Original Research Article

Advanced maternal age and obstetric outcome

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Abstract

Background: Background: In obstetric practice, maternal age is an important determinant of the outcome of pregnancy. In recent times women have postponed childbearing due to lifestyle changes such as the pursuit of higher education and career advancement. This results in an increasing maternal age that leads to many complications during pregnancy, labor and also for the baby. This study was designed to assess pregnancy outcomes in elderly primigravida by evaluating the effect of advanced maternal age on the mode of conception and the obstetric and perinatal outcomes. **Methods:** This study was a prospective hospital-based study done in 100 elderly primigravida enrolled after suitable exclusion criteria in Vijay Marie Hospital and Educational Society and Akshaya Fertility Center from July 2018 to June 2019. The Inclusion criteria allows for pregnant women >35 years - both primigravida (delayed childbearing) and multiparous women (continued childbearing). **Results:** The most common cause of delayed conception was infertility (35%). Miscarriage rate was 11% and ectopic pregnancy 4%. The rate of caesarean section was very high (70%). 65% of them developed complications in pregnancy of which the most common was gestational diabetes mellitus (22%), gestational hypertension (12%), and preterm labour (17%). Out of 115 babies delivered, the most common complications were preterm (17%),FGR (8%) and 32 babies required NICU admission for various reasons like preterm and respiratory distress. There was no incidence of maternal and neonatal mortality. **Conclusion:** Pregnancies in women of advanced maternal age are considered high risk for perinatal and maternal morbidity and mortality. A proper preconception counselling and intensive antenatal care assessment can individualize and potentially reduce the risks for women with advanced maternal age.
keywords: Elderly primigravida; Pregnancy; Maternal complication

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Email: drmeera1962@gmail.com
Received Date: 04/07/2021 Revised Date: 12/08/2021 Accepted Date: 09/09/2021

Access this article online

Quick Response Code:

Website: www.medpulse.in

DOI: https://doi.org/10.26611/10122111

INTRODUCTION

The last three decades have shown an increasing trend of delayed childbearing – up to and beyond the age of 35. The reasons for this development could be the increasing use of reproductive techniques[1] and the enormous changes in work and society, which include higher levels of female employment (particularly in high-level jobs) and educational attainment.[2] These social trends combined with effective birth control and a greater range of treatments for infertility, despite the risks associated with the latter,[3,4] have resulted in a steadily expanding population of women who become pregnant after the age of 35. Pregnant women aged over 40 are no longer uncommon.[5] Studies have also identified several prototypical groups of women who decide to become pregnant beyond the age of 35.[6-9] It is well established that a woman's fertility decreases dramatically with age.[10] A brief discussion of relevant literature pertaining to the various risk factors follows. It is commonly known that conception success is reduced, and aneuploidies are increased in AMA (Advanced Maternal Age) due the degrading nature of oocyte genetic content[11,12] The likelihood of fetal chromosomal abnormalities is higher in older women due to ineffective completion of the oocyte cell cycle.[13] The contribution of the ageing oocyte to pregnancy complications is difficult to investigate as oocyte donation (as part of IVF or in vitro fertilization) is an independent risk factor for adverse pregnancy

How to cite this article: Meera Rajagopal, Bodepalli Sravani. Advanced maternal age and obstetric outcome. *MedPulse International Journal of Gynaecology.* January 2022; 21(1): 01-06. http://medpulse.in/Gynacology/index.php

