Research Article

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PREGNANCY OUTCOME IN WOMEN OF ADVANCED MATERNAL AGE

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Abstract: To study the incidence and general outcome of pregnancy in advanced maternal age attending IMCH for delivery from July 1st 2008 to June 30th 2009. To compare the pregnancy outcome of gravitas of AMA and the younger counter parts with special reference to incidence of pregnancy morbidities like GDM, hypertension, abnormal placentation, incidence of LSCS and other instrumental delivers, preterm deliveries and neonatal outcome and maternal mortality. A prospective study of all women of advanced maternal age (≥35 yrs) admitted for delivery in Institute of Maternal and Child Health (IMCH) during a period of one year. The study design is Prospective cohort study and it was conducted in Institute of Maternal and Child Health, Calicut, a Tertiary referral center catering to around 16000-18000 deliveries per year, with 508 beds. The duration of study period is one year, July 1st 2008 to June 30th 2009. Data was collected by interviewing subjects, their relatives, attending doctors and reviewing their records. The sample size is 286 women admitted to IMCH labour room above 35 years of age and 300 controls belonging to 20-25 years age group admitted to labour room for delivery. From the study results our conclusions are Incidence of Pregnancy in advanced maternal age is 1.78% in 2009. Treatment for infertility, Bad obstetric history, Hypertensive disorders of pregnancy, Gestational diabetes, Preterm delivery, Intrauterine growth restriction, Foetal distress, Still births, Cesarian section rate, and Co morbidities like leiomyomas and maternal mortality rates were more and statistically significant in Advanced maternal age compared to the younger counter parts.

Key word: Advanced Maternal Age, Pregnancy, Women

INTRODUCTION

A young mother giving birth is a social rather than a medical problem, whereas the reverse is true for older mothers. Advanced maternal age, generally held to signify age after 35 years at the time of delivery, it is a term that implies decreased fertility and increased risk. Most reports suggests 35yrs as the limit as recommended by the Council of International Federation of Gynecology and Obstetrics.

As a result of rising education levels among women, effective birth control and an increasing number of women in the work force, birth rate has been dramatically reduced in the recent years all over the world and the proportion of older women turning motherhood has considerably increased in the population. There is no doubt that the elderly gravida is somewhat more likely to encounter complications which are the natural process of growing older, but even more important is the fact that her diminishing chances of further pregnancies put more of a premium on the present one. The reasons for this shift toward later childbearing are multiple. Women are attaining higher educational levels than in previous decades, within non industrialized countries, the age of first birth and the interval, between births increases as women's status increases. Factors in particular that are related to this phenomenon are related to the free choice of a partner, women's education and the wealth of the family. Level of the education correlates with knowledge and use of contraception, age at first birth and total number of children. The changing role of women in the workplace, with more career opportunities available, has undoubtedly affected childbearing. Control fertility with increased contraceptive options plays a part. Likewise the availability of assisted reproductive technologies to older women allowed many to achieve pregnancy and childbearing. An oldest woman to conceive naturally was 57 years old; births to women as old as 66 years have been reported using assisted reproductive technology.

Pre-conception Issues:

Fertility declines with advancing maternal age. In 2002, fertility rates for women aged 35-39 years were 41.4/1000, for women aged 40-44 years 8.3/1000, and for women aged 45-54years 0.5/1000 as compared to 103.6/1000 for women aged 20-24 years and 113.6/1000 for women aged 25-29 years[1]. There are multiple factors both physiological and acquired that contribute to this diminished fertility with increasing age. Acquired pathology contributing to infertility, particularly tubal disease, also uterine fibroids and endometrial polyps also accumulates over time and may also play a role. Ovarian occyte reserve declines with age, oocyte quality diminishes over time as well[2].

