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Original Research Article

Maternal and fetal outcome in pregnancy with advanced maternal age- a prospective study

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ABSTRACT

Background: Advanced maternal age defined as the age of mother ≥ 35 years at the time of delivery has become common in last two to three decades. It is considered to have more adverse obstetric and perinatal outcomes as compared to those in younger women. Therefore, it requires a proper understanding of the effect of age during her antepartum, intrapartum, and postpartum period that prevent a healthy outcome.

Methods: The primary objective was to study the maternal and foetal outcome of pregnancy in women aged ≥ 35 years. This was a prospective observational study conducted in 122 pregnant women over a duration of 18 months in the multispecialty hospital in an urban setting.

Results: In this study, pregnant women aged ≥ 35 years had a higher incidence of obesity (88.9%). Among antenatal complications, mothers aged ≥ 35 years had higher incidence of anaemia (21.3%), gestational diabetes mellitus (GDM) (37.7%), gestational hypertension (32.8%), fetal growth restriction (13.1%). There was no significant difference in the incidence of miscarriage, multiple pregnancy, malpresentation, preterm premature rupture of membranes (PPROM), intrauterine fetal demise between the two age groups. The incidence of preterm delivery (41%) and caesarean section (72.4%) were higher in advanced age group. Perinatal complications like low birth weight (29.3%), neonatal intensive care unit (NICU) admissions (32.8%) were higher in neonates of women aged ≥ 35 years.

Conclusions: Advanced maternal age was significantly associated with adverse obstetrical and fetal complications. Therefore, proper preconceptional counselling and intensive antenatal care assessment can individualize and potentially reduce the risks for women with advanced maternal age.

Keywords: Advanced maternal age, Elderly gravida, Maternal outcome, Obstetric outcome, Pregnancy outcome, Perinatal outcome

INTRODUCTION

The question of whether women who delay childbearing are at an increased risk of having an adverse outcome of pregnancy is of importance because of increasing proportion of primigravida at older age. In developed countries there are several explanations for advanced maternity age like more late marriages and remarriages, women's pursuit of higher education, success in the workforce, improvement in the use of assisted reproduction methods (ART) availability of efficient, secure contraception and in developing countries like

India, there can be other reasons like concept of large family size and desire for male child.¹

Physiologically, women of advanced maternal age are more prone to obstetric complications. These risks are often compounded by pre-existing medical conditions and lifestyle factors, necessitating vigilant prenatal monitoring and personalized management strategies.² Moreover, the age-related decline in ovarian reserve and the increased prevalence of chromosomal abnormalities in oocytes contribute to higher rates of miscarriage, stillbirth, and

genetic disorders in pregnancies with advanced maternal age.³⁻⁵

Fetal growth restriction, preterm birth, and neonatal intensive care unit (NICU) admissions are also more common in this population.⁶ The perinatal morbidity like low birth weight and birth asphyxia as well as perinatal mortality is also increased in these women as compared to their younger counterparts.⁷ According to NFHS-5 2019-21 prevalence of diabetes mellitus and obesity is increasing exponentially in Kerala.^{8,9} Thus, the aim of this study is to evaluate the maternal and foetal outcome in pregnancy with advanced maternal age in our hospital.

METHODS

This prospective observational study was conducted in the Department of Obstetrics and Gynaecology at a multispecialty hospital, Kerala after obtaining clearance from the Institutional Ethical Committee and scientific committee. The study spanned 18 months, from 01 December 2022, to 01 June 2024.

Sample size

Based on the results of proportion of hypertensive disorder of pregnancy in study group (26.6%) and in control group (4.4%) observed from an existing literature and with 95% confidence, 80% power, the minimum sample size comes to 51 in each group totalling to 102.¹⁰ A total of 122 participants were recruited using random sampling method.

Inclusion criteria

All pregnant women with age ≥ 20 years were included.

Exclusive criteria

Pregnant women of age < 20 years and those with no informed consent were excluded.

Data collection

All patients who presented to the antenatal clinic at Credence Hospital, Thiruvananthapuram, Kerala, India during the study period were enrolled after taking informed consent from the patients. Pregnant women satisfying the inclusion criteria were divided into two groups based on their age as women of 35 years or more and other group comprising of women 20 to 34 years. The demographic profile was recorded using pretested proforma. History of pre-existing medical conditions included pre gestational diabetes, chronic hypertension, thyroid diseases, and history of using medication before conception, such as insulin, antihypertensive or antithyroid medication were also obtained. Mode of conception, whether a natural conception or assisted reproductive techniques used were recorded. Previous adverse pregnancy outcomes were noted. Patient's reports of prior

miscarriage, history of fibroid uterus was recorded. They were also enquired about the reason for being pregnant at advanced maternal age. They were followed up during pregnancy, delivery, until discharge. Outcome of mother and foetus were studied and recorded in the research proforma. No interventions were undertaken specifically for the study.

