

Evaluation of Fetomaternal Outcome in Advanced Age-group Mothers: A Comparative Prospective Study in a Tertiary Care Maternity Hospital in Kashmir Valley

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ABSTRACT

Aim: The study was aimed to investigate the effect of maternal age on fetomaternal outcomes in primigravida singleton women aged above 35 years vs the younger age-group of 22–35 years.

Materials and methods: The study was carried out for a period of 18 months in the Department of Obstetrics and Gynaecology, Government Medical College, Srinagar, Jammu and Kashmir, India. The data were prospectively collected on 209 primigravida singleton pregnant women admitted to the hospital and were divided into two groups, one above 35 years and the other between 22 and 35 years. The fetomaternal outcome of each pregnancy was recorded and exported on the data editor of Statistical Package for the Social Sciences (SPSS) version 20.0. The comparative analysis between the two groups was done using the Student's independent *t*-test or Mann-Whitney *U* test.

Results: Comparative analysis between two groups of primigravida singleton pregnant women showed that advanced-age pregnancy was significantly associated with increased incidence of gestational hypertension (38.6 vs 22.4%, $p = 0.018$), antepartum hemorrhage (APH) (21.1 vs 9.9, $p = 0.031$), spontaneous abortions (17.5 vs 7.2%, $p = 0.027\%$), and cesarean delivery rate (64.3 vs 46.3, $p = 0.042$) as compared to younger age-group.

Advanced-age pregnancy was associated with adverse fetal outcomes like low birth weight (26.2 vs 13.2%, $p = 0.047$), preterm delivery (38.1 vs 22.1%, $p = 0.029$), intrauterine fetal demise (IUID) (16.7 vs 6.6%, $p = 0.047$), and intrauterine growth retardation (IUGR) (33.3 vs 16.21%, $p = 0.016$) as compared with younger age-group.

Conclusion: This study shows a strong association of advanced maternal age with adverse fetomaternal outcomes, and the rising trend of delaying pregnancy makes it imperative to educate women about the risks of advanced-age pregnancy and the need for specialized care during the antenatal period.

Keywords: Advanced age, Adverse, Fetomaternal, Pregnancy, Risks.

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INTRODUCTION

Pregnancy with a maternal age of 35 years or older is called an advanced maternal age which predisposes the mother and baby to enormous adverse outcomes.^{1–4}

The last 3 decades have seen a rise in women delaying childbearing globally.^{5,6}

In Sweden, the mean maternal age of first childbirth increased from 24.4 to 28.5 years between 1974 and 2001.^{5,6} In Norway, 33.4% of women among a cohort of 6,619 singleton pregnancies were of 35 years of age and above between 2004 and 2007.^{3,7} A study in the United Kingdom showed 18.2% prevalence of maternal age 35 years or older.^{3,8} In the United States of America, conception after the age of 35 years currently comprises 15% of pregnancies.⁹

Easy accessibility of family planning methods, delaying of pregnancy due to career goals, and advances in assisted reproductive methods have contributed to this increment.¹⁰

It has been established in some studies that after the age of 35, the risk for obstetrical and fetal complications rises.^{11,6} Older women who have age-dependent chronic illnesses like hypertension, diabetes, or poor physical condition usually have readily apparent risks and hence more prone to adverse pregnancy outcomes than younger women.¹¹

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The maternal mortality rate is 2.5 times higher in women aged 35–39 years and older and 5.3 times higher in women aged 40 years or above.¹²

Women older than 35 years constituted 27% of maternal deaths in the United States from 2006 to 2010.¹³

Fecundity has been shown to decrease with increasing maternal age. Nowadays, the easy availability of other assisted reproductive techniques has made conception in advancing age possible, and even postmenopausal women can conceive through egg donation.⁶

The risk of spontaneous abortions, intrauterine fetal death, pregnancy-induced hypertension, severe preeclampsia, gestational diabetes, and lower (uterine) segment caesarean section (LSCS) mode of delivery increases with maternal age 35 years or older, as proven in previous studies.^{6,14}

An increase in the risk of stillbirths, preterm birth rate, low birth weight, neonatal intensive care unit (NICU) admissions, and neonatal deaths have also been reported with increasing maternal age.^{3,6} Delayed marriages and hence delayed conception also create psychological problems and increase chances of depression, domestic abuse, drug addiction, and immoral behavior.¹⁵

There has been a rising trend of delaying childbirth in the state of Jammu and Kashmir due to delayed marriages.^{16,17} Setting professional goals, seeking higher education, and the availability of assisted reproductive technology are some of the reasons.^{16–18} The dowry system is another major cause of late marriages in Kashmir. A survey conducted in Kashmir Valley in 2017 by a non-governmental organization Tehreek e Fala-UI-Muslimeen revealed that about 50,000 girls across the Valley had crossed the marriageable age whose parents were too poor to arrange dowry.¹⁵

According to National Health survey-5, Jammu and Kashmir has the fourth lowest total fertility rate (TRF) in the country.

