

To Evaluate the Effect of Increasing Maternal Age on Maternal and Neonatal Outcomes in Pregnancies at Advanced Maternal Age

Abstract

Introduction: Late pregnancies have been a sensitive issue in the society and medical field for many years. The reason for this development could be the increasing use of reproductive techniques, women empowerment and late conceptions. The increased level of education in women, having more responsibilities at work, giving priority to their professional career could be leading to delay in conception and childbearing. Many studies have investigated the effect of advanced maternal age on fetal outcome suggesting higher risk of poor neonatal outcome. Recent studies have debated these outcomes.^[1-4] **Aims and Objectives:** To evaluate the effect of increasing maternal age on maternal and neonatal outcomes in pregnancies at advanced maternal age. **Material and Methods:** The study was conducted on 843 women above the age of 35 years who delivered at Dayanand Medical College and Hospital during 2015-2020. Patients were categorized into 2 groups, Group A comprised of pregnant women aged 35-40 years; group B included pregnant women aged >40 years. Various other parameters including parity, gestation at delivery, whether the pregnancies were spontaneous or conceived through ART (assisted reproductive techniques) and other associated co-morbid conditions were noted. The obstetrical, gynecological, medical, surgical, fetal and neonatal complications were studied in both the groups and the data was analyzed with release 9.4 (SAS Institute Inc, Cary, NC). **Results:** Out of 843 patients in our study, 81.4% (n=687) belonged to the age group of 35- 40 years. 18.5% (n=156) belonged to the age group of > 40 years. Patients more than 40 years underwent ART for conception more often as compared to group A. Co-morbid medical conditions including chronic hypertension, thyroid diseases, auto immune disorders and obstetric complications such as abortions, oligohydramnios, GDM, placenta previa, PPH was significantly more common in patients with group B. Cesarean delivery rate was significantly more in group B as compared to group A. Neonatal outcome in terms of NICU admissions and preterm birth at less than 35 weeks gestation was seen more frequently in group B as compared to Group A. **Conclusion:** Our study concludes that the decision to delay childbearing should be discouraged owing to increased maternal and fetal morbidity associated with advanced maternal age, the risks being higher with increasing maternal age.

Keywords: *Advanced maternal age, comorbidities, preterm birth*

Introduction

Every woman has a right to become a mother. Late pregnancies have been a sensitive issue in the society and medical field from many years. Indeed, maternal age has been increasing for several decades with many of these late pregnancies over 40 years of age.^[1,2] The reason for this development could be the increasing use of reproductive techniques, the enormous changes in work and society which include higher levels of female employment and educational attainment, and higher number of women working in higher level jobs. The increasing level of education in women who have more

responsibilities at work, giving priority to their professional career, delay their childbearing. It has always been a clinical tenet that childbearing in mature age carries elevated maternal and perinatal morbidity and mortality.^[3] Many studies have investigated the effect of advanced maternal age on fetal outcome suggesting higher risk of poor neonatal outcome. Recent studies have debated these outcomes.^[4] There is a conflicting data supporting motherhood at advanced age in present times. Furthermore there is scarcity of data evaluating the effect of advanced maternal age from Indian population.

Novelty of the study: Advanced maternal age is a significant risk factor for higher maternal and fetal morbidity.

How to cite this article: Juneja SK, Tandon P, Kaur G. To evaluate the effect of increasing maternal age on maternal and neonatal outcomes in pregnancies at advanced maternal age. *Int J App Basic Med Res* 2022;12:239-42.

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Submitted: 12-Mar-2022

Revised: 20-Jul-2022

Accepted: 21-Oct-2022

Published: 19-Dec-2022

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Access this article online

Website:
www.ijabmr.org

DOI:
10.4103/ijabmr.ijabmr_193_22

Quick Response Code:



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Aim

To evaluate the effect of increasing maternal age on maternal and neonatal outcomes in pregnancies at advanced maternal age.