Outcome measurement

Antenatal complications, onset of labour, mode of delivery, complication like post-partum haemorrhage were noted. Neonatal outcomes, antepartum, intrapartum, postpartum, and perinatal complications between the two groups were measured.

Statistical analysis

The data was entered in Microsoft Excel (MS Excel) sheet. All analyses performed using the statistical package for social science (SPSS) 22.0 (Armonk, NY: IBM Corp), and $p < 0.05$ was considered as statistically significant. The qualitative variables were expressed as percentage or proportion and the quantitative variables as mean with standard deviation. To test the statistical significance of difference in the proportions between two groups, Pearson Chi square test/Fishers exact test was applied and to test the statistical differences in mean values between two groups, independent sample t test was used. Relative risk with 95% confidence interval was computed for follow up outcomes.

RESULTS

83.6% of women < 35 years of age and 88.5% of women ≥ 35 years of age were from the upper middle class in contrast, 16.4% of women < 35 years of age and 11.5% of those ≥ 35 years were from the lower middle class. 42.6% of women < 35 years of age and 45.9% of women ≥ 35 years of age were primigravidae. While 57.4% of women < 35 years of age and 54.1% of those ≥ 35 years were multiparous. There was no statistically significant difference in the distribution of socioeconomic status and parity between the two age groups (Table 1).

In our study, there were no statistically significant difference in the distribution of previous medical history and obstetric problems between the two age groups (Table 2). Women ≥ 35 years had a higher risk of overweight as well as obesity compared to women < 35 years. There was statistically significant difference in the incidence of obesity between the two age groups. Our data showed that women ≥ 35 years are twice as likely to use ART compared to younger women, but this result was not statistically significant (Table 3). Our data indicated in pregnant women ≥ 35 years, the incidence of anaemia 21.3%, GDM 37.7%, GHTN 32.8%, FGR 13.1% were higher than younger counterparts and were statistically significant. Study variables such as PPROM, multiple pregnancy,

spontaneous labour was found to be not statistically significant (Table 4).

Women aged ≥ 35 years had 2.5 times the risk of preterm delivery (GA- <37 weeks) than women at younger age. For women aged ≥ 35 years, 27.6% had vaginal deliveries, and 72.4% underwent LSCS. This indicated that there was a

statistically significant difference in the mode of delivery between groups (Table 5). Our study showed that incidence of having a low-birth weight baby (29.3%) and NICU admission of neonate (32.8%) in women aged ≥ 35 years were higher than the younger counterpart (Table 5)

Table 1: Comparison of demographics between age groups.

Study variables	Age				Total		χ^2	P value
	<35 years		≥35 years					
Socioeconomic status	N	%	N	%	N	%	0.615	0.602
Upper middle	51	83.6	54	88.5	105	86.1		
Lower middle	10	16.4	7	11.5	17	13.9		
Obstetric score								
Primigravida	26	42.6	28	45.9	54	44.3	0.133	0.715
Multigravida	35	57.4	33	54.1	68	55.7		

Table 2: Comparison of pre-existing complication between age groups.

Variables	Age				Total		χ^2	P value
	<35 years		>35 years					
	N	%	N	%	N	%		
Medical history								
Chronic hypertension	2	3.3	5	8.2	7	5.7	1.364	0.243
Overt diabetes	3	4.9	7	11.5	10	8.2	1.743	0.323
Hypothyroidism	22	36.1	22	36.1	44	36.1	0	1.00
Obstetric problems								
Prev miscarriage	13	21.3	22	36.1	35	28.7	3.245	0.072
H/O fibroid	3	4.9	8	13.1	11	9.0	2.498	0.205
Prev LSCS	14	23	17	27.9	31	25.4	0.389	0.533

Table 3: Comparison of BMI and mode of conception between groups.

