

## Advanced Maternal Age and Adverse Pregnancy Outcomes in Muar, Johor, Malaysia

(Umur Lanjutan Maternal dan Kesan Mudarat Kehamilan di Muar, Johor, Malaysia)

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### ABSTRACT

Various factors may contribute to adverse pregnancy outcomes; either maternal or foetal outcomes. This study aimed was to determine the association between advanced maternal age and adverse pregnancy outcomes. This is a cross sectional study. Data were collected from the birth records from January 1st 2012 until December 31st 2012 in Muar District. Descriptive and multiple logistic regression analyses were done and the results were presented as adjusted odds ratio (aOR) with p-value <0.05. The proportion of birth in Muar district, Johor was 14.8% among mothers aged 35 years and older and 85.2% among mothers aged 20 to 34 years. Advanced maternal age was associated with pregnancy-induced hypertension (aOR: 5.00; 95%CI: 1.95-12.65), gestational diabetes mellitus (aOR: 2.32; 95%CI: 1.35-4.00) and Caesarean section (aOR: 2.21; 95%CI: 1.53-3.19). Anaemia was negatively associated with advanced maternal age (aOR: 0.50; 95%CI: 0.32-0.78). No significant association was found between advanced maternal age and adverse foetal outcomes. In view of the findings, special attention should be paid to the antenatal mothers aged 35 years and older, even to those without any pre-existing medical problems.

**Keywords:** Adverse pregnancy outcomes; anaemia; maternal age

### ABSTRAK

Terdapat banyak faktor yang menyumbang kepada kesan mudarat kehamilan sama ada terhadap ibu atau fetus. Kajian ini bertujuan untuk menentukan hubungan antara umur lanjutan maternal dengan kesan mudarat kehamilan. Kajian ini adalah kajian keratan rentas. Data dikumpulkan daripada rekod kelahiran yang berdaftar dari 1 Januari 2012 sehingga 31 Disember 2012 di daerah Muar. Analisis deskriptif dan logistik regresi berganda telah dijalankan dan keputusan dibentangkan sebagai nisbah ganjil terlaras (aOR) dengan nilai  $p < 0.05$ . Pecahan jumlah kelahiran di daerah Muar, Johor adalah 14.8% dalam kalangan ibu berumur 35 tahun dan ke atas dan 85.2% dalam kalangan ibu berumur 20-34 tahun. Umur lanjutan maternal dikaitkan dengan penyakit darah tinggi semasa mengandung (aOR: 5.00; 95%CI: 1.95-12.65), penyakit kencing manis semasa mengandung (aOR: 2.32; 95%CI: 1.35-4.00) dan pembedahan Caesarean (aOR: 2.21; 95%CI: 1.53-3.19). Anemia pula berhubungan secara negatif dengan umur lanjutan maternal (aOR: 0.50; 95%CI: 0.32-0.78). Tiada hubungan yang signifikan ditemui antara umur lanjutan maternal dan kesan mudarat kepada fetus. Dengan penemuan ini, perhatian istimewa perlu diberikan kepada ibu mengandung pada umur 35 tahun dan ke atas walaupun ibu tersebut tidak mempunyai masalah kesihatan sebelumnya.

**Kata kunci:** Anemia; kesan mudarat kehamilan; umur maternal

### INTRODUCTION

Pregnancy at an advanced maternal age (AMA); defined as age 35 years and older is associated with adverse pregnancy outcomes (Biro et al. 2012; Gravena et al. 2013; Hoque 2012; Joseph et al. 2005; Schimmel et al. 2014). However, women still pregnant at AMA especially in developed countries due to delay in marriage (Cooke et al. 2012; Khalil et al. 2013; Rosniza Aznie et al. 2013). In the United States, the proportion of first birth to women

of 35 years and older rose nearly 8 times from 1970 to 2006 (Mathews & Hamilton 2009). While in Canada, the percentage is increased nearly three times from 4% to 11% (Bushnik & Rochelle 2008).

