack of population immunity could have precipitated the outbreak and the absence of outbreaks in Africa and Asia could have been a result of pre-existent immunity from regular exposure to the endemic ZIKV. Another possibility may be due to under-reporting, as clinical presentation is similar to a mild illness associated with Zika, dengue, and chikungunya viruses, the three of which co-circulate through their common vector. Subsequently a 2013 outbreak in French Polynesia affected more than 11.5% of the inhabitants – an estimated 30,000 persons. Subsequently, more outbreaks of ZIKV infection occurred in New Caledonia, Easter Island and the Cook Islands, indicating rapid spread of the virus in the Pacific area.

By February 2015, north-eastern Brazil was next to report increased outbreaks of exanthematic disease affecting thousands of patients. The Pan American Health Organisation (PAHO) issued an alert in May 2015 confirming the presence of ZIKV. In fact, the country has since become the epi-centre of the current ZIKV epidemic which rapidly spread across the Americas.

As at the 10th March 2017, vector-borne ZIKV transmission was reported in 84 countries, 59 of which reported their first transmission since 2015 and with some also being included in the 13 countries with evidence of person-to-person transmission. Moreover, Australia, Japan and several European countries, have confirmed cases of Zika virus in travellers returning from countries with ongoing ZIKV transmission.

Association with Microcephaly and other Neurological Complications

Initially, ZIKV infection was considered a benign illness, even less severe than dengue or chikungunya. However, following a systematic review of the scientific literature up to 30th May 2016, on 7th September 2016, WHO concluded that ZIKV infection is a trigger of Guillain-Barré syndrome (GBS) and is a cause of congenital brain abnormalities, manifesting as microcephaly, in the unborn foetus.

In the French Polynesia outbreak between October 2013 and April 2014, 42 patients were admitted to hospital with GBS. This represented a 20-fold increase in GBS incidence, suggesting that ZIKV was the cause of this syndrome. As of 10th March 2017, 23 countries and territories worldwide have reported an increased incidence of GBS and/or laboratory confirmation of ZIKV among GBS cases.

In Brazil, by the second half of 2015 alone, more than >2700 cases of microcephaly were reported, which were suggested to be linked to ZIKV infection, marking a dramatic increase over the 150 microcephaly cases recorded in 2014. Moreover, in October 2015, Brazilian authorities declared a national public emergency due to this significant 20 fold increase of reported microcephaly in ZIKV-affected areas, including three foetal deaths. As of 10th March 2017, microcephaly and/or central nervous system malformations potentially associated with ZIKV infection or suggestive of congenital infection had been reported in 31 countries.

Zika in Europe

In May 2016, the WHO European Region released an interim risk assessment which assessed each European country's risk for a ZIKV outbreak. The likelihood of local ZIKV transmission was based on the presence and climatic suitability for *Ae. aegypti* and *Ae. albopictus*, and factors related to the introduction and onward transmission of ZIKV, such as a history of previous arboviral outbreaks, shipping and air connectivity, population density and urbanisation. A country capacity score was then derived by evaluating integrated vector management, clinical surveillance, laboratory capacity and emergency risk communication.

The most important factor in the assessment was ultimately the presence of the vectors. *Ae. albopictus* is considered to have lower vector capacity than *Ae. aegypti* for transmitting arboviruses, including ZIKV; however, *Ae. albopictus* is established in many countries in the

European Region and has been implicated in recent arboviral outbreaks in continental Europe.

Three localized geographical areas with established *Ae. aegypti* populations were categorized as having a high likelihood for transmission: Madeira Island, the Black Sea coastal area of Georgia and the Black Sea coastal area of the Russian Federation. Eighteen countries, mainly concentrated in Southern Europe, were classified as having a moderate likelihood, due to established populations of *Ae. albopictus*. Malta was classified as moderate likelihood, along with France and Italy. Consequently, it is predicted that future climate trends will increase the risk of establishment of *Ae. albopictus* in northern Europe, due to wetter and warmer conditions.

Another factor assessed was the history, if any, of past arboviral outbreaks. ZIKV has essentially the same epidemiology and mosquito vectors in urban areas as dengue virus and chikungunya virus. For example, from 2012 to January 2013, the autonomous island province of Madeira, Portugal, reported its first dengue outbreak with 2168 dengue cases. In fact, Madeira is now classified as the geographical area at highest risk. Furthermore, a potential for arbovirus outbreaks in Italy was demonstrated by chikungunya virus outbreak in the province of Ravenna, region of Emilia Romagna, in August 2007.

Currently, imported cases are being reported in several European countries. The European Centre for Disease Prevention and Control (ECDC) is collecting data on cases imported into the European Union and the European Economic Area from the media and official government communications. As of 1st March 2017, ECDC recorded 2141 cases in 21 countries, including 108 in pregnant women. These data are important, as returning travellers who are infected with Zika virus could initiate local transmission if there are established competent vectors. As of 1st March 2017, no autochthonous case of Zika virus transmission had been reported in the WHO European Region but 7 European countries have reported person-to-person ZIKV transmission mainly through sexual contact.

Zika in Malta

Until the 27th March 2017, Malta had two confirmed cases of imported ZIKV infection from residents travelling to countries with active transmission. Even though, no direct air connections currently exist with any countries with active Zika transmission, Malta does have direct air routes to several major hubs throughout Europe and the Middle East from where onward travel to Zika affected countries is possible. Furthermore, the multiple global shipping connections could be additional introductory routes. If ZIKV reaches our island, the locally established vector *Ae. albopictus* living amongst our highly dense population, places Malta at moderate risk for further ZIKV transmission. In view of the potential serious complications of ZIKV infection, especially during pregnancy, it is imperative that we invest major efforts to prevent the establishment of ZIKV in Malta.

The currently introduced measures include entomological surveillance and vector management plans. In addition, clinical surveillance for rash and fever in people returning from high risk areas exists and ELISA and PCR laboratory confirmatory testing is available.

However, being a small island, we should be even better able to prevent this serious public health threat from becoming a reality. In fact, major efforts are necessary for Malta to strengthen its vector control activities, with improved entomological surveillance and source reduction strategies through public education and awareness campaigns. Moreover, local options to decrease vector numbers include diminishing the habitats of *Ae. albopictus*. Notably, in Brazil, vector reduction strategies have involved the release of genetically modified mosquitoes, such as Wolbachia-infected and Oxitec mosquitoes which eliminates their ability of transmitting viruses. It has yet to be proven if these interventions can result in a reduction of the associated vector-borne diseases in humans.

Lastly, it should be of utmost importance to increase awareness amongst Maltese individuals, especially those who are pregnant, to avoid travelling to endemic areas. Returning travellers from the 2016 Summer Olympics held in Rio de Janeiro, Brazil created a potential for ZIKV introduction in Malta. In circumstances where travel cannot be avoided, more up-to-date advice on protection against ZIKV should be more readily available, including methods of avoiding mosquito bites and preventing ZIKV acquisition during sexual activity. Barrier methods during sex as well

as avoiding blood donation for at least 1 month from return have to be emphasised. Additionally, pregnant women whose sexual partners live in or travel to endemic areas need to ensure appropriate barrier methods during sexual intercourse or the abstention from sex during the pregnancy. Screening of persons returning to Malta from Zika affected areas is a pragmatic approach in preventing the introduction of the virus in the local *Ae. albopictus* population through appropriate isolation measures.

On 18th November 2016, at the fifth meeting of the Emergency Committee (EC), the Director-General of the WHO declared the end of the Public Health Emergency of International Concern (PHEIC). However, ZIKV and its associated consequences remain a significant enduring public health challenge. The potential of the ZIKV to spread geographically to areas where competent vectors are present remains a concern and appropriate vigilance needs to remain in place to prevent introduction of this virus to Malta.

Cover Picture:
'Old Farm house'
Ink
By Daren J Caruana

Daren J. Caruana has an interdisciplinary background, having read Biochemistry at the University of Warwick, PhD in Electrochemistry at the University of Southampton, then after a spell at the Department of Biomedical Sciences in Malta he spent a postdoctoral fellowship at the Chemical Engineering department at the university of Texas at Austin working with Prof. Adam Heller. He was awarded the Marlow Medal and prize (2004) for the development of gas phase electrochemistry and is now a Reader in Physical Chemistry at the Department of Chemistry at UCL. His research interests are focused towards understanding the electrochemical properties of plasmas and extending electrochemical science to the gas phase through new applications, including developing new analytical methodology for bioaerosols.

Original Article

Life expectancy, mortality and elections: their association during elections in Malta

Elaine Claire Lautier, Kathleen England, Natasha Azzopardi Muscat, Neville Calleja, Dorothy Gauci

Abstract

Introduction: While life expectancy has increased over the past thirty years, such increases have not been constant around election times in Malta. This study seeks to explore the relationship between the time of elections in Malta and specific mortality rates.

Aim: To determine if there is an association between mortality and elections in Malta.

Method: Yearly age specific death rates for all-cause mortality, mortality from ischaemic heart disease, cerebrovascular disease, other heart diseases and all circulatory diseases as well as suicides were calculated from the Malta National Mortality Register for the period between 1985 and 2013. Years when elections and referenda were held between 1985 and 2013 were obtained from the Electoral Commission.[1] The years 1985 – 2013 were coded using dummy variables to categorise them into pre-election, post-election, election year or any other year. Data was analysed using Poisson's regression technique in STATA with Mortality Rate Ratio (MRR) presented as the outcome measure.

Results: A significant increase in overall mortality during election years resulted for circulatory disease MRR 1.058 (p<0.001; 95% CI 1.029-1.087), cerebrovascular disease MRR 1.09 (p=0.002; 95% CI 1.032-1.155) and other heart diseases MRR 1.36 (p<0.001; 95% CI 1.276-1.449). A significant increase was also noted during pre-election years in circulatory disease MRR 1.046 (p=0.002; 95% CI 1.017-1.075) and other heart diseases MRR 1.33 (p<0.001; 95% CI 1.248-1.422) and post-election years for cerebrovascular disease MRR 1.08 (p=0.009; 95% CI 1.020-1.150) and other heart diseases MRR 1.19 (p<0.001; 95% CI 1.108-1.273)) relative to the other years.

Conclusion: This ecological study provides an indication that mortality patterns may be associated with the electoral cycle in Malta. Further research on individual physical and psychological responses to political events, particularly around election time is warranted.

