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Advanced Maternal Age at the First Pregnancy and Obstetric Performance:

A Retrospective Study

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Running Title: Evaluation of the influence of age and parity on female reproductive capacity.

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ABSTRACT:

Maternal Age of 35 years or more at first pregnancy and childbirth is considered advanced reproductive age and a high pregnancy risk associated with increased adverse maternal and perinatal outcomes. The industrialized and developing countries are replete with supporting scientific literatures but only a few data on nulliparous women in our setting hence our interest to appraise the correlates of advanced maternal age at first childbirth and obstetric performance in Nigerian women. The objectives were to determine the influence of advanced maternal age at first pregnancy on the obstetric and perinatal outcomes. To compare the obstetric performance of women advanced in maternal age at first delivery with their younger counterparts and to determine the trend of identifiable adverse outcomes with increasing maternal age at first delivery. This was a retrospective comparative study of 1684 nulliparous women that had their childbirth between 2009 and 2013 at a mission Hospital. Those aged 35 years and above were the study subjects while those aged 20 - 34 years the control. Relevant database was raised from the case files. The prevalence of elderly nullipara in this study was 1.6%. They were statistically significant different in primary level of education (OR = 4.1, P = 0.02), prenatal care lack (OR = 2.6, P = 0.02), caesarean section (OR = 2.5, P = 0.0006), incidental myomectomy (OR = 19.1, P < 0.0001), prolonged pregnancy (OR = 0.6, P = 0.04) and episiotomy at vaginal delivery (OR = 0.5, P = 0.01). They were also insignificantly worse in ante partum hemorrhage (APH), induction of labor, perineal tear, HIV infection, postpartum hemorrhage (PPH), preterm birth, Low birth weight (LBW), Intrauterine growth restriction (IUGR), stillbirth ,neonatal birth asphyxia and Perinatal mortality. Caesarean section rate, caesarean myomectomy, APH, induction of labor, stillbirth rate, LBW and Perinatal mortality each maintained a statistical significant linear tendency (P < 0.05) with maternal age. First pregnancy at advanced maternal age is fraught with increased maternal morbidity, perinatal morbidity and mortality. We proffer early education, marriage or and childbearing, quality prenatal care and skilled attendance at delivery for safe motherhood.

INTRODUCTION:

Maternal age and parity have been considered among the key determinants in obstetric performance and pregnancy outcomes [1 - 5]. The extremes of reproductive life and parity have been respectively widely associated with increased adverse obstetric outcomes. Pregnancy in women aged 35 years or above are termed advanced maternal age and for the first time mother elderly nullipara. The International Federation of Gynecology and Obstetrics (FIGO) in 1958 defined 'Advanced maternal age' as 35 years and older and recommended that a nullipara aged ≥ 35 years should be accepted as the international standard for elderly nullipara [3, 6 - 8]. They are high risk pregnancies because available scientific data suggest that they are prone to poor obstetric outcomes which tend to accelerate from age of 35 years and steeper from 40 years of age [1]. A woman's fertility and potential to have a conception end in a live birth within a year peak in her early to mid twenties [9] . The highest natural monthly fecundity of only 20 - 25% occurs in women under 30 years of age and drops to less than 10% at 35 years and above [10,11]. The yearly rate declines from a peak of about 90% in women in their 20s to 65% at 35 years, 40% at 40year and 10% at 45years [4-5], [9-12]. This is due to the decline in quality and quantity of the ovarian capital with increasing women age. Again at advanced maternal age there is increase in chronic medical disorders and the conception at increased risk of congenital disorder mostly of chromosomal origin leading to various degrees of birth defects [4, 12, 13]. This indicates an increased need for preconception care for safe motherhood especially in these high risk pregnancies. The results of analysis showed that age at first pregnancy depends on geopolitical zone, location of residence, level of educational attainment, marital status, religion and the age of first sexual initiation [14]. Work from Asia showed only increased incidence of Intrauterine growth restriction (IUGR) and Caesarean Section rate with advanced maternal age [15]. There is plethora of other scholarly scientific literatures on this but only a few of them from our setting. This study therefore sets out to appraise the correlates of advanced maternal age at first pregnancy and delivery in Nigerian.