Besides that, women also seldom have their own cut-off point for completing the family (Bayrampour et al. 2012). Various studies observed the proportion of mothers who are still pregnant at AMA (Rajee et al. 2010; Schimmel et al. 2014). A woman who is pregnant at AMA is associated with adverse pregnancy outcomes which can further divided into maternal, delivery and fetal outcomes. As for maternal diseases, AMA mothers are at higher risk of developing pregnancy-induced hypertension and gestational diabetes mellitus (Ahmed et al. 2015; Matsuda

et al. 2011). Another common maternal disease during pregnancy is iron deficiency anaemia. A study conducted in Ethiopia found that anaemia in pregnancy was more likely to occur in AMA (Alem et al. 2013).

Pregnancy at AMA is associated with adverse delivery outcome in which is defined as instrumental delivery or Caesarean section. There was an increased in the rate of emergency Caesarean section among AMA mothers compared to mothers aged 24 to 27 years (Schimmel et al. 2014). Other study observed increase rate of both Caesarean section before labour and in labour in nulliparous AMA. There was also evidence on higher odds of instrumental delivery among AMA mothers compared to non-AMA mothers (Wang et al. 2011).

AMA also associated with adverse foetal outcomes. There were evidence on the association between AMA and prematurity, stillbirth and low birth weight in previous studies (Carolan & Frankowska 2011; Fretts 2005). A finding from Italian study observed higher odds of preterm delivery among AMA mothers (Astolfi et al. 2005).

Currently, there is limited published data in Malaysia to show the association between maternal age and pregnancy outcomes. This study aimed to investigate the pregnancy outcomes in relation to maternal age in Muar district, Johor.

#### MATERIALS AND METHODS

Muar district was chosen as the study location in view of it has the comparable maternal and child health status as compared to the national cumulative data (UNICEF 2011). All births were delivered by skilled birth attendants in the year of 2012. Of the total deliveries in that year, 64% had antenatal check-up in government facilities and the remaining had ante-natal check-up in private facilities.

Data from the registered births from January 1st, 2012 to December 31st, 2012 were collected from 11 health clinics and 38 community clinics in Muar District, Johor, Malaysia. The inclusion criteria were all pregnant mothers aged 20 and older with singleton pregnancy and have no pre-existing diseases. The exclusion criteria were teenage pregnancy and mothers aged 20 and older with multiple pregnancy and have pre-existing diseases. Mothers with incomplete pregnancy and birth records also excluded from this study.

Maternal age was categorised into two groups; 20 to 34 years as the reference group and 35 years and older as the case group. Socio-demographic profiles of the respondents included ethnicity, occupation, education level, pre-pregnancy body mass index, gestation weeks at the first visit and parity status. The adverse pregnancy outcomes were divided into either adverse maternal outcomes or adverse foetal outcomes. The adverse maternal outcomes included pregnancy-induced hypertension, gestational diabetes mellitus, anaemia in pregnancy and instrumental delivery or Caesarean section. Meanwhile, the adverse foetal outcomes consisted of prematurity, low or high birth weight and stillbirth.

Data were analysed using Statistical Package of the

Social Science (SPSS) version 21 (SPSS Incorporation, Chicago). Descriptive analysis was used to calculate the proportion of pregnancy outcomes and the socio-demographic profiles of the respondents. Chi square test was used to determine the statistically significant differences between the variables. Simple logistic regression was used for calculating crude odd ratios, followed by multiple logistic regressions for each adverse pregnancy outcomes as the dependent variable. Multinomial logistic regression was used for dependent variables with more than 2 outcomes such as delivery outcomes, birth weights and gestation at births. The findings were considered as significant when the p-value was less than 0.05. This study has been approved by the Medical Research Ethic Committee, Ministry of Health with registration number of NMRR-13-1619-18603.

