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Original Research Article

Association between advanced maternal age and adverse pregnancy outcome

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ABSTRACT

Background: AMA (advanced maternal age) is associated with a wide range of adverse pregnancy outcomes. The purpose of this study is to review the impact of maternal age on a range of adverse pregnancy outcomes in order to assist in accurate counselling of women considering delaying pregnancy or those who are already pregnant and concerned about the risk of developing complications due to their age.
Methods: The present study is a prospective cohort study conducted in Sree Avittom Thirunal Hospital, Medical College, Thiruvananthapuram, India. The study population was divided into two groups. The exposure cohort included 200 elderly pregnant women (at or above 35 years). The control cohort included 200 younger women (<35 years). The two groups were followed up throughout their pregnancy period and pregnancy outcomes studied.
Results: The mean age of the study group was 37.1 years while the mean age of the control group was 25.2 years. Induction rates were higher among younger gravidae (50%) while Caesarean before labour was higher ($p<0.001$) in the elderly. Preterm delivery and Caesarean sections were higher ($p<0.001$) in the study group. However primary CS rates were higher in the control group. PPH was significantly higher (p 0.019) in the elderly group.
Conclusions: It is concluded in the present study that women with advanced maternal age are at higher risk of developing complications during and after delivery. Effective counselling should be given to mothers who plan to delay childbirth.

Keywords: Advanced maternal age, Elderly gravidae

INTRODUCTION

Advanced maternal age or elderly gravida refers to women who have their conception at or above the age of 35 years. Both extremes of age are associated with adverse outcomes in both mother and the foetus. The increasing educational and occupational status in women, late marriages, remarriages, rise in nuclear families, financial responsibility of raising children, knowledge, and use of various contraceptive methods, rise in infertility rates, assisted reproductive techniques has led to the rise in prevalence of elderly gravidae. A rise in the divorce rates nowadays also contributes to delayed conception and old age conception.[1] Increase in elderly multigravidae may be due to contraceptive failures, lack of knowledge and awareness on contraception, desire for male child, etc. According to the CDC (Centre for disease control and Prevention) report in 2014, the number of people who gave birth to their first babies between the age of 30 to 35 has been rising over time. It also states that first conception after 40 years age has risen 4 times than previous data. Nearly 19% of all pregnancies and 11% of all first pregnancies in the United States were in women aged 35 years and older.[2] The mean age of women having their first birth in 2020 was 27.1 years compared with 21.4 years in 1970.[2,3] In the United Kingdom (UK) the proportion of

maternities in women aged 35 years or over has increased from 8% in 1985-87 to 20% in 2006-2008 and in women aged 40 years and older has trebled in this time from 1.2% to 3.6%. According to the National Family Heath Survey 4 (NFHS-4), the percentage of unwanted births increases with maternal age (one percent for women <20 years, while 33 percent for women between 45 to 49 years). Pregnancy in the elderly is associated with a lot of complications to both mother and the foetus. Fertility decreases as age increases.

According to the Ministry of Health and Family Welfare (MoHFW), India (2017 data), the age specific fertility rate in Kerala is 101.2% (in age group between 20-24 years), 129.7% (25-29 years), 74.2% (30-34 years), 23% (35-39 years), 2.6% (40-44 years) and 0.5% (45-49 years). The percentage of women who ever had a non-live birth increases with age, peaking between 30 to 34 years (NFHS-4). Advanced maternal age is even associated with maternal near miss and maternal deaths.[4] AMA (advanced maternal age) is associated with a wide range of adverse pregnancy outcomes including miscarriage, chromosomal abnormalities, stillbirth, foetal growth restriction (FGR), preterm labour, preeclampsia, gestational diabetes mellitus (GDM) and increased rates of caesarean section (CS). The purpose of this study is to review the impact of maternal age on a range of adverse pregnancy outcomes in order to assist in accurate counselling of women considering delaying pregnancy or those who are already pregnant and concerned about the risk of developing complications due to their age.

The southern state of Kerala has a literacy rate of 96.2% with 96.11% in males and 92.07% in females, according to the 2011 population census. Also a highly career oriented life of Kerala women, especially in their early reproductive years which we consider as low risk, leads to late conception. Hence a study about the pregnancy outcome in the elderly gravidae in Thiruvananthapuram, the capital city of Kerala will help in anticipating risk factors. It will also improve early diagnosis and management of the various complications and comorbidities in them.

