International Academic Journal of Medical and Clinical Practice
Vol.6, No.4, 2021;
ISSN (5353 – 5523);
p –ISSN 8156 – 7532
Impact factor: 3.15

INCIDENCE OF BIRTH DEFECTS AND ITS ASSOCIATION WITH MATERNAL AGE AND MULTIPLE PREGNANCIES AT NNAMDI AZIKIWE UNIVERSITY TEACHING HOSPITAL (NAUTH) NNEWI: A RETROSPECTIVE STUDY

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Abstract: Tremendous efforts have been made by scientists over the years to demystify the causes of birth defects. This study seeks to find any possible association with maternal age & multiple pregnancies with the frequency of birth defect. This retrospective study was carried out at Nnamdi Azikiwe Teaching Hospital (NAUTH) Nnewi within a 10-year period. The research design is a descriptive survey non-experimental research. After due application and permission from the hospital management, the maternity register of the hospital within the period of 2010 to 2019 was retrieved and the required information extracted. No personal patient data was handled and the data cannot be traced directly to any patient. All data obtained was analyzed using the statistical package for social sciences (SPSS) version 20.1 and the Microsoft Office Excel 2010. During the period under review, 7,997 babies were born in NAUTH. In these 7,997 deliveries were 766 multiple pregnancies. Also, during the considered period 36 birth defects were recorded. Among the mothers that gave birth to defected babies, 4 were 18-28 years; 7 were 29-39 years while the remaining 26 were 40 years and above. This study shows that prevalence of birth defect occurs mostly in mothers aged over 40 Years. Multiple pregnancies on the other hand contributed to only two percent of the birth defects. In spite of the underlying mechanisms, these findings confirm the negative impact of advanced maternal ages on the outcome of pregnancy. These results providing evidence-based knowledge on the implications of late marriage and multiple pregnancies necessitated by drugs or artificial reproductive technology on birth outcome.

Keywords: Advanced maternal age, multiple pregnancies and birth defects.

1.0 INTRODUCTION

Our previous studies drew attention to the association between birth weight and maternal age in south east Nigeria (Agathokleous *et al*., 2013) as well as in Madonna University Teaching Hospital (MAUTH) (Agathokleous *et al*., 2013). The current study is aimed at drawing a similar association between high maternal age, multiple pregnancies and the prevalence of birth defects. With the recent debatable arguments on how maternal age and multiple pregnancy has increased birth defects and how mortality rate has increased in infants because of birth defects like congenital heart disease (CHD); advance maternal age is reported to increase chances of multiple pregnancy, both of which increases the chances of a birth defect (Scivastava, 2006).

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Birth defects can be caused by genetic or environmental factors or a combination of both. These may result in various forms of structural and functional disorders.

Genetic causes of birth defects are mostly present prior to conception in the gametes of either or both parents. Down syndrome, sickle cell anemia, muscular dystrophy, cleft lip & palate and club foot. However, not all children who inherit flawed genes from one or both parents will develop birth defects (Thorsen 2013). The higher the age of the mother, the more chances of having a chromosomal disorder which ultimately leads to a birth defect.

Birth defects can also occur from environmental factors after conception. This mainly occurs due to prenatal exposure to harmful substances during gestation. These toxic substances are called teratogens and include things like drugs, alcohol, medications, vaccines, radiation, stress and illness. Inadequate consumption of vital nutrients and minerals during pregnancy is another potential cause of environmental birth defects. Fetal alcohol syndrome, microcephaly, limb deformities and discoloration of the teeth are examples of environmental birth defects (Ribeil *et al*., 2017).

Advanced maternal age which is considered 35 years and above (Weymouth *et al*., 2017) may increase the risk of birth defect like Down syndrome, spina bifida, phocomelia, club foot, cleft lip and cleft palate (Holmbeck and Devine, 2010). Teenage mothers and mothers at their twenties are less likely to give birth to babies with birth defect than advanced age mothers. This may generally be due to (Hoffman, 2002). Birth defect, also known as congenital disorder, is a condition present at birth regardless of its cause (Canick, 2012). Birth defects may result in disabilities that may be physical, intellectual, or developmental. Maternal age is the age of the mother at the time of delivery. In addition, maternal age at childbearing has dramatically shifted in the last decades due to a broad range of social and cultural determinants (LaCroix, 2017). This is likely to also exacerbate the incidence of birth defects.

