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Research Article

The perinatal and maternal outcome in pregnancy with advanced maternal age 35 years and >35 years

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ABSTRACT

Background: Purpose of this study is to evaluate maternal and perinatal outcome in advanced maternal age women. As numbers of pregnancies in advanced maternal age continue to grow, obstetric care provider would benefit from up to date outcome data to enhance their preconceptional and antenatal counseling.
Methods: It is observational prospective analytic study, conducted in Nowrosjee Wadia maternity hospital, Parel, Mumbai. Total 100 patients were included in study, fulfilling inclusion criteria over period of 1 year.
Results: In 100 patients, most common cause of delay conception is infertility (27%). 24% of patients conceived after treatment. out of 100 patients 23% of patients had pre-existing medical and surgical disorders, 50% developed complications in pregnancy. Out of 100 patient 58 patients undergone through biochemical study, 3 patients had high risk for chromosomal disorders. The rate of caeasarean section in our study is 68%. Perinatal mortality and morbidity is high in our study, rate of preterm delivery is 23.7%. Out of 105 babies (including multiple gestation), 42.8% babies are low birth weight out of which 9.5% babies are very low birth weight. Rate of NICU admission is 33%, perinatal mortality rate, neonatal mortality rate and still birth rate is 19.4 per 1000 births. Advanced maternal age is related to high maternal and perinatal morbidity and mortality rate.
Conclusions: Pregnancies in women of advanced maternal age are considered high risk for Perinatal and maternal morbidity and mortality. A proper preconception consultation and intensive antenatal care assessment can individualize and potentially reduce the risks for women with advanced maternal age.

Keywords: Advanced maternal age, Maternal outcome, Perinatal outcome

INTRODUCTION

Advanced maternal age, defined as age 35years and older at estimated date of delivery. There is a growing trend for child-bearing to occur later in women's lives. Many of the reasons why women are choosing to postpone child-bearing reflect the availability of safe, effective, and reversible contraception, which has allowed women the reproductive autonomy to decide if and when they will have children. In pursuit of higher education and entry work force and career advancement outside the home, delayed marriage, increased rate of divorce followed by remarriage all contribute to this upward trend. In a developing country like India, this trend is sometimes because of multiparity in view of male child and poor acceptance of contraceptive method.[1-3]

After 35 years of age, fecundity decreases, and the chance of miscarriage, spontaneous abortion, pregnancy complications, and adverse pregnancy outcomes (including PTD and multiple birth) increases. As women age, many opt for fertility treatment to improve their chance of conception. The effectiveness of various reproductive technologies declines steadily after the age of 35, while the risk of pregnancy complications and adverse outcome increases with both maternal age and the use of reproductive assistance.[4-8]

Purpose of this study is to evaluate maternal and perinatal outcome in advanced maternal age women. As number of pregnancies in advanced maternal age continues to grow, obstetric care provider would benefit from up to date outcome data to enhance their preconceptional and antenatal counselling.

METHODS

Inclusion criteria

All pregnant women age 35 years or above 35 years with:

1. Single/multiple pregnancy
2. Mother with any pre-existing medical history i.e. hypertension, pregnancy induced hypertension, diabetes mellitus, gestational diabetes militias, anaemia, fibroids etc.
3. Conceived spontaneously/after treatment

This study initiated only after the ethics committee permission. This is prospective observational study, conducted in Nowrosjee Wadia Maternity Hospital, Parel.

100 patients fulfilling the inclusion criteria were enrolled. Signature and consent of the patient taken at the time of study. At any point of the study if the patient fell short of the laid criteria she was omitted from the study and the next patient taken.

Both indoor and outdoor patients were included in study. Each one of them was evaluated by detailed history which included the menstrual, obstetric and clinical examination.

Patient was followed up once monthly till 28 weeks, once fortnightly till 36 weeks and weekly there after till term. Minimum 3 to 4 visits are necessary. More frequent visits in high risk pregnancies like PIH, GDM, D.M, primary infertility etc. We observed the effect of advance maternal age on fetal growth closely.

1. Patient who had registered in first trimester were subjected to - USG for NT and NB, Dual marker biochemical study.
2. In 2nd trimester or who registered in 2nd trimester (before 20wk) were subjected to malformation scan, triple marker or Quadruple biochemical screening.

After 20 weeks of gestations-only malformation scan was performed.

Patient showing high risk in above screening test were managed according to routine obstetrics protocol. The patients were followed up to the delivery and 4 days post-delivery.