Keywords

cerebrovascular disorders, heart diseases, life expectancy, Malta, suicide

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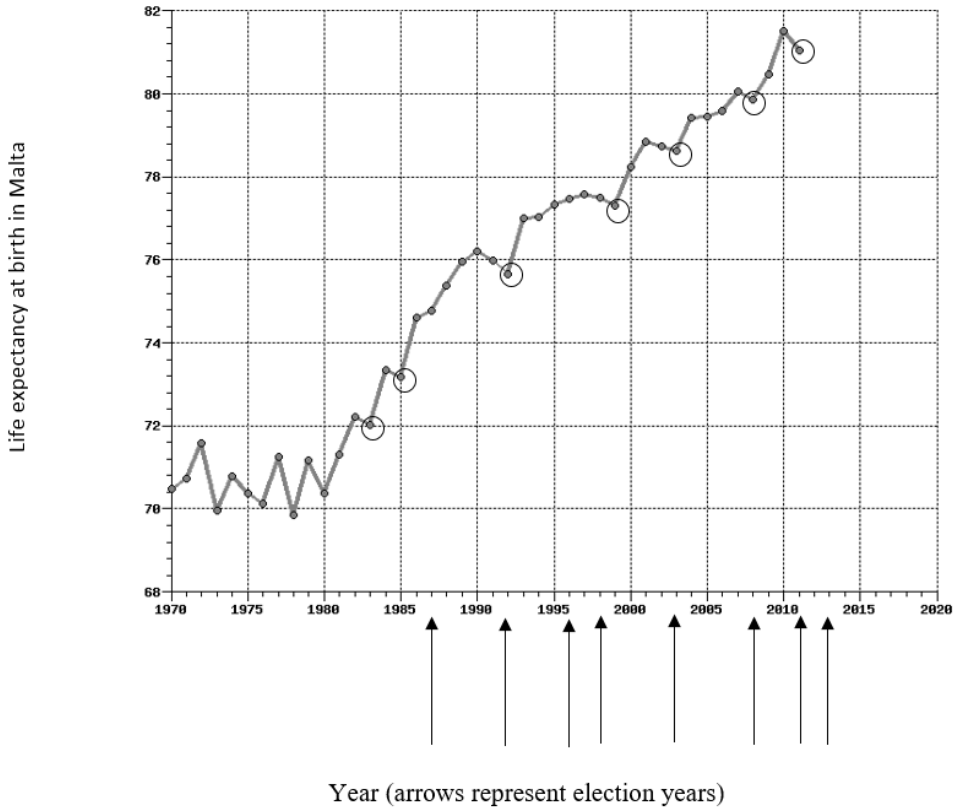
Introduction

Malta is a democratic republic country where the general public aged 18 years and over who are eligible to vote for their preferred Members of Parliament in a first past the post system every five years.[1] The elected party has a five year mandate to govern. Voting turnout in Malta is very high and during the seven general elections held between 1985 and 2013 there was a voting turnout of around 95%.[1]

Between 1985 and 2013, seven general elections and two national referenda were held in Malta. Graphs showing life expectancy (statistical measure of the average time an individual is expected to live) evolution since 1970 indicate that there is a stagnation of life expectancy during election time (Fig. 1).

Figure 1: *Life Expectancy at Birth in Malta (circled dates represent election years)*



There is very little information about pattern of mortality rates during election times in Malta. A study carried out by Sammut[3] suggested that the incidence of both non-fatal, as well as fatal, acute cardiac coronary events was increased during the election period compared with other control periods. In light of the above data, it is of interest to explore whether there is a population level phenomenon associating mortality with the electoral cycle.

Literature Review

Democracy, is the most important system of government. It is a system in which the citizens of a country rule by the majority vote. The United Nations describes democracy as "a universally recognized ideal".[4] Nowadays approximately 60% of the world's nations are democracies. The most important aspect of democracy is that every adult person has equal political rights irrespective of race, gender or religious belief. Citizens living in a democratic country are protected from oppression by laws and limits on governmental power.[5]

Elections bring a certain amount of stress. Waisel –Manor et al.[6] concluded that elections are exciting but very stressful events. The Oxford Dictionary[10] defines stress as 'a state of mental or emotional strain or tension resulting from adverse or demanding circumstances'. Stress is associated with an increased risk of mortality from several major causes including death from all causes, cardiovascular diseases including cerebrovascular disease, all cancers and deaths from external causes.[7]

The 'House of Representatives' consists of 65 members who are elected for a five-year term unless an election needs to be called beforehand due to problems in government.[1] Since 1985 Malta had seven general elections in 1987, 1992, 1996, 1998, 2003, 2008 and in 2013. Two referenda in important policy issues were held in 2003 (EU Referendum) and in 2011 (Divorce Referendum).[1]

Two studies were conducted in Malta regarding body responses (the behaviour of the individual that results from an external or internal stimulus) during election times. A study carried out by Sammut[3] on the Maltese population showed that the incidence of both non-fatal and fatal acute cardiac coronary events increased during the election period and this was compared to other control periods. It is possible that this difference can be explained by the effects of heightened acute mental stress levels that are generated among the Maltese population in general by public events such

as general elections.

A study by Grech[8] concluded that stress leading up to elections in Malta caused a reduction in the male-to-female birth ratio. Previous studies did conclude that population level socio-economic scarcity such as when a country passes through economic depressions may lead to a reduction in the ratio of males to females at livebirth.[9] Other studies conducted in different populations during or after stressful events confirmed the physiological and psychological responses these events brought about.[11-13] Several studies showed an increase in cardiac complications after the September attacks on the Twin Towers in New York in 2001. Feng at al.[11] found a significant increase in tachyarrythmia, acute myocardial infarction and a smaller increase in unstable angina after the September attacks. The difference did not appear to have taken place due to temporal variation but was more likely to be related to stress.

Wilbert-Lampen et al.[12] showed that viewing important football matches like the World Cup more than doubles the risk of an acute cardiovascular event, particularly in men with already known coronary heart disease.

There is a strong correlation between committing suicide or attempting suicide and stressful life events.[13] Individuals who committed suicide would have experienced more undesirable events when compared to controls. On the other hand Patterson and Pegg[14] concluded that people are committing more and more suicides because of increased boredom. People with a fulfilling social life and those that keep themselves busy have a decreased risk of committing suicide or attempting deliberate self-harm. Even though elections bring about with them stress, for some people elections bring about with them a sense of hope and something to look forward to in life.

Method

The exact dates of the elections and referenda taking place in Malta during the period between 1985 and 2013 were obtained from the Electoral Commission.[1] Data for all-cause mortality and mortality from all circulatory diseases, ischaemic heart disease, other heart diseases, cerebrovascular disease and suicides for all ages, for each year since 1985 was obtained from the Malta Mortality Register (Malta National Mortality Register, Directorate for Health Information & Research).

All the data was analysed for both males and females separately, on a yearly basis for the period between 1985 and 2013 and at 5 year age group intervals from birth onwards. The total population of Maltese residents for each age group for the period between 1985 and 2013 was obtained from the National Statistics Office (NSO) website.[16]

Each year was categorised and labelled as election year, pre-election year, post-election year, or any other year. The same was done for the referenda. These years were coded using dummy variables as follows with election year coded as 2, post-election year as 3, pre-election year as 4 and any other year as 1. Since in 1996 and in 1998 there was an election in each year, this created some difficulty for the classification of the year 1997. Since the 1998 election was unforeseen it was decided to designate 1997 as a post-election year.

Poisson's regression was carried out using STATA[18] (Data Analysis and Statistical Software used mainly for data management, statistical analysis, graphics, simulations, regression and custom programming). STATA was chosen as this was the statistical software available to the analyst but the model could have been run in other packages such as SPSS, R or SAS. All data was adjusted for age and gender and the Mortality Rate Ratio (MRR) calculated. The MRR is a ratio quantifying the increase/decrease in mortality. Poisson's regression was chosen since it allows for the analysis of count data using linear trends while adjusting for multiple explanatory variables such as age group, gender and year. A p-value of <0.05 was taken as significant in the analysis.

Results

No difference was found in all-cause mortality risk between all the years (p=0.055; 95% CI 1.00 – 1.04). When looking at ischaemic heart disease, we found no difference in mortality risk when comparing pre-election (p-value of 0.90), election (p-value of 0.40) and post-election (p-value of 0.84) years to non-election years.

The likelihood of dying from circulatory diseases (including heart diseases, cerebrovascular diseases and diseases of arteries and veins) was significantly elevated during pre-election and election years compared to non-election years. The highest risk was during election years where the risk of death from circulatory diseases was found to be 1.058 times greater when compared to non-

election years (p<0.001; 95% CI 1.029 – 1.087). This increase in the likelihood of death from circulatory diseases was observed to be higher in pre-election years than in non-election years with an MRR of 1.046 (p=0.002; 95% CI 1.017 – 1.075) in pre-election years compared to non-election years. There was no association with post-election years.

For other heart diseases (including heart failure, pulmonary embolism, pericarditis, cardiac valve disorders and cardiomyopathies) we noted an increased probability of dying in all years associated with the election – pre, election and post year – when compared to non-election years. The highest likelihood of death was during the election year itself with death from other heart diseases being 1.36 times more likely during election years compared to non-election years (p<0.001; 95% CI 1.276 - 1.449). This risk was marginally lower during pre-election years with an MRR of 1.33 (p<0.001; 95% CI of 1.248 - 1.422). While the risk decreases during post-election years, the likelihood of dying from other heart diseases still remains significantly high when compared to non-election years with an MRR of 1.19 (p<0.001; 95% CI 1.108 - 1.273).

Similar to the previous causes of death the risk of death from Cerebrovascular diseases was significantly elevated during election years when compared to non-election years (MRR 1.09, p=0.002; 95% CI 1.032 - 1.155). In contrast with circulatory diseases however the elevated risk did not begin in the pre-election period but was carried into the post-election period with an MRR of 1.08 (p=0.009; 95% CI of 1.020 - 1.150) in post-election years compared to non-election years.

In contrast to the patterns exhibited by the previous causes of death, death by suicide exhibited an opposite pattern in relation to election cycles. During election years the risk of death due to suicides was found to be approximately 40% lower when compared to non-election years (p<0.001; 95% CI of 0.500 - 0.820). There was no association for the pre and post-election years.

Table 1 is a summary of the results including MRR, p value and CI.

Table 2 shows a graphical summary of the pattern of mortality risk for all-cause mortality and diagnosis specific causes of death when comparing election related years to non-election years.

***Table 1**: Summary of the results*

Cause of Death	Year	*p Value*	MRR	95% CI
All cause mortality	**Election year**	***p=0.055***	**1.018**	**1.00-1.04**
	Pre-election year	*p=0.52*	1	0.98-1.01
	Post-election year	*p=0.6*	1.01	0.99-1.03
Ischaemic Heart disease	Election year	*p=0.4*	1.02	0.98-1.06
	Pre-election year	*p=0.9*	1.002	0.96-1.04
	Post-election year	*p=0.8*	1.004	0.96-1.05
Circulatory disease	**Election year**	**<0.005**	**1.058**	**1.029-1.087**
	Pre-election year	**<0.005**	**1.046**	**1.017-1.075**
	Post-election year	*p=0.2*	1.02	0.99-1.05
Other heart disease	**Election year**	**<0.005**	**1.36**	**1.28-1.45**
	Pre-election year	**<0.005**	**1.33**	**1.25-1.42**
	Post-election year	**<0.005**	**1.19**	**1.11-1.27**
Cerebrovascular disease	**Election year**	**<0.005**	**1.09**	**1.03-1.15**
	Pre-election year	*p=0.07*	1.05	0.99-1.12
	Post-election year	**<0.05**	**1.08**	**1.02-1.15**
Suicides	Election year	<0.005	0.64	0.497-0.82
	Pre-election year	*p=0.06*	0.8	0.62-1.01
	Post-election year	*p=0.7*	1.04	0.82-1.32

***Table 2**: Summary of mortality risk patterns by cause of death 1985 - 2013, reference group non-election year. An upward arrow indicates elevated risk, a downward arrow indicates lower risk while an equal sign indicates no difference between the year and reference group.*

Cause of Death	YEAR		
	Pre-Election	Election	Post-Election
All Cause Mortality	=	=	=
Ischaemic Heart Disease	=	=	=
Mortality from circulatory Diseases	↑	↑	=
Other Heart Diseases	↑	↑	↑
Cerebrovascular diseases	=	↑	↑
Suicides	=	↓	=

Discussion

From the results obtained, when adjusted for the effect of age and gender, the most significant health impact of elections appears to be on the category 'Other heart diseases'. According to the International Statistical Classification of Diseases and Related Health Problems (ICD 10)[17] 'Other heart diseases' includes conditions like heart failure, pulmonary embolism, pericarditis, cardiac valve disorders, conduction disorders and cardiomyopathies. In Malta the main condition captured under the heading 'Other heart diseases' is mortality from heart failure. The results show that in Malta the chances of dying from heart failure during election years compared to non-election years increased substantially. Similarly this is also seen in pre and post-election years. Individuals who are already diagnosed with heart problems and tend to take elections very seriously need to be more cautious during this period. This is very similar to what Wilbert-Lampen et al.[12] found with regards to stress during World Cup matches. They concluded that during this period men who already have a history of heart problems tend to experience a higher risk of mortality.