Causes of advanced maternal age ranges from sociocultural factors to economic or career factors. Others may be due to infertility and some unknown causes (Alberman, 2002). Advanced maternal age is associated with adverse reproductive effects such as increased risk of infertility, and higher risk that the children may have chromosomal abnormalities (Leridon, 2004). Advanced maternal age continues to be associated with a range of adverse pregnancy outcomes including low birth weight, pre-term birth, stillbirth, unexplained fetal death, and increased rates of Caesarean section. However, over time, improvements in (and improvements in access to) medical services and social resources have decreased the negative association between older maternal age and low birth weight (Myrskylä, 2018). It is reported that higher parents' age, especially of the mother increases the possibility of birth defects on the children (Alliance, 2010). It has also been documented that higher maternal age increases the possibility of multiple births. This study is designed to verify these claims.

Multiple pregnancies is a condition wherein the mother delivers two or more offspring. Multiple pregnancies may be the result of the fertilization of a single egg that then splits to create identical fetuses, or it may be the result of the fertilization of multiple eggs that create fraternal fetuses, or it may be a combination of these factors (Pamela, 2014). In human, the average length of pregnancy (two weeks fewer than gestation) is 38 weeks with a single fetus. This average decreases for each additional fetus: thirty-six weeks for twin, thirty-two weeks for triplets, and thirty weeks for quadruplets. This will decrease the maturity of fetus which may cause a defect to be present at birth. Recent history has also seen increasing numbers of multiple births. In the United States for example, it was estimated that by 2011, more than 36% of births will be multiple births. This is owing to the huge advances in assisted reproductive technology (ART) (Gallo, 2013).

Numerous studies have found that multiple births have a higher risk of preterm delivery, low birth weight, and

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neonatal mortality (Alexander, 1998). Many epidemiological studies have observed that multiple births also have a higher risk of birth defects compared to singletons (Anderson *et al.*, 2006). For example, central nervous defects, cardiovascular defects, alimentary tract defects, ear defects, respiratory defects have all been observed more frequently among multiple births. Increased risks of specific birth defects among multiple births have been noted for macrocephaly, encephalocele, hydrocephaly, cleft lip and palate, anomalies of the diaphragm, cardiac septal defects, atresia or stenosis of the large intestine or anus, tracheoesophageal fistula,malformations of the alimentary tract, inguinal and umbilical hernias, and cystic kidney (Bezerra *et al*., 2000).

2.0 MATERIALS AND METHODS

2.1. Research Design

This was a descriptive survey non-experimental research. It was aimed at determining an association between multiple pregnancies, maternal age and the prevalence of birth defects in Nnamdi Azikiwe University Teaching Hospital Nnewi between 2010 and 2019 (10years) period.

2.2 Location of Study

The study was carried out at Nnamdi Azikiwe University Teaching Hospital Nnewi. The hospital is located at Uruagu Nnewi, in Nnewi North local government area of Anambra State, Nigeria.

2.3 Instrument of Data Collection

This study was done using records from delivery and special baby care units of the Nnamdi Azikiwe University Teaching Hospital Nnewi. Records considered are reports of births that took place in this tertiary hospital within the 10-year period under review. Records obtained are cases of birth defect with reference to the age of the mother as well as the number of children delivered at once.

2.4 Data Analysis

All data obtained was analyzed using the statistical package for social sciences (SPSS) version 20.1 and the Microsoft Office excel 2010.

3.0 RESULTS AND DISCUSSION

3.1 Results

During the considered period, 7,997 babies were born in NAUTH. Of these 7,997 deliveries, 766 were multiple pregnancies. This represents approximately 9.6% of all deliveries. Also, during the considered period 36 birth defects were recorded representing 1 in every 222 births.

Among the mothers that gave birth to defected babies, 4 were 18-28 years; 7 were 29-39 years while the remaining 25 were 40 years and above.

Table 3.1: Showing the frequency of birth defects and percentage over the years of study.

