ORIGINAL ARTICLE

Effect of Advanced Maternal Age on Pregnancy Outcomes

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ABSTRACT

Introduction: Advanced maternal age generally denotes age after 35years during the time of delivery. Despite the fact that being pregnant at any reproductive age is not risk free, older gravidity usually culminates with adverse outcomes both to mother and fetus or neonates. The objectives of this study is to investigate the impact of advanced maternal age on perinatal and neonatal outcomes of primiparous singleton pregnancies.

Methods: This was a prospective cohort study conducted in Kathmandu Model Hospital/Kirtipur Hospital including 60 elderly pregnant Women from exposed groups (35-40 years) and 60 pregnant women from unexposed groups (30-34 years) and analyzed for maternal and fetal outcomes. Data was collected in the proforma and statistical analysis was done using IBM SPSS v 26.

Results: A total no. of 120 pregnant patients were selected for the study. The average age of the patients was 36.561.61years and 31.53±1.27years in exposed and unexposed groups. The risk of pregnancy induced Hypertension (55%), preterm labour (30%) and low birth weight (28.3%) were significantly higher in exposed group as compared to non-exposed group. There was little evidence of increased risk of oligohydramnios (13.3%) and cesarean delivery rates (63.4%) in exposed group. Rate of neonatal intensive care unit admission was high in exposed group (46.7%) than unexposed group (30%).

Conclusions: This present study showed that pregnancy at advanced maternal age associated with increased risk of certain maternal and fetal complication and these finding emphasize the importance of age-appropriate prenatal care and early intervention to improve outcomes of elderly pregnant women.

Keywords: Advanced maternal age, Maternal and Perinatal outcomes, Preterm labour

INTRODUCTION

Pregnancies at an advanced maternal age has become more common in both developed and developing countries over the last decades.[1] Advanced maternal age is generally defined as pregnancy in women aged 35 years or older. Primary and secondary infertility due to various reason may also cause a delayed conception. Cultural, Social, economic changes & reproductive technologies such as egg donation contributes to the increasing incidence of pregnancies in women who are older than the usual biological reproductive age.[2]

Pregnancy after the age of 35 years can be challenge because of the maternal and fetal risk. The various maternal and perinatal risk is chronic hypertension, subfertility, anemia, pregnancy induced hypertension (PlH), preeclampsia, gestational diabetic mellitus (GDM), oligohydramnios, antepartum hemorrhage (APH), malpresentation, premature rupture of membrane, increased incidence of instrumental deliveries and cesarean sections, postpartum hemorrhage (PPH), chromosomal abnormalities (mainly down syndrome), intrauterine growth

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retardation (IUGR), still birth, prematurity leading to higher number of neonatal intensive care unit (NICU) admission. Perinatal morbidity and mortality increased in these patients.[3] A study done in 29 countries revealed that the overall prevalence of advanced maternal age was 12.3%.[4] However, there are not adequate studies that assess the effect of age on pregnancy outcomes in Nepal. Hence, we aimed to find out the association of maternal and perinatal outcomes in advanced maternal age.

METHODS

We conducted a cohort prospective study conducted in the Department of Obstetrics and Gynecology, Kirtipur Hospital during the study period of 7 months from February to August 2023.

Sample was calculated using the formula for comparing two groups of age 30-34 year (control/unexposed groups) and 35-40 years (advanced maternal age / exposed groups)

n =z2pq/d2, where q =1-p, Level of confidence is 95% (Z) =1.96, Margin of error (d) = 5%, Power = 80%.

A total of 120 admitted primi gravida pregnant women with >28 weeks of gestation of exposed groups (35-40 years) and unexposed groups (30-34 years) were selected. Exclusion criteria were pregnant women with age < 30 years, multiple pregnancies, uterine and adnexal masses, with history of previous cesarean section, women who conceive with the use of assisted reproductive technology (ART). Patients with chronic renal disease, cardiac disease, liver disease, lung disease and not willing to participate in the study were also excluded.

All patients were analyzed for maternal and fetal outcomes as pregnancy induced hypertension, diabetes mellitus, preterm labor, preterm premature rupture of membrane (PPROM), oligohydramnios, antepartum hemorrhage, postpartum hemorrhage, low birth weight, IUGR, NICU admission, and mode of delivery. Information related to patient's demographical information, antenatal booking status, associated medical disorder, complication during pregnancy, mode of delivery, maternal and neonatal outcomes was collected in predesigned proforma.