SUBJECTS AND METHODS:

One thousand six hundred and eighty four (1684) women of the 1726 that had their first delivery between June 2009 and Dec 2013 in St Philomena Catholic Hospital (SPCH) Benin City Edo state Nigeria were retrospectively studied. All the adolescent mothers and those whose pregnancy ended in abortion were excluded. Data on the socio-demographic characteristics, prenatal and delivery details, maternal and perinatal outcomes were

extracted from the case files into the computer. The main outcome measures were maternal and perinatal complications. The women were stratified into two clinically important age groups for comparative analysis. The study groups were those aged ≥35 years (elderly nulliparae) and those aged 20-34 years served as the control group. The control group was further subdivided into three groups for intra-group analysis for trend testing where necessary. For the purpose of this study a nullipara or nulliparous woman is defined as a woman who has never carried any pregnancy to viability and delivered irrespective of the number of early pregnancy losses (abortions, ectopic gestations or gestational trophoblastic disease) she has had previously and or the gestational age of the pregnancy she is currently carrying. Viable gestational age by World Health Organization (WHO) is 24 completed weeks or greater. Those women aged 35 years or more are termed advanced or elderly nullipara while those aged 20 - 34 years are termed normal aged or young nullipara (FIGO). Preterm birth is childbirth at earlier than 37 completed weeks of gestation while prolonged pregnancy is that beyond 40 weeks of gestation from the day of onset of the last normal menstrual period (LNMP). Low birth weight newborn weighed less than 2500 grams while macrosomic newborn weighed 4000grams or more each at birth. SPCH is a secondary tier mission hospital with fairly well equipped and staffed maternity department. It

has over a thousand deliveries annually. The medical record unit was fairly satisfactory. The facility has adequate obstetric and pediatrics coverage. The study was approved by the hospital ethics and research committee. Analysis was done with EPI-INFO version 3. 5. 1 and INSTAT statistical software where appropriate. Chi-square (X^2), Fisher's Exact test and Student t-test statistical packages were used as appropriate setting the Statistical significance at p-value < 0.05.

RESULTS:

Total deliveries at the center during our study was 3976, the first deliveries were 1726 out of which 1684 (42.4%) met the study criteria and were included for this study. The women aged 35 years and above at their first delivery constituted 1.6% of all the deliveries at the centre during this study and 3.8% of the nulliparae. The mean age of the study group was 36.5 ± 1.4years and modal age 35 years while the values for the control counterparts were 26.9 ± 1.7 and 27 years respectively. There was statistically significant difference in their mean age (t = 44.9, P < 0.0001). The study group was significantly more of primary (7.1% v 1.8% OR = 4.1, P = 0.02), but similar in secondary (23.2% v 26.8% OR = 0.8, P = 0.6) and tertiary (69.7% vs. 71.1%, OR = 0.9, P = 0.8)) levels of education respectively (Table 1). All the study group were married while 11 (0.7%) of the control group were unmarried at the time of their first childbirths (OR 1.1, P =

1.0). Eight (12.3%) of the study group and 82 (5.1%) of the control group had no prenatal care (OR = 2.6, P = 0.02). This was statistically significant but did not maintain a statistical significant linear trend (X^2 = 0.4859, P = 0.5). The study group though not statistically significant, was twice as likely as the control counterparts to be unemployed at the time of their child birth. In Table 2, among those who had prenatal care at the center the study group comparatively had reduced risk of anemia (5.3% vs. 9.8%, OR = 0.5, P = 0.4) at their first visit though the difference was not statistically significant. They more than twice tested positive to human immunodeficiency virus infection (HIV) screening than the control group (6.2% vs.3.0%, OR = 2.1,P = 0.1) but this failed to maintain a significant linear trend (X^2 = 2.851, P = 0.09). The study group were more prone to ante partum hemorrhage (OR = 2.5, P = 0.6) relative to the control group and there was statistical significant linear trend (X^2 = 7.481, P = 0.01).There was a slight increase risk of premature rupture of membranes at advanced maternal age at first delivery when compared with the control group (9.7% vs. 8.4%, OR = 1.1, P = 0.8). There was a non-significant increase of induction of labor among the study group (28.0% vs. 22.3, OR = 1.4, P = 0.4) with a significant linear trend (X^2 = 5.128, P = 0.02). The two groups were similar in augmentation rate (26.0% vs. 26.3, OR = 1.0, P = 1.0). The study group were less likely to have assisted vaginal delivery (0. 0% vs. 0.95, OR =

0.8, P = 1.0). Caesarean section rate was more than twice increased among the study group (43.1% vs. 23.45, OR = 2.5, P = 0.0006) relative to the control group. The difference was statistically significant and followed a statistically significant linear trend (X^2 = 12.669, P = 0.0004). The mothers in the study group were significantly at increased risk of incidental caesarean myomectomy (7.7% vs. 0.4% OR = 19.1, P < 0.0001) and this also maintained a statistically significant linear trend (X^2 = 17.431, P < 0.0001).