Years	Frequency	Percent (%)
2010	3	8.3
2011	7	16.7
2012	5	13.9
2013	1	2.8
2014	3	8.3
2015	4	11.1
2016	2	5.6
2017	4	11.1
2018	3	8.3
2019	5	13.9
Total	36	100

The table 3.1 above shows the distribution of cases of birth defect per year within the 10 year period under review. 2011 was the year with the highest number of cases while 2013 had the lowest.

Fig 3.1 Area chart showing prevalence of birth defect based on maternal age.

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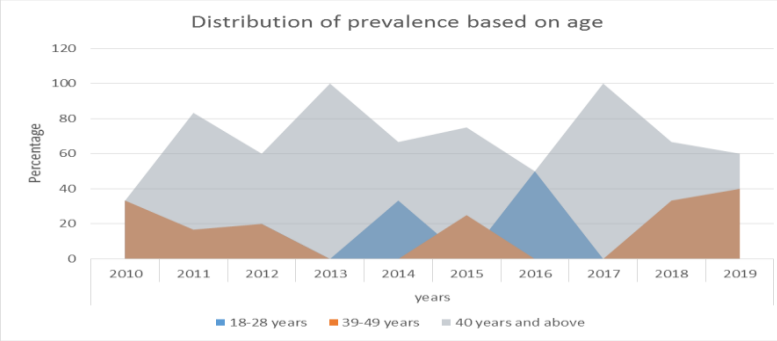

Table 3.2: Showing the frequency of birth defects based on maternal age.

Age Range	Frequency	Percent
18-28years	4	11.1
29-39years	7	19.4
40years and above	25	69.4
Total	36	100

This table shows the frequency of birth defects according to maternal age. The table shows that 69.44% of cases of birth defect are born mothers aged 40 years and above. The trend follows that the higher the maternal age the more cases of birth defect. So 19.44% were born to mothers aged 29-39 years while 11.11% were born to mothers aged 18-28 years. This table shows that there is a correlation between advanced maternal age and birth defects.

Table 3.3: Showing percentage of male and female with birth defect during the considered years of study.

Sex	Number	Percentage
Male	22	61.1
Female	14	38.9

Our result in Table 3.3 shows that 61.1% of children born with birth defects are male as against 38.9% who are female.

Table 3.4: Comparing multiple pregnany and the frequency of birth defect

Congenital anomaly	Single births	Multiple births	Total
Phocomelia	2	5	7
Congenital heart disease	3	1	4
Spina bifida	1	2	3
Club foot	2	1	3
Down syndrome	13	4	17
Cleft palate	2	-	2
Sickle cell anaemia	1	-	1
Total	24	13	37

Table 3.4 shows the distribution of birth defects between single and multiple deliveries.

Several disparities were seen in the frequencies of different forms of birth defect among single and multiple births. Phocomelia for example appeared to be very high among multiple births than singleton births. Down syndrome on the other hand was very high among single births compared to multiple births. This may suggest a pattern for these congenital anomalies. In all, 24 out of 7231(0.33%) representing approximately 1 in every 300 singleton births had a congenital anomaly. On the contrary, 13 out of 766 (1.7%) of multiple births had birth defect. This represents approximately 1 out of 60 multiple pregnancies came down with a birth defect

Table 3.5: Percentage distribution of birth defects

Congenital anomaly	Single births	Multiple births
Phocomelia	28.6	71.4
Congenital heart disease	75	25

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Spina bifida	33.3	66.7
Club foot	66.7	33.3
Down syndrome	76.5	23.5
Cleft palate	100	-
Sickle cell anaemia	100	-
Total	64.9	35.1

Table 3.5 shows the percentage distribution of the birth defects based on single or multiple pregnancy. Multiple pregnancies had 71.4 % cases of all phocomelia reported in the work. They also had 66.7% of all cases of spina bifida. On the other hand, all cases of cleft palate and sickle cell diagnosed at birth were single pregnancy each. Congenital heart disease (CHD) was 75% of cases for singleton pregnancies. It now appears that certain congential malformations are more common in singleton births than in multiple births.