Materials and Methods

The study was conducted on 843 women above the age of 35 years who delivered at Dayanand Medical College and Hospital during 2015–2020. Patients were categorized into two groups: Group A comprised pregnant women aged 35–40 years and Group B included pregnant women aged >40 years. Various other parameters including parity, gestation at delivery, whether the pregnancies were spontaneous or conceived through assisted reproductive techniques (ARTs), and other associated comorbid conditions were noted. The obstetrical, gynecological, medical, surgical, fetal, and neonatal complications were studied in both the groups, and the data were analyzed with release 9.4 (SAS Institute Inc, Cary, NC).

Maternal age was considered as the age at the time of delivery. Gestational age was determined on the basis of either date of last menstrual period or ultrasound examination and in patients with IVF according to date of embryo transfer. Comorbid conditions including cardiac disease (cardiomyopathy, cardiac valvular disease), chronic kidney disease, thyroid disorders, bronchial asthma, chronic liver disease, and autoimmune disease were identified.

The obstetrical, gynecological, medical, and surgical complications observed were gestational hypertension (defined as systolic >140 mmHg and/or diastolic >90 mmHg without proteinuria), preeclampsia (systolic >140 mmHg and/or diastolic >90 mmHg associated with a proteinuria of 24 h >300 mg or severe features), gestational diabetes, abruptio placenta, premature rupture of membranes, postpartum hemorrhage (PPH) (loss of more than 500 cc of blood within 24 h after vaginal delivery or cesarean section), blood transfusion, rupture of ovarian cyst, torsion of ovary or fibroid, red degeneration of fibroid, urinary tract infection (UTI), cholecystitis, appendicitis, and pancreatitis. Admission of women to the intensive care unit during their pregnancies and after delivery was noted.

The fetal and neonatal complications studied were prematurity (birth before 37 weeks), need for neonatal intensive care unit (NICU) care just after the birth, and intrauterine fetal demise.

Statistics

Categorical variables were reported as number and percentage (percentages were calculated excluding missing data) and were compared by Chi-square test or Fisher's exact test, as appropriate.

A $P < 0.05$ was considered significant unless otherwise specified. All statistical analyses were performed with

Table 1: Distribution of patients with regard to age

Age distribution (years)	No. of patients
35-40	687
40-45	92
45-50	64
Total patients	843

Table 2: Distribution of patients according to the mode of conception

Distribution according to conception	Number of patients	
	Group A (%)	Group B (%)
Spontaneous	620 (90.25)	23 (14.7)
IUI	20 (2.91)	12 (7.7)
IVF	47 (6.84)	121 (77.6)
Total patients	687 (100)	156 (100)

IUI: Intrauterine insemination; IVF: *In vitro* fertilization

Table 3: Distribution of patients according to gestation at the time of delivery

Gestational age	Number of patients	
	Group A (%)	Group B (%)
<28 weeks	46 (6.7)	26 (16.7)
28-32 weeks	98 (14.3)	46 (29.5)
32-35 weeks	157 (22.9)	38 (24.3)
>35 weeks	386 (56.1)	46 (29.5)
Total	687 (100)	156 (100)

χ^2 : 55.359, $P < 0.0001$

Table 4: Distribution of patients according to comorbid medical condition

	Number of patients with comorbidities		χ^2	P
	Group A (%)	Group B (%)		
Cardiac disease	13 (1.89)	14 (8.9)	20.567	0.001
Chronic renal disease	8 (1.2)	6 (3.8)	5.598	0.018
Diabetes	17 (2.5)	34 (21.7)	83.492	0.001
Chronic hypertension	9 (1.3)	44 (28.2)	156.082	0.001
Thyroid disorder	46 (6.7)	45 (28.8)	64.776	0.001
Bronchial asthma	23 (3.3)	12 (7.7)	6.029	0.0141
Chronic liver disease	12 (1.7)	5 (3.2)	1.368	0.242
Autoimmune disorder	34 (4.9)	23 (14.7)	19.345	0.001

SAS release 9.4 (SAS Institute Inc, Cary, NC) statistical software package.