The study was approved by the Institutional Review Committee of the Public Health Concern Trust, Nepal (phect-NEPAL) (IRC approval number: 042-2022). Data were obtained from patients and de-identified. Written informed consent was obtained from the patients. Data were then entered in MS Excel 2016 and was analyzed using IBM SPSS v 26.

Means ± SD (continuous variables with normal distribution), while number and percentages were used to characterise the categorical variables. The unpaired Student's t-test was used to examine continuous variables, while the Chi-square or Fisher's exact tests were used to compare categorical variables. In order to compare the results of women by maternal age group, we conducted a univariate analysis. P values less than 0.05 were regarded as statistically significant. Multinomial multivariable logistic regression modelling of the relationship between maternal age and delivery method includes variables that were significant on univariate analysis (not presented) for the key outcomes.

RESULTS

A total of 120 pregnant women were included in this study. In exposed and non-exposed groups 60 pregnant women were included in each groups. The average age of the patients was 36.56±1.61 years and 31.53±1.27 years in exposed and unexposed groups respectively. Similarly, mean gestational age, married duration, past medical history is shown in table 1.

Out of 120 deliveries, vaginal delivery was observed in 40% and cesarean section was 60%. All the women had primigravida and primiparous. Regarding CTG, 88.9% were normal, 4.2% were pathological and 6.7% were suspicious (Table 1).

Comparison of maternal complication between exposed and unexposed groups is shown in Table 2. Risk of GDM, oligohydramnios, APH, malpresentation, PPROM, PPH were not statistically significant between groups. However, gestational hypertension was 2 times more likely in exposed group than non-exposed group RR=2.22; 95%CI: 1.10-4.47; p=0.019 and was statistically significant. Similarly, risk of pre-eclampsia/eclampsia and preterm birth was 2-3 times more likely in exposed group than in non-exposed groups [RR=3.25 95%CI: 1.18-12.67; p=0.018] and [RR=2.78; 95%CI:1.10-7.04; p=0.027] respectively and was statistically significant.

Table 1: Demographic characteristics of women according to groups

Variables	Exposed (n=60)	Non-Exposed (n=60)
	Mean ± SD	Mean ± SD
Age (Years)	36.55±1.61	31.53±1.27
Gestation Age (Weeks)	37.66±1.97	38±2
Married duration (Years)	5.77±2.60	3.86±2.01
BMI (kg/m^2)	28.45±1.92	29.01±1.77
No. of ANC visit	5.27±1.91	6.65±1.61
Medical History	**n (%)**	**n (%)**
Pre-eclampsia	1 (1.7%)	0
PIH	3 (5.0%)	0
Hypothyroidism	7 (11.7%)	13 (21.7%)
Gestational Hypertension	5 (8.3%)	2 (3.3%)
Gestational Diabetic Mellitus	3 (5.0%)	3 (5.0%)
Obstetrics Cholestasis	2 (3.3%)	2 (3.3%)
Smoker	2 (3.3%)	0
Vaginal Delivery	**19 (31.7)**	**29 (48.3%)**
Episiotomy	6 (31.6%)	17 (58.6%)
1st Degree	0	3 (10.3%)
2nd Degree	8 (42.1%)	6 (20.7%)
3rd Degree	2 (10.5%)	2 (6.9%)
Normal	3 (15.8%)	1 (3.4%)
Cesarean Section (CS)	**41 (68.3%)**	**31 (51.7%)**
Elective CS	15 (36.6%)	12 (38.7%)
Emergency CS	26 (63.4%)	19 (61.3%)
Menstrual Cycle		
Regular	52 (86.7%)	55 (91.7%)
Irregular	8 (13.3%)	5 (8.3%)
Cardiotocography		
Suspicious	3 (5%)	5 (8.3%)
Pathological	4 (6.7%)	1 (1.7%)
Normal	51 (87.9%)	54 (90%)

Table 2: Comparison of maternal complication between exposed and unexposed groups

