Original Article

Maternal risks associated with pregnancy in women with advanced maternal age

Mandy Collict, Yves Muscat Baron, Miriam Gatt, Neville Calleja

Abstract

Introduction: The trend towards delayed motherhood has accelerated in developed countries over the last few decades. Advanced maternal age (AMA) is defined as age 35 years and older at the estimated date of delivery.

Objective: The aim of this large retrospective cohort study is to assess for the association between AMA and adverse maternal outcomes after adjustment for confounding factors in maternal characteristics and in the obstetric history.

Study Design: Mothers of 20 years and older, who delivered singleton babies in Malta and Gozo between 1st January 2000 and 31st December 2014 were studied. All data was derived from the National Obstetric Information System.

Results: The study population included 55,943 singleton births. 12.2% (6,838) of mothers were between 35 – 39 years and 2.4% (1,325) were 40 years and older. Significant difference was found between maternal age and BMI (p<0.0001), maternal smoking status (p<0.0001), non-insulin dependent diabetes mellitus (p=0.004), history of stillbirth (p<0.0001), gestational diabetes (p<0.0001), pregnancy – induced – hypertension (p=0.008) and pre-eclampsia (p=0.008). Significant difference was also found between maternal age and mode of delivery (p<0.0001). Regression analysis revealed persistent significant differences between maternal age and different maternal outcomes.

Conclusion: This study demonstrates that AMA in Malta significantly increases the risk for hypertension in pregnancy, gestational diabetes and caesarean delivery. Care providers need to be aware of these increased risks and adjust their obstetric management according to the individual to ensure optimal maternal outcomes.

Mandy Collict* MD, MSc (Reproductive Health), MRCSEd
Department of Obstetrics & Gynaecology
Mater Dei Hospital
Msida, Malta
mandy.caruana@gov.mt

Yves Muscat Baron MD, FRCOG, FRCPI, PhD
Department of Obstetrics & Gynaecology
Mater Dei Hospital
Msida, Malta

Miriam Gatt MD, MSc (Public Health Medicine), MSc.HSCR(Sheffield)
Department of Health Information and Research

Neville Calleja MD, PhD, FFPH, CStat
Department of Health Information and Research

**Corresponding Author*

Keywords

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Introduction

The trend towards delayed childbearing has accelerated in developed countries over the last three decades.[1] Advanced maternal age (AMA) is commonly defined as age 35 years an older at the estimated date of delivery. The reasons motherhood is postponed are manifold. Women's pursuit of higher education, effective contraception, advances in assisted reproductive technology, delayed marriage, and longer life expectancy have all been mentioned as possible reasons for this phenomenon.[1-4] Women should be supported in their decisions of whether to have children or not and when to plan childbearing. Accordingly, women with AMA need to be counselled regarding how fertility and pregnancy outcomes change with age.

Published studies and data on the obstetric risks associated with childbirth at 35 years or over are various and inconsistent. AMA continues to be associated in various numbers of studies with a range of adverse pregnancy outcomes including antepartum haemorrhage, malpresentation, low birth weight, pre-term birth, stillbirth, operative vaginal delivery and increased rates of Caesarean deliveries.[5-6] However, other studies have yielded inconsistent conclusions about both the specific outcomes adversely affected by maternal age and the strength of their association.[7-8]

The only published study on AMA and pregnancy outcomes in Malta was back in 1987 by Savona Ventura and Grech on risks factors in elderly obstetric patients, in the European Study Group on Social Aspects of Human Reproduction, V annual meeting.[3] The scope of this research is to present a clearer picture of what the actual risks to these Maltese elderly women are and also help to compare our findings with that of other countries.

Methodology

This research project is a Retrospective Cohort Study which analyses maternal complications associated with AMA.

All data was derived from the National Obstetric Information System (NOIS) of Malta. This research analyses almost all deliveries in Malta and Gozo over a fifteen-year period from the year 2000 to 2014. The study population was recruited from the NOIS according to the following inclusion and exclusion criteria.