Compared with the control group, the study group were significantly less likely to require episiotomy at delivery (27.7% vs. 45.1%, OR = 0.5, P = 0.01) but there was no significant linear trend. However the results also indicate that though insignificant, there was an increased risk of perineal tear among study group (15.9% vs. 11.9% OR = 1.5, P = 0.2). The elderly mothers were more prone to postpartum hemorrhage (4.6% vs. 2.8%, OR = 1.7, P = 0.4) though none received blood transfusion unlike the younger group (0% vs. 1.6%, OR = 0.5, P = 0.6). There was no difference in the risk of gestational hypertension (16.9% vs. 16.7%, OR = 1.0, p = 1.0) and twining (P = 0.6) between the two groups. As can be seen in Table 3 there was an increased rate of preterm delivery among the elderly nulliparae (OR = 1.5, P = 0.4). They were significantly 40% less likely to have prolonged pregnancy than the control group (28.1% vs. 40.9%, OR = 0.6, P = 0.04) but

there was no significant linear tendency (X^2 = 0.3164, P = 0.6). Again relative to the newborns of the control group, those of the elderly mothers were twice (OR = 2.1, P = 0.2) more prone to having Apgar score of less than 7 at 5 minute.

TABLE 1: Maternal Characteristics

Variables	AGE GROUPS IN YEARS (N = 1684)						
	Age groups	20-24yrs	25-29yrs	30-34yrs	≥35yrs	≥35yrs vs. 20-34yrs	
	N (%)	383 (22.7)	876 (52.0)	360 (21.4)	65 (3.9)	OR	P-value
Education Attainment	Primary	7(2.0)	13(1.6)	8(2.4)	4(7.1)	4.1	0.02 *
	Secondary	150(41.9)	185(22.3)	72(21.7)	13(23.2)	0.8	0.6
	Tertiary	201(56.1)	628(75.9)	251(75.6)	39(69.7)	0.9	0.8
	Nil	0(0.0)	2(0.2)	1(0.3)	0(0.0)	3.5	1.0
Marital Status	Married	376(98.2)	867(99.8)	352(99.4)	62(100.0)	0.9	1.0
	Unmarried	7(1.8)	2(0.2)	2(0.6)	0(0.0)	1.1	1.0
Mean height (cm)	At booking	162.0 ± 7.4	161.3± 9.2	161.3.±11.6	159.7±7.5	t=1.2	0.2
Mean weight (kg)	At booking	66.3±11.4	70.1±13.3	73.3±14.3	73.8±12.1	t=2.2	0.03*
	At last prenatal visit	74.9±11.6	78.4±12.4	81.0±14.4	78.6±12.0	t=0.2	0.8
Booking status	Booked	357(93.2)	841(96.0)	339(94.2)	57(87.7)	0.4	0.02*
	Un-booked	26(6.8)	35(4.0)	21(5.8)	8(12.3)	2.6	0.02 *
Employment status	Unemployed	22(5.7)	33(3.8)	22(6.1)	6(9.2)	2.0	0.1
	Employed	361(94.3)	843(96.2)	338(93.9)	59(90.8)	0.5	0.1

* = significant, (All values in brackets are percentages)