outcome.[14] Furthermore, comparing outcomes of pregnancies conceived using 'young' donor eggs in women of AMA compared to women of optimal childbearing age is complicated by confounding primary infertility issues in the latter group of women. The risk of aneuploidy rises significantly with advancing maternal age. Data from the FASTER (First and Second Trimester Evaluation of Risk) trial, in which approximately 30,000 women at 10 to 14 weeks of gestation were enrolled in a prospective multicenter investigation of singleton pregnancies, revealed increasing rates of both threatened abortion and miscarriage with advancing maternal age. Women aged 35 years or older can expect to have twice the rates of antepartum hospitalization than the younger counterparts. Older women have a twofold higher risk of being diagnosed with hypertension. Studies on this topic have been plentiful in literature over several decades.[15] The prevalence of diabetes mellitus increases with age. The rates of both pre-existing and gestational diabetes increase 3- to 6-fold in women 40 years of age or older compared to women aged 20-29 years. Diabetes during pregnancy could result in severe or fatal complications to mother or the unborn. The rate of diabetes in primigravida of 35 years or more was shown to be 4.1% when compared to multiparous controls of younger age group where it is only 1.7%.[16] Gilbert W.M *et al.*[17] did find a 10-fold increased risk of placenta praevia in nulliparous women 40 years of age or older when compared to women aged 20-29 years, although the absolute risk of this was small (0.25% vs 0.03%). It was also observed that preterm delivery was more common in older mothers (19% vs 5%).[18] There was a clear tendency of increased incidence of breech births with age, with lowest frequency in the 15-19 year age group and almost 7 times the frequency among 35 and above. The most important cause of multiple pregnancy in older women currently is conception with assisted reproductive technologies (ART) and ovulation induction (OI). According to a 2002 Centers for Disease Control (CDC) study, 0.7% of all 3.9 million births in the US in 1998 were the result of these techniques. The risk of Leiomyoma increases because as a woman gets older, she naturally has more time to develop gynecological abnormalities – fibroids being the most common. Maternal age below 20 years and above 30 years were significantly associated with the risks of low birth weight and preterm birth. Advanced maternal age is responsible for a substantial proportion of the recent increase in rate of low birth weight (LBW) and preterm (PTD) delivery[19] A significant proportion of perinatal deaths seen in older women were due to lethal congenital and chromosomal anomaly. Maternal mortality is higher in women aged 35 years and older but improved medical care may ameliorate this risk.[20] This is further influenced by the fact that in many countries, women do not have access to maternity hospitals or to skilled professionals for delivery. Pre-existing medical conditions such as heart disease, diabetes and hypertension are more common in women over 35 years.[21] Other lifestyle factors such as maternal obesity[22] are prevalent in this cohort and these are all risk factors for poor pregnancy outcome including SGA (small for gestational age), FGR (fetal growth restriction), LGA (large for gestational age), preterm birth and stillbirth.[23] AMA has been proposed to play a role in the rising intrapartum caesarean section rates.[24] Women of AMA can also suffer dystocia – a long and difficult labour. Another study found that 40-45% of mothers aged >35 years had a prolonged second stage of labour compared to only 16% of 20-24 year-olds.[25] The higher rates of dysfunctional labour may be due to decreased uterine contractility with AMA. Several studies have tried to examine the relationship between maternal age and pregnancy outcome, but as evidenced from the above studies, most studies have reported contradictory results with regard to advanced maternal age.[26-29] The aim of this study was therefore to evaluate pregnancy and delivery outcomes in a cohort of women at the higher spectrum of maternal age and to consider the complex impact of medical and obstetrical factors on delivery outcomes. Wherever appropriate, other risk factors and causes were examined and contrasted to those present in existing literature.

MATERIALS AND METHODS

The study was a prospective observational study conducted at the department of Obstetrics and Gynaecology, Vijay Marie Hospital and Educational Society and Akshaya Fertility Clinic; both located in the city of Hyderabad. The study period spanned one year from July 2018 to June 2019. The study population consisted of pregnant women more than 35 years of age including primigravida (delayed childbearing) and multiparous women (continued childbearing). The sample size was calculated by using the statistical formula:

$$N = \frac{Z^2 P(1-P)}{L^2}$$

where Z is the Z-value (1.96 for 95% confidence interval), P is the anticipated prevalence and L is the allowance error. The hospital data from the last three years was reviewed and the average prevalence of advanced maternal age was considered as 10% for sample size calculation. The sample size came out to be 36 pregnancies of advanced maternal age. Therefore, the sample size for this study was 40. To account for any potential dropouts the sample size was increased to 100 cases. The pregnant women admitted for delivery in Vijay Marie Hospital in the study period who satisfy the inclusion criteria were enrolled for this study.