Maternal complications	Exposed n=60	Un-Exposed n=60	RR [95%CI]	P-Value
Gestational HTN				
Yes	20 (33.3%)	9 (15%)	2.22[1.10-4.48]	0.019
No	40 (66.7%)	51 (85%)	Ref	
Preeclampsia/Eclampsia				
Yes	13 (21.7%)	4 (6.7%)	3.25[1.18-12.67]	0.018*
No	47 (78.3%)	56 (93.3%)	Ref	
GDM				
Yes	8 (13.3%)	6 (10%)	1.38[0.45-4.26]	0.570
No	52 (86.7%)	54 (90%)	Ref	
Oligohydramnios				
Yes	8 (13.3%)	3 (5%)	2.92[0.74-11.61]	0.114
No	52 (86.7%)	57 (95%)	Ref	
APH				
Yes	1 (1.7%)	1 (1.7%)	1[0.06-16.37]	0.999
No	59 (98.3%)	59 (98.3%)	Ref	

Malpresentation				
Yes	6 (10%)	8 (13.3%)	0.72[0.23-2.24]	0.777
No	54 (90%)	52 (86.7%)	Ref	
Preterm labor				
Yes	18 (30%)	8 (13.3%)	2.78[1.10-7.04]	
No	42 (70%)	52 (86.7%)	Ref	0.027*
PPROM				
Yes	6 (10%)	2 (3.3%)	3.22[0.62-16.65]	0.272
No	54 (90%)	58 (96.7%)	Ref	
PPH				
Yes	5 (8.3%)	3 (5%)	1.73[0.39-7.57]	0.717
No	55 (91.7%)	57 (95%)	Ref	

The mean duration of hospital stay was 4.80±3.49 vs 3.10±1.48 in exposed and non exposed groups respectively. The details of descriptive statistics of fetal characteristics according to groups is shown in table 3.

Table 3: Descriptive statistics of fetal characteristics according to groups

Variables	Exposed n=60	Non-Exposed n=60
	Mean ±SD	Mean ±SD
Apgar score at 5 min	7.62±1.57	8.05±5.65
Birth Weight (g)	2885.33±706.16	3156.33±523.64
Total Hospital Stay (days)	4.80±3.49	3.10±1.48
Duration of NICU (Days)	n=28	n=18
	4.69±3.90	2.72±0.95

According to fetal complications, Risk of IUGR, IUFD, fetal distress, low Apgar score was also not statistically significant between groups. However, risk of low birth weight was 3 times more likely in the exposed group as compared to the unexposed group [RR= 3.4 95%CI: 1.34-8.62; p=0.005] and was statistically significant. Similarly, rate of NICU admission was also higher in the exposed group than the non-exposed group (46.7% vs. 30% p=0.091) but was not statistically significant as shown in table 4.

Table 4: Comparison of fetal complication between exposed and unexposed groups

Fetal Complications	Exposed n=60	Un-Exposed n=60	RR [95%CI]	P-Value
IUGR				
Yes	4 (6.7%)	2 (3.3%)	2.07[0.36-11.76	0.679
No	56 (93.3%)	58 (96.7%)	Ref	
IUFD				
Yes	2 (3.3%)	0	NA	0.496
No	58 (96.7%)	60 (100%)	Ref	
Fetal distress				
Yes	8 (13.3%)	7 (11.7%)	1.14[0.44-2.95]	0.999
No	52 (86.7%)	43 (88.3%)	Ref	
Low Apgar Score				
Yes	3 (5%)	0	NA	0.244
No	57 (95%)	60 (100%)	Ref	
Low birth weight				
Yes	17 (28.3%)	5 (8.3%)	3.4[1.34-8.62]	0.005*
No	43 (71.7%)	55 (91.7%)	Ref	
Neonatal ICU(NICU)				
Yes	28 (46.7%)	18 (30%)	1.55[0.97-2.49]	0.091
No	32 (53.3%)	42 (70%)	Ref	
Congenital anomalies				
Yes	0	0	NA	NA
No	60 (100%)	60 (100%)	Ref	
Neonatal Death				
Yes	0	0	NA	NA
No	60 (100%)	60 (100%)	Ref	

Multivariate analysis showing the relationship between the maternal and fetal complication and advanced maternal age pregnancy but there were no significant changes in risk of maternal and fetal outcome except risk of low birth weight was still significant in multivariate analysis [aRR=4.8; 95%CI: 1.19-19.34; p=0.027] after adjusted of other neonatal complication

as shown in table 5 and 6. Other demographic variables were not included in the multivariate model because the rate of complications were not high.