TABLE 2: Maternal Outcome Variables

Variables	Age groups in years (N = 1684)					
Age groups	20-24yrs	25-29yrs	30-34yrs	≥35yrs	≥35yrs vs. 20-34yrs	
N (%)	383(22.7)	876(52.0)	360(21.4)	65(3.9)	OR	P-value
Positive HIV test	13(3.4)	18(2.1)	18(5.1)	4(6.2)	2.1	0.1
Twining	7(1.8)	10(1.1)	11(3.1)	0(0.0)	0.4	0.6
Anaemia (at booking)	53(15.0)	70(8.2)	28(8.4)	3(5.3)	0.5	0.4
Induction of labour	57(16.4)	189(23.7)	80(25.1)	14(28.0)	1.4	0.4
Augmentation of labour	104(30.0)	208(26.1)	73(22.9)	13(26.0)	1.0	1.0
Caesarean section	69(18.0)	209(23,8)	101(28.0)	28(43.1)	2.5	0.0006 *
Incidental caesarean myomectomy	0(0.0)	5(0.6)	2(0.6)	5(7.7)	19.1	<0.0001*
Perineal tear	49(12.8)	105(12.0)	39(10.8)	11(16.9)	1.5	0.2
Episiotomy	187(48.8)	387(44.2)	156(43.8)	18(27.7)	0.5	0.007 *
Postpartum hemorrhage	8(2.1)	23(2.6)	14(3.9)	3(4.6)	1.7	0.4
Pregnancy induced hypertension/preeclampsia	64(16.9)	140(16.0)	66(18.3)	11(16.9)	1.0	1.0
Antepartum hemorrhage	2(0.5)	19(2.2)	13(3.6)	2(3.1	1.5	0.6
Malpresentation	14(3.7)	29(3.3)	7(1.9)	2(3.1)	1.0	1.0
Premature rupture of membranes	20(5.3)	74(8.4)	42(4.6)	6(9.2	1.1	0.8
Blood transfusion	3(0.8)	17(1.9)	6(1.7)	0(0.0)	0.5	0.6

*=significant, (All values in brackets are percentages)

TABLE 3: Perinatal Outcome Variables

Variables	Age groups in years (N = 1684)					
Age groups	20-24yrs	25-29yrs	30-34yrs	≥35yrs	≥35yrs vs. 20-34yrs	
N (%)	383(22.7)	876(52.0)	360(21.4)	65(3.9)	OR	P-value
Intrauterine growth restriction	11(2.9)	30(3.4)	17(4.8)	3(4.6)	1.3	0.5
Preterm birth	29(7.6)	84(9.6)	26(7.2)	8(12.3)	1.5	0.4
Apgar score at 5 min <7	14(3.7)	43(4.9)	21(5.8)	6(9.2)	2.1	0.2
Mean birth weight (g)	3215.3±518.6	3247.0±549.5	3201.1±594.4	3166.2±645.5	t=0.5	0.6
Prolonged pregnancy	152(39.7)	364(41.5)	146(40.6)	18(28.1)	0.6	0.04 *
Stillbirth	5(1.3)	21(2.4)	15(4.2)	3(4.6)	1.9	0.2
Early neonatal death	1(0.3)	1(0.1)	1(0.3)	0(0.0)	3.5	1.0
Perinatal mortality rate	6(15.7)	22(25.1)	15(41.7)	3(46.2)	1.8	0.4
SCBU Admission	5(1.3)	6(0.7)	5(1.4)	0(0.0)	0.7	1.0
Low birth weight	16(4.2)	55(6.3)	33(9.1)	7(10.8)	1.8	0.2
Macrosomia	21(5.5)	65(7.4)	29(6.9)	5(7.7)	1.1	0.8

*=significant, (All values in brackets are percentages)

The mean birth weight of their neonates was similar (t = 0.5, P = 0.6) despite about double the risk of LBW (OR = 1.8, P = 0.2) and 30% more likelihood of intrauterine growth restriction (IUGR) among the older group. The former followed a significant linear trend (X^2 = 8.136, P = 0.004) unlike the latter (X^2 = 1.840, P = 0.2).There was a slight increase of rate of fetal macrosomia (7.7% vs. 7.1%, OR = 1.1, P = 0.8) among the study group. The study group had more stillbirths relative to the control group (OR = 1.9, P = 0.2).This followed a significant linear trend (X^2 = 5.748, P = 0.02). The Perinatal mortality was about twice increased among the elderly mothers (4.6% vs. 2.7%, OR = 1.8, P = 0.4). This was not statistically

significant but it maintained a statistically significant linear tendency (X^2 = 5.197, P = 0.02).The other maternal and Perinatal outcome variables did not maintain significant linear relationship. Among all the subjects, there was no maternal death or hysterectomy at the center within the period of this study.