Data is taken from July 2018 to June 2019 in a monthly pattern. The women were enrolled for the study from the labour ward after taking verbal consent. The demographic data of these women, gestational age at the time of delivery and complications during pregnancy were noted. They were monitored till discharge and mode of delivery; perinatal outcome and any intrapartum and postpartum complications were recorded in a specially designed research proforma. The study was approved by the ethical committee of the hospital. The major obstetrics parameters were parity, obstetric complication (antepartum hemorrhage and premature rupture of membrane), medical disorder associated with pregnancy (hypertension in pregnancy and gestational diabetes) and mode of delivery (normal vaginal delivery, instrumental delivery and caesarean section). The perinatal information compared were birth weight, NICU (neonatal intensive care unit) admissions and so on. Antepartum hemorrhage (APH) was defined as any vaginal bleeding after 28 weeks of gestation and before delivery of the baby. Women who were diagnosed as having pre-existing hypertension were categorized as chronic hypertension whereas those who had new onset hypertension after 20 weeks of gestation with or without proteinuria were labelled as preeclampsia and pregnancy induced hypertension respectively. Eclampsia was convulsion occurring in women with hypertension. All these types of hypertension were collectively categorized as hypertensive disorder of pregnancy. Women were classified as diabetic if they had a history of pre-existing diabetes or that were diagnosed for the first time during pregnancy (GDM - carbohydrate intolerance of variable severity first recognized during pregnancy). Pregnancy termination before 37 completed weeks of gestation was termed preterm delivery. Mode of delivery categorized as normal vaginal delivery or caesarean section. Birth weights less than 2500 grams were termed as low birth weight. Very low birth weight was defined as < 1500 g; macrosomia was defined as birth weight ≥ 4000 g. Nuchal translucency (NT) scan was carried out at 11–13 (+6) weeks pregnancy and assessed for the quantity of fluid collecting within the nape of the fetal neck cut-off: 2.5 or 3.0 mm. TIFFA performed between 18-23 weeks of pregnancy involves a detailed scanning and examination of the fetus for any abnormalities. For females in all age groups, the Triple Marker Test for Alpha Fetoprotein rises during pregnancy from 0.20 ng/ml to 250 ng/ml at 32 weeks' gestation, hCG is 4,060 - 165400 mIU/ml and Estriol is <14.60 ng/ml (Pregnancy Third Trimester). Data is collected by interviewing the participants. The observations were then inferred with use of univariate and bivariate analysis. SPSS (version 17) and Microsoft Excel software were used for the statistical analysis.

RESULTS

It is important to recall that the objective of this study is to provide an update of our current knowledge about the impact of advanced maternal age on pregnancy outcome. The population used for the current work was studied in three broad categories: demographics, maternal outcomes and neonatal outcomes. In what follows, the results in each category are presented, discussed and contrasted with earlier works from literature.

Table 1: Age Distribution

Age (years)	Number	Percentage (%)
35 – 36	43	43
37 – 38	32	31
38 – 39	12	12
> 40	14	14

Table 2: BMI

BMI	Number	Percentage (%)
20 – 25	19	19
25 – 30	61	61
> 30	17	17

Table 3: Marital Life

Marital Life (years)	Number	Percentage (%)
< 5	23	23
5 – 10	29	29
10 – 15	33	33
> 15	31	31

Table 4: Educational Status

Educational Status	Number	Percentage (%)
Primary School	10	10
High School	30	30
Higher Secondary	28	28
Graduate / Post-graduate	32	32

Table 5: Reasons for Late Childbearing

Cause	Number	Percentage (%)
Idea of Large Family	4	4
Remarriage	15	15
History of Subfertility	35	35
Failure of contraception	5	5
Desire for Male Child	12	12
Late Marriage	17	17
Pursuit of Career	10	10
Bad Obstetric History	2	2

Table 6: Parity

Parity	Number	Percentage (%)
Primiparous	34	34
Multipara	66	66

In analyzing the demographics of the study population, the variables used were age, body-mass index (BMI), educational status, marital life, parity and reasons for late childbearing. These results are presented in Tables 1-6.

The mean age group was 37.6 years in this study, which is higher than the 36.8 years reported by Moses V *et al*.[30] The largest BMI category of the population (61%) was observed to be that of overweight. Majority of them were married for a longer time – two possible explanations arise for this distribution: either a history of subfertility or pursuit of their career. In terms of educational status, our findings mirror.[30,31] The top reason for late childbearing was a history of subfertility (35%) followed by remarriage and late marriage (totaling to 32%). These incidences are comparable to Kalewad P *et al.*[31] in which infertility (47%), remarriage and late marriage (24%) were reported as the biggest causes for late childbearing. The majority of pregnant females above 35 years were multipara (66%). This could probably be because of the increase in the rate of divorce and remarriage, and an idea of a large family. Another potential reason could probably be because the study site (Vijay Marie Hospital) caters to the lower socio-economic class of people. They have poor knowledge about contraceptive usage or family planning accounting for the higher multiparity. There also appears to be less spacing between pregnancies. The incidence of multipara is higher (and hence primipara is lesser) than the 57.5% reported by Neerja Singal *et al.*[32]