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The risk of aneuploidy rises significantly with advancing maternal age[3,4]. Normal physiology predicts higher rates of aneuploidy with aging, errors accumulated over time seem to increase the risk of non-disjunction, leading to unequal chromosome products at completion of division. In a recent RCT involving pre-implantation genetic diagnosis for women of AMA aneuploidy rate was 43.2% of the tested embryos[5]. A woman's chance of progressing from the beginning of ART to pregnancy and live birth (using her own eggs) decreases at every stage of ART as her age increases (25.7% in younger versus 2.9% in older)[6]. Age specific risk for Trisomy 21 and chromosomal anomalies in 20 years is 1/1667 and 1/526 respectively and in above 35 years is 1/378 and 1/192 respectively.

First trimester complications:

Difficult to quantify the number of spontaneous abortions accurately, it is well established that older women are at increased risk. From the faster (First and Second Trimester Evaluation of Risk) trial, in which approximately 30,000 women at 10-14 weeks gestational age were enrolled in a prospective multicenter investigation of singleton pregnancies[7], revealed increasing rates of both threatened abortion and miscarriage with advancing maternal age. The leading cause of death in early pregnancy, ectopic gestation, remains one of the most significant obstetric complications older data suggests up to an 8-fold increased risk of ectopic pregnancy in women >35 years compared to younger women[8,9]Advanced maternal age (35-40 years) was associated with a small increased incidence in several congenital anomalies including all heart defects, tricuspid atresia, right outflow tract defects, hypospadias second degree of higher, other male genital defects and craniosynostosis[10]

Maternal complication:

Non genetic adverse outcomes reported in association with advanced maternal age include increased risk of (1) Gestational diabetes (2) hypertensive disorders of pregnancy (3) pre-term birth (4) abnormal placentation (5) cesarean section (6) Still birth (7) BOH.

Gestational diabetes:

Prevalence of diabetes increases with maternal age. Rate of overt diabetes and gestational diabetes increases 3-6 times in AMA[11,12,13]

Chronic hypertension:

More frequent in patients older than 35 yrs. Present in approximately 5% of pregnant patients. Patients who have chronic hypertension are more likely to develop superimposed pre-eclampsia[14], to deliver by cesarean section, placental abruption, congestive heart failure, IUGR, hypertensive encephalopathy etc. than normotensive patients.

Pre-eclampsia, Gestational hypertension:

It is defined as the development of hypertension with proteinuria after 20 weeks of gestation. AMA (Advanced maternal age) can be considered as one of the many risk factors for pre-eclampsia[15]

