



Original Research Article

Effect of advanced maternal age on pregnancy outcome - A retrospective cohort study

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ABSTRACT

Aim: To determine the risks of pregnancy and to study the adverse maternal and fetal outcomes of pregnancy in advanced maternal age.

Materials and Methods: This study was a retrospective cohort study. Which was conducted in the Department of Obstetrics and Gynaecology, Government Medical College, Kozhikode. Data were collected from Department Medical Records Library. Data consisted of study group with maternal age above 35 years and control group with age less than 35 years. Cases beyond 28 weeks of gestation, both primiparous and multiparous patients were included. Minimum 262 patients were included in each group. Gestational age, presentation, mode of delivery, indications for caesarean, maternal complications and fetal outcomes were analysed. Statistical analysis was done by SPSS16.0 statistical software.

Results: In this study statistically significant difference in maternal complications like incidence of gestational diabetes, gestational hypertension and preterm labour were observed in advanced maternal age women.

Conclusion: Increasing incidence of maternal complications both obstetric and medical were observed in the advanced age mothers (AMA). There was a significant increase in preterm labour, increased caesarean delivery, PROM, PPRM, gestational hypertension, gestational diabetes, VLBW babies, intrauterine death in these elderly mothers. Due to the increase and advances of infertility treatments has made it common for mothers to become pregnant even at late forties.

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1. Introduction

Advanced maternal age (AMA) is defined as childbearing in a woman over 35 years of age and is a growing trend in high income countries. In many contemporary studies, the cut-off for AMA has been changed to the age of 40.¹⁻³ The trend of pregnancy occurring in mothers of advanced age is most commonly due to older primi gravid women who delay childbearing by lifestyle choice or due to underlying subfertility, but also includes multiparous women continuing childbearing. This is also due to advancements in assisted reproductive technologies.⁴

The prevalence of advanced maternal age was 17.5% in a retrospective comparative study conducted in South Africa.⁵

Delayed childbearing is believed to be associated with an increased rate of obstetrical and perinatal complications, i.e greater risk of congenital disorders, placenta previa, ectopic pregnancy, spontaneous abortion, stillbirth, preterm birth, induction of labour, caesarean delivery and small for gestational age (SGA) unlike younger women. Prevalence of chronic medical conditions like diabetes mellitus, hypertension and other diseases with a possible influence on a course of pregnancy (such as cancer) are higher among older patients.⁶ Multiple studies suggest that the

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incidence of perinatal complications only begins to increase after the age of 35, but the most significant increase in incidence can be observed after the age of 40.^{7,8} AMA also results in neonatal complications, such as low Apgar score, NICU admission, preterm delivery, low birth weight, birth defects, chromosomal abnormalities and perinatal death.^{9–13} Fertility in women starts to decrease in the early thirties and even decreases faster after mid and late thirties. Women with advanced age usually have a relatively lower tendency to achieve pregnancy within a short period. The probability of achieving pregnancy in a single menstrual cycle, i.e fecundability, is decreased in these group of women.^{14,15}

2. Aim and Objectives

To determine the risks of pregnancy in advanced maternal age and study the adverse maternal and fetal outcome.

3. Materials and Methods

3.1. Study design

Retrospective cohort study.

3.2. Study settings

Department of Obstetrics & Gynaecology, Government medical college, Kozhikode.

3.3. Study population

Study group (S) – Pregnant women ≥ 35 years with gestational age ≥ 28 weeks.

Control group (C) – Pregnant women between 20 to 35 years with gestational age ≥ 28 weeks.

Study period was during January 1st 2017 to December 31st 2017. All mothers with age 20-35 years as control group and ≥ 35 years as study group, who had either vaginal or caesarean deliveries were included. Women with multiple pregnancies were excluded from study.

3.4. Sample size

535.