Variables	Age group		RR (95% CI)	P value
	<35 years N (%)	≥35 years N (%)		
BMI				
Normal (18.5-22.9 kg/m ²)	15 (44.1)	5 (23.8)	-	
Overweight (23-24.9 kg/m ²)	19 (55.9)	16 (76.2)	1.363 (0.930-1.999)	0.128
Obese (≥25 kg/m ²)	27 (64.3)	40 (88.9)	1.383 (1.079-1.772)	0.006*
Mode of conception				
Natural)	54 (88.5)	47 (77)	2 (0.868-4.610)	0.093
Assisted reproductive techniques	7 (11.5)	14 (23)		

*denoted as statistically significant.

Table 4: Comparison of maternal and fetal outcomes between age groups.

Study variables	Age group				RR (95% CI)	P value
	<35 years		≥35 years			
	Yes, N (%)	No, N (%)	Yes, N (%)	No, N (%)		
Anaemia in pregnancy	2 (3.3)	59 (96.7)	13 (21.3)	48 (78.7)	6.5 (1.53-27.59)	0.002*
GDM	8 (13.1)	53 (86.9)	23 (37.7)	38 (62.3)	2.875 (1.397-5.918)	0.002*
GHTN	6 (9.8)	55 (90.2)	20 (32.8)	41 (67.2)	3.33 (1.438-7.725)	0.002*
Fetal growth restriction	1 (1.6)	60 (98.4)	8 (13.1)	53 (86.9)	8 (1.032-62.040)	0.038*
PPROM	1 (1.6)	60 (98.4)	4 (6.6)	57 (93.4)	4 (0.460-34.767)	0.361
Multiple pregnancy	1 (1.6)	60 (98.4)	3 (4.9)	58 (95.1)	3.00 (0.321-28.044)	0.611
Spontaneous labour	23 (39.7)	35 (60.3)	14 (24.1)	44 (75.9)	0.609 (0.349-1.061)	0.073

*denoted as statistically significant.

Table 5: Comparison of maternal and fetal related variables.

Variables	<35 years N (%)	≥35 years N (%)	RR (95% CI)	P value
Gestational age (weeks)				
<37	10 (16.4)	25 (41)	2.5 (1.316-4.75)	0.003*
>37	51 (83.6)	36 (59)		
Mode of delivery				
Vaginal delivery	30 (15.7)	16 (27.6)	1.5 (1.1-2.045)	0.008*
LSCS	28 (48.3)	42 (72.4)		
Birth weight (kg)				
<2.5	7 (12.1)	17 (29.3)	2.429 (1.09-5.413)	0.022*
2.5-4	51 (87.9)	41 (70.7)		
NICU admission				
Yes	6 (10.3)	19 (32.8)	3.16 (1.364-7.354)	0.003*
No	52 (89.7)	39 (67.2*)		

*denoted as statistically significant.

DISCUSSION

In current scenario delayed marriage and delayed child bearing have been increasing day by day due to higher female literacy rates and increasing independence among women. As a result, the number of women having their first pregnancy at the age ≥35 years is on the rise. The incidence of elderly primigravida in our study was 45.9%. The incidence of pregnancy at advanced maternal age was reported as 21% in US by Goldmen et al, 33.4% in Norway by Wang et al.^{7,11}

In our study, 8.2% of women ≥35 years of age had chronic hypertension, 11.5% had overt diabetes mellitus. The prevalence of hypothyroidism in both the groups was 36.1%. There was no statistically significant difference in the distribution of previous medical history between the two age groups. Obstetric problems like history of previous miscarriage were 36.1%, history of fibroids 13.1%, history of previous lower segment caesarean section (LSCS) 27.9% in women ≥35 years. Barbara et al reported increased obstetric complications due to underlying medical disorders.⁶

Elderly gravidas had a higher incidence of obesity (88.9%) compared to women aged <35 years. We found that women aged ≥35 years had 1.38 times risk of obesity when compared to <35 years and this was statistically significant RR 1.383, (95% CI 1.079-1.772) (p=0.006). This was comparable to the study by Meera et al and indicates the increasing burden of obesity as an epidemic in Kerala.¹² Obesity and overweight have been associated with preterm births, low Apgar scores, stillbirths and neonatal death.¹³ The world's largest and most comprehensive meta-analysis of pre-pregnancy body mass index (BMI) in 20 million women included 86 studies found that pre-pregnancy overweight and obesity significantly increased the risk of pre-eclampsia and GDM during pregnancy. The OR for obesity was 4.10 and 3.57, respectively.¹⁴