Inclusion criteria:

- Mothers of 20 years of age and over
- Who delivered singletons babies, live births or even still births
- In Malta or in Gozo
- Between 1st January 2000 and the 31st of December 2014

Exclusion criteria:

- Mothers of less than 20 years
- Mothers with multiple pregnancies
- Missing maternal age

All the data analysis was performed by the Statistical Package for the Social Sciences.

Results:

Between the year 2000 and the year 2014, a total of 61,365 deliveries were registered in Malta and Gozo (Figure 1).

1. Demographic Data

All women studied were divided into 5 maternal age groups (Table 1). The average maternal age was 29.2 years (range 20 years – 55 years) and the median age was 29 years. Figure 2 represents the maternal age over this 15-year period.

The maternal weight at booking visit and height were also analysed and the body mass index (BMI) was worked out. In the studied population, 3.2% (1,258 mothers) were underweight, 53.8% (21,019 mothers) had normal BMI, 26.4% (10,324 mothers) were overweight and 16.5% (6,450 mothers) were obese.

The data was analysed by the Medical Statistician (NC) in the employ of the Department of Health Information and Research. The Pearson Chi- Squared (PCS) test was used to assess the significant difference between maternal age and BMI and the results were statistical significant $p<0.0001$. It was noted that although the most common BMI was the normal BMI, a large percentage of mothers were overweight and obese (Figure 3).

***Figure 1**: Study plan*

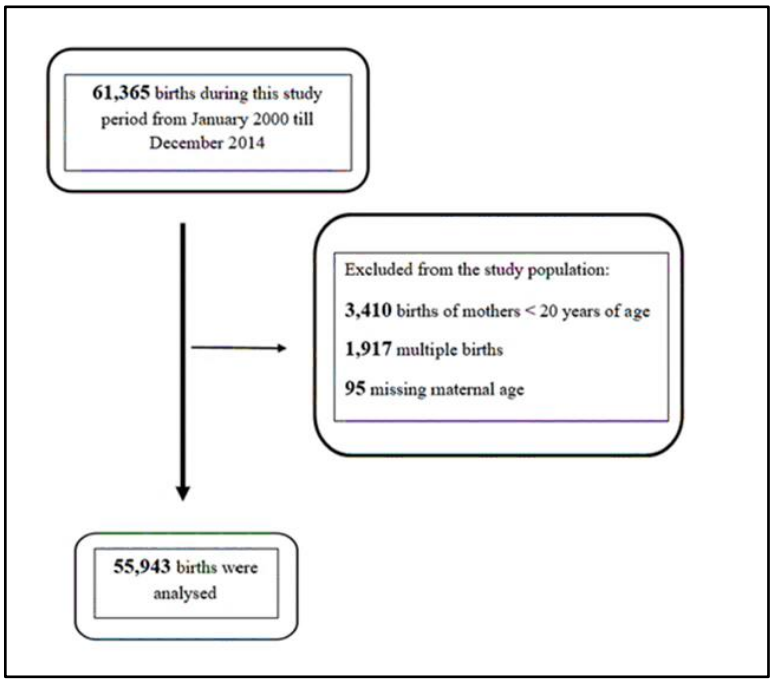


***Table 1**: Patient Age Distribution*

Maternal Age Groups	Number of Mothers	Percentage of Mothers
20 – 24 years	9,814	17.5%
25 – 29 years	20,417	36.5%
30 – 34 years	17,549	31.4%
35 – 39 years	6,838	12.2%
≥ 40 years	1,325	2.4%