Perinatal outcome was recorded in terms of birth weight, any chromosomal abnormalities, gestational age of delivery, NICU admission, cause of NICU admission, NICU course.

Maternal outcome was recorded in terms of mode of delivery, obstetric complication, and systemic complications.

Preterm labour was defined as onset of labour before 37 completed weeks of gestation. Low birth weight was defined as <2.5 kg.

Outcome

Outcome of the study calculated in terms of fetal outcome - average birth weight, chromosomal/congenital anamolies, gestation age at delivery, NICU admission and maternal outcome - mode of delivery, obstetrics complications, systemic complications.

RESULTS

Table 1: Reason for late conception.

Reason for late conception	Frequency	%
Both, primary and secondary infertility	3	3.00%
Late marriage	24	24.00%
Multigravida	22	22.00%
Planned pregnancy	3	3.00%
Primary infertility	23	23.00%
Secondary infertility	24	24.00%
Unplanned pregnancy	1	1.00%
Total	100	100.00%

Table 2: Mode of conception.

Spontaneously/after treatment	Frequency	%
IUI conception	1	1.00%
IVF conception	13	13.00%
Male infertility	1	1.00%
OI	9	9.00%
Spontaneously	76	76.00%
Total	100	100.00%

Purpose of this study was to evaluate maternal and perinatal outcome in advanced maternal age.

Total 100 patients were included in study, fulfilling inclusion criteria over period of 1 year.

Reason for late conception

Most common causes of late conception in our study was late marriage and secondary infertility (24%) followed by primary infertility (23%) followed by multiparity (22%).

In the pursuit of higher education, a stable job, securing a higher salary, and for increasing career prospects, women

are postponing their conception and with increasing age fertility rate is reduced and rate of infertility increases.

Table 3: Distribution of pre-existing medical and surgical illness.

Pre-existing medical/surgical illness	Frequency	%
Uterine fibroid	8	8.00%
HTN	5	5.00%
DM	3	3.00%
Ectopic pregnancy	2	2.00%
Beta thalassemia trait	1	1.00%
Chronic liver disease	1	1.00%
Epilepsy	1	1.00%
HBSAG positive	1	1.00%
Vaginal septum removed	1	1.00%

Table 4: In pregnancy complications.

In pregnancy complication	Frequency	Percent
GDM	15	15.00%
PIH	15	15.00%
Gestational HTN	4	4.00%
Pre-eclampsia	2	2.00%
Hypothyroid	12	12.00%
PPROM	6	6.00%
Twins	8	8.00%
Placenta previa	5	5.00%
Malpresentation	6	6.00%
Miscarriage	2	2.00%
Stillbirth	2	2.00%
Oligohydramnios	2	2.00%
Chromosomal abnormalities	1	1.00%
Abruption	1	1.00%
No	50	50.00%

There is 1% of accidental pregnancy because of poor acceptance of contraception, 3% are planned pregnancies and 3% are having history of bad obstetric history with secondary infertility.

Mode of conception

Out of 100 cases, 76% conceived spontaneously and 24% conceived after treatment.

Out of 50% infertility cases 24% conceived after treatment and 26% conceived spontaneously.

In our study 13% cases were IVF conceptions, 9% cases are conceived on ovulation induction and 1% case conceived on IUI.

There was one case of male infertility in our study, patient conceived after treatment of male factor.

Rise in the proportion of pregnancies achieved with assisted reproductive techniques (ART) has reflected in subsequent increased incidence of twin gestation. The superovulation in ARTs is responsible for the release of two or more ova in a single menstrual cycle and so increased incidence of multiple pregnancies.

In our study out of 8 twins, 6 were conceived after in vitro fertilisation and 2 were conceived spontaneously.

Table 5: Biochemical screening.

Biochemical screening	Frequency	%
Yes	58	58.00%
No	42	42.00%
Total	100	100.00%

Pre-existing medical/surgical illness

It is known that older women are more likely to have pre-existing medical disorders such as diabetes mellitus hypertension, some chronic illness and pre-existing surgical disorders like uterine fibroid and past surgical history.

Most common pre-existing medical condition associated with advanced maternal age was hypertension (5%) and diabetic mellitus (3%) in our study.

4% of cases had chronic medical conditions like epilepsy (1%), beta thalassemia trait/anaemia (1%), chronic liver disease (1%) and HBsAG positive (1%).

In our study 2% of cases had history of ectopic pregnancy which indicates advanced maternal age is a risk factor for ectopic pregnancies. This is due to an accumulation of risk factors over time, such as pelvic infection, and tubal pathology and ARTs and one case had history of vaginal septum removal which is one of factor which affects conception.