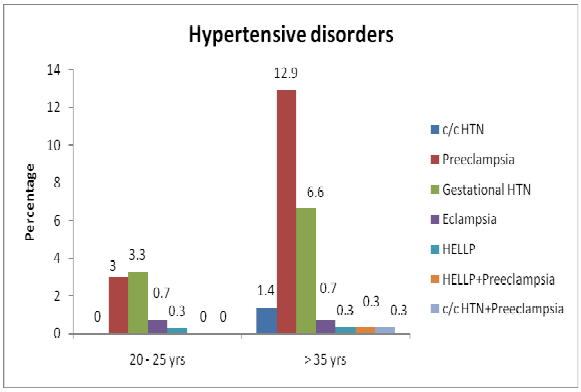

Figure.1: Hypertensive disorders of pregnancy

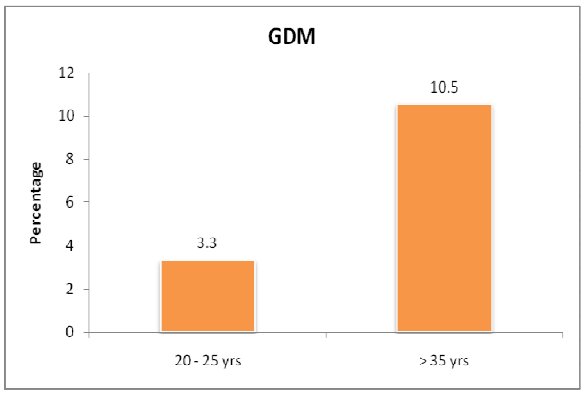

Figure.2: Gestational Diabetes

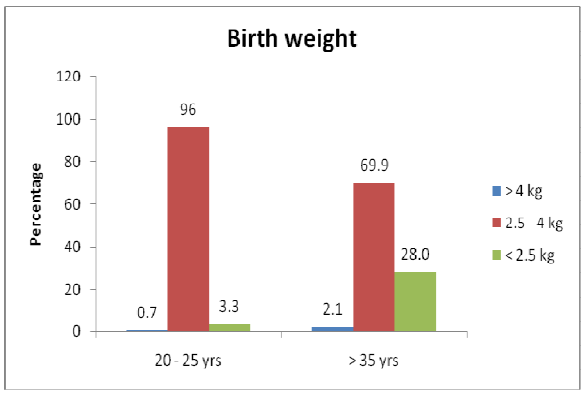

Figure.3: Birth Weight

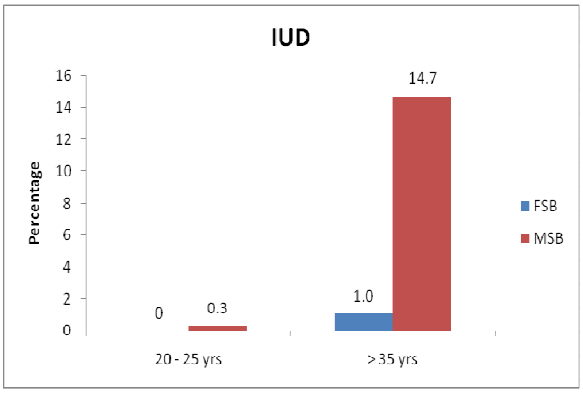

Figure.4: Intra uterine deaths

Table.1: Maternal mortality

	Advanced Maternal Age Group	Control Group
Maternal Mortality Rate	699.3	52.6*

(*P<0.05 significant compared control group with advanced age group)

Abnormal placentation:

Placental abruption and placenta previa. Lahmann and Chism reported placental abruption can occur in approximately 3.2% of pregnancies in AMA compared with 0.4% in younger counter parts.

Cesarean section and dysfunctional labour:

LSCS is performed with more frequent in women of AMA[13,16]. In some cases it is related to confounding problems such as HTN, pre-eclampsia, placental abruption or fetal macrosomia. Cesarean section is associated with increased maternal risk like Immediate Hemorrhage, infection, and aspiration pneumonitis. Hysterectomy following a cesarean section occur 10 times more frequently than vaginal delivery. The risk of maternal morbidity is 16 times more. Long term morbidity includes adhesions, bowel obstructions, bladder injuries and increased risk for placenta previa and ectopic gestation in next pregnancy.

Maternal mortality:

AMA is associated with increased risk of mortality[17,18]

Fetal complications:

AMA associated with increased incidence of multiple pregnancy, mal-presentations, IUGR, prematurity, perinatal morbidity[19]and perinatal mortality[20,17]. To summaries care of the pregnant patient of advanced maternal age is often the case of a high risk pregnancy. Co-morbidities (Pre-existing and pregnancy related) combined with high maternal expectation place these patients at greater need for intervention during pregnancy and parturition.

Aims and Objectives:

1. To study the incidence and general outcome of pregnancy in advanced maternal age attending IMCH for delivery from July 1st 2008 to June 30th 2009.
2. To compare the pregnancy outcome of gravidas of AMA and the younger counter parts with special reference to incidence of pregnancy morbidities like GDM, hypertension, abnormal placentation, incidence of LSCS and other instrumental delivers, preterm deliveries and neonatal outcome and maternal mortality.

MATERIALS AND METHODS

A prospective study of all women of advanced maternal age (≥35 yrs) admitted for delivery in Institute of Maternal and Child Health (IMCH) during a period of one year.

Study design:

Prospective cohort study

Inclusion criteria:

All pregnant women with advanced maternal age attending IMCH. Equal number of women between 20 and 25 years as control group.

Exclusion criteria:

Pregnant women less than 20 years and women between above 25years and below 35 years of age.

Study setting

Institute of Maternal and Child Health, Calicut, a Tertiary referral center catering to around 16000-18000 deliveries per year, with 508 beds.

Study period:

One year, July 1st 2008 to June 30th 2009.

Method of data collection

Data was collected by interviewing subjects, their relatives, attending doctors and reviewing their records.