***Figure 2**: Trends in maternal age in Malta from 2000 - 2014*

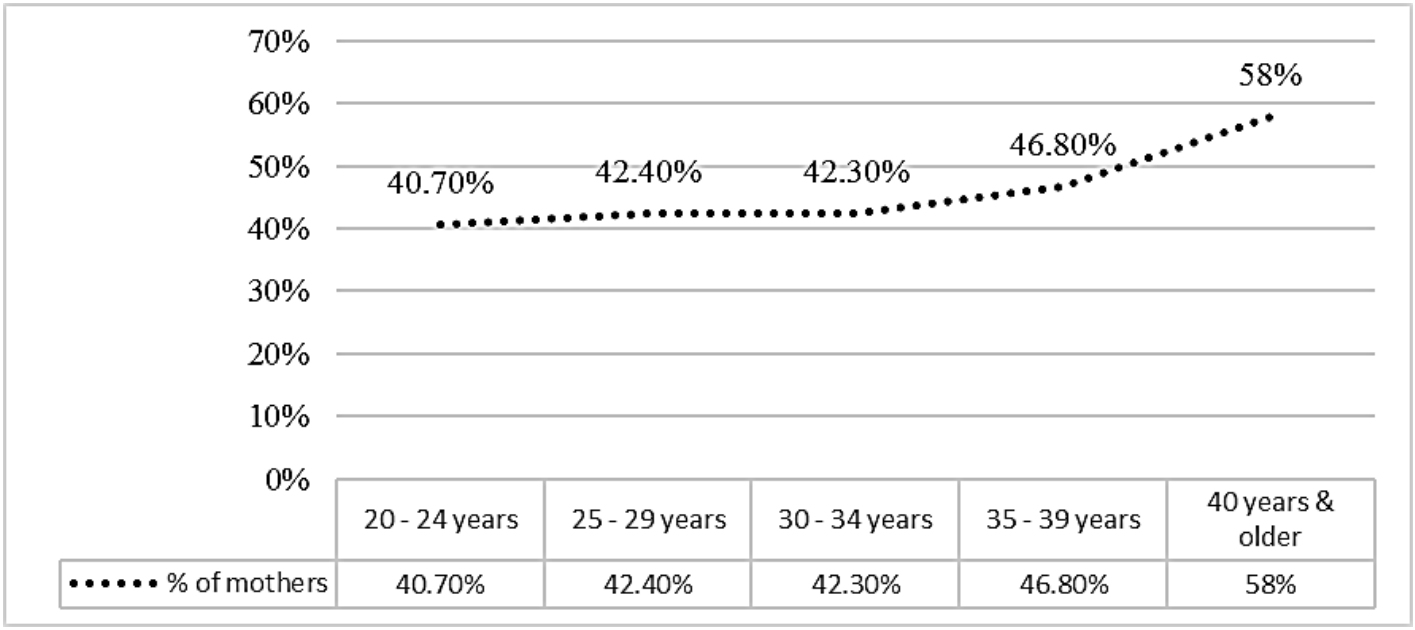
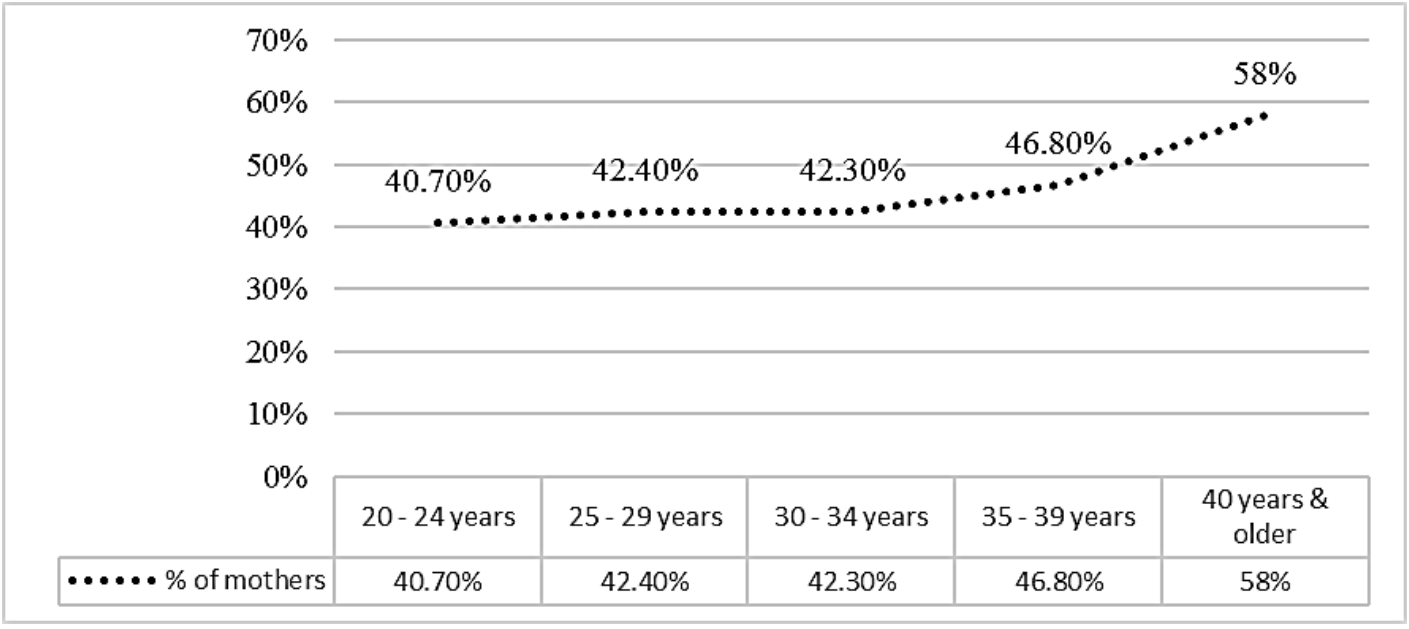