#### RESULTS

A total of 1772 birth records were collected for this survey. Of the total number, 357 birth records were excluded from the analyses due to; multiple pregnancies, teenage pregnancies, cases had pre-existing medical problems and incomplete records (no documentation on variables of interest). The remaining 1415 antenatal records were then analysed. Profiles of the cases according to maternal age group were shown in Table 1.

The proportion of birth in this study showed 14.8% among mothers aged 35 years and older and 85.2% among mothers aged 20 to 34 years. There was higher number of the respondents who were from Malay ethnicity when compared to Non-Malay ethnicity which were 61.7% and 73.8% in mothers aged 20-34 years and mothers aged 35 years and older, respectively. Both groups had majority of respondents with secondary and lower level of education, normal pre-pregnancy body mass index (BMI), booking at the first visit before 20 weeks of gestation and multipara. However, in terms of occupation, 53.3% of mothers aged 20-34 years were employed and less than half of mothers aged 35 years and older were employed.

Table 2 shows the relationship between pregnancy outcomes and maternal age groups. AMA mothers were associated with higher cases of pregnancy-induced hypertension, gestational diabetes and Caesarean section, however lower in cases of anaemia. There was no significant association between AMA mothers and adverse foetal outcomes.

Logistic regression analysis showed that AMA mothers were associated with pregnancy-induced hypertension (adjusted odds ratio [aOR]: 5.00; 95% confidence interval [CI]: 1.95-12.65), gestational diabetes mellitus (aOR: 2.32; 95%CI: 1.35-4.00), Caesarean section (aOR: 2.21; 95%CI: 21.53-3.19) when other socio-demographic variables were held in constant. Anaemia was negatively associated with AMA mothers (aOR: 0.50; 95%CI: 0.32-0.78). No significant association was found between AMA mothers and adverse foetal outcomes (Table 3).

TABLE 1. Socio-demographic profiles in relation to maternal age in Muar, Johor (*n*=1415)

	20-34 years ( <i>n</i> =1205)	35 years and older ( <i>n</i> =210)
<i>Ethnicity</i>		
Malay	743(61.7)	155(73.8)
Non-Malay	462(38.3)	55(26.2)
<i>Occupation</i>		
Housewife	563(46.7)	121(57.6)
Employed	642(53.3)	89(42.4)
<i>Education</i>		
Secondary and below	935(77.6)	160(76.2)
Tertiary	270(22.4)	50(23.8)
<i>BMI pre-pregnancy</i>		
Normal (18.5-24.9)	853(70.8)	112(53.3)
Obese (25 or more)	352(29.2)	98(46.7)
<i>Gestation weeks at first ANC visit</i>		
Less than 20 weeks	1103(91.5)	195(92.9)
20 weeks and more	102(8.5)	15(8.3)
<i>Parity</i>		
Primigravida	460(38.2)	16(7.6)
Multipara	745(61.8)	194(92.4)

TABLE 2. The association between pregnancy outcomes and maternal age in Muar, Johor (*n*=1415)

	20-34 years <i>n</i> =1205	35 years and older <i>n</i> =210	<i>p</i> -value*
	N (%)	N (%)	
<i>Maternal outcomes</i>			
Antenatal problems			
Pregnancy-induced hypertension			
Yes	10 (0.8)	11(5.2)	<0.001*
No	1195 (99.2)	199 (94.8)	
Gestational diabetes mellitus			
Yes	48 (4.0)	24 (11.4)	<0.001*
No	1157 (96.0)	186 (88.6)	
Anaemia			
Yes	249 (20.7)	26 (12.4)	0.006*
No	956 (79.3)	184 (87.6)	
Delivery Outcomes			
SVD	944 (17.2)	145 (69.0)	
Instrumental delivery	54 (4.5)	9 (4.3)	
Lower segment caesarean section	207 (17.2)	56 (26.7)	0.005*
<i>Foetal Outcomes</i>			
Birth weight			
Normal	1102 (91.5)	191 (91.0)	
Low	75 (6.2)	10 (4.8)	
High	28 (2.3)	9 (14.3)	0.839
Gestation at birth			
Term	1078 (89.5)	17 (8.1)	
Premature	112 (9.3)	190 (90.5)	
Postdate	15 (1.2)	3 (1.4)	0.195
Stillbirth			
Live birth	1182 (98.1)	205 (97.6)	
Stillbirth	23 (1.9)	5 (2.4)	0.651