In the present study, for women ≥35 years, 77% conceived naturally and 23% used ART RR 2.00, (95% CI 0.868-4.610) (p=0.093) This implies that women 35 years and older are twice as likely to use ART compared to younger women and with increasing age the rate of spontaneous conception reduced, but this result was not statistically significant. This was comparable with Meera et al in which 70% of women aged ≥35 years conceived spontaneously, while 30% of them utilized ART.¹² Among the study group the incidence of women utilizing ART was high when compared to Pawde et al, 12.6%.¹⁵

Both pregnant women, <35 years of age and ≥35 years of age had miscarriage rate of 4.9%. this can be due to the fact that many of the first trimester bookings were in late gestational age (10-11weeks) and we might have missed early miscarriages. Incidence of miscarriage in a study by Kalewad et al was 2%. Other studies by Sasirekha et al (15.2%), Pawde et al (18.9%) showed higher incidence of miscarriages.¹⁵⁻¹⁷

In our study 21.3% of women of advanced maternal age had anaemia compared to 3.3% in younger pregnant women, the difference was statistically significant RR 6.5, (95% CI 1.53-27.59) (p=0.002). Moses et al reported anaemia in 19% of cases despite close supervision. This was attributed to failure to take prescribed haematinics, food preference and food taboo in pregnancy.¹⁸ Suchita et al reported 20 % pregnant women had anaemia which was comparable to our study.¹⁹

The incidence of glucose intolerance increases with age owing to reduced insulin sensitivity and increased level of serum lipids. Fulop et al explained the reduction in insulin sensitivity with age by progressive deterioration of pancreatic β-cell function.²⁰ In our study the incidence of GDM was higher in the study group 37.7% as compared to 13.1% in control group, the difference was statistically significant RR 2.87, (95% CI 1.397-5.918) (p=0.002). However, we did not observe an age-related increase in the risk of large for gestational age (LGA). This was in

agreement with Kahveci et al.²¹ Suchita et al recorded 22.34% of elderly primigravida who developed gestational diabetes mellitus and /or pre- eclampsia during antenatal period compared to 6.38% in the younger control group.¹⁹

Incidence of gestational hypertension in our study group was 32.8% and we found women with ≥ 35 years have 3.33 times the risk of developing GHTN as compared to women < 35 years of age RR 3.33, (95% CI 1.438-7.725) ($p=0.002$). Similarly, Dixit et al reported an incidence of 30% in women ≥ 35 years.²² Kahveci et al reported the risks of preeclampsia and gestational hypertension were significantly higher in pregnant women aged over 35 years.²¹

In present study, the incidence of FGR in pregnant women ≥ 35 years was 13.1% and they had 8 times risk of developing FGR when compared to their counterparts' RR 8, (95% CI 1.032-62.040) ($p=0.038$). In a study by Suchita et al, 23% had FGR due to placental insufficiency and associated medical or obstetric disorders like preeclampsia, diabetes mellitus causing maternal vasculopathy.¹⁹ Odibo et al identified a positive dose-response relationship between advanced maternal age and increased risk of FGR.²³ They noted that advanced maternal age is an independent risk factor for FGR and suggested that screening for FGR should be conducted among women aged ≥ 35 years.

The incidence of PPROM and preterm labour in pregnant women aged ≥ 35 years were 6.6% and 8.2%. The risks of developing PPROM and preterm labour were 4 and 2.5 times higher in advanced maternal age group when compared to younger age group, but was not statistically significant in our study. Aghamohammadi et al showed that there is a statistical significant relation between the age of above 35 and preterm labor ($p=0.006$). This finding was supported by other reports by Diejomaoh et al, and Joseph et al.²⁴⁻²⁶ But a study by Kamalesh et al claimed that age doesn't have a significant association with PROM.²⁷

Our study showed that in women aged ≥ 35 years, 4.9% had multiple pregnancy ($p=0.611$). Mahmoud et al also found no significant difference between younger primigravida and elderly primigravida regarding multiple pregnancy (1.8% versus 3.7 %). Gaikwad et al, in their study found the rate of multifetal gestation (22.8%) was higher in elderly gravidas, largely because of artificial reproductive technologies.^{28,30}

Both pregnant women, < 35 years of age and ≥ 35 years of age had malpresentation of 3.3% in this study. Aghamohammadi et al and Sahu et al also did not find any statistically significant difference in malpresentation when aged and young women were compared.^{24,29} But malpresentation was observed in 10.5% in Gaikwad et al study and 9.1% in Ezechi et al study.^{30,31} Kalewad et al reported an increased risk of malpresentation with an incidence of 6% which may be due to uterine fibroids and poor abdominal muscle tone.¹⁶

We had no case of antepartum haemorrhage.