***Figure 3**: The percentage of mothers with BMI > 25 and maternal age*



2. Maternal Complications

As part of this study, the pathology that arises in pregnancy was also studied and specifically we looked into gestational diabetes and hypertension in pregnancy.

For gestational diabetes, mothers were further divided into those who were treated without insulin and those who were treated with insulin. The results show that as the maternal age increase, the percentage of mothers that developed gestational diabetes increases (Table 2). The PCS test was used to analyse the effect of age on the results obtained and the results were statistically significant (p<0.0001).

The data was further analysed by regression analysis (Table 3). A forward stepwise logistic regression model was used and the significant confounders were maternal age (p<0.0001), parity (p<0.001) and BMI (p<0.0001).

As regards hypertension in pregnancy, pregnancy induced hypertension, pre-eclampsia and eclampsia were specifically studied in the 5 different age groups (Table 2). In pregnancy induced hypertension, a sharp rise is noted in the advanced maternal age groups. PCS test was used and the results were statistically significant (p<0.0001). Pre-eclampsia was also much commoner in the elderly age groups. In the elderly age groups, 1.0% of mothers had pre-eclampsia (p=0.008). There were only 12 cases of eclampsia reported in this 15-year study period (p=0.668).

Further data analysis was carried out on hypertension in pregnancy (Table 4). Forward stepwise logistic regression analysis was also carried out. In this latter analysis pregnancy – induced hypertension, pre-eclampsia and eclampsia were grouped into this single group – hypertension in pregnancy. The significant confounders for this model were maternal age (p<0.0001), parity (p<0.0001), IDDM (p<0.0001), cigarette smoking (p=0.01), and BMI (p<0.0001).