3.2 DISCUSSION

Birth defects constitute a lifelong trauma both to the child and to the parents who care for them beyond the required time, and sometimes into adulthood. Numerous scientific efforts have been made to drastically reduce and possibly eliminate birth defects. Notwithstanding the various scientific efforts at curtailing birth defects, approximately 8 million babies are born with defects each year (Edwards *et al*., 2004). With improvements in quality of life and health care in various nations of the world, the incidence of birth defects is on the decline (Dobbs and Gurnett, 2012). According to a report carried out by Center for Disease Control CDC, birth defects affect one in every 33 babies (about 3% of all babies) born in the United States each year. Official statistics published by New Life Charity in the summer of 2012 revealed that around 42 children are born with a significant birth defect each day in the UK. That is one in every 45 live births and up to 1 in every 202 pregnancies. Although our results shows 1 out of every 222 live births had a birth defect which is relatively low compared to what is obtainable in the US and the UK.

The high level of birth defect in our report may be traceable to the poor standard of living and deformed medical system in the country.

Studies have shown that increased maternal age is associated with increased chances of multiple pregnancy and possibility of birth defects (Holmbeck, 2010).

The result of this study shows that maternal age is directly associated with increased frequency of birth defects. Mothers aged 40 and above produced 69.44% of children with the reported birth defects.

Our results therefore show a clear association between maternal age and birth defect.

Spina bifida is an abnormal closure of the neural tube during the fourth week of development. Spina bifida is a general term for neural tube defects affecting the spinal cord. It consists of splitting of the vertebral arches and may or may not involve underlying neural tissue (Holmbeck, 2010).

Phocomelia is characterized by the absence of proximal limb elements to various degrees combined with the presence of distal limb structures (e.g., autopod). Historically, this condition was associated with thalidomide ingestion during pregnancy. However, many congenital syndromes can manifest with phocomelia (e.g., Holt-Oram, TAR, Roberts, and Schinzel syndromes). (Weymouth *et al.*, 2010)

Multiple pregnancies on the other hand contributed to only two percent of the birth defects. Birth defects may result from genetic or chromosomal disorders, exposure to certain medications or chemicals, or certain infections during pregnancy. Risk factors include folate deficiency, drinking alcohol or smoking during pregnancy, poorly controlled diabetes , and a mother over the age of 35 years old (John, 2007).

Most of the birth defected babies that came from mother's under the age of 35 were chromosomal anomalies or due to attempted abortions. Some of the mothers in this study have parity of P6-A3 which shows that they might have had complications with pregnancies. Some of the birth

defects like the most known defect "Down Syndrome" (Trisomy 21) have proven according to this study that it occurs mostly in mothers with advanced maternal age, the extra chromosome is believed to occur by chance, with no known behavioral activity or environmental factor that changes the probability (Marteau, 1999).

The number of multiple pregnancy and the number of babies with defects due to multiple pregnancy as shown in the result proves that the risk of birth defect in mothers with multiple pregnancy is related which makes maternal age the high risk factor that can cause birth defects.

Multiple pregnancy is often associated with premature birth in which the babies require special care and incubation. This prematurity may be a predisposing factor to birth defect as some organ systems may not fully form before the time of birth. A report from the work of Aguwa *et al.,* (2016) shows that maternal age was highest among women from the south-east part of Nigeria compared to the other major regions of the country. This could possibly imply that the chances of birth defect may be higher in the south east compared to any other region of the country. Result from table 3.3 shows that majority of the birth defects recorded occurred in male children than in female children.

The main limitation of this study is its retrospective design. Meanwhile, its strengths lie firstly in the fact that it allows the possibility to take important confounding factors into account, secondly it better contributes to evidence-based knowledge of possible risk factors of delayed childbearing in an aging population.

4.1 CONCLUSION

In spite of the underlying mechanisms, the findings of this study confirm the association between high maternal ages and increased risk of birth defects. More caution and care should therefore be taken in handling mothers with high ages, especially the primigravid. Therefore, among the factors to consider to inform women adequately, providing evidence-based knowledge to support their procreation choices, and to improve clinical surveillance aiming to identify early signs of adverse outcomes.

4.2 RECOMMENDATION

Further studies should be done in other teaching hospitals across the country the properly document the incidence of birth defects in Nigeria.

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