The still birth rate among mothers ≥ 35 years and 20 – 34 years was 8.5% and 2.8% respectively by study conducted by Salihu HM et al,¹⁶ expecting similar rates, the sample size required calculated by the below formula:

$$n = 2(Z\alpha/2 + Z 1-\beta)^2 pq/d^2, \text{ where } p = (p_1 + p_2)/2 \text{ and } d = p_1 - p_2 = 257.3$$

273 patients in study group and 262 patients in control group were included in this study. Patients were categorized according to maternal age group into two groups. The case records were retrieved from the medical records department. Information on age, parity, reason for delaying pregnancy, whether there is history of treatment for infertility or not,

gestational age, risk factors, maternal co morbidities, mode of delivery, maternal complications, apgar scores, sex of baby, birth weight and NICU admissions were collected. Fetal outcomes like still birth and fetal growth restriction, neonatal death, small for gestational age, NICU admissions, preeclampsia, placental abruption, preterm birth, and gestational diabetes mellitus were studied. Primary outcome studied were maternal complications like preterm labour, antepartum haemorrhage, premature rupture of membranes, incidence of gestational diabetes, gestational hypertension, incidence of caesarean delivey, and also comparing these in study and control groups. And secondary outcomes like intrauterine death, intrauterine growth restriction, low apgar scores also compared among two groups. Data analysed using SPSS16.0 statistical software.

4. Results

This retrospective study was conducted from 1st January 2017 to 31st December 2017. Of the 273 cases in AMA group studied 92.6% patients were between 35 to 39 years, 6.6% cases with age between 40 to 44 years, one patient with age above 45(0.3%), and one with above 50 (0.3%) years. In below 35 age group(control), of the total 262 patient 49.2% were below 25 years and 50.7% between 25 to 34 years.(Figure 1)

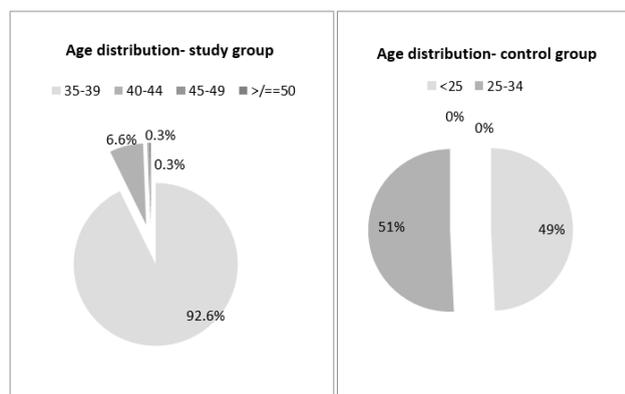


Fig. 1: Age distribution

Among the study group majority of patients were multies 76.7%, 16.9% cases were primies, 6.2% grand multies. In control group 48.4% were primies, 51.1% multies and only 0.38% grand multies. Parity wise there was a significant difference in two groups. p value < 0.001 in nullipara. (Figure 2)

According to gestational age 70.8% patients in study group belonged to gestational age between 37 to 40 weeks, 14.7% between 34 to 37 weeks, 11.7% less than 34 weeks, 3.35% above 40 weeks. Control group also majority belonged to gestational age between 37 to 40 weeks i.e 75.9%, 8% of less than 34weeks, 6.4% between 34 to 37 weeks, and 10.3% more than 40 weeks. (Figure 3)

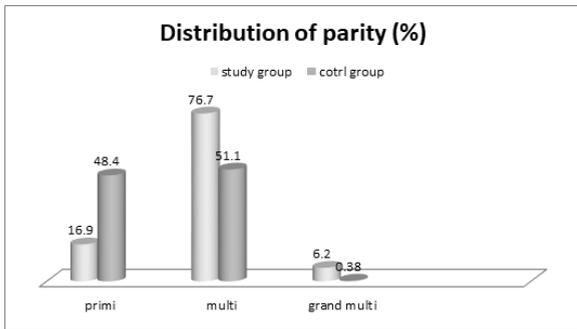


Fig. 2: Distribution of parity (%)

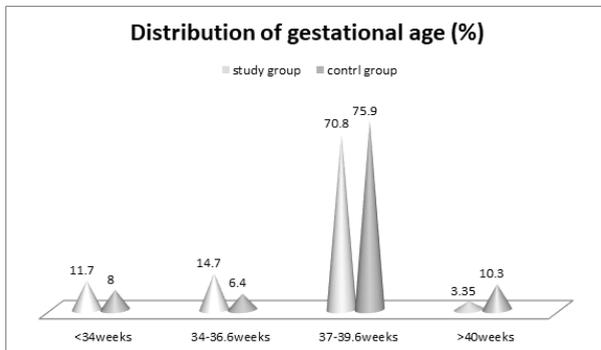


Fig. 3: Distribution of gestational age (%)