Dikavonic[15] and Russ T C[7] found a strong correlation between stress and cerebrovascular disease. A similar result was seen here with an increased risk of mortality from cerebrovascular diseases during election and post-election years compared to non-election years.

Elections in Malta have a positive impact when it comes to suicide and people tend to commit less suicides during election years. Since Malta is such a small country, during election time people might feel more involved and have something additional to look forward to in life. Democratic elections, not just in Malta can bring with them a sense of hope for some people and as Patterson and Pegg[14] concluded, boredom and lack of hope makes people think of committing suicide more often and if people are kept busy, this can prevent them from committing suicide or attempting deliberate self-harm.

The main limitation in this study is the small numbers of mortalities. Even though all deaths in residents were considered between the years 1985 and 2013, Malta being a small island with an average population of about 400,000 means that analysis is conducted on small numbers allowing for wider fluctuations in rates . The accuracy with which death certificates are completed varies and coding variability between different coders over time may also lead to discrepancies. This variation can be assumed constant since variations in coding discrepancies can be assumed to remain constant

throughout the years and over the years considered in this analysis and the completion and coding of death certificates should not vary during election years.

Conclusion

Sammut[3] and Grech[8] both discussed the impact Maltese elections have on our mental and general physical health. Together with this study they all highlight the paramount importance of anticipating when more medical complications can arise. This should translate into more health promotion and increasing awareness amongst health care workers during election times.

Democracy entails that there should be a general election every five years to allow the general public to vote for their preferred party in government. As happens every time a general election is approaching, from a year before the end of term of Government in Parliament, the Health Promotion and Disease Prevention Directorate should come up with an awareness campaign advising the public how they can recognise better and from an earlier stage cardiac symptoms. Individuals, especially those with a history of cardiac problems, should visit their GP/Health Centres in order to check their blood pressure and other cardiovascular parameters on a regular basis. Emphasis should also be placed on maintaining the mental health of individuals. There should be an education campaign in place advising the public on how to keep generally healthy, and how to avoid unnecessary stress especially during the election period.

Recommendations should also be placed on increasing the amount of physical activity and taking up more hobbies during the election period so as to avoid thinking continuously and worrying of what can happen during this period and after.

Family Doctors should be made aware of this situation and rate the opportunity to flag patients at risk according to their medical and social history. They should be the first line of doctors who are most likely to identify certain individuals at an increased risk from certain complications like heart failure, cerebrovascular disease and circulatory disease.

Further research in this area should be conducted. More research at an individual level (e.g. by conducting surveys and questionnaires on people admitted to hospital complaining of heart problems, cerebrovascular diseases and circulatory diseases, especially those who already have a history of heart problems) would help us to clarify the results concluded in this study. Similar studies should also be conducted in other countries and the results compared to the local scenario.

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Original Article

Lack of leisure time: a cause of psychological distress in international medical graduates

Anton Grech, Rachel Taylor-East

Abstract

Background: Previous research has shown that migration for a newly graduated doctor is a risk factor for psychological distress.

Aims: In this paper we examine the risk factors for psychological distress in a group of international medical graduates.

Methods: We studied the potential risk factors of Cultural Distance, gender, uncertainty and lack of leisure time for psychological distress in a group of 30 international medical graduates in Malta undergoing their foundation training.

Results: Psychological distress was measured using the General Health Questionnaire. Lack of leisure time was found to be significantly related to psychological distress (B 1.558, S.E. 1.226, Wald 6.677, Sig. 0.010). Cultural Distance, gender and uncertainty were not found to be significantly associated with psychological distress in the group studied.

Conclusions: We suggest that helping such doctors having more leisure time is an important part of their coping mechanisms in dealing with the stress of their profession.

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Introduction

Medical training can be emotionally difficult and usually takes up a significant number of years. Issues of equality, diversity and fairness are often overlooked. Doctors in general have been found to be among the most stressed professionals[1-3] and several studies have shown high rates of psychiatric morbidity in medical students and young doctors at various stages of their training.[4-8] Medical students and young doctors who migrate for their training may be an under-represented group, and possibly have specific stressors and needs. Migration includes a variety of processes, influencing factors and conditions that have an impact on emotional well-being.[9] The process of migration is known to be highly heterogeneous, in both quantitative and qualitative aspects. Its psychological and biological effects and implications depend on the nature, scale and reasons for migration. These effects are varied and the relationship between migration and mental health is complex.[10] Doctors moving to Malta are usually fluent in English, though for many it is not their first language. Foreign doctors moving to Malta do not have any social relations in place before their move; however, the Foundation Training Programme (FTP) provides a short induction course for doctors once they take up employment. Lack of emotional support and the difficulties associated with long-distance relationships exacerbate distress.[9] Availability of a social network and support system has been found to be crucial in preventing depressive symptoms.[11] The concept of cultural distance reflects the dissimilarities between cultures, including aspects such as language, religion, values, the status of women, individualism-collectivism, attitudes to authority, forms of government and the legal system.[12-13] According to the cultural distance

hypothesis,[13] the greater the gap between host and home cultures, the more difficulties newcomers (sojourners, international students, and immigrants) will experience. Babiker, Cox and Miller[14] developed a measure of individual cultural distance. Using this instrument, they found that cultural distance was related to anxiety and medical consultations among international students in Edinburgh. In another study, Furnham and Bochner[15] found a strong relationship between cultural distance and new migrants having difficulties interacting and settling down in their host culture. It is well known that doctors travel all over the world, for employment as well as for educational purposes. A study we conducted on a cohort of newly graduated doctors in Malta doing their foundation training, found that psychological distress was significantly related to being a migrant. Other risk factors for this distress were lack of leisure time, uncertainty and being female.[16] We wanted to focus further on the potential causes of psychological distress in the cohort of the international medical graduates. To do this the Cultural Index Score (CDI) was used. We also used logistic regression analysis to understand further the sub group of international medical graduates within this cohort and their risk factors for psychological distress as identified by our previous analysis.

Method

The population included all doctors in the FTP (years 1 and 2), including those originally from Malta, and those who had migrated to Malta. Doctors attend a lecture every week where they were recruited. A short explanation was given on the research being conducted; each doctor was given an information leaflet and consent form. There were no exclusion criteria. Those doctors that did not attend the lecture on the day of data collection could not be identified and followed up due to confidentiality reasons.

A self-report questionnaire was completed by the participants consisting of Demographic Details, the Genaral Health Questionnaire (GHQ-28) (Appendix 1),[17] and the Cultural Distance Questionnaire (CDQ) (Appendix 2).[18]

Results:

In February 2013, 149 doctors were registered with the FTP in Malta. On the day of sampling 117 (78.5%) of FY doctors had attended the lecture, and they have all participated in the study. Out of these 87 (74.4%) graduated from Malta Medical School, 35 (39.1%) were males, 39 (44.9%) were female, and 14 (16.1%) did not report sex. The remaining 30 international medical graduates were: 20 (66.7%) were males, 9 (30%) were females and 1 (3.3%) did not report sex, and they all had migrated to Malta following completion of their university degree in Europe. Out of these 30, 13 were in the first year of the programme and the remaining 17 were in the second year. The local graduates were significantly younger than the international graduates, with only 23(26.4 %) being older than 25 years old, compared to 27 (90.0%) of the international graduates.

Psychological distress was assessed using the GHQ-28. A cut-off point of 6 was used in order to define 'caseness', and thus two groups were created. In the group of 30 international medical gaduates on which this paper is focusing there were 20 (66.7 %) doctors who reached the level of 'caseness' and 10 (33.3 %) of doctors who did not reach the level of 'caseness'.

Analysis was carried out on this particular sub group only, to asses if within this group cultural distance was a contributory factor to those in mental distress. This was done by independent samples t-test to examine the relationship between the cultural distance index scores (CDI) using the CDQ[18] and psychological distress (caseness). No association was found between cultural distance and psychological distress (p=0.35).

Logistic regression analysis was carried out on this sub group of doctors who had migrated. The variables that were entered were gender, uncertainty and lack of leisure time. These were the variables that were found to be significantly associated with caseness and thought to be hypothesised as predictors for stress and anxiety. The forward step-wise Wald method was used, with n=30. The results showed that in those who had migrated, out of these three variables, lack of leisure time was significantly associated with caseness (B 1.558, S.E. 1.226, Wald 6.677, Sig. 0.010).

Discussion

This study had identified being female, lack of leisure, migration and uncertainty as risk factors associated with mental distress of newly graduate medical doctors during medical internship, while

being married, age, religiousness were not. Out of the 87 local medical graduates 38 (43.7%) reached caseness.[16]

In this paper we focused specifically on the psychological effect of migration within this group. Migration has increased over the years, and since the introduction of the FTP, the administration began to provide added support with introductory meetings at the beginning of the year. This situation is relatively new for Malta, but it has been happening for much longer in other countries. In 2007, in the USA, 26% of all physicians were international medical graduates. The American Medical Association[19] published a paper on the facts and issues concerning the international medical graduates. It was reported that international medical graduates are more likely to serve in medically underserved areas. These may be busier with even less resources. These individuals bring unique perspectives and experiences that enrich the educational process; however, IMGs tend to face a unique set of challenges in getting residency positions in the US, securing legal immigration status and finding the right job. This situation is comparable to that in Malta.

Within the international medical graduate group studied here, lack of leisure time was found to be the single factor that accounted for distress in the migrant group of doctors. Being overworked, or not having enough leisure time is a reason that doctors have cited for leaving medicine altogether.[20] A Swiss study[21] makes clear recommendations for reduction in work intensity and workload. Lack of leisure time can also be a proxy measure for other important factors for mental wellbeing. For example, leisure time is a potential way of forming social contacts and friendships outside the immediate working environment, especially for migrants who do not have the social support of a family.

In this study no relationship was found between cultural distance and psychological distress. All doctors who were at the Foundation Training in Malta would have already attained their medical degree in a European Union country. It is thus possible that the doctors in question were already accustomed to living in a culturally different country by the time they settled in Malta.

A limitation of this study is the relatively small number of subjects studied. Non-statistical significance present in potential risk factors studied could be related to this fact.

The study was based on reporting by the doctors themselves, and the trainees could have been tempted to under or over report. The fact that both the GHQ and the CDI are validated questionnaires will reduce this potential bias.

In conclusion, we need to be attentive to the well-being of young doctors, particularly in the case of migrants. Having so many doctors from overseas come to Malta to work and train is both a challenge and a new opportunity. This study shows that a cause of psychological distress in those doctors is lack of leisure time. Thus, these doctors must be helped in having more leisure time as an important part of their coping mechanisms in dealing with the stress of their profession.

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Appendix 1.

General Health Questionnaire (GHQ)

Please read this carefully.
We would like to know if you have had any medical complaints and how your health has been in general – *over the past few weeks*. Please answer all the questions on the following pages simply by underlining the answer that you think most nearly applies to you. Remember that we would like to know about present and recent complaints, not those that you have had in the past.
Thank you!

Have you recently:

A1	Been feeling perfectly well and in good health?	Better than usual	Same as usual	Worse than usual	Much worse than usual
A2	Been feeling in need of a good boost?	Not at all	No more than usual	Rather more than usual	Much more than usual
A3	Been feeling run down and out of sorts?	Not at all	No more than usual	Rather more than usual	Much more than usual
A4	Felt that you are ill?	Not at all	No more than usual	Rather more than usual	Much more than usual
A5	Been getting any pains in your head?	Not at all	No more than usual	Rather more than usual	Much more than usual
A6	Been getting a feeling of tightness or pressure in your head?	Not at all	No more than usual	Rather more than usual	Much more than usual
A7	Been having hot or cold spells?	Not at all	No more than usual	Rather more than usual	Much more than usual

Have you recently?