Table 7: Mode of Conception

Conception		Number	Percentage (%)
	Spontaneous	70	70
	IVF	8	8
ART	Donor Egg	16	16
	Donor Sperm	2	2
	Ovulation Induction	4	4

Table 8: Number of Fetus

Number of Fetus	Number	Percentage (%)
Singleton	86	86
Multiple	14	14

Table 9: Medical and Surgical Disorders

Maternal Diseases	Number	(%)
Overt Diabetes Mellitus	6	6
Chronic Hypertension	8	8
Rheumatoid Arthritis	1	1
Fibroid Uterus	2	2
Colloid Hyperplastic Goiter	1	1
Mild Concentric LVH* with mild TR and mild LR	1	1

*Left ventricular hypertrophy

Table 9: Pregnancy Losses

Pregnancy Losses	Number	Percentage (%)
Miscarriage	11	11
Ectopic Pregnancy	4	4

Table 10: Mode of Delivery

Mode		Number	(%)
Normal Vaginal		22	25.88
Caesarean	Elective	38	44.71
	Emergency	22	25.88
Instrumental		3	3.53

Table 11: Second and Third Trimester Complication

Complications	Number	Percentage (%)
Severe Oligo	2	2.35
Fetal Anomalies	1	1.17
Preterm Labor	17	20
Abruption	3	3.52
Placenta Previa	4	4.70
Preeclampsia	1	1.17
Eclampsia	0	0
Gestational Hypertension	12	14.11
Gestational Diabetes Mellitus	22	25.88

The variables used to study the next category, i.e., maternal outcomes are presented in Tables 7-11. 70% of the study population conceived spontaneously, while 30% of them utilized ART. Among the study group the incidence of women utilizing ART was high when compared to Refs.[31 and 33] which reported 26% and 12.6% respectively. Among the study group majority were singleton pregnancies (86%), and 14% comprised multiple pregnancies (twins 12%, triplets 2%) which is significant when compared with other studies - 10.6%, 1.1% and 4% reported by Refs.[31,34 and 35] respectively. The most common pre-existing medical conditions in our study population were hypertension (8%) and overt diabetic comprises (6%). We also found some surgical conditions - two cases having fibroadenoma of breast who got operated after delivery. There was one case with rheumatoid arthritis who was on prednisolone. Two cases with fibroid uterus were found who delivered at full term. One case with thyroid swelling got operated on and histology showed colloid hyperplastic goiter. She was later prescribed a thyroid supplement. One patient suffering from chronic hypertension developed mild concentric left ventricular hypertrophy, with mild MR (Mitral Regurgitation) and mild TR (Tricuspid Regurgitation) whose peripartum was uneventful. The incidence of chronic or essential hypertension was high when compared to Kalewad P *et al.*[31] (5%) and was less when compared to Palival V *et al.*[36] (9%). Similarly, the incidence of diabetes was high when compared toKalewad P *et al.*[31] (5%) and was less when compared to Ref Palival V *et al.*[36] (9%). Also, the incidence of uterine fibroids was higher (8%) in [31] 11 miscarriages were reported in the study population: eight of which were missed abortions, two were incomplete abortions and one blighted ovum. A patient got aborted at 22 weeks because of premature rupture of membranes. 4 ectopic pregnancies were also reported in which three of them underwent salpingectomy and one got medical management. The incidence of miscarriage and ectopic was high when compared to Moses V *et al.*[30] (9%) and less when compared to Sasirekha K *et al.*[35] (15.2%), Pawde Anuya A *et al.*[33] (18.9%) and Kalewad P *et al.*[31] (3%). Patients who had registered in the first trimester were subjected to USG for NT and NB (Nasal Bone). which came out to be normal. The study population in the