Sample size:

286 women admitted to IMCH labour room above 35 years of age and 300 controls belonging to 20-25 years age group admitted to labour room for delivery.

Observations:

Statistical analysis was done using SPSS 16.0. Data was analyzed using chi square test and Fisher's exact test. A p value < 0.05 was considered as statistically significant.

Incidence:

Total number of Deliveries-16081
Total number of cases-286

Total Incidence of Advanced Maternal Age Pregnancy-1.78%.

Total Incidence of Primigravida in the Advanced Maternal Age-0.45%.

Age Group:

89.9% belonged to 35-40 years, 9.4% belonged to 41-45 age group,0.7% belonged to >45 years age group. The mean age group was 35.8years in this study. In the study group 65% were Multigravida were as in the control group 70% were primigravida. Marriage to conception interval in elderly primigravida was analyzed and found that 63.88% the interval was 2-5 years, whereas 97.14% of primigravida in 20-25 age groups conceived in 2 years. The study group 3 cases was >10 years. Age related difference in fecundity between 2 groups was significant statistically with a p=0.00001.

Treatment for Infertility:

54 (18.8%) cases of study group underwent treatment whereas only 3 (1%) cases in the control group underwent treatment. The result was statistically significant with p value of 0.00001. RR18.88 (5.97-59.7). BOH-there were a total of 28 (9.7%) cases with Bad obstetric history in the study group and 2 (0.6%) cases in the control group, p value of 0.00001 RR=14.69 (3.53-61.08).

Hypertensive disorders: of pregnancy were more among study group, RR=5.68 (3.14-10.29), p=0.00001.Preeclampsia, RR=4.31 (2.21-8.77), p=0.00001 and GHTN p=0.00001.Incidence of HELLP and Eclampsia were not significantly different p =0.74, p=0.67 resp.

Antepartum hemorrhage: There was no significant difference between the study group and control when incidence of APH was considered, p=0.08.Studies suggests an Increased risk of abruption as age increases and parity increases.

Gestational diabetes: the incidence in the study population was 10.5% and in the control group was 3.3%.In our study the rate of Gestational diabetes was significantly more in the study population p=0.002,RR=2.94(1.45-5.94). There was 2 cases of Overt Diabetes in the study group.

Uterine leiomyoma: 3.1% of the study population pregnancy was complicated by uterine leiomyomas, whereas no cases in the control population had myomas. This observation was statistically significant with a p=0.002.

Intrauterine growth restriction: 28% of the study population and 3.3% of the control group had growth restriction. The rate of growth restriction was more in the study population we could establish a statistical significance, p value=0.00001 RR=8.39 (4.44-15.87).

Preterm labor: 24.1% of the study group had preterm delivery and 5% of the control group had preterm delivery. This association between Advanced maternal age and preterm delivery in our study was found to be statistically significant, p value=0.00001, RR=4.83 (2.83-8.23).

Multiple pregnancy: rates were more in the study group, 1% and 0.3% in the control group. But we could not establish a statistically significant correlation between multiple pregnancy and advanced maternal age in our study.

Mal-presentation: Though the number of cases of Breech were more in the study population we could not establish a statistical significance between the groups, p value=0.21. There were 3 cases of brow and transverse lie in the control group only.

Foetal distress: the rate of foetal distress in the study group was4.2% and in the control group was 1.3%. The association between Advanced maternal age and foetal distress was significant statistically, p value=0.03, RR=3.15 (1.03-9.64).

Still birth: The study population had a still birth rate of 15.7%, the control group had a rate of 0.3%. So in our study we could establish that the rate of pregnancy loss in the advanced maternal age was significantly more, p value=0.00001, RR= 47.2 (6.55-340.18).

Mode of delivery: Vaginal delivery rate was 47.2%, Caesarean section rate was 48.3%, 1.1% was Instrumental delivery, VBAC was1.7%, and Assisted breech delivery was1.1%. In the control group 83.3% vaginal deliveries, 14% CS, 2.7%Instrumental delivery. In our study, the Caesarean section rate was significantly more in the advanced maternal age group, p value=0.00001, RR= 3.45 (2.54-4.68).