B1	Lost much sleep over worry?	Not at all	No more than usual	Rather more than usual	Much more than usual
B2	Had difficulty in staying asleep once you do?	Not at all	No more than usual	Rather more than usual	Much more than usual
B3	Felt constantly under strain?	Not at all	No more than usual	Rather more than usual	Much more than usual
B4	Been getting edgy and bad-tempered?	Not at all	No more than usual	Rather more than usual	Much more than usual
B5	Been getting scared or panicky for no good reason?	Not at all	No more than usual	Rather more than usual	Much more than usual
B6	Found everything getting on top of you?	Not at all	No more than usual	Rather more than usual	Much more than usual
B7	Been feeling nervous and highly strung all the time?	Not at all	No more than usual	Rather more than usual	Much more than usual

Have you recently?

C1	Been managing to keep yourself busy and occupied?	More so than usual	Same as usual	Rather less than usual	Much less than usual
C2	Been taking longer over the things you do?	Quicker than usual	Same as usual	Longer than usual	Much longer than usual
C3	Felt that on the whole you were doing things well?	Better than usual	About the same	Less well than usual	Much less well
C4	Been satisfied with the way you carried out your tasks?	More satisfied	About the same	Less satisfied than usual	Much less satisfied
C5	Felt that you are playing a useful part in things?	More so than usual	Same as usual	Less useful than usual	Much less useful
C6	Felt capable of making decisions about things?	More so than usual	Same as usual	Less so than usual	Much less capable
C7	Been able to enjoy your normal day-to-day activities?	More so than usual	Same as usual	Less so than usual	Much less than usual

Have you recently?

D1	Been thinking of yourself as a worthless person?	Not at all	No more than usual	Rather more than usual	Much more than usual
D2	Felt that life is entirely hopeless?	Not at all	No more than usual	Rather more than usual	Much more than usual
D3	Felt that life isn't worth living?	Not at all	No more than usual	Rather more than usual	Much more than usual
D4	Thought of the possibility that you might do away with yourself?	Definitely not	I don't think so	Has crossed my mind	Definitely have
D5	Found at times that you couldn't do anything because your nerves were too bad?	Not at all	No more than usual	Rather more than usual	Much more than usual
D6	Found yourself wishing you were dead and away from it all?	Not at all	No more than usual	Rather more than usual	Much more than usual
D7	Found that the idea of taking your own life kept coming into your mind?	Definitely not	I don't think so	Has crossed my mind	Definitely have

Appendix 2.

Cultural Diversity Questionnaire (CDQ)

In this questionnaire you are asked to make physical and cultural comparisons between your home environment (your home country) and your new environment (Malta). Please answer each question in relation to your new environment as accurately as you can, by putting a tick next to the sentence which represents your answer.

	YOUR HOME	**MALTA**
1A	What is the climate like?	Similar to Malta A little hotter or a little colder Much hotter or much colder
1B	How much rainfall?	Similar to Malta A little more or a little less Much more or much less
2A	What do men usually wear?	Similar to Malta Modified western clothes National costume
2B	What do women usually wear?	Similar to Malta Modified western clothes National costume
3A	What is the main language?	English Other European language Other language
3B	Is English spoken?	By most people By some people Hardly ever
4A	Is education free?	Free to secondary level Free to primary level Not free
4B	What level of education would most people attain?	Secondary (high school) Primary level None
5A	What food do most people eat?	Similar to Malta Somewhat different Altogether different

5B	Are there religious dietary rules?	No. Yes but not mandatory. Yes, mandatory.
6A	What is the main religion?	Largely Christian Mixed Largely non-Christian
6B	Does religion play a role in most people's lives?	Similar to Malta Somewhat greater than in Malta Affects all aspects of life
7A	What is the standard of living?	Similar to Malta A little better or a little worse off Much better or much worse off
7B	Do most people have electrical appliances (TV, fridge, iron) in their homes?	Yes, many appliances Yes, a few appliances No
8A	Are leisure activities (sport, music, drama, etc)...?	Similar to Malta Somewhat different Very different
8B	Are social interactions (parties, informal visiting, etc)...?	Similar to Malta Somewhat different Very different
9A	What respect is shown to elderly people?	Similar to Malta Treated with more respect Revered
9B	What roles do women fulfil?	Go to work if they wish Only look after house and children Rigidly housebound

10A	What is the system of marriage?	Similar to Malta
		Bride or groom brings a dowry
		Financial settlement by families
10B	Can young men and women meet each other socially?	
		At parties and social occasions
		Only through the family
		No

Original Article

Optimal gestational age for delivery in uncomplicated dichorionic twin pregnancies: a population-based study

Mark R Brincat, Mark Sant, Neville Calleja

Abstract

Objectives: To identify the optimal gestational age for delivery in uncomplicated dichorionic twin pregnancies.

Study Design: A retrospective analysis of gestational age-specific neonatal morbidity and mortality data was performed for 254 uncomplicated dichorionic twin pregnancies. Outcome measures included 1st and 5th minute Apgar scores, NICU admission, RDS, TTN, sepsis, seizure, hyperbilirubinemia, hypoglycaemia, neonatal length of hospital stay, birthweight and overall outcome. After correcting for confounding variables by regression analysis, adverse variable trends were assessed in each of the gestational-age-at-birth groups.

Results: A significant drop in the incidence of LBW, RDS, TTN and hypoglycaemia, accompanied with the lowest NICU admission rate and neonatal length of hospital stay occurred concordantly at 38 completed weeks of gestation. The incidence of severe hyperbilirubinemia requiring phototherapy decreased significantly by 36 weeks. No correlation was found between advancing gestation and foetal, perinatal or neonatal mortality.

Conclusion: Elective delivery in uncomplicated dichorionic twin pregnancies should be delayed until at least 38 completed weeks of gestation as this significantly reduces neonatal morbidity with no impact on mortality.

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MeSH keywords

Twins, Pregnancy, Outcome

Introduction

In recent years, multiple pregnancy has been on the rise secondary to a delay in childbearing age and more widespread use of assisted reproductive technology.[1-2] Records show that twin births in the Maltese islands have increased from 1.04% in the 1960-1969 period, when the use of ART was presumably minimal, to 1.51% in 2015.[3]

Twin pregnancies are associated with increased fetal, perinatal and neonatal risks and complications when compared to their singleton counterparts. This is attributable to the higher incidence of preterm birth, lower birth weight and the associated physiological instability and lung immaturity of the infant.[4-6]

Preterm birth is a leading cause of death and complications in the neonatal period and one of the key causes for poor developmental outcomes in childhood.[7] Gestational age at delivery is thus a key factor affecting neonatal outcome in twin pregnancies.[8-9] Appropriate timing for delivery of twin pregnancies is a matter of acknowledging the dynamic balance that exists between in-utero foetal stillbirth risk and ex-utero neonatal risk.[10]

In general, clinical practice guidelines regarding the optimal gestational age of delivery in uncomplicated dichorionic twin pregnancies favour delivery in the early-term period (37^{+0}-38^{+6} weeks). A consensus opinion from a 2011 workshop held by the Society for Materno-foetal Medicine (SMFM) and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

suggests delivery at 38 weeks of gestation for uncomplicated dichorionic twins and 34 to 37 weeks for uncomplicated monochorionic diamniotic twins.[11] The National Institute for Health and Clinical Excellence (NICE) recommends elective delivery of dichorionic twin pregnancies from 37 weeks of gestation and monochorionic twin pregnancies from 36 weeks (after a course of corticosteroids).[12] The American College of Obstetricians and Gynaecologists (ACOG) recommends delivery of uncomplicated dichorionic twins at 38^{+0} to 38^{+6} weeks and uncomplicated monochorionic twins at 34^{+0} to 37^{+6} weeks of gestation.[13-14]

Although several investigators have undertaken studies to define the optimal delivery time for twin pregnancy, some results are controversial due to lack of chorionicity data and the confounding effect of pre-pregnancy or pregnancy-induced conditions on neonatal morbidity, mortality or the decision for delivery. This study deals solely with uncomplicated dichorionic twin pregnancies. It eliminates the confounding effect of relatively higher risk monochorionic pregnancies as well as eliminating the effect that maternal comorbidities, pregnancy-induced conditions and congenital anomalies have on the obstetric decision for delivery and outcome. These exclusion criteria allow for clearer inquiry into the interplay between gestational age and neonatal outcome variables. Such a consideration should drive the empowerment of both obstetricians and parents towards more informed decision-making when balancing the risks and benefits of discretionary delivery.

Methods

Population-based retrospective data for all twin deliveries occurring in the Maltese islands in the 2008-2014 period was obtained from the National Obstetric Information System (NOIS) database. Systematic neonatal data collection for NOIS commences from the point of delivery and lasts until discharge from hospital or until 28 days of neonatal life.

Exclusion criteria were applied to the data sequentially, eliminating births that occurred prior to 34 weeks of gestation, as well as excluding neonates with major congenital anomalies as defined by the European Registration of Congenital Anomalies (EUROCAT). Pregnancies involving maternal chronic ill health and pregnancy-induced conditions including gestational hypertension, gestational diabetes, pre-eclampsia, and intrauterine growth restriction were excluded. Growth restriction was defined as birthweight below the 10^{th} percentile for gestational age or inter-twin weight discordance of more than 20%.

To ensure exclusion of monochorionic pregnancies only twin deliveries with clear documentation of chorionicity data (separate gestational sacs / lambda sign in ultrasound scans done up to 14 weeks of gestation) or different sex at birth were included.

Data collection concerning neonatal outcome included 1^{st} and 5^{th} minute Apgar scores, admission to the neonatal intensive care unit (NICU), perinatal morbidity (respiratory distress syndrome (RDS), transient tachypnoea of the newborn (TTN), sepsis, seizure, hyperbilirubinemia, hypoglycaemia), neonatal length of hospital stay, birthweight and overall outcome (perinatal death and early/late neonatal death). Variables that represented potential confounders included maternal age, parity, smoking, alcohol intake, drug abuse, antenatal maternal steroid administration, twin birth order and infant sex.

Valid data entries were allocated into gestational-age-at-birth groups, starting from 34^{+0}-34^{+6} weeks and continuing upwards at one week intervals. Regression models were built up using gestational age and neonatal outcome variables, and forward stepwise regression was applied to eliminate the confounding effect of risk factors that were initially found to also have a significant effect on the dependant outcome variable. Statistical analysis was done using the IBM SPSS Statistics package Version 22 and Microsoft Excel 2013. Ethical approval was acquired from the University of Malta University Research Ethics Committee on 16^{th} November 2015.

Results

In the period studied (2008-2014), there were 29,497 deliveries and 474 twin sets. Out of the 474 twin sets, 254 pairs met the inclusion criteria. These mothers had a mean maternal age of 30.6 years (95%CI 30.21-30.99), 53.43% of which were primiparous women.

The highest proportion of deliveries occurred by elective caesarean section (CS) at 37 and 38 completed weeks of gestation. (*Figure 1*) The

majority of deliveries prior to 37 weeks of gestation were via CS after the onset of spontaneous labour or rupture of membranes (ROM).

Figure 2 depicts a logistic-function pattern of birthweight gain with advancing gestation. The birthweight of twin neonates born to non-smoking mothers was found to be 148.60 grams higher (95%CI 28.50-268.70g) than twin neonates of smokers ($p<0.005$).

Male infant birthweight was a mean 90.26 grams ($p<0.0009$, 95% CI 37.22-143.31g) higher than female infants. The percentage proportion of twin neonates with LBW (<2500g) was highest at 35 weeks of gestation, decreasing linearly to 35.20% and 26.28% at 37 and 38 weeks respectively (*Figure 3*).