METHODS

This is a prospective cohort study conducted in Government medical college, Thiruvananthapuram. All women with a singleton pregnancy at or above 20 weeks of gestation were selected till we obtained a sample size of 200 in exposure cohort (at or above 35 years) and 200 in control cohort (below 35 years). Consecutive sampling technique was used.

The major outcomes that are studied include onset of labour, pregnancy outcome, mode of delivery, primary caesarean section rates, indications of caesarean section and PPH.

The onset of labour will be recorded as either spontaneous or induced. Another category included CS before labour.

Both study group and control group will be followed up to study their pregnancy outcomes which may be one among the following:

Second trimester abortion was an expulsion of a foetus between 20-24 weeks gestation, IUD- death of a foetus above 24 weeks gestation in utero. Preterm delivery was a birth of a live child above 24 weeks gestation but below 37 weeks gestation. Term delivery was a birth of a live child at or above 37 weeks gestation. The mode of delivery will be noted as vaginal delivery/caesarean section, instrumental delivery (forceps or vacuum). In case of caesarean section, the following details will be documented. Postpartum haemorrhage is defined as blood loss more than 500 ml in normal delivery or more than 1000 ml in a caesarean section.

RESULTS

The study group consisted of elderly gravidae who were pregnant women aged more than or equal to 35 years. The mean age distribution of the study group in this study was 37.1±2.2. The control group included pregnant women between 19 to 34 years age and the mean age distribution of the control group in this study was 25.2±3.3 (Table 1).

Table 1: Mean age distribution of the study population.

Category	N	Age in years		p
		Mean	SD	
Control	200	25.24	3.333	<0.001
Case	200	37.11	2.279	

Induction rates were higher among the control group while caesarean section before labour was common in the elderly gravidae. Among the elderly gravidae, 47% had spontaneous onset of labour, 33.5% were induced and 19.5% had caesarean section before labour while among the younger gravidae, 41.5% had spontaneous onset of labour, 50% were induced and 8.5% had caesarean section before labour (Table 2).

There was a significant increase in the rates of second trimester abortions, intrauterine death and preterm delivery among the elderly group. There were no second trimester abortions among the younger gravidae while it was 5.5% among the elderly. The percentage of IUD was 1.5% among the younger group and 3.5% among the elderly group. Preterm delivery rates were 32% and 24.5% among the study group and control group respectively (Table 3).

Caesarean section rates were significantly higher among elderly gravidae. 51% of the elderly gravidae had undergone caesarean section while only 32.5% of the younger women underwent caesarean section. Instrumental delivery and caesarean hysterectomy were slightly higher among the control group (Table 4).

Primary caesarean section rates were observed to be significantly higher among the younger gravidae group, which may be probably due to the more number of primigravid population in this group. The primary caesarean section rate was 39.4% in the elderly group, while it was 69.8% in the younger population (Table 5).

Table 2: Onset of labour among the study group and control group.

Onset of labour	Control group		Study group		Total		χ^2	df	p
	N	%	N	%	N	%			
Spontaneous labour	83	41.5	94	47	177	44.3	15.85	2	<0.001
Induced labour	100	50	67	33.5	167	41.8			
CS before labour	17	8.5	39	19.5	56	14			
Total	200	100	200	100	400	100			

Table 3: Pregnancy outcome among study group and control group.

Pregnancy outcome	Control group		Study group		Total		χ^2	df	p
	N	%	N	%	N	%			
Second trimester abortion	0	0	11	5.5	11	2.8	17.98	3	<0.001
IUD	3	1.5	7	3.5	10	2.5			
Preterm delivery	49	24.5	64	32	113	28.2			
Term delivery	148	74	118	59	266	66.5			
Total	200	100	200	100	400	100			

Table 4: Mode of delivery among study group and control group.

Mode of delivery	Control group		Study group		Total		χ^2	df	p
	N	%	N	%	N	%			
Normal vaginal delivery	130	65	96	48	226	56.5	15.51	3	0.001
C section	65	32.5	102	51	167	41.8			
Instrumental delivery	2	1	0	0	2	0.5			
Caesarean hysterectomy	3	1.5	2	1	5	1.3			
Total	200	100	200	100	400	100			

Table 5: Primary caesarean section rates among study group and control group.

Primary CS	Control group		Study group		Total		χ^2	df	p
	N	%	N	%	N	%			
No	19	30.2	63	60.6	82	49.1	14.53	1	<0.001
Yes	44	69.8	41	39.4	85	50.9			
Total	63	100	104	100	167	100			

Table 6: Indications of caesarean section among the study group and control group.