There was only one case of intrauterine fetal demise in advanced maternal age group in our study. Karbala et al reported that the risk of intrauterine death was significantly higher in the older women, these results were in agreement with study done by Jacobsson et al.^{32,33} Sahu et al found an increased incidence of still birth in advanced maternal age group (6.3%).²⁹

The present study in women aged ≥ 35 years, 75.9% had induced labour ($p=0.073$). This suggested that there was an increase in induction of labour in mothers with advanced maternal age. Similarly, Blomberg et al showed an increase in induced labour in elderly mothers.³⁴ But in contrast, Smitha et al showed less of labour inductions in elderly patients.³⁵

Our study showed that women aged ≥ 35 years have 2.5 times the risk of a preterm delivery than those aged < 35 years, and this was statistically significant ($p=0.003$). Kalewad et al showed maternal age was significantly associated with preterm delivery as advanced age women (19.2%) had higher rate of preterm delivery ($p<0.026$).¹⁶ A multi country assessment undertaken by WHO also reported a significant association maternal age with preterm delivery (OR 1.2, 1.4 and 1.3 for women aged 35–39, 40–45 and ≥ 45 years old, respectively).³⁶ This might be attributed to iatrogenic prematurity and to the fact that pregnancy complications are more abundant in this age group. Nevertheless, this finding was contradicted by the studies done in Malaysia and UK which showed no association of maternal age with preterm delivery.^{37,38}

In the present study for women aged ≥ 35 years, 27.6% had vaginal deliveries, and 72.4% underwent LSCS RR 1.5, (95% CI 1.1-2.045) ($p=0.008$). In a similar study by Karbala et al, they showed that there was statistically significant association between the age over 35 and caesarean section ($p<0.0001$). In a systematic review of twenty-one studies, Bayrampour et al found an increased risk of caesarean birth among women of advanced maternal age compared with younger women for both nulliparas and multiparas.³²

In our study when low birth weight of babies was considered, elderly gravidas showed an incidence of 29.3% RR 2.4, (95% CI 1.09-5.413) ($p=0.022$) which was statistically significant. Similarly, incidence of low birth weight in elderly women was reported as 23.08% and 27.9% by Basa et al and Kalewad et al.^{16,39} 32.8% and 10.3% of neonates of elderly gravidas and younger age group had NICU admissions respectively. We found that neonates of women ≥ 35 years have 3.16 times the risk of NICU admissions compared to neonates of women aged < 35 years ($p=0.003$). 38.5% neonates required neonatal ICU admission for close observation and management of complications due to preterm and low birth weight in a study by Bhankar et al.⁴⁰ Dixit et al in their study found significant difference in NICU admission between

advanced age group and younger age group (45% versus 18.3%).²² There were no case of still birth or neonatal death in our study. Immediate resuscitative measures by trained person have reduced perinatal morbidity and neonatal mortality.

Limitations

This was a hospital-based study. 86% of the study population belonged to upper middle class socioeconomically. As most of our patients booked late in first trimester, early events of miscarriage had not been reported.

Strengths

This was a prospective study and there was no attrition.

CONCLUSION

This study showed that there was significant increase in obstetric complications and operative interventions required with increasing maternal age. Among antenatal complications, women of advanced maternal age had higher incidence of anaemia complicating pregnancy, gestational diabetes mellitus, gestational hypertension, fetal growth restriction. Vaginal deliveries were significantly less in elderly gravidas. There was significant increase in the incidence of preterm deliveries and caesarean section rates in women with advanced maternal age. Also, low birth weight and neonatal intensive care unit admissions were significantly higher in newborns of elderly gravida. These findings may have significant implications in clinical practice. Larger studies are needed to establish the exact magnitude of these associations and to show any significant difference in antepartum obstetric problems and fetal and neonatal outcome measures. Unwarranted intervention in labour based on age alone is not acceptable. Management will largely depend on attempts at improving perinatal outcome without compromising the health and well-being of the mother. As more women delay childbearing, older parturient constitute a large and growing fraction of our obstetric patient population, women should realistically appraise the risks of pregnancy in later life. Hence these women should be counselled, and their complications managed with utmost care. This group of patients should be considered as high-risk categories and need special attention and vigilant care in the multidisciplinary tertiary care centre. Modification of follow-up protocols to account for these age-related risk factors could also improve pregnancy outcomes in women of advanced maternal age.

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