***Figure 1**: Mode of delivery of twin neonates according to gestational age at birth*

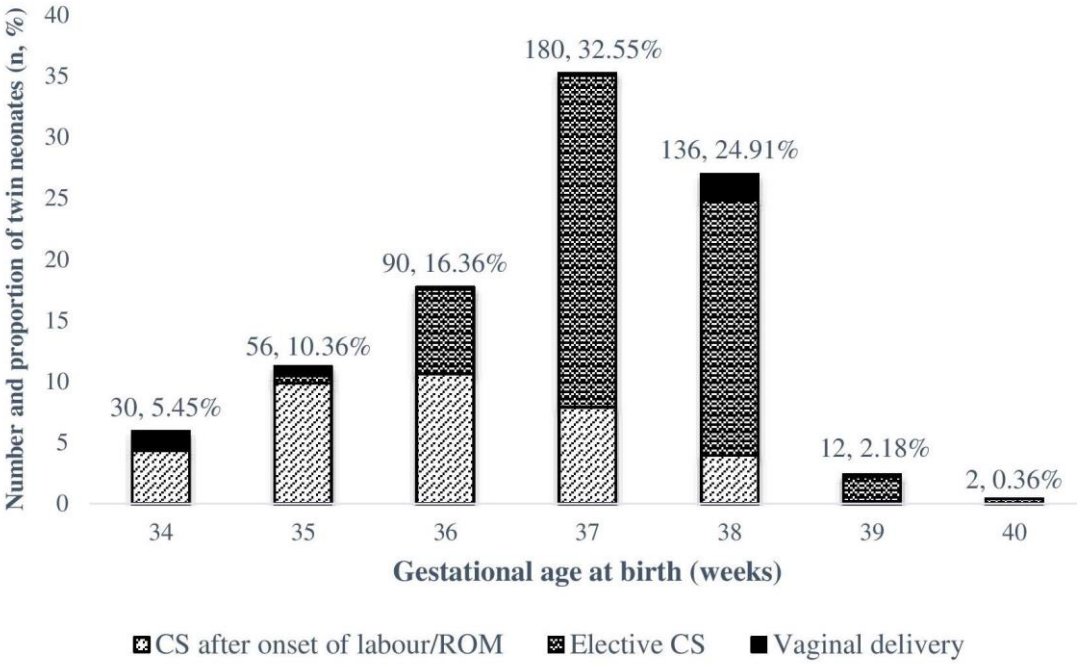


***Figure 2:** Mean birthweight according to gestational age at delivery in uncomplicated dichorionic twin pregnancies*

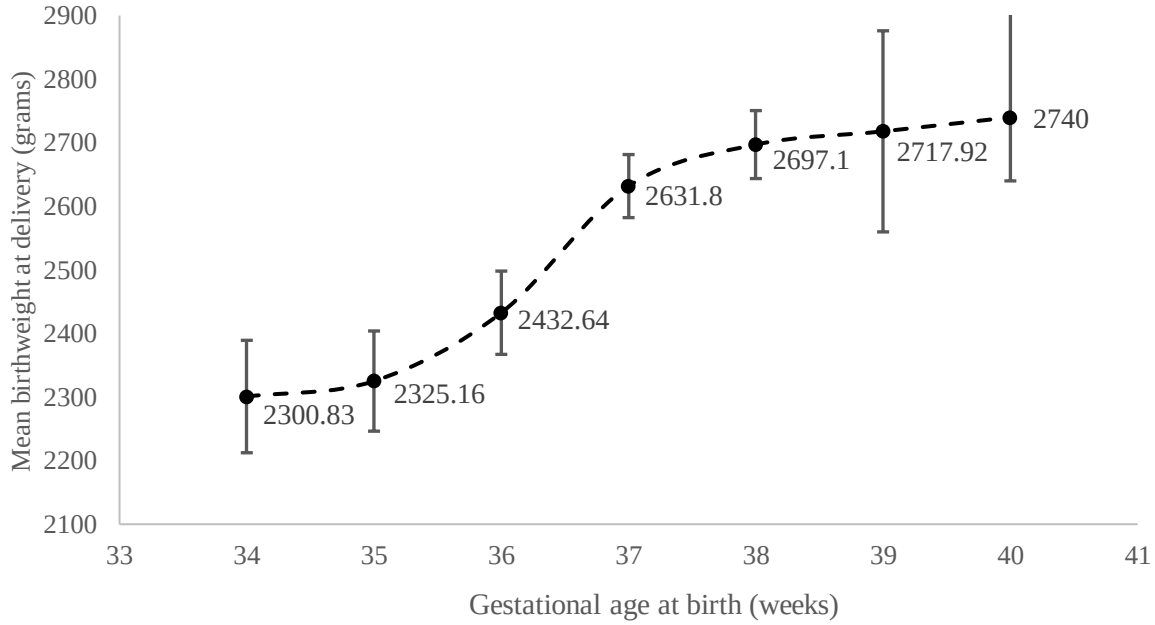


Figure 3: *Incidence of LBW (1500g-2499g) in twin neonates according to gestational age at birth*

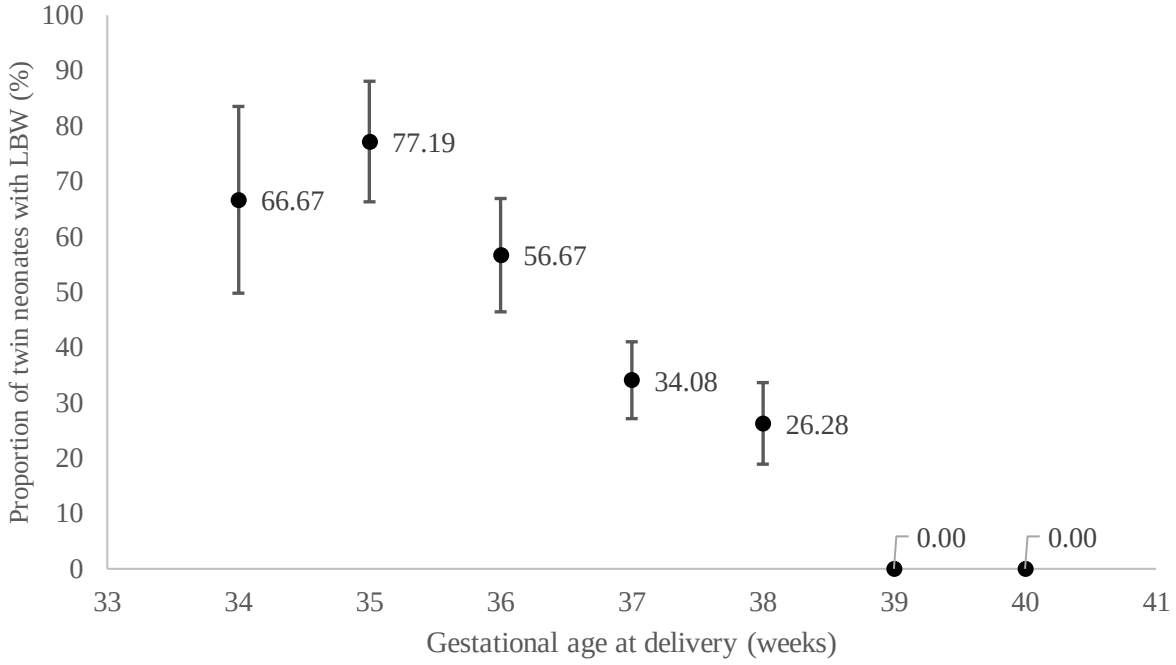
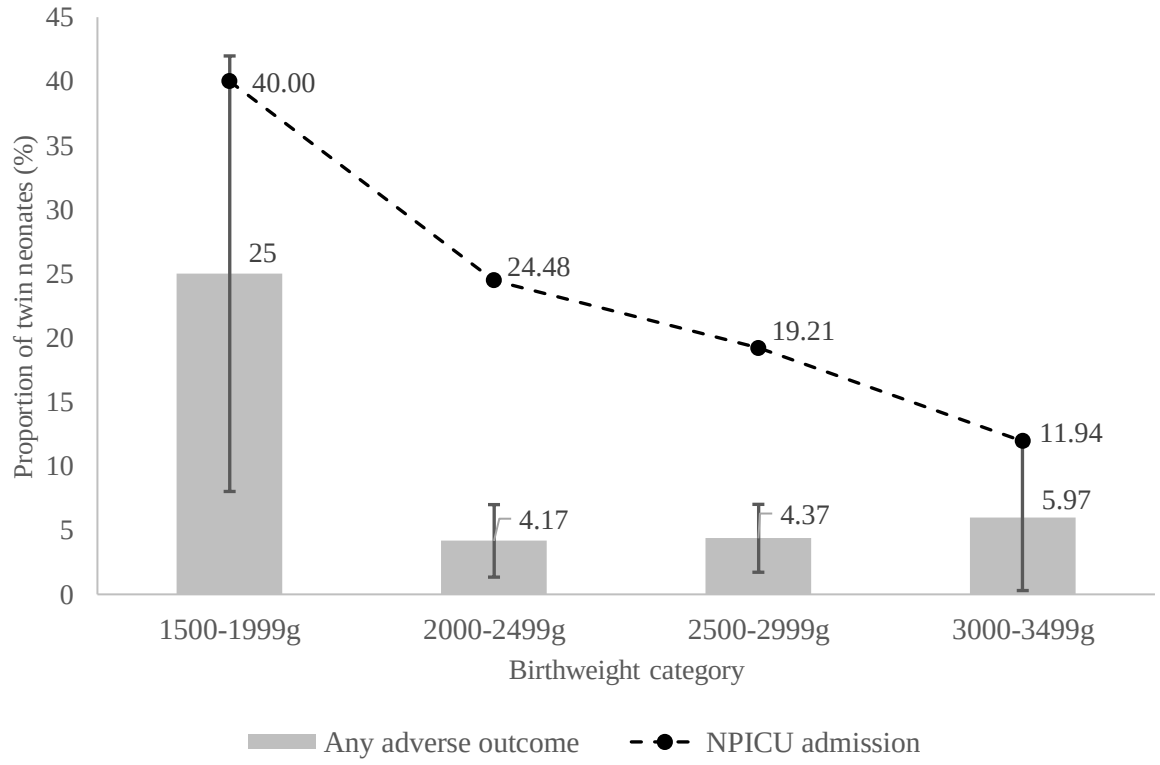


Figure 4: *Incidence of any adverse outcome (RDS, TTN, 1st/5th Apgar <7, Hyperbilirubinemia, Hypoglycaemia or Sepsis) and NICU admission according to birthweight category*



LBW was associated with RDS (RR 3.00 95%CI 1.63-5.50, $p<0.0001$), hypoglycaemia (RR 4.65 95%CI 1.30-16.71, $p=0.009$) and intensive care requirement (RR 1.48 95%CI 1.06-2.07 $p=0.02$). (*Figure 4*).

The mean first minute Apgar score was significantly higher in neonates born at 39 or 40 completed weeks of pregnancy. This intergroup difference was no longer detected at the fifth minute. (*Figure 5*)

RDS affected 9.45% of the twin cohort. There was a sharp statistically significant drop in the incidence of RDS at 38 completed weeks of gestation with only 1.46% being diagnosed ($p<0.001$). The incidence of RDS decreased significantly as gestational age increased, each additional week of gestation after 34 weeks decreasing the risk of RDS by 57.10% ($p<0.001$, 95%CI 45.13-72.38).