The TRF, which was 3.6 in 1991, declined to 2.3 in 2007 and stood at 1.4 in 2019–20.^{19,20}

National Health Profile 2015 shows that the mean age of marriage for females in Jammu and Kashmir state is the highest in India.^{1,6}

Hence it became imperative to conduct a study on the Kashmiri population about the effect of increasing maternal age on fetal and maternal outcomes, as no such study has been done to date in the state.

MATERIALS AND METHODS

The main aim of this study was to investigate the influence of maternal age on fetomaternal outcomes in a primigravida with singleton pregnancies by comparing the fetomaternal outcome of advanced-aged mothers with age above 35 years with that of younger mothers with age between 22 and 35 years.

After being approved by the Institutional Ethical Committee, the study was conducted in the Postgraduate Department of Obstetrics And Gynaecology, Government Medical College, Srinagar, Jammu and Kashmir, India. Lalla Ded hospital is the lone tertiary care center that caters to the whole population of Kashmir Valley in the Department of Obstetrics and Gynaecology.

The comparative analysis of the prospectively collected database of patients admitted to the hospital was done to study the association between advanced maternal age and adverse fetomaternal outcomes.

Inclusion criteria—the study group included ($n = 209$) all primigravida, singleton pregnancies who were admitted to the hospital during their antenatal care visits with maternal age of 22 years and above from April 2020 to October 2021.

Table 1: Age distribution of study patients

Age (years)	Number	Percentage	Mean \pm SD
22–35 years (group I)	152	72.7	27.6 \pm 2.85
>35 years (group II)	57	27.3	36.7 \pm 2.78
Total	209	100	30.1 \pm 4.92

Exclusion criteria—multigravida and pregnant women with uterine and adnexal masses were excluded from the study to prevent any discordance in conclusion due to confounding bias.

Proper written informed consent was taken. The study population was grouped according to maternal age into two groups—group I and group II.

Group I included all pregnant women aged 22–35 years ($n = 152$).

Group II included all pregnant women aged above 35 years ($n = 57$).

All primigravida who was admitted to the hospital underwent proper evaluation with a detailed history taken and physical examination admission according to the predesigned format. A proper document like a birth certificate or adhaar card for proof of age was checked. The fetomaternal outcome of each admitted pregnant female was evaluated, and a comparative analysis of the outcome variables was done between the two groups. The fetomaternal outcome parameters which were compared between the two groups are as under.

Maternal parameters	Fetal parameters
Gestational hypertension	Low birth weight
Gestational diabetes mellitus (GDM)	Intrauterine fetal growth restriction
Spontaneous abortions	IUFD
APH	NICU admissions
Mode of delivery (vaginal/CS)	Preterm births
Mode of conception	

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to the data editor of SPSS version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean \pm standard deviation (SD), and categorical variables were summarized as frequencies and percentages. The data was represented graphically. Student's independent *t*-test, or Mann-Whitney *U* test, was used for comparing continuous variables. The Chi-squared or Fisher's exact test was applied to compare categorical variables. A *p*-value of <0.05 was considered statistically significant.

OBSERVATION AND RESULTS

The study was conducted for a period of 18 months on 209 pregnant women out of which 27.3% belonged to advanced age-group II (>35 years) and 7% belonged to the younger age-group I (22–35 years), as shown in Table 1.

As shown in Table 2, 81.6% of women in the group I had conceived spontaneously, while 68.4% of women in group II had conceived spontaneously; the *p*-value was statistically significant (0.041) hence proving that with advancing maternal age, fecundity decreases.

As shown in Table 3, the incidence of gestational hypertension (38.6%), GDM (10.5%), prelabor rupture of membranes (PROM)

Table 2: Spontaneous conception in relation with maternal age

Spontaneous conception	22–35 years (I)		> 35 years (II)		<i>p</i> -value
	No.	% age	No.	% age	
Yes	124	81.6	39	68.4	0.041*
No	28	18.4	18	31.6	
Total	152	100	57	100	

*, statistically significant

(12.3%), APH (21.1%), spontaneous abortions (17.5%), ectopic pregnancy (5.3%), and molar pregnancy (3.5%) was increased in the advanced age-group of >35 years (group II) as compared with the younger age; group I (22–35 years) where results of maternal complications were found as under gestational hypertension (22.4%), GDM (7.2%), PROM (7.2%), APH (9.9%), spontaneous abortions (7.2%), ectopic pregnancy (2.6%), and molar pregnancy (0.7%).