***Table 2**: Gestational diabetes, Pregnancy induced hypertension, pre-eclampsia, eclampsia and maternal age*

Maternal Age Group	**20 – 24 years**	**25 -29 years**	**30 – 34 years**	**35 – 39 years**	**≥ 40 years**
Diagnosis of Gestational Diabetes					
No	98.3% (9,646)	97.3% (19,872)	96.7% (16,974)	95.9% (6,555)	94.4% (1,251)
Yes: not treated with insulin	1.5% (144)	2.3% (475)	3.0% (531)	3.9% (264)	5.3% (70)
Yes: treated with insulin	0.0% (0)	0.1% (12)	0.1% (9)	0.0% (1)	0.0% (1)
Diagnosis of Pregnancy Induced Hypertension					
No	94.4% (9,260)	94.1% (19,206)	94.1% (16,519)	92.9% (6,350)	89.0% (1,179)
Yes	5.4% (526)	5.6% (1,147)	5.7% (993)	6.9% (471)	10.9% (144)
Diagnosis of Pre-Eclampsia					
No	99.1% (9,724)	99.2% (20,246)	99.2% (17,401)	98.8% (6,755)	98.9% (1,310)
Yes	0.7% (64)	0.5% (111)	0.7% (116)	1.0% (69)	1.0% (13)
Diagnosis of Eclampsia					
No	99.7% (9,785)	99.7% (20,349)	99.8% (17,511)	99.8% (6,822)	99.7% (1,321)
Yes	0.0% (2)	0.0% (4)	0.0% (3)	0.0% (2)	0.1% (1)

Table 3: *Adjusted results for gestational diabetes and maternal age*

Gestational Diabetes	Adjusted Rates	Standard Error	Confidence Interval (Lower)	Confidence Interval (Upper)
20 – 24 years	3%	0.005	0.02	0.04
25 – 29 years	4%	0.007	0.03	0.06
30 – 34 years	6%	0.009	0.04	0.08
35 – 39 years	7%	0.011	0.05	0.09
40 years & older	9%	0.017	0.06	0.13

Table 4: *Results for Hypertension in Pregnancy*

Hypertension in Pregnancy	Adjusted Rates	Standard Error	Confidence Interval (Lower)	Confidence Interval (Upper)
20 – 24 years	7%	0.013	0.05	0.10
25 – 29 years	7%	0.013	0.05	0.10
30 – 34 years	7%	0.013	0.05	0.10
35 – 39 years	9%	0.015	0.06	0.12
40 years & older	11%	0.021	0.08	0.16