Figure 5: *Mean 1st (blue) and 5th minute (red) Apgar score according to gestational age of dichorionic twin neonates*

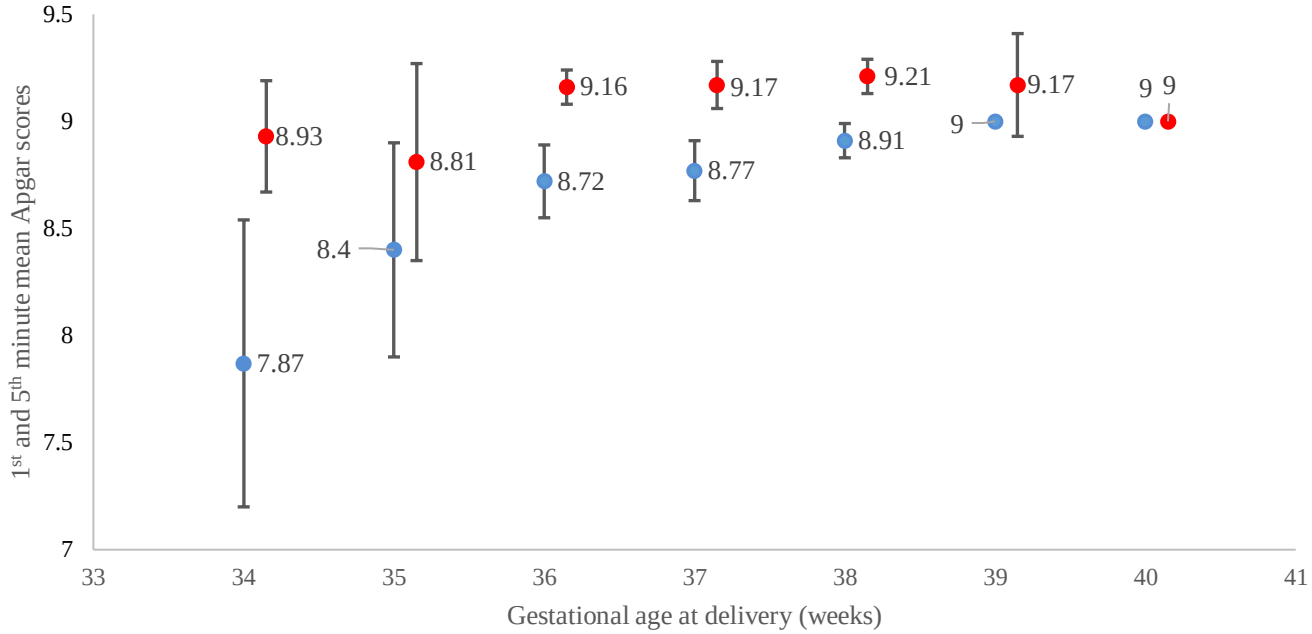


Figure 6: *Percentage of twin neonates affected by RDS according to gestational age at delivery*

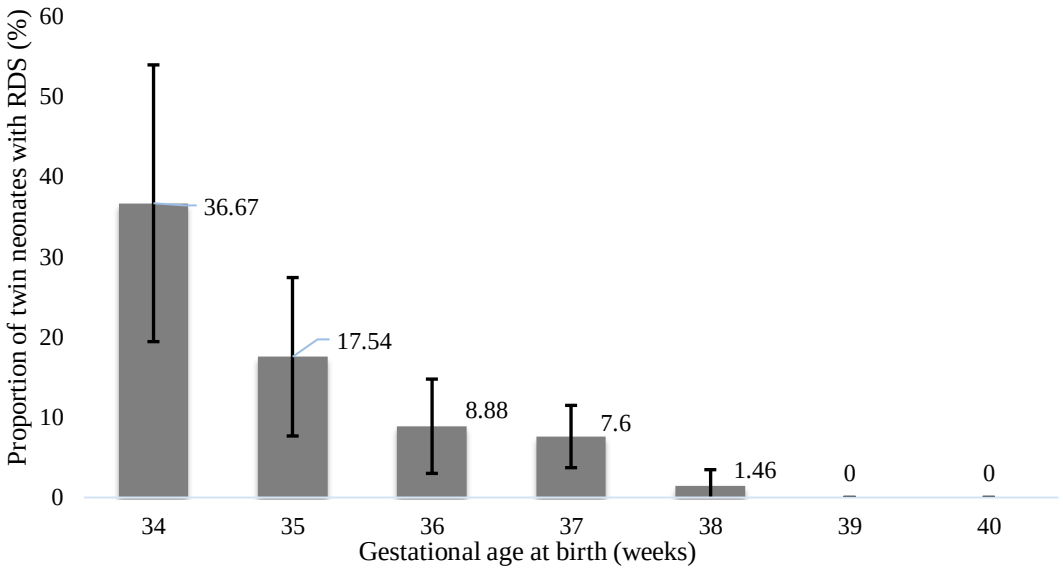


Figure 7: *Percentage of twin neonates affected by TTN according to gestational age at delivery*

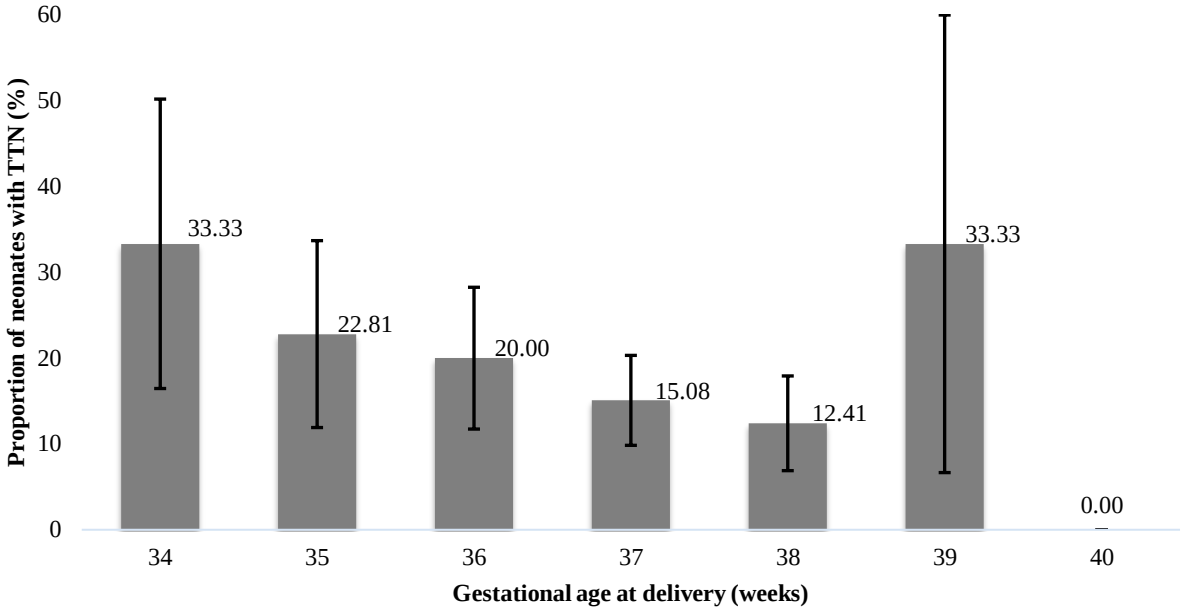
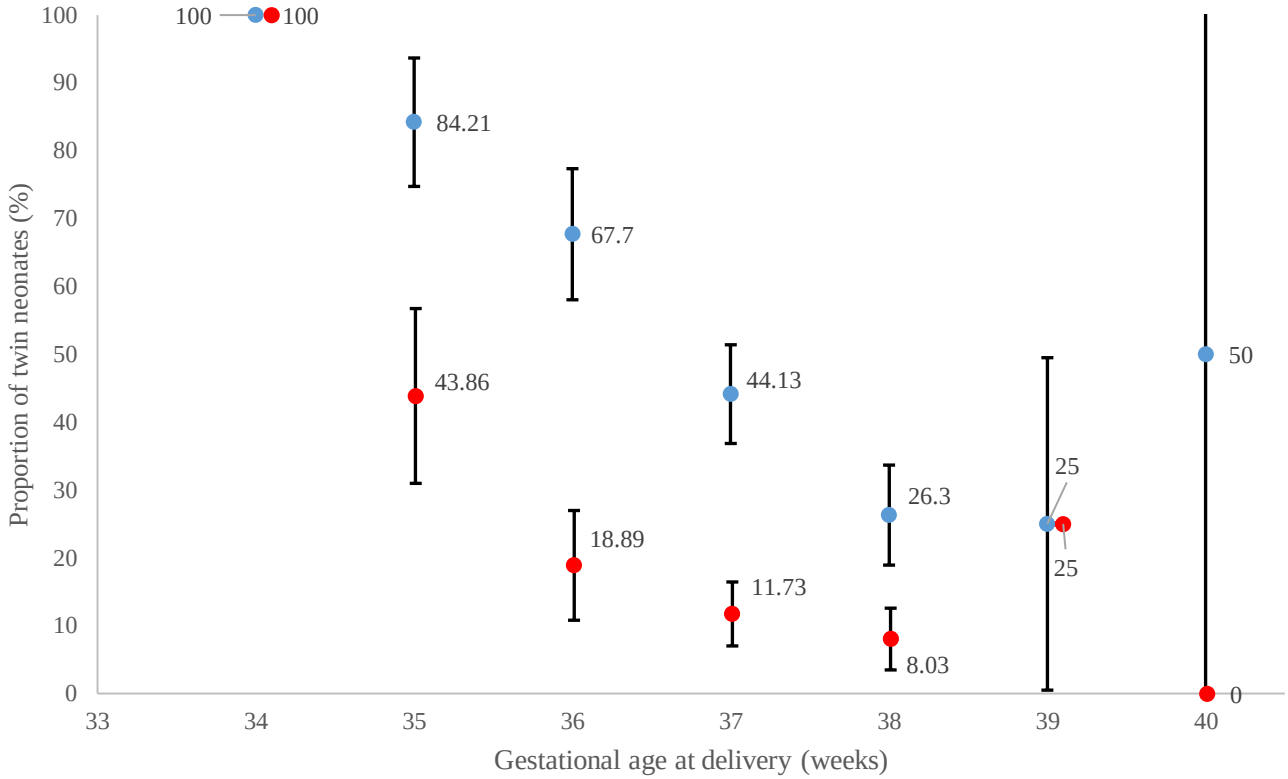


Figure 8: *Proportion of twin neonates with at least one adverse outcome (blue) and NICU admission (red) according to gestational age at birth*



The proportion of twin neonates with TTN also decreased with advancing gestation. Each additional week of gestation from 34 weeks onwards decreased the risk of TTN by 22.51% (p<0.001, 95%CI 12.33-55.21). A considerable but non-significant rise in TTN was observed at 39 weeks gestation. (*Figure 7*)

A total of seven neonates had hyperbilirubinemia that necessitated phototherapy. The highest proportion of neonates requiring phototherapy were born at 34 completed weeks of gestation, followed by a significant reduction from 36 weeks onwards. Prevalence of hypoglycaemia decreased gradually, with no cases reported at 38 weeks gestation. There were no recorded neonatal seizures in the studied cohort and no significant trends in sepsis rates were detected.

All neonates born at up to 34^{+6} weeks of gestation were admitted to NICU for a period of observation due to departmental policy. NICU admission rate was lowest in neonates born at early term (37^{+0}-38^{+6} weeks). Each additional week of gestation beyond 34 weeks decreased NICU admission rate by 43.88% (p<0.001, 95%CI 38.10-50.51). A considerable but non-significant rise in NICU admission rate occurred at 39 weeks gestation. The trend for mean neonatal length of stay in hospital is dependent on and follows the pattern of gestational age-specific NICU admission rates.

On evaluation of the different gestational age at birth groups and the incidence of *any* adverse neonatal outcome (RDS, TTN, 1st or 5th minute Apgar <7, hyperbilirubinemia requiring phototherapy, sepsis, hypoglycaemia), a significant reduction in overall morbidity at 38 weeks of gestation was noted (*Figure 8*). This coincides with a nadir in NICU admission rate and neonatal length of hospital stay.

Discussion

During the period under study, overall twin pregnancies amounted to a mean 67.7 per year. 254 of these were dichorionic twin pregnancies which satisfied our inclusion criteria; a mean 40.7 pregnancies per year. Uncomplicated dichorionic twin pregnancies thus represent a small but noteworthy proportion of pregnancies at this state hospital.