On the statistical analysis of study data, the increase in the incidence of gestational hypertension, APH, and spontaneous abortions in group II than group I was found to be statistically significant with a p -value < 0.05.

The increased incidence of GDM, PROM, ectopic pregnancy, and molar pregnancy in the advanced maternal age-group was not found to be statistically significant.

As shown in Table 4, we found a higher rate of CS, 64.3%, in group II as compared to group I, with a CS rate of 46.3% which was found to be statistically significant with p -value = 0.042.

The results of the study for the fetal outcome variables (Tables 5 to 7) showed that the incidence of preterm births, IUGR, NICU admission, low birth weight, IUFD, and low 5-minute Appearance, Pulse, Grimace, Activity and Respiration (Apgar) score were found to be increased in advanced maternal age-group >35 years (group II). However, on comparative analysis of the data between the two groups, we found that preterm births were 38.1% in group II whereas 22.1% in group I, which was found to be statistically significant p -value = 0.029.

Intrauterine growth retardation (IUGR) in advanced maternal age; group II was found to be 16.7% as compared to 6.6% in group I with p -value = 0.047.

Table 3: Maternal complications in relation with maternal age

Maternal complications	22–35 years (I) (n = 152)		> 35 years (II) (n = 57)		p-value
	No.	% age	No.	% age	
Gestational hypertension	34	22.4	22	38.6	0.018*
GDM	11	7.2	6	10.5	0.439
PROM	11	7.2	7	12.3	0.247
APH	15	9.9	12	21.1	0.031*
Spontaneous abortions	11	7.2	10	17.5	0.027*
Ectopic pregnancy	4	2.6	3	5.3	0.346
Molar pregnancy	1	0.7	2	3.5	0.181

*statistically significant

Table 4: Mode of delivery in relation with maternal age

Mode of delivery	22–35 years (I)		> 35 years (II)		p-value
	No.	% age	No.	% age	
Vaginal delivery	73	53.7	15	35.7	0.042*
LSCS	63	46.3	27	64.3	
Total	136	100	42	100	

*statistically significant

Table 5: Fetal complications in relation with maternal age

Fetal complications	22–35 years (n = 136) group I		>35 years (n = 42) group II		p-value
	No.	% age	No.	% age	
Preterm	30	22.1	16	38.1	0.029*
IUGR	9	6.6	7	16.7	0.047*
NICU admission	7	5.1	3	7.1	0.623
IUFD	22	16.2	14	33.3	0.016*

*statistically significant

Table 6: Birth weight in relation with maternal age

Birth weight (kg)	22–35 years		>35 years		p-value
	No.	% age	No.	% age	
<2.5 kg	18	13.2	11	26.2	0.047*
≥2.5 kg	118	86.8	31	73.8	
Total	136	100	42	100	

*, statistically significant

Table 7: Apgar score in relation with maternal age

Apgar score	22–35 years		>35 years		p-value
	No.	% age	No.	% age	
<7	40	29.4	18	42.9	0.104
≥7	96	70.6	24	57.1	
Total	136	100	42	100	

Intrauterine device in group II (>35 years) was found to be 33.3% as compared to 16.2% in group I (22–35 years) with p -value = 0.016.

As shown in Table 6, low birth weight (<2.5 kg) was found to be increased in the advanced maternal age-group (group II) with an incidence of 26.2% as compared with an incidence of 13.23% in group I with p -value = 0.047.

Low 5-minute Apgar score (<7/10), as shown in Table 7 (42.9%) and NICU admission rate (7.1%) (Table 5), although increased in group II but the results were not statistically significant.

DISCUSSION

Advancing age itself is a risk factor for many chronic diseases like chronic hypertension, diabetes, and metabolic syndrome.

So advancing age with the pregnancy would further complicate the process, and this study does show the association between adverse fetomaternal outcomes with advancing maternal age by doing a prospective comparative study on 209 singletons primigravida women for a period of 18 months.

The results showed a significant increased incidence of gestational hypertension, APH, and spontaneous abortions in the advanced maternal age-group (>35 years) as compared to the younger age-group (22–35 years)

We also found an increased rate of assisted conception in advanced age-group II as compared to younger age-group I.