DISCUSSION:

The prevalence of elderly nullipara in this study was 1.6 % which compares with previous reports of 1.4-2.0% in other centers in this south –south geopolitical region [6],[16] but lower than an earlier finding of 4.4% in this setting over a decade ago [17] and other reports from other regions [18-19]. The average age at first childbirth is on increase globally [19-20]. This is mainly due to educational, social and most importantly economic reasons. Pursuit of higher educational attainment as a key for stable job, a higher salary and increasing career prospects is common globally not only among the males but the females alike especially in countries like ours with high level of gender inequality ,limited job and high employment insecurity. This quest for increase earning power of career women increases their labor force participation at the expense of early marriage and childbearing.

The decline in prevalence in this setting over the previous decade as observed in this study can be because the earlier study [17] was in a tertiary hospital while this took place in a secondary mission hospital in the same setting.

Both studies were however, hospital based and may not be the true representative of the zone. Increasing the level of awareness of the consequences of delay in childbearing and the benefits of early completion of family size among the people might reduce the incidence of elderly nulliparity. A low incidence of elderly nulliparity of 0.42% was reported from the northern part of the country [21]. This may be explained by cultural and religious variations that encourage a high prevalence of early marriage and childbearing in the north. This is supported by the national demographic and health survey report [20].

Evidently, greater proportion of mothers in each category in this study attained tertiary level of education though double the older ones were unemployed at the time of their first child birth. It has been shown that median age at first birth increases with the level of education and socioeconomic status [20].

In all, seven out of the 15 maternal outcomes measured and 8 out of 10 perinatal complications in this study were unfavorable in the study group relative to the control counterparts. Among maternal outcome variables, Caesarean section and incidental caesarean myomectomy were statistically significant different. Others were induction of labor, ante partum hemorrhage, postpartum hemorrhage, and premature rupture of membranes, perineal tear and HIV infection. These compared with these reports [16, 22-25] and at variant with others [6].

Our results were not different in gestational hypertension but compared to other findings [23] but were different from other reports of increased occurrence among the elderly nulliparae [21, 24, 25]. The study group appeared more prone to perineal tears and will require more episiotomy at delivery compared to the control group.

The study group was comparatively significantly more delivered abdominally confirming reports by other workers [17, 23-28]. A significant number of the study group had incidental myomectomy. Advancing age without childbirth has been associated with increased occurrence of uterine fibroids this is supported by other findings [25]. At booking for antenatal care the study group were less prone to anemia because the older mothers have more reserves and less likely to develop anemia as presented in Table 2. This compares with previous reports [28].

The increased likelihood of the older nullipara to have interventional delivery therefore obstetric hemorrhage were not unconnected to their high rate of co-existing uterine fibroids, malpresentation, rigid perineum and ante partum hemorrhage. This confirms another report of increased likelihood of primary postpartum hemorrhage with advanced maternal age [29].

Perinatal adverse outcomes were relatively higher among the older mothers though none was to a statistically significant level. These were preterm birth, low birth weight, early neonatal death, perinatal mortality and stillbirth similar to other findings [24, 25, 30]. Report from southwestern Nigeria revealed no adverse perinatal outcome in advanced maternal age pregnancy [14]. This was not on first time pregnancies and their findings are therefore not strictly comparable with our present study.

Congenital malformation was higher in younger mothers similar to findings by other authors [23]. This may be due to the small sample size of the study group. Congenital anomaly tends to increase with advancing maternal age [12-13]. This work also confirmed the significant increase of prolonged pregnancy among the younger group as earlier reported [21]. There is the need for increased campaign against excessively widened bio-social gap to forestall delay in commencement of childbearing.

Our data indicate that the maternal and perinatal morbidities tend to increase with increasing maternal age.

One of the limitations in our study is that it is retrospective and hospital based therefore it may not be a true representative of the geopolitical region. A multicenter study would have a better spread and representation. A randomized prospective study with statistically appropriate sample size is hereby suggested for further study.

It is evident from this study that early and regular prenatal care in a well equipped health facility for proper screening, regular evaluation, and health education especially on nutrition in

pregnancy, pregnancy and childbirth, continuous counseling and psychological support through the gestational period and childbirth is essential for safe motherhood and healthy neonates among this group. The need for skilled attendance at their delivery need not be overemphasized.

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