A large proportion of twin neonatal complications are related to low birth weight and respiratory problems, namely RDS. This study identified an inverse association between birthweight and RDS, hypoglycaemia and intensive care requirement. Low birthweight implies metabolic instability in the neonate as well as a higher body surface area to volume ratio that makes the newborn susceptible to heat loss and hypothermia. There were no very low birthweight infants in this study population. This is because of the lower gestational age cut-off of 34 weeks, coupled with the exclusion of twin neonates with intrauterine growth restriction.

With a 5% mortality rate, RDS can be severe, however it becomes less common in infants born at 33 to 36 weeks of gestation and is rare in full-term infants.[15-16] The observed trends in RDS incidence reflect the different stages of foetal lung development. Remarkable changes in lung appearance begin at around the 28th week of gestation, when there is a decrease in interstitial tissue, and airspace walls become narrow and more compact. As reflected in the drop in RDS incidence at 36 completed weeks of gestation, alveoli then start appearing. From then onwards, during the saccular stage, the surfactant-secreting Type 2 pneumocytes are formed and the foetal ex-utero morbidity decreases significantly.

In general, RDS rates in our study population were higher than those in published literature. In a prospective study over 2 years, Bakr AF et al identified an RDS rate of 7% in deliveries at 36^{+0}-36^{+6} weeks and 0.8% at 37^{+0}-38^{+6} gestational weeks.[17] These investigators excluded maternal risk factors and congenital anomalies however included pregnancy-related conditions such as PIH and GDM. In our study, despite excluding these high-risk pregnancies, RDS rates at 36, 37 and 38 completed weeks were still marginally greater at 7.8, 8.4 and 1.5% respectively.

An important reason for this incongruity is the higher caesarean section (CS) rate in our local population, with 56.10% undergoing elective CS and another 38.58% undergoing CS after the onset of labour or ROM. This represents a total 94.68% of cases as opposed to 44.67% in Bakr AF et al's cohort.[17] Gerten KA et al reported that at any given gestational age, the incidence of RDS is greater for infants born by CS, especially without established labour, than for those born by vaginal delivery.[18] This could be due to a combination of delayed expulsion of pulmonary fluid and a lack of the

cortisol response associated with spontaneous labour.[19]

In our cohort, the incidence of RDS in neonates at 38 completed weeks of gestation was significantly lower than those born at 37 weeks. This benefit, and its secondary impact on NICU admission and neonatal length of hospital stay supports delaying delivery to 38 completed weeks whenever possible.

Within the CS subgroup we found that elective caesarean delivery was associated with a decreased age-adjusted risk of RDS (RR 0.79, $p<0.04$) and an increased risk of TTN (RR 2.21, $p<0.04$) when compared to CS after onset of labour/ROM. This observation may be secondary to information bias. Since surgery occurred electively with no suspected foetal prematurity or distress, hospital staff may have been more likely to label respiratory symptoms as TTN rather than RDS. A prospective study with strict diagnostic criteria would clarify this observation.

Hyperbilirubinemia in preterm infants is also more prevalent, more severe, and its course is more protracted than in term neonates.[20-22] Our findings are in keeping with those by Sarici SU et al[23] who studied 365 neonates and found that late preterm infants had a higher incidence of hyperbilirubinemia than those at 38 to 43 weeks gestation. There are numerous reasons for this observation. Primarily, there is an increased bilirubin load in hepatocytes as a result of decreased erythrocyte survival, higher erythrocyte volume, and increased enterohepatic circulation of bilirubin. In addition, a delay in the initiation of enteral feedings, which is common in the clinical management of sick premature newborns, may limit intestinal flow and bacterial colonisation resulting in further enhancement of bilirubin enterohepatic circulation.[24] In our study population severe hyperbilirubinemia was most prevalent in those born at 34 and 35 weeks, decreasing to almost nil from 36 weeks onwards.

Gestational age-specific NICU admission rates have been widely studied as these give a general picture of the neonate's condition at birth and physiological maturity. In a study by Lee HJ et al[25] the nadir of composite morbidity rate was observed at ≥39 weeks of gestation, where there was no NICU admission, neonatal morbidity or mortality. Lee HJ's study is a retrospective analysis of 18 years' worth of data on uncomplicated dichorionic twin pregnancies. Very similar data was obtained from the prospective cohort study by Bakr AF et al[17], with NICU rates decreasing significantly to 4.5% at early term (37^{+0}-38^{+6}) and to 0% at 39 completed weeks. Similarly, local NICU admission rates were lowest in neonates born at 37 and 38 weeks with a non-significant increase at 39 weeks of gestation. A wide confidence interval at this gestation reflects the data group's susceptibility to the effect that aberrant single data entries could have on the variable mean.

Any attempt to identify the optimal gestational age of delivery must counterbalance the neonatal benefits of advancing gestation with any possible increase in foetal/neonatal mortality risk. Luke B et al[26] concluded that there is a U-shaped pattern of mortality with the best outcomes observed at birth weights of 2,500-2,799g and 35-38 weeks gestation. This late surge in mortality beyond 38 weeks, they concluded, reflected the combined influence of growth retardation and advancing gestation on mortality. Over the seven year period under study we identified two stillbirths and no perinatal or neonatal deaths. These stillbirths occurred at 35 weeks gestation. This gave our study population a prospective intrauterine foetal death risk of 0.39% beyond 34^{+0} weeks. Unlike Luke B et al's study which included cases with maternal or pregnancy induced complications, this study did not identify a mortality surge in twin neonates at term.

Conclusion

Local population-based data suggests that in the absence of complication, dichorionic twin neonates continue to benefit from advancing gestation to at least 38 weeks with no consequence on foetal, perinatal or neonatal mortality. Delaying discretionary delivery to 38 weeks of gestation decreases the prevalence of LBW, RDS, TTN and hypoglycaemia while decreasing NICU admission rate and neonatal length of hospital.

Acknowledgements

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Case Report

Ruptured abdominal aortic aneurysm with a horseshoe kidney: an uncommon but potentially troublesome coexistence

Nebojsa Petrovic, Stephen Micallef Eynaud, Sinisa Pejkic

Abstract

We report a case of an elderly patient with a ruptured abdominal aortic aneurysm (AAA) associated with a horseshoe kidney (HSK) treated by an emergency open repair and discuss the anatomical features and surgical challenges attendant to this rare combined pathology.

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Introduction

Horseshoe kidney is the most frequent congenital renal malformation, with the prevalence in a general population of up to 0.25%.[1] It is characterized by the presence of an anomalous strip of tissue or *isthmus*, comprised in the vast majority of cases of a functional renal parenchyma, crossing in front of the abdominal aorta and interconnecting the two renal moieties at their inferior (~95% of cases) or superior poles; the least frequent variant of this fusion anomaly is a "cake kidney", in which both the upper and the lower poles of the two kidneys are conjoined. Clinical significance of HSK includes frequent association with other congenital malformations, susceptibility to medical and surgical renal disease (e.g., nephrolithiasis, hydronephrosis, urinary tract infection), as well as posing technical difficulties during retroperitoneal surgical procedures, such as the abdominal aortic aneurysm repair.[1-3] Cases of HSK coinciding with a *ruptured* AAA, as described in this report, represent true surgical rarities.

Case report

A 71-year-old man presented to Mater Dei Hospital Emergency Department four hours after a sudden onset of excruciating abdominal pain followed by a transitory syncope. Apart from being an ex-smoker, his past medical history was unremarkable and there was no family history of aneurysmal disease. On examination, his blood pressure was 102/53 mm Hg, heart rate 92 bpm and oxygen saturation 92% on room air. Routine laboratory investigations revealed a haemoglobin level of 125 g/L, haematocrit of 0.38 L/L, serum creatinine level of 211 μmol/L and eGFR of 22 mL/min/1.73m.[2] On palpation of abdomen, tender pulsating mass was noted around the umbilicus. In view of patient's hemodynamic stability, *contrast-enhanced computed tomography (CT) was* urgently performed. It confirmed the diagnosis of an acute

rupture of a large juxtarenal AAA measuring 9.6 cm in maximum transverse diameter (Fig. 1).

Patient was immediately taken to the operating theatre for an emergency open repair. After placing him under general anaesthesia, median laparotomy was performed and transperitoneal route used to approach the abdominal aorta. The findings of a large AAA surrounded by acute retroperitoneal hematoma (RPH) in combination with the HSK confirmed the preoperative diagnosis. After mobilization of the left hepatic lobe and systemic heparinization, supraceliac aortic cross-clamp was initially placed, followed by its prompt repositioning at infrarenal level once the distal duodenum was mobilized, the left renal vein identified and the short infrarenal aneurysmal neck dissected free. Both common iliac arteries were then exposed and cross-clamped after finding them to be moderately atherosclerotic but without aneurysmal lesions. Finally, HSK isthmus was carefully isolated and retracted away from the aneurysm, enabling us to proceed with the aortic repair. Upon longitudinal opening of the aneurysm sac and removal of a mural thrombus, laceration of the aneurysm left posterolateral wall was identified as the site of rupture. Aortic continuity was restored by interpositional grafting from infrarenal aorta to aortic bifurcation using the 20-mm polyester prosthesis tunnelled behind the preserved HSK isthmus (Fig. 2). Operative time was 125 minutes and blood loss 1700 mL, with intraoperative cell saver device usage enabling for 420 mL re-transfusion of autologous packed red blood cells. Patient tolerated the procedure well and was subsequently transferred to an intensive therapy unit in a hemodynamically stable condition. Postoperative course was marked by oliguria (30 mL/h while on inotropic support) and difficulty weaning from mechanical ventilation. Deteriorating renal function necessitated continuous renal replacement therapy. Follow-up CT performed at postoperative day 6 showed patent aortic graft with competent anastomoses and intact distal arterial system without embolism, but also revealed loss of normal parenchymal perfusion in relation to the lower pole of the left renal moiety, with the right renal moiety maintaining normal perfusion. The main renal arteries on either side appeared patent all the way down to the corresponding hila (Fig. 3). Unfortunately, patient expired of multiorgan failure on postoperative day 7.