The study showed that gestational hypertension was in 38.6% of pregnant females in advanced age-group II as compared to 22.4% of pregnant females in the younger age-group I with p -value = 0.018. This shows a significant increase in the incidence of gestational hypertension with advancing maternal age.

Similar observations were obtained in a comparative cross-sectional study conducted on similar groups in a north Ethiopian hospital in 2017 by Mehari et al.²³ where advanced-age mothers (≥35 years) were four times more likely to encounter gestational hypertension than their younger counterparts (20–34 years) [odds ratio (OR) 4.15, (95% CI 2.272–7.575), p < 0.001].

The study conducted by Kahveci et al.,¹⁰ Lipipuspa et al., Blomberg et al.,⁴ and Rendtorff et al.²¹ also showed similar results.

This could be possible by the fact that endothelial response to vasodilators diminishes as mothers get older and increases the peripheral; the resistance of blood vessels as age advances.

A study conducted in India by Nagarwal et al.²², however, finds no association between pregnancy induced hypertension and maternal age. This contradiction in results may be due to the difference in sample size.

Advancing maternal age was found to be significantly associated with APH (primarily caused by placenta previa and abruption placentae) with an incidence of 21.1% in the advanced age-group as compared to 9.9% in the younger age-group with p -value = 0.031. This finding is supported by studies done by Dr Pattnaik et al.,² Mehari et al.,²³ and Suneela.²⁴

This is due to the fact that advanced maternal age is itself associated with increased risks of complications like

placenta previa and placental abruption due to sclerosis of intramyometrium arteries, which decreases placental blood flow.²⁵ However, a study from Turkey done in 2016 by Yilmaz et al.²⁶ showed no significant association of maternal age with APH. However, this study was done in a private hospital which deals with mostly high-risk pregnancies

The study also showed a significant increased incidence of spontaneous abortions (early pregnancy loss with gestational age <20 weeks) in advanced age-group II (17.5%) as compared to younger age-group I (7.2%) with p -value = 0.027.

Many studies have proved a strong association between advancing maternal age and spontaneous abortions. There is a decline in fertility accompanied by an increased risk of aneuploidy and spontaneous abortions with advancing age, according to American College of Obstetricians and Gynecologists committee report in 2014.²⁷

A study conducted by Magnus et al.,²⁸ and Almeida et al.,²⁹ demonstrated advancing maternal age is the strongest known risk factor for spontaneous abortions.

Advancing maternal age is associated with increased chromosomal aberrations. The most common causes of early pregnancy failure are nondisjunction and reciprocal translocations. Submicroscopic chromosomal alterations, which remain hidden during cytogenetic analysis, cause some unexplained miscarriages.³⁰ Contrary to our results, a Danish study by Nybo et al.³¹ found an increased risk of miscarriages among young women; however, after a crude adjustment of results was done, this increase in results did not persist.

This study found that advanced-age mothers in group II had a significantly higher CS rate which was 64.3%, as compared to younger age-group I, which was 46.3% with p -value = 0.042.

The results are supported by a study conducted by Rosa Rendtorff et al.,²¹ which found CS was the most common mode of delivery in older mothers, with an incidence of 59% as compared to younger mothers, with an incidence of 29%, p < 0.001.

Kahveci et al.¹⁰ explained that the increasing rate of CS in advanced-age mothers could be explained due to myometrial muscle weakness with age; also, oxytocin receptors decrease with age, and increased rates of maternal systemic diseases and obstetric complications with age.

Prolonged and abnormal labor is the cause of increased CS rate in older age-group women, as proved by a study done by Luke et al.³² Study by Greenberg et al.³³ and Elmes et al.³⁴ showed similar results and proposed that myometrial contractility reduces with maternal age hence leading to prolonged labor.

This study also found that spontaneous conception rates were higher in the younger maternal age-group I, that is, 81.6%, as compared to the advanced maternal age-group, which was 68.4%.

31.6% of advanced age-group mothers required assisted methods for conception, like ovulation induction and *in vitro* fertilisation, as compared to 18.4% of younger age-group mothers. The results were statistically significant, with a p -value = 0.041.

Pertinent to mention here is that we found 18.4% of women in the younger age-group also needed assisted methods to conceive. This could be because of the fact that polycystic ovary syndrome (PCOS) is on the rise in Kashmir Valley. A cross-sectional study conducted on Kashmiri women aged between 15–40 years by Ganie et al.³⁵ found that the prevalence of PCOS was 28.9% by National Institutes of Health criteria which is probably the highest in a published series globally.