95.2% of fetuses in study group were in cephalic presentation, 4.4% of breech and 0.36% transverse lie. In the control group 92.7% cephalic, breech 6.8%, transverse 0.38%. In the patients of age more than 35 years 51.2% had caesarean and 49.4% delivered vaginally. In the control group 63% delivered vaginally, 37% delivered by caesarean. Of the LSCS 56.8% were done as emergency and 43.1% as elective. And in control group as 67% emergency and 32.9% as elective. Caesarean rate was significantly more among advanced maternal age, $RR=1.38(1.13-1.67)$, $p = 0.001$ and this is statistically significant. Of the vaginal delivery group there were 11 cases of assisted breech delivery and 6 instrumental delivery in patients above age 35 years. In the control group 2 cases of assisted breech delivery and 4 instrumental delivery. (Table 1).

Commonest indication for LSCS was previous LSCS, i.e about 49.6%, out of that 84% cases were for previous one CS, 14.4% for previous 2 CS, 1.4% for previous 3CS, other common indications were prolonged period of infertility 16.7%, severe preeclampsia 7.2%, HELLP 2.1%, unfavourable cervix 7.2%, fetal distress 4.3%, placenta previa 4.3% etc. In control group also most commonest indication was previous caesarean about 27.8%, other indications are failed induction 17.5%, fetal distress 16.4%, oligamnios 11.3%, abruption 11.3%, cephalo pelvic disproportion 11.3%, breech 6.1%, prolonged period of infertility 6.1%.

Maternal complications commonly seen in the advanced age group were diabetes in about 44.2%, and 38% cases of hypertensive disorders. In the control group 20.2% cases of diabetes and 14% cases of hypertensive disorders. Among the 44.2% cases of diabetes in AMA 90% belonged to gestational diabetes and 10% cases to pre gestational diabetes. In the control group out of 20.2% cases of diabetes, 92.4% were of gestational diabetes and 7.5% cases of pre gestational diabetes. Proportion of diabetes complicating pregnancy was significantly more among advanced maternal age, $RR= 2.19 (1.66-2.88)$, $p < 0.001$.

And of hypertensive disorders 51.4% cases belonged to gestational hypertension, 29% cases of severe preeclampsia 11.6% cases of chronic hypertension, 6.7% cases of HELLP in the study group. In the control group hypertensive disorders of pregnancy were of 14%, of which gestational hypertension 56.7%, severe preeclampsia 27%, HELLP syndrome 10.8%, chronic hypertension 2.7% and eclampsia in 2.7%. Proportion of hypertension complicating deliveries was significantly more among advanced maternal age, $RR=2.67 (1.91-3.73)$, $p < 0.001$. Proportion of gestational hypertension was significantly more among advanced maternal age, $RR=2.8 (1.74-4.48)$, $p < 0.001$, And also proportion of severe preeclampsia was significantly more among advanced maternal age $RR=3.54 (1.78-7.07)$, $p < 0.001$. There was no significant difference in proportion of HELLP between the two maternal age groups $RR=2.28(0.68-7.66)$ $p = 0.221$.

There was 25.8% cases of preterm delivery in the study group compared to 14.5% cases in control group. Proportion of preterm deliveries were significantly more among advanced maternal age group, $RR=1.78(1.25-2.54)$, $p = 0.001$. 7.3% cases of antepartum haemorrhage in study group and 3% cases in control group. Proportion of APH was significantly more among advanced maternal age, $RR=2.42(1.08-5.39)$, $p < = 0.025$. Preterm premature rupture of membranes 4.7% in advanced maternal age compared to 3% in less than 35 years. This also significantly more among advanced maternal age, $RR=6.28 (1.43-27.58)$ $p = 0.005$. Premature rupture of membranes 4.05% in study group and 1.9% in control group. There is no significant difference in proportion of PROM between 2 groups $RR = 2,22 (0.78-6.29)$, $p = 0.121$. (Figure 4)

Other maternal complications were oligamnios 6.6%, fibroid 4.05%, previous myomectomy 1.8%, polyhydramnios 2.2%, heart disease 1.47%, and anaemia 1.47%, past date 0.73% in study group. In control group incidence of oligamnios 4.9%, fibroid 0.76%, anaemia 2.2%, past date 2.6% respectively.