\**p* value <0.005

TABLE 3. The adjusted odd ratios for adverse maternal outcomes in women aged 35 years and older in Muar district compared to women aged 20-34 years

Variables	Women aged 35 years and older			<i>p</i> -value	
	Crude OR (95%CI)	Adjusted Wald Test	<i>df</i>	Adjusted OR (95%CI)†	
<i>Maternal outcomes</i>					
Antenatal problems					
Pregnancy-induced hypertension					
Yes	6.61(2.76-15.76)	11.33	1	5.00(1.95-12.65)	0.001
No <sup>ref</sup>	1.00			1.00	
Gestational diabetes mellitus					
Yes	3.11(1.86-5.20)	9.19	1	2.32(1.35-4.00)	0.002
No <sup>ref</sup>	1.00			1.00	
Anaemia					
Yes	0.54( 0.35-0.84)	9.16	1	0.50(0.32-0.78)	0.003
No <sup>ref</sup>	1.00			1.00	
Delivery Outcomes					
SVD <sup>ref</sup>	1.00		1	1.00	
Instrumental delivery	1.09 (0.52-2.25)	0.72		1.39 (0.65-2.98)	0.397
Lower segment caesarean section	1.76(1.25-2.48)	17.65		2.21(1.53-3.19)	<0.001
<i>Foetal Outcomes</i>					
Birth weight					
Normal <sup>ref</sup>	1.00		1	1.00	
Low	0.76(0.39-1.52)	0.52		0.81(0.40-1.64)	0.470
High	1.86(0.86-3.99)	0.14		1.18(0.54-2.61)	0.706
Gestation at birth					
Term <sup>ref</sup>	1.00		1	1.00	
Premature	0.86(0.51-1.47)	0.52		0.82(0.47-1.42)	0.577
Postdate	1.14(0.33-3.96)	0.14		1.29(0.35-4.78)	0.677
Stillbirth					
Live birth <sup>ref</sup>	1.00		1	1.00	
Stillbirth	0.86(0.51-1.46)	0.56		0.81(0.47-1.41)	0.651

# adjusted with variables age, ethnicity, occupation, education, BMI pre-pregnancy, gestation weeks at first ANC visit and parity.  
<sup>ref</sup> and 1.00 as reference variables

## DISCUSSION

The proportion of pregnancy at AMA in this study was 14.8% which was nearly similar with the findings in Israel and Iran, 14.0% and 14.3% (Rajee et al. 2010; Schimmel et al. 2014), respectively. A study conducted by the World Health Organization (WHO) in 29 countries from Africa, Asia, Latin America and Middle East observed much lower proportion of AMA cases; 12.3% (Laopaiboon et al. 2014). Although the proportion of first birth at 35 years and older are increasing in the developed countries such as in the United States and Canada (Bushnik & Rochelle 2008; Mathews & Hamilton 2009), the proportion of AMA are still less than one fifth out of the total pregnancy. However, this situation needs a special attention in managing pregnant mothers at AMA.

Our study had observed that AMA was an important risk factor for adverse pregnancy outcomes. The association between adverse pregnancy outcomes and AMA as noted in our study also had been observed in the United Kingdom and Norway (Kenny et al. 2013; Wang et al. 2011).

The most common adverse maternal pregnancy outcomes are diseases that occurred during pregnancy such as pregnancy-induced hypertension and gestational diabetes mellitus. Mother with AMA in this study had the higher odds of developing pregnancy-induced hypertension and gestational diabetes mellitus. This finding is similar with previous studies elsewhere (Aghamohammadi & Nooritajer 2011; Cleary-Goldman et al. 2005). A study from the United States with a large scale of cohort reported that AMA had higher odds of pregnancy-induced hypertension, gestational diabetes compared to mothers aged 30-34 years (Luke & Brown 2007).