Observations

Out of 843 patients in our study, 81.5% ($n = 687$) belonged to the age group of 35–40 years. 18.5% ($n = 156$) belonged to the age group of >40 years.

Results

Out of the 843 patients in our study, 81.5% ($n = 687$) belonged to the age group of 35–40 years. 18.5% ($n = 156$)

Table 5: Distribution of patients according to the obstetrical, gynecological, and surgical complications

Complications	Number of patients		χ^2	P
	Group A	Group B		
Obstetrical complications				
Abortions	25	16	12.032	0.001
Oligohydramnios/ anhydroamnios	50	37	37.125	0.001
FGR	48	43	55.901	0.001
Hypertensive disorder of pregnancy	48	56	98.252	0.004
GDM	34	47	92.801	0.001
Placenta previa	12	17	32.648	0.001
Abruption placenta	6	8	14.093	0.001
PROM	26	30	48.904	0.001
Preterm labor	68	56	68.498	0.007
PPH	13	12	14.862	0.001
Peripartum cardiomyopathy	3	6	13.992	0.001
Gynaecological complications				
Rupture of ovarian cyst	3	1	0.112	0.737
Torsion of ovary	2	1	0.438	0.507
Torsion of fibroid	2	3	5.743	0.017
Red degeneration of fibroid	1	3	8.506	0.004
Surgical complications				
Cholelithiasis	4	5	8.281	0.004
Cholecystitis	2	4	9.294	0.002
Appendicitis	1	2	4.631	0.032
Pancreatitis	1	3	8.506	0.004

FGR: Fetal growth restriction; GDM: Gestational diabetes mellitus; PROM: Premature rupture of membrane; PPH: Postpartum hemorrhage

Table 6: Distribution of patients according to the mode of delivery

Mode of delivery	Number of patients		χ^2	P
	Group A	Group B		
Vaginal	209	5	178.06	0.0001
Assisted vaginal	25	8	1.483	0.223
LSCS	453	143	40.623	0.0001
Total	687	156		

LSCS: Lower-segment cesarean section

Table 7: Distribution of patients according to the fetal and neonatal outcomes

Fetal outcome	χ^2		χ^2	P
	Group A	Group B		
Preterm delivery	54	65	119.85	0.0001
Still birth	16	9	5.228	0.22
NICU admission	45	59	114.946	0.0001
5 min Apgar <7	35	24	20.68	0.0001

NICU: Neonatal intensive care unit

Table 8: Distribution of patients according to mortality

	Number of patients (%)		χ^2	P
	Group A	Group B		
Maternal mortality	7 (1.01)	3 (1.9)	0.886	0.347

belonged to the age group of >40 years [Table 1]. Patients more than 40 years underwent ART for conception more often (85.3%) as compared to (9.75%) in Group A [Table 2]. Preterm birth was significantly higher in Group B as compared to Group A [Table 3]. Comorbid medical conditions including chronic hypertension, thyroid diseases, autoimmune disorders and obstetric complications such as abortions, oligohydramnios, gestational diabetes mellitus (GDM), placenta previa, and PPH were significantly more common in patients with Group B [Tables 4 and 5]. Cesarean delivery rate was significantly more in Group B as compared to Group A [Table 6]. Neonatal outcome in terms of NICU admissions and preterm birth at <35 weeks gestation was seen more frequently in Group B as compared to Group A [Table 7]. Maternal mortality was higher in Group B than Group A, though the difference was not significant [Table 8].

Discussion

Advanced maternal age is an independent risk factor for certain adverse outcomes in pregnancy.^[1-3] In our study, out of the 843 patients, 81.5% (n = 687) belonged to the age group of 35–40 years. 18.5% (n = 156) belonged to the age group of >40 years.