Figure 4: *Maternal age groups and their mode of delivery*

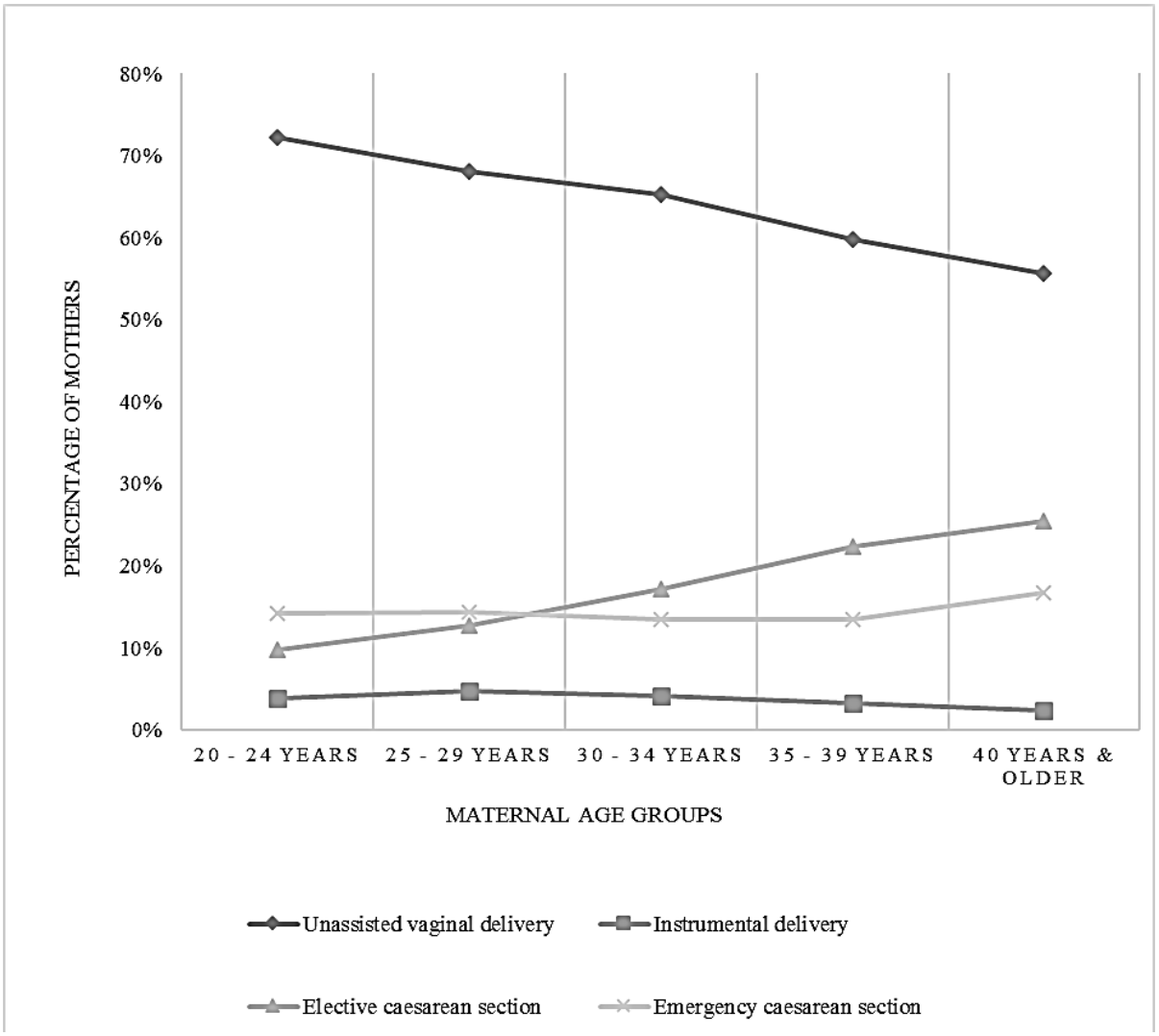


Table 5: *Adjusted results for Mode of Delivery and Maternal Age*

Mode of Delivery	Normal Vaginal Delivery OR (95% CI)	P-value	Instrumental Delivery OR (95% CI)	P-value	Elective Caesarean Section OR (95% CI)	P-value
20 – 24 years	2.507 (2.117 – 2.968)	< 0.0001	1.346 (0.899 – 2.015)	0.149	0.868 (0.713 – 1.056)	0.158
25 – 29 years	2.070 (1.760 – 2.436)	< 0.0001	1.761 (1.189 – 2.607)	0.005	0.965 (0.802 – 1.161)	0.706
30 – 34 years	1.716 (1.458 – 2.020)	< 0.0001	1.860 (1.256 – 2.755)	0.002	1.056 (0.879 – 1.269)	0.558
35 – 39 years	1.247 (1.050 – 1.480)	0.012	1.562 (1.037 – 2.353)	0.033	1.036 (0.854 – 1.256)	0.722
40 years & older	Reference		Reference		Reference	

3. Mode of Delivery

In this study, the mode of delivery was also analysed (Figure 4). The PCS test was used to analyse the effect of maternal age on the mode of delivery and the results were statistically significant ($p<0.0001$).

For the mode of delivery, forward stepwise multinomial regression analysis was carried out (Table 5). The significant confounders were maternal age ($p<0.0001$), year of delivery ($p<0.0001$), IDDM ($p<0.0001$), parity ($p<0.0001$), cigarette smoking ($p<0.0001$), BMI ($p<0.0001$) and history of stillbirth ($p<0.0001$).

Discussion

In the Western world, the average maternal age at which mothers are giving birth is continually rising. Risks associated with pregnancy in women of AMA have been addressed in numerous studies, mostly focusing on the medical risks associated with advancing maternal age. The main purpose of this study was to analyse the Maltese local data. The importance of this research lies in the fact that it is the first recent research of its kind carried out locally after the study published by Savona-Ventura and Grech in 1987.[3]

In the present study, a significant increase in medical complications were noted in mothers with AMA. A significant increase was noted in pregnancy – induced hypertension ($p<0.0001$), pre – eclampsia ($p=0.008$) and gestational diabetes ($p<0.0001$). Similar findings were noted in other studies carried out in Europe,[9-10] in Asia,[11-12] and in USA.[13-14]

The regression analysis carried out showed that hypertension in pregnancy increased steadily with age. A sharp rise in hypertension was seen after the 35 years. For gestational diabetes, a steady increase in mothers with advancing age was noted after the effect of the significant confounders was removed.