In pregnancy complications

It is well established that advancing maternal age is associated with the higher incidence of antepartum complications such as miscarriage, fetal chromosomal abnormalities, pregnancy induced hypertension, pre-eclampsia, gestational hypertension, gestational diabetes, placenta previa, placental abruption, twin gestation, preterm premature rupture of membrane, oligohydramnios and malpresentation have been documented.

In our study there was 15% risk of gestational diabetic mellitus, 15% risk of pregnancy induced hypertension, 4% risk of gestational hypertension, 2% risk of pre-eclampsia, 12% risk Of hypothyroidism, 6% risk of preterm premature rupture of membrane, 8% risk of multiple gestation,5% risk of placenta previa, 6% risk of

malpresentation, 2 % risk of miscarriage, 2% risk of still births,2% risk of oligohydramnios, 1% risk trisomy 21 and 1% risk of abruption. 50% patient doesn't have any in pregnancy complications.

Table 6: Invasive procedure.

Biochemical screening	Result	Amniocentesis	Result	Count	%
Yes	High risk	Yes	Normal	3	3%
			Trisomy 21	1	1%
		No		2	2%
	Low risk	Yes	Normal	1	1%
		No		51	51%

Table 7: Mode of delivery.

Mode of delivery	Frequency	%
LSCS	66	68.04%
Vaginal delivery	31	31.96%
Total	97	100.00%

Biochemical screening

It is the standard of care to offer all pregnant women with advanced maternal age, non-invasive screening for chromosomal aneuploidy using various combinations of ultrasound and maternal serum markers to adjust the mother's age related risk. Women whose screening tests suggest a high risk of aneuploidy are offered diagnostic invasive testing (amniocentesis, chorionic villus sampling).

In our study, biochemical screening was done in 58 patients, of the others some patients are registered late and others refused to do this screening because of some financial problems.

Out of 58 patients who did biochemical screening, 6 patients were diagnosed as high risk for chromosomal abnormalities and other 52 patients were low risk for chromosomal abnormalities.

Out of 6 patients which were high risk, 4 patients were subjected to invasive confirmative procedure and 2 patients refused invasive testing because of cost.

The 4 patients who were subjected to invasive procedure one fetus diagnosed as trisomy 21 which was terminated. Other 3 fetus were chromosomally normal.

Out of the 52 low risk patients one patient subjected to invasive procedure in view of previous history of trisomy 21 which came out normal.

Post-delivery biochemically low risk babies were healthy, not suspected to have any chromosomal abnormalities. This indicates biochemical screening with nuchal scan has higher efficacy to diagnosed chromosomal abnormalities. It's not necessary to performed invasive procedure in all advanced maternal age with avaibility of such highly efficient screening procedure.

Table 8: Reason of LSCS.

Reason of LSCS	Frequency	%
Abnormal colour Doppler	1	1.52%
Absent fetal movement	1	1.52%
Cord prolapse	2	3.03%
Deep transfer arrest	1	1.52%
Fetal distress	7	10.61%
Malpresentation	5	7.58%
MSAF	4	6.06%
Noninducible cervix	1	1.52%
NPOL	3	4.55%
Placenta previa	4	6.06%
Precious pregnancy	4	6.06%
Previous LSCS	23	34.85%
Prolonged lacking per vaginum	2	3.03%
Twins	7	10.61%
Worsing preeclampsia	1	1.52%
Total	66	100.00%

Mode of delivery

Out of 97 patients (excluding 2 miscarriages and 1 MTP) 66 patients delivered by caesarean section and 31 patients delivered by vaginal delivery.

Rate of caesarean section is higher in advanced maternal age.

There are various reasons which contribute to higher section rate in advanced maternal age.

Most common reason for caesarean section was previous LSCS, 23 (34.8%) patient out of 66 underwent to caesarean section.

Next common cause of caesarean section was twin gestation (10.61%) and fetal distress (10.61%).

The third most common cause were malpresentation (7.58%) which is common in advanced maternal age due to poor abdominal tone and uterine fibroids followed by placenta previa (6.06%) and precocious pregnancy (6.06%).

Sometime the physician's attitude contributes to the higher rate of Caesarean births in older gravidas by considering them to be at high risk or their pregnancies to be more precious.

Other causes were non-progress of labour followed by prolonged leaking per vaginum (4.55%) and cord prolapsed (3.03%)

Table 9: Distribution of babies delivered tern/ preterm.