A study by Maheshwari et al.³⁶ found that fecundity in females begins to decrease during the 4th decade of life. Fecundity decreases due to oocyte atresia, and also, oocyte quality is reduced near perimenopause.

The capacity to reproduce decreases with age, as proved by a study conducted by Nicole et al.³⁷; causes could be a reduction of oocytes in the ovary and a decrease in egg quality.

In this study increased incidence of gestational diabetes was found in the advanced age-group II 10.5% as compared to 7.2 % in group I of younger age-group mothers. However, the results were statistically insignificant. Similar results were found in a study conducted by Mehari et al.²³ The insignificant difference could be due to the fact of increased prevalence of PCOS in young Kashmiri women, as reported by Ganie et al.³⁵ PCOS is found to be an independent high-risk factor for the development of gestational diabetes.^{38,39}

Fetal Outcomes

The findings of this study showed that advanced maternal age has a significant association with preterm delivery (<37 weeks), low birth weight (<2.5 kg), growth-restricted fetuses, and in- utero fetal demise.

The study showed that the advanced maternal age-group is associated with an increased incidence of preterm labor, with 38.1% in Group II as compared to 22.1% in Group I of younger aged mothers. The difference was statistically significant with p value=.029. Similar results were found in a study conducted by Mehari et al.²³ advanced-age mothers were almost four times more likely to have preterm babies than younger age-group mothers. (adjusted OR—3.622%, cephalic index (1.469–8.930), $p = 0.005$).

The increased rate of preterm birth among advanced-aged mothers is largely explained by the need for induction of labor for medical conditions like chronic hypertension and diabetes associated with advanced age.

This is in contrast to the study by Dietl et al.⁴⁰ found no significant differences in the rates of preterm delivery between different age-groups.

This study found a significant increase in the incidence of low birth weight babies(26.2%), IUGR fetuses (16.7%), and IUFD (33.3%) in advanced age-group mothers (>35 years) as compared to younger age-group mothers (22–35 years) with an incidence of low birth weight babies 13.2% (p -value = 0.047), growth restricted fetuses 6.6% (p -value = 0.047), in utero fetal demise 16.2 % (p -value = 0.016).

The study by Mehari et al.²³ also showed that advanced maternal age was a major risk factor for low birth weight (OR 3.14, $p = 0.009$), which could be explained due to the abundance of obstetrical complications in advanced-age pregnancy and iatrogenic prematurity accompanying these adverse pregnancy complications.

In her study, Suneela²⁴ also concluded an increased incidence of IUGR fetus 8.4% in the advanced maternal age-group as compared to in younger age-group mothers 6.1 %, RR = 3.26 (1.22–8.72) p -value = 0.011.

Increased incidence of IUGR fetuses in advanced age-group mothers was also found in studies conducted by Jacobsson et al.⁶ and Hansen et al.¹⁴ Poor oxygenation of tissues due to myometrial under perfusion due to sclerosis of arteries could be the cause of small for gestational age babies with older age mothers.¹⁰

Significant increased incidence of IUFD has also been found in a study by Lipipuspa et al.² The study reported an increased number of IUFD in the advanced maternal age-group, which was 4%, as compared to the younger age-group which was 0.77%.

Pasupathy et al.⁴¹ also found similar results. One of the causes of increased rates of IUFD in advanced-age mothers could be attributed to intrapartum anoxia. Other causes could be maternal morbidity and congenital malformations, for which advanced maternal age is a risk factor.⁴² Incidence of congenital anomalies in the advanced maternal age-group was also reported by Suneela.²⁴

CONCLUSION

This study proved that advanced maternal age is associated with a significant increased incidence of gestational hypertension, APH, CS rate, and spontaneous abortions. The advanced maternal age-group was associated with decreased fecundity.

The study found a significant increase in the incidence of preterm births, low birth weight babies, growth-restricted fetuses, and in utero fetal demise in advanced-age-group mothers.

Therefore, it becomes important to educate women who want to delay childbirth to their later ages about the adverse outcomes of advanced-age pregnancy.

Clinical Significance

Thus, this study proves that advanced maternal age is associated with significant adverse fetomaternal outcomes.

Hence for better pregnancy outcomes, the frequency of antenatal visits should be increased in advanced age-group mothers. Advanced-age mother needs proper evaluation by a senior obstetrician and proper monitoring according to the known risk factors.

The delivery should be conducted at a highly specialized tertiary care center with a team with excellent expertise in neonatal care to reduce adverse outcomes.

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