With advancing age, pancreatic B cell function and insulin sensitivity diminish, increasing risk in developing type 2 diabetes.[15] Due to the diminished pancreatic B cell response to glycaemic stimulation women with AMA may be more insulin-resistant than younger women, which, when combined, make gestational diabetes more likely. The presence of gestational diabetes increases the risk for foetal macrosomia.[16] Inherently the Maltese population as in most Mediterranean populations is at risk of gestational diabetes which is further augmented in women with AMA.[17]

There is increased risk of gestational hypertensive disorders with AMA.[18] It has been hypothesized that haemodynamic response to pregnancy and ageing might be associated with differences in blood pressure levels during pregnancy between younger and older women.[19] Maternal blood pressure is associated with impaired foetal growth during pregnancy especially during the third trimester of pregnancy and increased risks of adverse outcomes.[20]

Pregnant women experiencing hypertensive disorders are also at greater risk of stillbirth.[21] This risk of foetal demise is further exacerbated in hypertensive women in the AMA cohort.[22] The risk of stillbirth is increased with the onset of pre-eclampsia, and pre-eclampsia is also more prevalent in women with AMA.[23]

Overarching the risks of women in the AMA group for both gestational diabetes and hypertension is the increased prevalence of high BMI. In this study 26.4% of pregnant women were overweight and 16.5% were obese. The combination of AMA and an elevated BMI increase the risk for the occurrence of gestational diabetes.[24] Similarly, hypertensive disorders and pre-eclampsia are associated with AMA and an elevated BMI.[25] Moreover the combination of AMA, elevated BMI, diabetes and hypertension have a multiplier effect on increasing the risk of adverse maternal and neonatal outcomes.[26-27]

In this research, statistical significant results were found between mode of delivery and the maternal age ($p<0.0001$). The percentage of women delivering by normal vaginal delivery was noted to decrease with advancing age, while the percentage of women delivering by elective caesarean sections was noted to increase with advancing age. In mothers over 35 years, an increase was also noted in the rate of emergency caesarean sections. The regression analysis carried out confirmed that these results were still noted after the effects of the other significant confounders were removed. Several studies published similar findings of high rate of caesarean sections in different countries from the year 1987 to the year 2014.[7, 28-31]

In contrast with other international studies, in this study population, instrumental deliveries were noted to decrease with AMA. Wang et al reported in their study carried out in Norway, that

instrumental deliveries were increased in nulliparous women.[7] Tan and Tan also reported in 1994, that the incidence of instrumental deliveries was higher in women over the age of 35 years.[29]

In this study the trend of increased elective caesarean section avoiding vaginal delivery and more so instrumental assistance suggests that obstetricians in this unit may have a lower threshold for intervention in pregnant women in AMA cohort. This is especially noted in nulliparous women with AMA. The obstetrician's decision to resort to elective caesarean section in women with AMA would be further catalysed in the presence of medical complications. Breech presentation also increases with AMA contributing to an increased caesarean section in this cohort of women.[32] In an effort to reduce the risk of sudden stillbirth in the postdates period, resort to induction of labour and subsequent failure to progress in women with AMA may also increase the rate of abdominal delivery.[33, 34] Maternal requests in cases of AMA possibly compounded by a period of subfertility may be another reason for of increased elective caesarean section.[35]

Conclusion

This study demonstrates that advanced maternal age in Malta significantly increases the risk for hypertension in pregnancy, gestational diabetes and caesarean delivery.

With the persistent rise in the number of mothers having their children at advanced age in Malta, the set- up of a multidisciplinary specialized clinic for pre-conception, antenatal and postnatal care for these mothers may prove useful in improving outcome in pregnancies of women with AMA.

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