Figure 1*: Preoperative transverse tomogram (left, level of 4th lumbar vertebra) and 3D reconstructed CT image (right), showing 9.6-cm large juxtarenal AAA with surrounding massive acute RPH. Anteriorly displaced by the AAA and the RPH, HSK is present, with its isthmus connecting the two renal moieties inferior poles (arrows) and displaying decreased perfusion in comparison to the rest of the HSK. Apart from two normal renal arteries, a small accessory left renal artery arising from the aneurysm neck posterior wall and supplying the isthmus of HSK was also noted.*

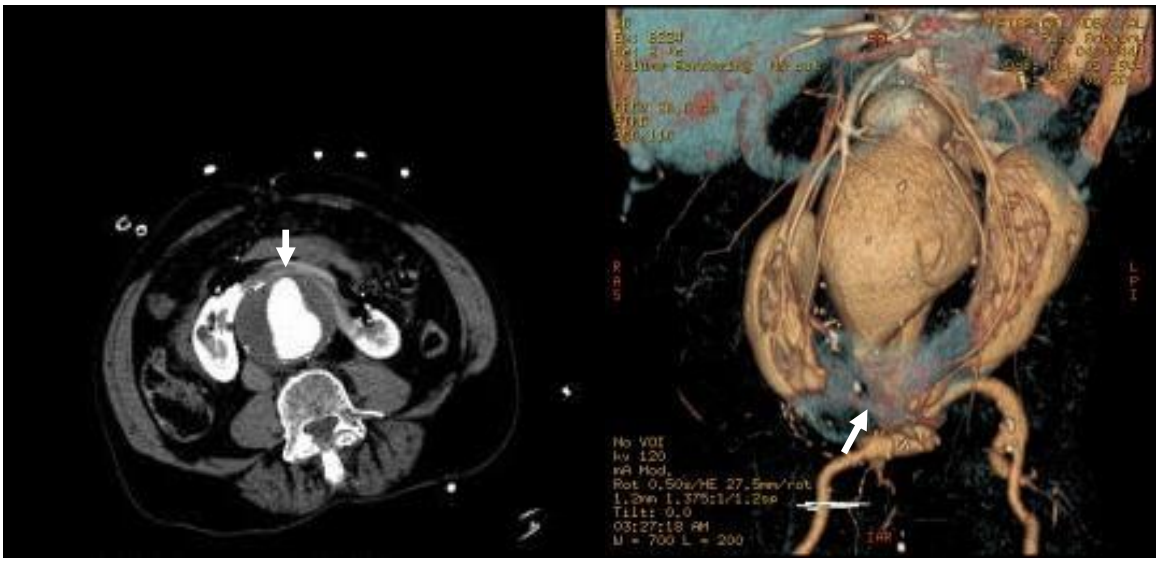


***Figure 2**: Intraoperative photograph after completing repair of ruptured AAA. Polyester aortic prosthesis is positioned behind the preserved HSK isthmus (retracted upward with umbilical tape).*

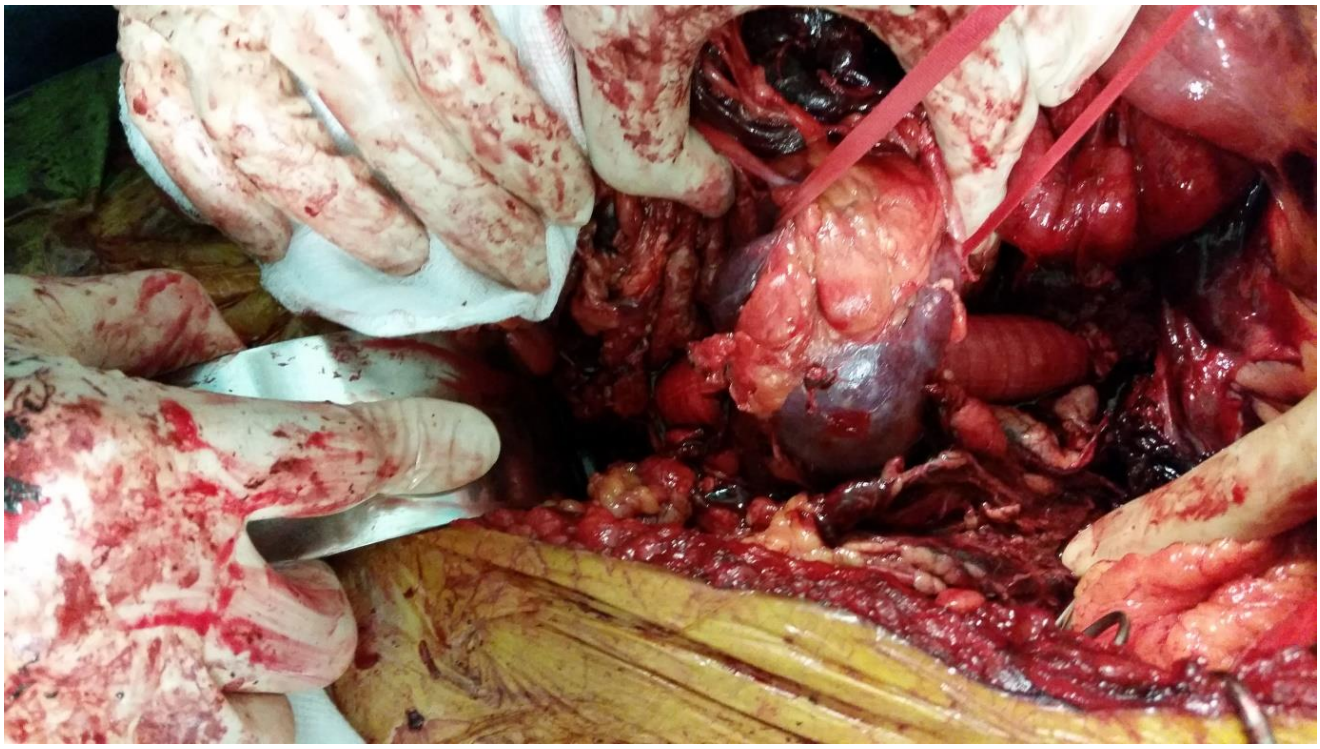
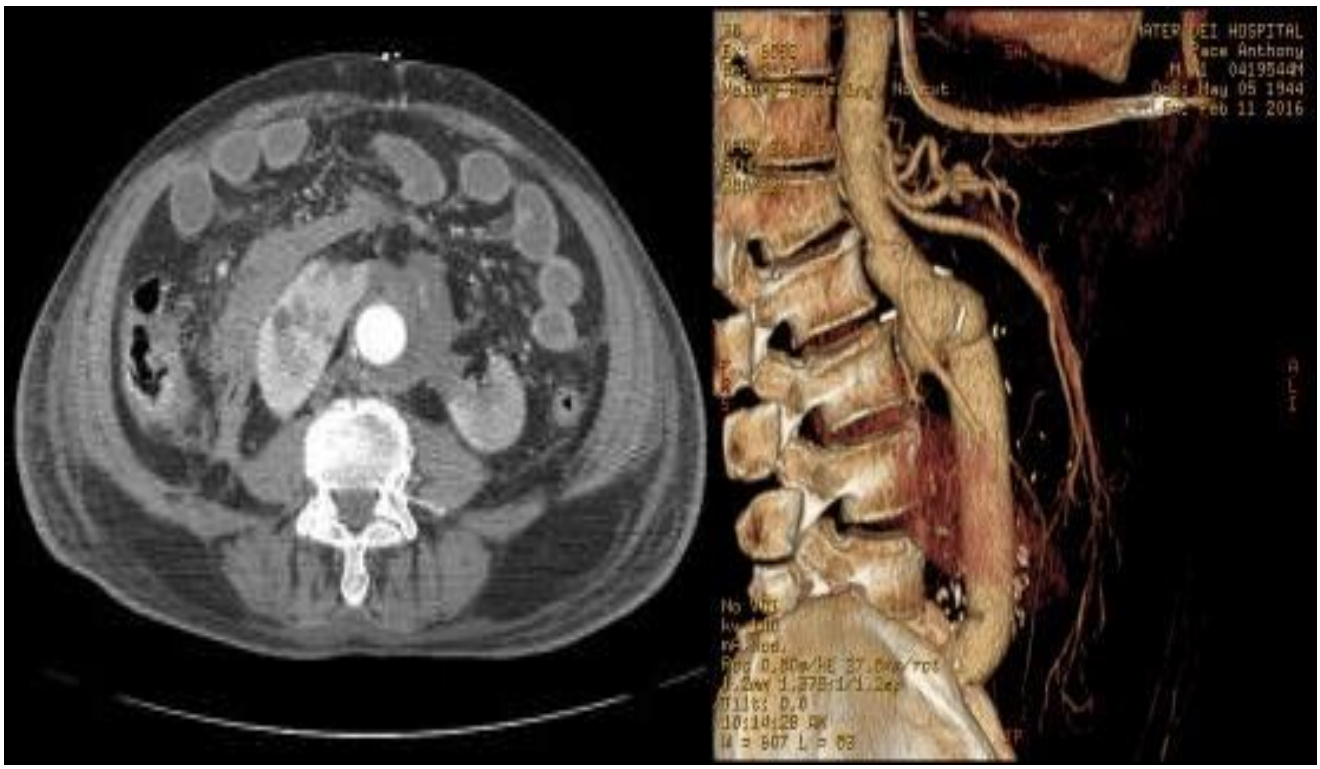


***Figure 3**: Postoperative transverse tomogram (left) and 3D reconstructed CT image (right) show patent aorto-aortic graft with competent anastomoses and intact HSK isthmus.*



Discussion

Co-existence of HSK and AAA is estimated at 0.12% of patients undergoing elective open aneurysm repair.[1] It is characterized by the presence of: 1) renal isthmus, usually thick and parenchymatous, 2) anomalous renal vasculature, and 3) anteromedially displaced ureters.[1-3] Each of these anatomical peculiarities requires special attention during AAA open repair in order to avoid HSK-related postoperative complications, which can have catastrophic consequences. Since the first case of successful treatment of an aortic aneurysm in association with a HSK was reported by Phelan et al. in 1957,[5] the fascinating progress in the field of vascular surgery in general and better understanding of this combined pathology in particular have led to considerable improvements and shifts in its treatment. In a review article published in 2001, Stroosma et al.[3] found a total of 176 cases of AAA with HSK reported in the literature over the 44-year period (1956–1999), of which 42 were of ruptured AAA. Different reconstructive strategies were described, including: 1) transperitoneal approach with or without division of HSK isthmus, 2) retroperitoneal approach, and 3) endovascular aneurysm repair, with its first use in this situation reported in 1997 by Ferko et al.[7] From this collective experience, several important lessons have been learned. Preoperative CT with a contrast enhancement is the preferred diagnostic modality, raising awareness of the unusual situation and allowing for more deliberate planning of aortic reconstruction.[1,3] In an elective setting, when dealing with an asymptomatic aneurysm, *endo*vascular repair (EVAR) or open surgical repair using the *retro*peritoneal approach to abdominal aorta offer clear advantages in avoiding or mitigating technical difficulties imposed by the aberrant anatomy.[1,3,6,8] General consensus is that minor accessory renal arteries (<3 mm) can be ligated/sacrificed without undue consequences, while more sizeable ones should be revascularized to avoid loss of renal parenchyma.[1,3,6] Special promise with regard to the preservation of dominant anomalous arteries holds rapidly evolving and ever more widely used EVAR technology (e.g., customized fenestrated stent grafts). Standard endoprostheses currently used for exclusion of infrarenal AAA still carry an upredictable risk of kidney devascularisation by shutting down potentially critical accessory renal arteries. [8]

The approach of choice for a ruptured AAA is anterior *trans*peritoneal,[1-3] whereby transection of HSK isthmus cannot always be avoided and was indeed necessary in as many as 50% of 42 collective cases identified by Stroosma et al. (double as frequent in comparison to 134 elective cases).[3] Bearing in mind this can lead to severe complications such as bleeding and urinary fistula, the latter also being associated with an ominous risk of aortic graft infection, an attempt at renal isthmus preservation should be made by its careful separation from the aorta and other adjustments in operative technique (e.g., isthmus retraction and posterior graft tunnelling), as seen in Fig. 2. Emergency repair for ruptured AAA is also associated with an increased hazard of anomalous renal arteries occlusion (74%, versus 51% in the elective group).[3]

In two largest single-centre studies of patients with HSK undergoing abdominal aortic repair (19 patients over a 31-year period described by O'Hara et al.[4] and 15 patients over a 20-year period in the study by Davidović et al.)[2] the strongest negative prognostic factor was preoperative renal failure. Because the anomalous HSK is inherently prone to various pathological conditions, chronically compromised renal function is a frequent occurrence in this clinical scenario and it adversely impacts postoperative morbidity and mortality. This is even more so true in an emergency situation, in which shock and suprarenal clamping independently contribute to a rise in serum creatinine.[1-3]

Summary

The presence of HSK increases the technical complexity and risks of AAA repair, especially in an emergency setting. CTA is the preoperative diagnostic modality of choice, enabling for better reconstruction planning. Recommended surgical approach in cases of ruptured AAA is midline transperitoneal. The renal isthmus should be preserved and as many anomalous renal arteries as technically feasible revascularized to avoid the HSK-related postoperative morbidity. In elective setting, endovascular aneurysm exclusion or open repair using retroperitoneal approach are preferred treatment options.

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