Term/pre-term	Frequency	%
PRETERM	23	23.70%
TERM	74	76.30%
Total	97	100.00%

Table 10: Weight distribution of babies.

Baby weight	Frequency	%
Below 1 Kg	2	1.90%
1 to 1.4 Kg	8	7.61%
1.5 to 1.9Kg	13	12.38%
2. to 2.4 Kg	22	20.95%
2.5 to 2.9 Kg	36	34.28%
3 to 3.9 kg	24	22.85%
4kg and above	0	0%
Total	105	100.00%

Term/preterm delivery

In our study out of 97(excluding 1 MTP and 2 miscarriages) deliveries 74 were term deliveries and 23 were preterm deliveries.

With higher incidence of multiple gestation and pre-existing/superimposed medical problem, risk of preterm deliveries is higher in advanced maternal age.

Careful antenatal monitoring and vigilance is required throughout pregnancy.

Baby weight

In our study total 105 babies were born (including twin pregnancies), the below chart shows the weight distribution of the babies in this group.

Out of 105 babies, 45 (42.85%) babies were low birth weight.

Out of there 45, 10 babies (9.5%) were very low birth weight.

The other 60(57.14%) babies were adequate for birth weight.

Incidence of multiple gestations, pregnancy induced hypertension; other medical disorder is high in very low birth weight babies. It indicates with underlying medical disorders risk of low birth weight were high.

Table 11: Number of NICU admission.

NICU admission	Frequency	%
Yes	34	33.00%
No	69	67.00%
Total	103	100.00%

NICU admissions

Total 103 live babies (excluding 2 still births), 34 babies (33%) were admitted in NICU for various reason. It includes PTD, LBW, GDM mother, distress, meconium stained liquor etc.

Table 12: Outcome of study.

Outcome	Frequency	%
Still birth rate	2	19.4 per 1000 birth
Neonatal mortality rate	2	19.4 per 1000 birth
Perinatal mortality rate	2	19.4 per 1000 birth
Maternal mortality rate	0	0
Post neonatal mortality rate	2	19.4 per 1000 birth

Outcome of study

Maternal mortality rate in our study was nil. Nonavaibility of maternal intensive care unit in our institute ,we referred high risk patients who need an intensive care unit to higher tertiary health care for further management.

DISCUSSION

The objective of this report is to provide an update of our current knowledge about the impact of maternal age on pregnancy outcome. Pregnancy in women 35 years old is associated with a higher maternal and perinatal mortality. The older gravida also has a higher chance of being delivered by Caesarean section. Most of the complications associated with older age are caused by age-related confounders such as leiomyomas, type II diabetes, hypertension and multiparity. Diabetes and hypertension increase almost linearly with age. Pregnant women with diabetes or hypertension are at increased risk of adverse pregnancy outcome irrespective of age.

It is generally assumed that women >35 years have an increased risk for complications during pregnancy. However, most reported age-related risk factors are only indirectly related to age through their association with age-dependent confounders such as hypertension, diabetes, high parity, uterine myomas and a history of infertility

With increasing age the rate of spontaneous conception reduced. Moreover, the likelihood of a successful response to ovarian stimulation resulting in egg retrieval decreases as the woman ages and this, compounded by the fact that older women have a poor ovarian response, makes women aged 35 years or older less than ideal candidates for ARTs. In our study incidence of infertility was 50%, of which 13% conceived on IVF, 9% conceived on ovulation induction, 1% conceived on IUI conception and other conceived spontaneously.

The most important effect of ageing on the cardiovascular system is a gradual loss of compliance. Thus the normal hemodynamic adaptation to pregnancy becomes more difficult with advancing age. Thus incidence of hypertension is more common in this age group. In our study incidence of pregnancy induced hypertension was 15%, gestational hypertension 4%, chronic hypertension 5%, and preeclampsia 2%.

With increasing age incidence of diabetes also increased, incidence in our study was 15%.

With increasing age risk of malpresentation was increased due to uterine fibroids and poor abdominal muscle tone. Our study shows incidence of fibroid as 8% and incidence of malpresentation 6%.

As a woman ages, the chance of having an aneuploidy pregnancy increases. Most common cause of miscarriage in advanced maternal age is aneuploidy. Incidence of miscarriage in our study is 2% and aneuploidy is 1%.

Incidence of placenta previa 5% and abruption 1%, with high risk of hypertension risk of abruption is high in advance maternal age.

The increasing rate of caesarean in aged women and claimed that there would be many reasons for this, including basic diseases, obstetric troubles, neonatal problems and decrease of the function with the increasing age of women. In our study incidence of caesarean section is 68%.