Indication of C section	Control group		Study group		Total	
	N	%	N	%	N	%
Arrest of descent	3	4.8	1	1	4	2.4
Previous CS	20	31.7	57	54.8	77	46.1
MSAF	4	6.3	1	1	5	3
Decreased FM	0	0	4	3.8	4	2.4
FGR stage 2/3	3	4.8	4	3.8	7	4.2
Placenta previa	4	6.3	8	7.7	12	7.2
Pathological CTG	6	9.5	3	2.9	9	5.4
Maternal request	0	0	6	5.8	6	3.6
Failed induction	8	12.7	8	7.7	16	9.6
Severe pre-eclampsia	1	1.6	1	1	2	1.2
Cord prolapse	0	0	2	1.9	2	1.2
Breech	6	9.5	6	5.8	12	7.2

Continued.

Indication of C section	Control group		Study group		Total	
	N	%	N	%	N	%
CPD	4	6.3	3	2.9	7	4.2
Abruption	2	3.2	0	0	2	1.2
Eclampsia	1	1.6	0	0	1	0.6
Brow presentation	1	1.6	0	0	1	0.6
Total	63	100	104	100	167	100

Table 7: Incidence of postpartum haemorrhage among the study group and control group.

PPH	Control group		Study group		Total		χ^2	df	p
	N	%	N	%	N	%			
No	198	99	190	95	388	97	5.50	1	0.019
Yes	2	1	10	5	12	3			
Total	200	100	200	100	400	100			

As far as the various indications of caesarean sections are concerned, previous caesarean was the commonest indication among the elderly, owing to the higher prevalence of multigravida and multiparous women in this group. The other indications that were slightly higher among the study group were decreased foetal movements, placenta previa, maternal request and cord prolapse (Table 6).

The incidence of postpartum haemorrhage (PPH) was significantly higher among the elderly gravidae. 5% of the elderly women developed PPH while only 1% of the younger gravidae developed PPH (Table 7).

DISCUSSION

The present study aims at demonstrating the association between advanced maternal age and adverse pregnancy outcome. Several other studies for studying this association, both hospital based and population based, as well as both prospective and retrospective studies have been conducted previously in various other countries as well as in Northern states of India. The results of majority of these studies are comparable to the present study.

The mean age of the study group was 37.1 years while that of the control group was 25.2 years.

Induction rates were observed to be higher among the control group (50%), while majority of the elderly women underwent caesarean section before labour onset (19.5%). These differences were statistically significant. In contrast, a study by Zapata-Masias et al demonstrated higher incidence of induced delivery among the elderly.[5] While, the finding of our study was similar to the study by Jacquemyn et al where induction of labour was significantly less in the older group.[6] A meta-analysis by Pinheiro et al supported that AMA women were more likely to undergo induced labour.[7] Kim et al found that labour induction increased the risk of emergency CS in elderly women above 35 years.[8]

Significant rise in the rates of second trimester abortions, preterm births and Intrauterine death were observed in the elderly group (p<0.001).These findings were consistent with previous studies. A 10 year birth database study in Scotland from 1994 to 2003 by Sutan et al showed that AMA was significantly associated with unexplained antepartum still birth.[9] A French study by Bouzaglou et al also showed a significant rise of preterm birth (p<0.001) and foetal death in utero (p<0.001) in elderly women above 40 years age.[10] A study in United States by Bahtiyar et al showed a significant increase in IUD rates with increasing maternal age (p<0.05) and the risk was highest for a maternal age of 40 to 45 years.[11] The US National Vital Statistics reports about foetal and perinatal mortality has shown that foetal mortality rates were higher among women aged above 35 years. Another study by Reddy, Ko and Willinger also reported a stillbirth risk of 1 in 382 in elderly women between 35 to 39 years age and 1 in 267 risk for women above 40 years, between 37 to 41 weeks gestation, when compared with younger age group.[12-14] Zapata-Masias et al revealed a higher incidence of preterm births among elderly, especially above 40 years age (p=0.001).[5] Ciancimino et al have also demonstrated higher preterm births among elderly women >35 years (p=0.001).[15] Another study by Jacquemyn et al showed significant rise in preterm births (both <35 weeks and <37 weeks as well as <29 weeks) in elderly.[6] In contrast to this, Islam et al observed no significant higher risk of stillbirth or preterm birth among the advanced age mothers.[16] A meta-analysis by Pinheiro et al showed higher stillbirth rates and preterm delivery rates among advanced maternal age women.[7] Barton et al found that nulliparous women above 40 years delivered at a significantly lower gestational age.[17] Frederiksen et al showed a higher incidence of preterm birth before 34 weeks gestation in elderly women above 40 years age, but no increased risk of stillbirth rates.[18] Celik et al found no differences in preterm birth and stillbirth rates between cases (>40 years) and controls (21-35 years).[19] Scime et al found that advanced maternal age only modified the association between preterm birth and preeclampsia, such that older