Table 5: Multivariate analysis showing the relationship between the maternal complications and advanced maternal age pregnancy

Maternal Complication	Adjusted RR	95% CI.		p-value
		Lower	Upper	
Gestational HTN (Yes vs. No)	1.96	0.53	7.18	0.307
Preeclampsia (Yes vs. No)	2.51	0.47	13.39	0.281
GDM (Yes vs. No)	1.52	0.45	5.08	0.500
Oligohydramnios (Yes vs. No)	3.17	0.74	13.56	0.12
APH (Yes vs. No)	0.72	.029	18.01	0.844
Malpresentation (Yes vs. No)	1.34	0.40	4.42	0.63
Preterm (Yes vs. No)	1.54	0.46	4.42	0635
PPROM (Yes vs. No)	2.78	0.36	21.52	0.327
PPH (Yes vs. No)	3.21	0.69	14.81	0.13

Table 6: Multivariate analysis showing the relationship between the fetal complication and advanced maternal age pregnancy

Fetal Complication	Adjusted RR	95% CI		p-Value
		Lower	Upper	
IUGR (Yes vs. No)	0.443	0.053	3.72	0.45
Fetal distress (Yes vs. No)	1.15	0.36	3.64	0.81
Low Birth Weight (Yes vs. No)	4.80	1.19	19.34	0.027
NICU admission (Yes vs. No)	1.32	0.55	3.18	0.53

DISCUSSION

Advanced maternal age (AMA) is defined as childbearing in women over 35 years of age and is growing trend with in high income countries.[5] Lower income countries differ significantly in the socio-demographic characteristics of expectant mothers and availability of obstetrics care services; however, AMA still represent a significant and growing fraction of pregnant women in these countries. As maternal age increases, fertility declines and rate of spontaneous abortion increases. The risk of trisomy 21 and chromosomal abnormalities also increases with increasing maternal age.[6]

In the present study the study sample consisted of women in their early to mid-30s, with a slightly older average age in the exposed group. The majority of women in both groups were employed. While few women reported hypothyroidism or gestational diabetes mellitus, chronic hypertension these conditions could potentially interact with smoker exposure and influence maternal and fetal outcomes. In present study few women had hypothyroidism and Obstetrics cholestasis. Vaginal delivery was observed in 40% and cesarean section was 60%. Most of them were with a regular menstrual cycle. Regarding CTG, 88.9% were normal, 4.2% were pathological and 6.7% were suspicious.

The study found a significantly increased risk of PIH (gestational hypertension/ pre-eclampsia/ superimposed pre-eclampsia with chronic hypertension/ eclampsia) and preterm birth in the older age group (35-40 years) compared to the younger age group (30-34 years). This suggests that advanced maternal age may be associated with an elevated risk of these adverse maternal outcomes. While the study did not observe significant differences between the groups for other maternal complications, such as GDM, oligohydramnios, APH, malpresentation, PPROM, and PPH, these outcomes should be closely monitored in older pregnant women. Contrary to the finding of some studies that AMA pregnancies were significantly associated with PIH, this study did also find a significant association between AMA pregnancies with PIH. The association with PIH was attributed to increased oxidative stress and the fact that endothelial response to vasodilators diminishes as mother get older.[12]

The most common adverse maternal and fetal outcomes due to advanced maternal age in our study pregnancy induced hypertension including GHTN (33.3% vs 15%) and pre-eclampsia/eclampsia (21.7%vs 6.7%), preterm labor (30% vs 13.3%), low birth weight (28.3% vs 8.3%). Similar observation was noted in studies of Asefu; Sharma; Awoyesuku but preterm labour was same in both AMA (≥35 Years) and control groups (20-34 years) in Awoyesuku study. Similarly, Pawde study also shows higher incidence of hypertension disorder

of pregnancy (17.54% vs 7.23%) and very low birth weight (12.28% vs 7%) in elderly groups (≥35yrs) than control groups (<35yrs). Likewise, study conducted in Rasheed et al also showed higher odds of developing pregnancy induced hypertension (5.2% vs 0.8%) in AMA than reference groups. [7,8,11,12 ,15]

In the present study, the risk of low birth weight was 3 times more likely in age 35-40 years. The study revealed a significantly increased risk of low birth weight in the older age group. This is a critical finding, as low birth weight is associated with various health problems in infants and children.