With higher incidence of multiple gestation and underlying medical disorder, risk of preterm delivery and low birth weight increases.

In our study incidence of preterm delivery 76.3%, low birth weight 42.8%.

Most of admissions in NICU are due to preterm deliveries and low birth weight.

The still birth rate in our study is 19.04 per 1000 births, the neonatal mortality rate is 19.4 per 1000 births, perinatal mortality rate is 19.4 per 1000 births, post natal mortality rate is 19.4 per 1000 births. There is no maternal mortality in this study.

In summary, as women become older, they become increasingly prone to perinatal complications above and beyond the medical complications concomitant with aging.

This study better defines the importance of both counselling and following patients for specific adverse outcomes associated with advancing maternal age. Patients aged 35 years and older are at an increased risk for miscarriage and fetal chromosomal abnormalities, many of which may be diagnosed prenatally. Age 35 years and older is an independent risk factor for gestational diabetes, placenta previa, placental abruption, caesarean delivery and perinatal mortality. The role of routine antenatal surveillance in women aged 35 years and older requires further investigation because these women seem to be at increased risk for perinatal mortality, including stillbirth. Although the likelihood of adverse outcomes increases along with maternal age, patients and obstetric care providers can be reassured that overall maternal and fetal outcomes are favourable in this patient population.

Study conducted in Department of Public Health, University of Limpopo (Medunsa Campus), South Africa. It is retrospective comparative study, conducted from 1st September to 30th November 2010 where the pregnancy outcomes of females who were more than 35 years old (advanced age women) were compared with adult women (aged between 20 and 34 years).

In this study maternal age was significantly associated with preterm delivery as advanced age women (19.2%) had higher rate of preterm delivery compared to adult women (14.7%) [p<0.026]. Mode of delivery was also associated with maternal age as caesarean delivery was more common among advanced age women (38.4%) compared with adult women (35.3%) [p<0.001]. Breech presentation was statistically more common among advanced age women (7.0%) compared to adult women (3.9%) [p=0.020]. Similarly, LBW rate was significantly higher among advanced age women (27.9%) compared to adult women (18.8%) [p<0.001]. Perinatal outcomes such as FSB and MSB rate was higher among advanced age women (5.6%) but the rate was not significantly high as compared to adult women (4.8%) [p=0.825]. The results show that advanced age women were 1.37 times more likely to have preterm delivery compared to adult women. Also advanced aged women were 1.67 times more likely to deliver LBW babies compared to adult women.[9]

A retrospective study conducted in the North West Thames Region, UK, between 1988 and 1997 by Jolly M, Sebire N, Harris J, Robinson S and Regan L. In this study a higher proportion of the women aged >35 years had gestational diabetes, hypertension, placenta praevia and a fetus with a breech presentation (malpresentation). There was no increased likelihood of anaemia in the older women and the increased risk for preeclampsia was only just significant in the 35–40 year old women. Rate of caesarean section is higher in advanced maternal age. Despite the higher proportion of older women having a fetus with a breech presentation, fewer had a vaginal breech delivery. The risk for preterm delivery and stillbirth was significantly greater in the older women. The incidences of small for gestational age and large for gestational age babies were higher in the older women.[10]

In population-based cohort study using the Centers for Disease Control and Prevention's "Linked Birth-Infant Death" file data. For this study, we assembled a 10-year cohort using data for the years 1995 to 2004 study findings concur with the literature in that advanced maternal age is an independent risk factor for having a stillbirth. The risk of stillbirths appeared to increase with increasing maternal age from 3.09/1000 births among 25- to 29-year and 8.89/1000 among women aged >45.[11]

CONCLUSION

Pregnancy and delivery are never risk-free.

As obstetricians and gynaecologists, we 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.

1. A proper preconception consultation and intensive antenatal care assessment can individualize and potentially reduce the risks for women considering a pregnancy at any age.
2. The rising trends of obstetric complications was observed in patients > 35 years of age so this group of patients should be considered as one of the obstetric high risk category and they need special attention and vigilant care in the multidisciplinary tertiary care centre.
3. With higher incidence of chromosomal abnormalities, women ≥ 35 years of age should be offered screening for fatal aneuploidy. With availability of non-invasive, sensitive biochemical tests in combination with nuchal scan, need for invasive procedures greatly reduced.
4. There is 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 contributes to the higher rate of Caesarean births in older gravidas by considering them to be at high risk or their pregnancies to be more precious.

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