Chromosomal anomaly: one case of downs syndrome was reported in the study group, patient had irregular Antenatal checkups was referred to our institute for delivery from peripheral hospital.

Congenital anomaly: one case of multiple congenital anomalies and two cases of Congenital Talipes Equino Varus were noted in the study group.

Maternal mortality: There were 2 cases of mortality in the study group. The mortality rate in study group was 699.3/1 lakh and in the control group in our institute was 52.6/1 lakh live births. The mortality rate was more in the study group and was statistically significant with a P value of 0.016, RR 13.29.

DISCUSSION

Pregnancy after 35 is becoming a fact of life in our society and one should have a realistic approach to this problem. The most significant hurdle for older women is their age related risk of infertility, changes in uterine or hormonal function and oocyte quality. The incidence of Pregnancy in advanced maternal age in our institute is1.78%, among this group the incidence of elderly primigravida is0.45%. Incidence of elderly primi according to Stalworthy, UK 1.4%. According to Sahu *et al.,*[21] the mean age group was 35.8years in his study. Age related difference in fecundity between 2 groups was significant statistically with a p=0.00001. According to studies by Sahu *et al.,* [21]5.9% of his study population underwent treatment for infertility. The rate in our study 18.8% was more owing probably to the increased literacy, early access to treatment facilities Similar study by Sahu *et al.,* the rate of BOH were 13.1% of the case group our study it was 9.7%. Goldman J *et al.,*[22] found an increased incidence of hypertensive disorders in the AMA group. According to Bobrowskei *et al*., Preeclampsia was 3 times more and chronic hypertension was 5 times more in AMA group. According to Sahu *et al.,*[21] the rate of gestational diabetes in their AMA group was 4.1% in our study it was 10.5%. According to Leeks *et al.,* Advanced Maternal Age is associated with a decreased growth possibly reflecting biological aging of maternal tissues and systems and the cumulative effect of aging. Studies by Edge and Laros showed an increase inpre term delivery AMA, p value<0.05.Studies by Sahu *et al.,* the study group rate of preterm was29.4% our study it was 24.1%. Bekowetz *et al.,* also demonstrated an increase in foetal distress in women with advanced maternel age. Studies by Fretts *et al.,* where the rate of still birth in the advanced maternal age was twice than the younger counter parts. According to Sahu *et al.,*[28] the rate was 6.3% our study it was 15.7%.

CONCLUSION

After analyzing 286 patients of advanced maternal age and 300 controls of 20-25 years admitted to labor room of Institute of Maternal and Child Health, our conclusions are

- Incidence of Pregnancy in advanced maternal age is 1.78% in 2009 and we can anticipate further rise owing to the better standards of education and socioeconomic developments.
- Treatment for infertility, Bad obstetric history, Hypertensive disorders of pregnancy, Gestational diabetes, Preterm delivery, Intrauterine growth restriction, Foetal distress, Still births, Cesarian section rate, and Co morbidities like leiomyomas and maternal mortality rates were more and statistically significant in Advanced maternal age compared to the younger counter parts.
- Though a statistically significant difference could not be established the rate of Ante partum hemorrhage, Mal-presentation, multiple pregnancy, failed induction were more in the advanced maternal age group.

SUGGESTIONS

- Young women should be encouraged to balance the biological advantages of having a child at younger age against the social and economic advantages of obtaining an education and establishing a career.
- They should be educated about the risks of delayed child bearing, age related risk of fetal anueplodies, the increased risk of both early and late complications of pregnancy.
- If conception has not occurred after 6 months of actively attempting pregnancy the couple should be referred to a clinician who can initiate an infertility evaluation and help formulate a plan to optimize the establishment of pregnancy.
- Older Women should be offered prenatal screening and prenatal diagnosis, targeted anomaly scan and liberal use of ante partum testing to ensure safe motherhood and a healthy foetus.
- In view of the increased morbidity and mortality associated with pregnancy in advanced maternal age they should preferably be taken care in tertiary referral centers.

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