In the present study incidence of Gestational diabetic mellitus (13.3% vs 10%) little high in advanced maternal age groups (35-40 years) than adult age group (30-34 years) which is comparable to study done by Mahoto (4.76% vs 0%); Asefa (2.4%vs 1.6%; Awoyesuku (2.1% vs1.7%) but study conducted in Rasheed observed GDM (11.4% vs 4%) which was statistically significant in case groups (≥35 years) than reference groups (<35 years) and also Shan D et al 2018 study observed 2-3 fold risk for AMA mother diagnosed with GDM.[4,7,12 ,13, 15]

Increasing maternal age also associated with higher risk of instrumental delivery and caesarean section. A systemic review on AMA and risk of Caesarean section observed an increasing risk of caesarean section in older mother.[15] However, this study only observed positive association between maternal age and cesarean section, the cesarean delivery rate (68.3%) was high in AMA in this study similar to study conducted in Asefu, (34.7%); Mahato, (75%); Radon-Pokracka, (64.8%); Pawde (35.2%); Rasheed (26.7%); San D, 2018. [4,7,10 ,11,13,15]

The rate of postpartum hemorrhage was not significantly different in this study similarly in Pawed AA, 2015; Shan D et al 2018 study. This may be due to timely intervention. A few studies have found higher rates of postpartum hemorrhage in women with advanced maternal age like study observed in Rajput PPH (9%). The incidence of PPH is higher in AMA because atonicity as a result of multiparty and poor myometrium function and decreased oxytocin receptor of uterus.[2]

Our study observed oligohydramnios (13.3%) cases more in AMA although not statistically significance comparable to study in Sharma (6%); Radon-Pokracka, (1.3%) but Awoyesuku study observed that no difference of oligohydramnios in both AMA and adult reproductive age (2% vs 2%). [8,10 ,12]

Incidence of IUGR was 6.7% in current study which is comparable to study done by Rajput (3.81%). Advanced maternal age is associated with a decrease potential for fetal growth possibly reflecting biological ageing of maternal tissue and systems or the cumulative effects of diseases.[14] The rate of NICU admission was higher in the older age group, although this difference did not reach statistical significance. This finding suggests that older maternal age may increase the risk of neonatal complications, necessitating intensive care.

In this study NICU admission rate higher (46.7% vs 30%), unlike in study Awoyesuku (16.8% vs 14.4%), Rajput (6.94%). The most common cause of NICU admission is low birth weight and preterm birth but Pawde study rate of admission similar in both groups (8.7 vs 8.68%) and Shan D, 2018 study also observed lower risks of neonatal NICU admission in older mother. [12, 2 ,11 ,13]

The results of this study highlight the potential impact of maternal age on both maternal and fetal health. The increased risk of pregnancy induced hypertension, preterm birth, and low birth weight in the older age group emphasizes the importance of providing specialized care and monitoring for elderly pregnant women. While the study did not find significant differences for all outcomes, it is important to note that the sample size may have limited the power to detect smaller effects. Further research in multi center with larger sample sizes is needed to confirm and extend these findings. Additionally, investigating the underlying mechanisms by which maternal age affects maternal and fetal health could provide valuable insights for developing targeted interventions. Implementing age-appropriate prenatal care and monitoring strategies can help improve maternal and child health outcomes in elderly pregnant women. As the trend in Advanced maternal age continues, obstetricians should work to provide rigorous surveillance, improved clinical counselling and optimized new approach to antenatal care as well as management for adverse pregnancy outcomes.

CONCLUSION

This study highlights the potential significant risks such as gestational hypertension, pre-eclampsia, preterm birth, low birth weight baby associated with advanced maternal age. Elderly pregnant women may benefit from increased surveillance and early intervention to address potential complications. In conclusion, this study provides evidence for the association between advanced maternal age and increased risk of certain maternal and fetal complications. These findings emphasize the importance of age-appropriate prenatal care and early intervention and modification of follow-up protocols to account for these age-related risk factors to improve outcomes for advanced maternal age.

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