second trimester, including those who registered in the second trimester (before 20 weeks), were subjected to malformation scan, triple marker or Quadruple biochemical screening. After 20 weeks gestations-only malformation scan was performed. From all those on whom the TIFFA scan was performed, one patient was diagnosed with multiple fetal anomalies and the pregnancy was terminated. From all those on whom biochemical screening was performed, 4 patients were diagnosed as high risk for chromosomal abnormalities. All 4 patients were subsequently subjected to an invasive confirmative procedure which came out normal. Incidence of abnormal biochemical screening was high when compared to Kalewad P *et al.*[31] (3%). Out of the 85 patients who ultimately delivered, 22 patients did so by normal vaginal delivery, 3 were instrumental delivery, 60 patients delivered by caesarean section. Among the mothers who delivered the incidence of caesarean section was less when compared to Palival V *et al.*[36] (74%) and high when compared to Giri A *et al.*[34] (30%), Kalewad P *et al.*[31] (40%), Chan BC *et al.* .[37] and Moses V *et al.*[30] (66%). Further, the incidence of instrumental delivery is less when compared to Giri A *et al.* [34] (6.6%). Only 27% of these 85 deliveries did not have any complications in the second and third trimester. Of the complications that arose, the largest numbers were seen in gestational diabetes mellitus (25.88%), preterm labour (20%) and gestational hypertension (14.11%). Among the mothers who delivered, the incidence of oligohydramnios is less when compared to Moses V. *et al.* .[30] (10%), and more when compared to Kalewad P *et al.*[31] (2%). The incidence of abruption was high when compared to Chan BC *et al.*[37] (1%), Moses V, *et al.*[30] Cleary Goldman J *et al.*[38] and Joseph KS *et al.*[39] (2.4%). The incidence of placenta previa was high when compared to Chan BC *et al.*[37] (4%) and Cleary Goldman J *et al.*[38] (1.8%). The incidence of preeclampsia was low when compared to Giri A *et al.*[34] (20%), Kalwad P *et al.*[31] (2%) and Moses V.[30] (4%). The incidence of gestational hypertension was less when compared to Moses V *et al.*[30] (24%) and Kalewad P *et al.*[31] (15%). Finally, the incidence of gestational diabetes mellitus was higher than Giri *et al.*[34] (1%), MosesV *et al.*[30] (6%) and Kalewad P *et al.*[31](15%).

Table 12: Neonatal Complications

Neonatal Outcome	Number	Percentage (%)
IUGR	8	7.92
Preterm	17	16.83
Macrosomia	5	4.95
Twins	12	11.88
Triplets	2	1.98
Normal Babies	43	42.57
Chromosomal Anomaly	1	0.99

The results for the next category (neonatal outcomes) are presented in Table 12. The incidence of IUGR was less when compared toGiri A *et al.*[34] (8.8%), and kalewad P *et al.*[31] (22%). The incidence of preterm delivery was higher than [30] (10%), Joseph KS.[39] (12%) andGiri A *et al.*[34] (1.1%) but was less when compared to Chan BC *et al.*[37] (17%). The incidence of macrosomia is higher than Chan BC *et al.*[37] The incidence of multiple pregnancy is higher than Kaliwad P *et al.*[31] (10.6%), Giri A *et al.* .[34] (1.1%). Finally, the incidence of NICU admissions was less when compared to Moses V *et al.*[30] (43%).

CONCLUSIONS

This paper has presented vital data on maternal and neonatal outcomes on the increasing trend of advanced maternal age seen in societies all around the world. Obstetricians and gynaecologists have a duty to address the growing epidemic of aging motherhood and the complications that arise from this, as well as to inform women of the risks associated with delayed childbearing. A proper preconception consultation and intensive antenatal care assessment can individualize and potentially reduce the risks for women considering a pregnancy at any age. The rising trends of obstetric complications were observed in patients > 35 years of age so this group of patients should be considered as a high-risk category for obstetrics, and they need special attention and vigilant care in the multidisciplinary tertiary care center. With higher incidence of chromosomal abnormalities, women ≥ 35 years of age should be offered screening for fetal aneuploidy. With availability of non-invasive, sensitive biochemical tests in combination with nuchal scan, the need for invasive procedures can be greatly reduced. There is a rising trend of caesarean section in advanced maternal age due to increased incidence of pregnancies following ARTs, multiple pregnancies, pregnancy complicated by medical disorders and the physician's attitude. The higher rate of caesarean births in older gravidas also occurs as they are defaulted to be at high risk or their pregnancies to be more precious. Due to these reasons, it is advised not to postpone conception and advise the women to become pregnant to avoid age specific complications.

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Source of Support: None Declared
Conflict of Interest: None Declared