This study observed that anaemia in pregnancy was less likely to occur in mother aged 35 years and older. This finding is similar with the finding from the study conducted earlier which observed higher prevalence of anaemia in pregnancy among teenage mothers compared to mothers from other age groups. The possible reason to this, was due to poor compliance to prophylactic oral iron and folate supplements among younger mothers (Haniff et

al. 2006). Another study conducted in Ethiopia showed that anaemia in pregnancy was more likely to occur in mother with high parity regardless of maternal age (Al-Farsi et al. 2011) however, a study in Nigeria found that there was no relationship between anaemia with maternal age and parity status as the prevalence of anaemia was higher in that region (Dim & Onah 2007).

Increasing maternal age also associated with higher risk of instrumental delivery and Caesarean section (Cleary-Goldman et al. 2005; Kenny et al. 2013; Luke & Brown 2007; Wang et al. 2011). However, this study only observed positive association between maternal age and Caesarean section. A systematic review on AMA and the risk of Caesarean section observed an increasing risk of Caesarean section in older mother (Bayrampour & Heaman 2010). The association of AMA with instrumental delivery was not significant in this study. The possible reason for this finding was the instrumental delivery had a very small number of cases in Muar District for that year.

Various studies observed the association between advanced maternal age and adverse foetal outcomes such as prematurity, low or high birth weight and stillbirth (Delbaere et al. 2007; Kenny et al. 2013; Lisonkova et al. 2010; Yadav & Lee 2013). A large scale study conducted by the World Health Organization (WHO) in 29 countries from Africa, Asia, Latin America and Middle East observed higher odd of preterm birth, stillbirths and low birth weight in AMA mothers when compared to mothers aged 20-34 years (Laopaiboon et al. 2014). However, there was no significant association between advance maternal age and foetal outcomes in our study. The reason to this finding is possibly due to improvement in antenatal care services in Muar district where the prevalence of adverse foetal outcomes is too small (UNICEF 2011).

This study only analysed birth records from the low risk mothers as we had excluded birth records from mothers with a known risk factors for adverse pregnancy outcomes such as pre-existing medical problems, multiple pregnancy and teenage pregnancy. Majority of the cases also had early antenatal visits and all of them had more than four antenatal visits which were considered as adequate antenatal care for low risk pregnancy (Villar et al. 2001). As such, the effect of maternal age on the adverse pregnancy outcomes is considered a significant finding in this study for pregnancy-induced hypertension, gestational diabetes mellitus and Caesarean section.

In current situation, the Ministry of Health, Malaysia has been practising the pre-pregnancy care to mother with pre-existing diseases such as hypertensive disorder, diabetes mellitus and heart disease (Ministry of Health Malaysia 2015). Pregnancy at AMA should be considered as pregnancy with a risk and needs special attention from the healthcare provider even though the mothers do not have any pre-existing disease. The pre-pregnancy care clinic aims to give pre-conception services three months prior to conception to the mothers and their partner regarding the pregnancy needs, the pregnancy risk, optimization of the health status of the mother and promoting the healthy life style to the couple.

As this study only analysed data in a selected district of Johor, the findings cannot be considered as the true situation in Malaysia due to selection of respondents who cannot represent the various ethnicities in Malaysia. A smaller percentage of birth in Muar might not be registered even though all births registered in the district were recorded in this analysis. This study also did not look into other factors that might be related to the adverse outcomes studied such as quality of the antenatal care and delivery services provided to the mothers. In addition, this is a cross sectional study design which limits the determination of causality.

## CONCLUSION

Advanced maternal age was significantly associated with adverse maternal outcomes; pregnancy-induced hypertension, gestational diabetes, anaemia in pregnancy and Caesarean section. However, there was no association between advanced maternal age and adverse foetal outcomes.

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