women with preeclampsia experience a higher risk for preterm birth than younger counterparts.[19] Marozio et al found a higher incidence of preterm birth in elderly women.[20]

The instrumental delivery rates in our study were slightly higher in the younger age group although statistically insignificant. Jacquemyn et al also proved that instrumental deliveries were less commonly used among the elderly.[6]

Caesarean section rates were significantly higher among elderly gravidae (51% in elderly and 32.5% in younger age) (P value 0.001). Pradhan et al demonstrated a higher incidence of C sections (29.52%) among the elderly.[21] Bouzaglou et al demonstrated significant increase in both scheduled caesarean section as well as emergency caesarean section (p<0.001) among elderly women >40 years.[10] Ciancimino et al showed higher rates of iterative caesarean section among elderly (p=0.026)(15). Higher c section rates in elderly was also supported in the study by Zapata-Masias et al. Islam et al also showed significantly higher caesarean delivery rates (15.6% in elderly vs 10.7% in younger age) among elderly.[5,16] Osmundson et al, in a study done in extremely advanced maternal age above 50 years, found that these women were less likely to undergo a trial of labour; however majority (74%) who underwent a trial of labour experienced a vaginal delivery.[22] A meta-analysis by Pinheiro et al showed that AMA women were more likely to undergo elective caesarean deliveries.[7] Barton et al found a greater incidence of caesarean delivery among nulliparous women above 40 years age.[17] Jean-ju Sheen et al also found higher caesarean delivery rates in women aged 45-54 years.[23] Celik et al found no differences in the route of delivery between cases (>40 years age) and controls (21-35 years age).[19] Bergholt et al found that in nulliparous women with induced labour, the rate of caesarean section increased from 14% in women less than 20 years of age to 39.9% in women 40 years or older.[24] In multiparous induced women, the risk of caesarean section was 3.9% in women less than 20 years to 9.1% in women 40 years or older. Callaway et al also demonstrated increased caesarean section rates in women of very advanced maternal age.[25]

The primary C section rates were significantly higher (p<0.001) in the younger age group (69.8% in younger and 39.4% in elderly) probably due to higher parity among the study group. This finding was in contrast to the results of Ciancimino et al who showed that first caesarean section was not significantly higher in elderly population (p=0.145).[15] Both primary and secondary caesarean section rates were found to be higher in the elderly in a study by Jacquemyn et al.[6]

Previous caesarean was the foremost cause among the elderly accounting for 54.8% while other indications were comparatively less common. The other indications that were slightly higher among the study group were decreased foetal movements, placenta previa, maternal request and cord prolapse. Timofeev et al, in their retrospective analysis found that previous uterine scar was the leading indication for caesarean delivery in women aged 25 or older, while for younger women, CPD, failure to progress and non-reassuring FHR were the predominant indications.[26] Kim et al proved that advanced maternal age was an independent risk factor for emergency CS due to non-reassuring FHR and arrest disorder during trial of vaginal delivery.[8]

The incidence of PPH was significantly higher among the elderly gravidae (p value 0.019). Pradhan et al showed a higher incidence if PPH (3.81%) among the elderly.[21] Jean-Ju Sheen et al in their retrospective cohort analysis showed a higher incidence of PPH in maternal age 45-54 years.[23] Luna Alvarez et al who compared women of 3 age groups (<35, 35-40, >40) found a higher incidence of PPH in women above 40 years of age.

CONCLUSION

Induction of labour was higher among the younger age group, while spontaneous onset of labour and caesarean section before labour were higher among younger age group. Caesarean section rates were higher in the elderly, while primary section rates were higher in the younger age group. The most common indications of caesarean section among the elderly were previous caesarean and placenta previa. AMA also was associated with increased risk of PPH. This outcome study will have a major influence in counselling of AMA women and a better antenatal and intrapartum care for this age group.

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