Incidence of infertility among advanced maternal age mothers was about 7.7%, compared to 2.67% in control group. $RR= 2.88 (1.24 -6.66)$ p value 0.009 which is statistically significant. Among the study group majority belonged to primary infertility, only 4.7% cases belonged

Table 1: Mode of delivery

Vaginal Delivery Study	Vaginal Delivery		Total	Elective	LSCS Emergency	Total
	Instrumental Delivery	Assisted Breech delivery				
126	6	2	134	60(43.1%)	79(56.8%)	139(51.2%)
Control 159	4	2	165	32 (32.9%)	65 (67%)	97(37%)

to secondary infertility.

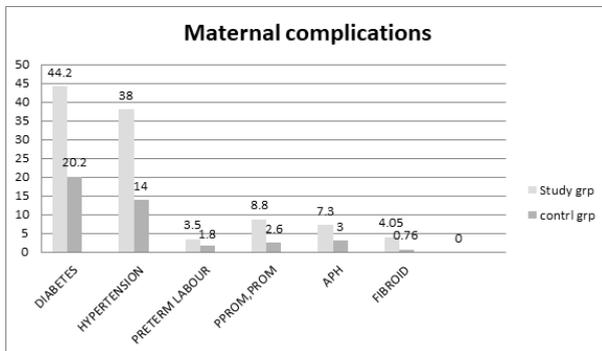


Fig. 4: Maternal complications

Of the babies 50.9% were females and 49% were males in study group. In the control group 52.8% males and 47.1% were females. When analysed the baby weight 53.8% babies belonged to the group with weight between 2.5 to 3.5kg, 28.7% with weight between 1.5 to 2.5 kg, 11% with weight less than 1.5kg and 6.2% with weight more than 3.5kg in study group. In the control group 69.4% belonged to birth weight between 2.5 to 3.5 kg 18.3% belonged to weight between 1.5 to 2.5 kg, 8.3% above 3.5 kg, and 3.4% with birth weight less than 1.5kg. (Figure 5). There was statistically significant difference in babies with birth weight below 1.5 kg in advanced maternal age group RR= 3.2 (1.55-6.6) p value 0.0007.

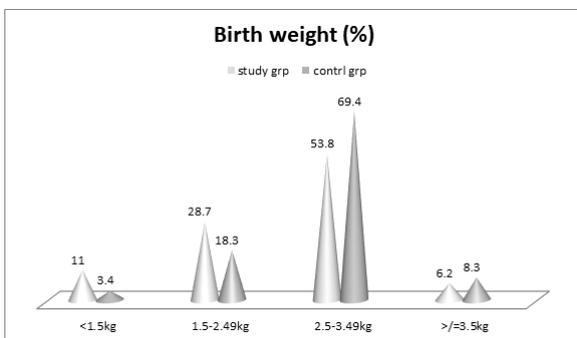


Fig. 5: Birth weight (%)

Incidence of intrauterine death in study group was 6.2% and in control group it was 1.9%. There were in 8.4% cases

of intrauterine growth restriction among AMA and 6.1% in control group RR =3.26 (1.22-8.72) p value being 0.011 which is statistically significant. There was no significant difference in proportion of IUGR between the two groups RR=1.39 (0.75-2.57), p=0.291.

And oligamnios in study group was 6.6% and 4.9% in control group. Incidence of babies with low apgar was 5.9% in study group and 2.2% in the control group. RR=2.56 (1.02-6.44) p value 0.038 which is also statistically significant.

Incidence of congenital anomalies in advanced maternal age group was about 5.9% and in control 2.8%. Major anomalies identified were congenital diaphragmatic hernia, duodenal atresia, non immune hydrops, omphalocele, fetal intracardiac echogenic focus, fetal bilateral hydronephrosis in study group and in control group the anomalies identified were cardiac anomaly and true knot. (Figure 6)

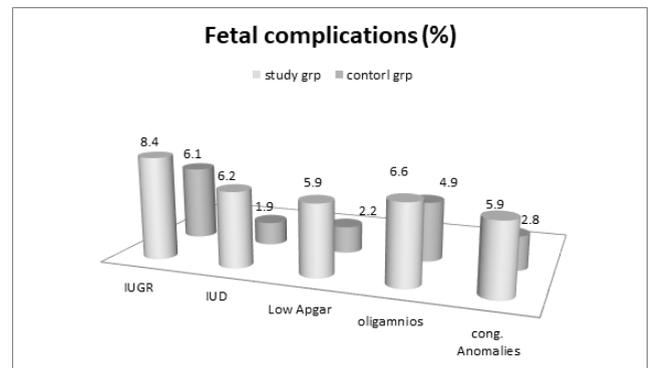


Fig. 6: Fetal complications

Induction of labour was very few in the study group i.e 4.4%, of which 50% induced with PGE2 gel, 25% with PGE1, 25% with foley plus PGE1 In the control group rate of induction was 25.9%, of which 52.9% patients were induced with PGE2, 25% with PGE1, 22% induced with foley plus PGE1.