The number of patients getting pregnant between the age group of 35 and 40 years is more than patients >40 years of age. In France, the INSEE report shows that the proportion of pregnant women over 35 years rose from 19.3% to 21.3% between 2010 and 2016. This report states that about 5% of women who give birth are 40 years old or older. The age of first pregnancy increased from 29.5 in 2003 to 30.4 in 2016.^[5] Decades earlier, a pregnancy was considered “late” if it was obtained after 35 years, today the threshold has shifted to 40 years or even 43 or 45 years according to the scientific literature.^[5-7] This is explained by a societal evolution marked by a constantly increasing level of studies by women who have more responsibilities at work and therefore delay their project of childbearing giving their first priority to their professional career.

Demographic trends have seen a significant group of women in their forties seeking reproductive treatments. Although it is well documented that natural fecundity declines with increasing maternal age and the success rates in ART are particularly low for women 40 or older,^[8] the cutoff age after which no pregnancies are observed with ART remains elusive and controversial, because there are still acceptable chances for pregnancy in women of this age group. Only recently, the Society for Assisted Reproductive Technology registry has been providing rates of pregnancy and live births for women 43 years of age and older (pregnancy rates of 10.8% and 7.4% for women at ages 43 and 44, with a live birth of 5.1% and 3.0%, respectively) but these data are still limited.

Advances in assisted reproductive technology and increases in the proportion of maternities in older women have

both contributed to the steep increase in the incidence of multiple pregnancies since the 1980s. Maternal and perinatal complications are higher in twins than in singleton pregnancies. A significant proportion of perinatal mortality and morbidity among multiple is due to the high incidence of preterm delivery.

Preterm birth is the most important factor determining neonatal morbidity and mortality and has a major impact on it. It has been seen that there is an association between prematurity and advanced maternal age. Lawlor *et al.*, in a population of Danish women, found a U-shaped relationship between maternal age and risk of preterm birth, with the lowest risk age at 24–30 years.^[9] Our study corroborates similar findings. A common hypothesis is that the increased risk of preterm birth among aged mothers is largely explained by early labor induction for medical conditions. UTI is associated with preterm labor and occurred more frequently in the women aged >40 years.

GDM was significantly more common in the older age groups as it was associated with decreased insulin sensitivity as with age the pancreatic B cell function and pancreatic sensitivity fall. Women with the predisposition to Type 2 diabetes are therefore more likely to have an inadequate B cell response to stimulation and be more insulin resistant than younger women, which when combined, make gestational diabetes more likely.

Myometrial function deteriorates with age. This mechanism may also be relevant to the increased age-related risk PPH, as uterine atony is the most common cause of PPH. There is also an increased incidence of placenta previa syndrome, retained placenta, and genital lacerations. The incidence of PPH (7.6% in Group B as compared to 1.8% in Group A) and placenta previa (10.8% in Group B as compared to 1.7% in Group A) shows that the incidence of obstetric complications was more in Group B.

We demonstrated a lower prevalence of labor and spontaneous delivery in women of advanced age and a higher rate of cesarean section. A lot of other studies came to similar conclusions citing various comorbidities, previous cesarean section, and fetal macrosomia associated with diabetes mellitus to be the reasons for high rate of operative delivery in older women.^[10]

The risk of stillbirth was significantly higher in older women. The risks of aneuploidy and fatal congenital anomalies increase with maternal age and, despite antenatal screening, they are likely to have contributed to the increased rate of stillbirth.

Conclusion

In view of the different maternal profiles, this work attempts to shed more light on the hypotheses surrounding

older mothers, postulating higher risks in pregnancy and poorer obstetrical and neonatal outcomes in pregnancies of older mothers. The aim of this study was therefore to evaluate delivery outcomes in a cohort of women at advanced maternal age and to consider the complex impact of medical, surgical, gynecological, and obstetrical factors on delivery outcomes. Our study concludes that the decision to delay childbearing should be discouraged owing to increased maternal and fetal morbidity associated with advanced maternal age, the risks being higher with increasing maternal age.

Ethical statement

The study was approved by the Institutional Ethics committee, Dayanand Medical College and Hospital, IEC -217.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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