When analysed among the study group patients with comorbidities and without, there was an increased incidence of preterm deliveries and babies born with low APGAR scores in advanced maternal age mothers with comorbidities. RR for preterm labour is 2.31 (1.49 – 3.81) p value = 0.0001 which is statistically significant. But p value for low APGAR score is statistically not significant.

Table 2: Subgroup analysis among AMA women

	AMA with Comorbidities 134		AMA without Comorbidities 139		P value	
Primi	24	17%	22	15.8%	0.646	
Multi	110	82%	117	84%		
LSCS	73	54%	75	53.9%		0.931
Preterm labour	46	34.3%	20	14.3%		0.0001
Intrauterine death	3	2.2%	4	2.8%		0.520
Low APGAR	7	5.2%	4	2.8%		0.324

5. Discussion

In this study of pregnancy outcome in advanced maternal age, the incidence of mothers with age above 40 years is 7.2%, increased compared to previous years. Of the women in the study group 92.6% belonged to age group between 35 to 39 yrs and 6.6% between 40 to 45years which is similar to the observation in the studies by Sobotka, Shan D et al. and Hamilton BE et al.¹⁷⁻¹⁹ This is mainly due to increased acceptance of advanced infertility treatment like assisted reproductive techniques, changes in female attitude towards education career importance. When analysed based on parity, increased incidence of multiparity was observed in advanced maternal age group and nulliparous mothers were of 16.9%, and almost equal incidence of nulliparous 48.4% and multiparous mothers 51.1% in control group. Incidence of preterm delivery was high in advanced age mothers in this study also i.e 25.8% in study group and 14.5% in control group. Advanced maternal age is an independent risk factor for preterm delivery. Medical comorbidities can also increase the effect of advanced age on pregnancy. This similar observation was reported in various studies.²⁰⁻²⁴

When assessed based on presentation of fetuses both in study group and control group there was no major difference in incidence unlike other studies.^{25,26} Incidence of breech was 4.4% in this study group compared to 6.1% in control group. Mode of delivery in study group was caesarean in more than 50%, where as in control group majority delivered vaginally. Cesarean rate in control group only 37%. The common indication for caesarean in the advanced maternal age were previous caesarean, prolonged period of infertility, severe preeclampsia, unfavourable cervix etc. In the control group the indications for caesarean were apart from previous caesarean, failed induction, fetal distress, cephalopelvic disproportion, oligamnios etc.²⁷⁻³¹

Maternal complications like hypertensive disorders were amounting to about 38% in the advanced maternal age group compared to 14% in the control group. Significant Incidence of chronic hypertension complicating pregnancy was high in the study group. Similar observation was obtained in studies conducted by^{32,33} Cavazos et al, Bateman BT et al. Similarly incidence of diabetes complicating pregnancy were almost double compared to control group.³⁴ There is also higher incidence of placenta praevia, premature rupture of membrane, fibroid complicating pregnancy in advanced maternal age group.³⁵ Pregnancies following

infertility treatment also was more in advanced age mothers. Patients conceived following ovulation induction, invitro fertilization also is more in study group.³⁶

Fetal complications like intrauterine growth restriction, oligamnios, intrauterine death of fetus were significantly higher in the study group compared to control group.^{37,38} Neonatal complications like low apgar, very low birth weight babies, NICU admission were higher in the study group. Similar observation is seen in studies by Koo Y-J et al, Almeida et al.^{39,40} Congenital anomalies in advanced age mothers also was high similar to study of E Lemyre et al.⁴¹

But unlike most of studies induction of labour was more in control group compared study group.⁴²

6. Conclusion

In this study of fetomaternal outcome in advanced maternal age, the maternal and neonatal complications were more in study group compared to younger age group women, similar to most of the studies. Even though medical complications were significantly higher, proper antenatal care and timely termination of pregnancy significantly reduced the major adverse outcome of hypertension and hyperglycemia in these women.

7. Source of Funding

None.

8. Conflict of Interest

None.

9. Acknowledgement

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