## ANTENATAL EVENTS AMONGST MOTHERS OF BABIES WITH OROFACIAL CLEFTS

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#### ABSTRACT

*Background:* Exogenous factors occurring in the antenatal period could be contributory to the formation of orofacial cleft. This study sought to determine the antenatal events in mothers that may have contributed to orofacial cleft deformity of their children.

*Methodology:* It was a prospective observational cross sectional study of consenting mothers of babies with orofacial cleft who met the inclusion criteria. The study instrument was a questionnaire.

*Results:* Seventy-two mothers participated in the study. Most of these mothers were below 35 years of age and more than half, 43 (59.7%) were of the low-intermediate socioeconomic status. Although majority, 70 (97.2) of the mothers had antenatal care, the mean gestational age at commencement of antenatal care was 4 months. Almost all, 69 (95.8%) mothers had ultrasound scans however the detection of the orofacial cleft was in only 2 (2.8%) mothers. The commonest medication taken was haematinics, 26 (36.1%). Herbal medication, 15 (20.8%) and antimalarial, 12 (16.7%) were the other drugs more frequently taken. The mean age of pregnancy at commencement of these medications was 3.6 months.

*Conclusion:* Although uptake of antenatal service was common practice among mothers of babies with orofacial clefts in this study, no antenatal predisposing factors were identified.

Keywords: Cleft lip and palate, Antenatal events, Mothers

### **INTRODUCTION**

Orofacial cleft is the commonest craniofacial congenital anomaly, which occurs approximately one in every 700 - 1,000 births<sup>1,2</sup>. The precise aetiology is unknown possibly due to the heterogeneous nature of the anomaly.<sup>2,3</sup> However several risk factors have been suggested for this anomaly.<sup>2,4-7</sup>, These factors have been reported variously among different populations as predisposition such as family history of cleft, parental tobacco smoking, alcohol intake during pregnancy, increased maternal and paternal age, smoking, exposure to insecticides, nutritional deficiencies, low socioeconomic status and residence in particular locations/geographical locations.4,6-8 This study was undertaken to describe the antenatal events in a Nigerian population of mothers with babies with orofacial clefts. Knowledge of practices among mothers of babies with cleft anomalies may aid in the identification of possible aetiological factors and steps that could be taken to reduce the incidence of these anomalies in our environment.

### MATERIALS AND METHODS

This was a prospective observational cross-sectional study of consenting mothers of babies with orofacial cleft who presented to the cleft clinic of the hospital from 2014 to 2015. Antenatal events in this study were defined as health related events both experienced and performed by the mothers in the antenatal period. Mothers with babies older than six months of age were excluded from the study because of the reliability of being able to recall the prenatal events. Questions pertaining to age of the parents and infants, socioeconomic status of the mothers, uptake of antenatal services, use of medications and traditional concoctions during pregnancy, occurrence of illness and trauma during pregnancy were asked. Documentations of the anomalies were also recorded regarding the type of orofacial cleft, laterality and extent of cleft anomalies as well as the frequency of other associated congenital anomalies. The socioeconomic status (SES) was categorized according to a modification of the classification by Ogunlesi, which described five classes.9 These classes were recategorized as in Table 1; high-intermediate SES (Classes 1 and 2), intermediate SES (Classes 3) lowintermediate SES (Class 4) and low (Class 5). An addition class of High SES was introduced and dependents were not categorized into a particular class (Table 1). The type of cleft was described as cleft lip with or without cleft palate (CL $\pm$ P), cleft palate only (CP) (Bell) and rare craniofacial clefts. Categorical variables were compared using Chi square and multiple means were compared using ANOVA. Significance was set at p  $\leq 0.05$ .

### RESULTS

Within the two-year study period, 72 mothers of infants with clefts anomalies participated in the study. More than half, 43 (59.7%) of these mothers were from the low-intermediate SES (Figure 1). The mean ages of the mothers and fathers were 29.2 years and 37.5 years respectively (Table 2). Majority (79.2%) of the mothers were younger than 35 years of age. Cleft of primary palate with or without secondary palate (CL $\pm$ P) was the most common, 56, (77.8%) and the rare craniofacial cleft was the least observed, 4(5.6%),

SES By Ogunlesi Components High Director of Oil companies, Senior politicians, Multinational company directors, Industrial and Bank Directors. High-intermediate Classes I and II Executive managers, Senior civil servants, Professionals (doctors, lawyers), Senior Clergy, High Scale Traders, University lecturer Class III Intermediate Intermediate grade civil servants, nurses, lab scientist, Photographers, junior clergy, secondary school teachers Low-intermediate Class IV Semi-skilled workers; Tailors, Bricklaver, Traders, Artisans, Drivers, Farmers, Mechanics, Market trader (shop owners), Auxiliary nurses, Hair dressers Low Class 5 Unskilled; Messengers, Roadside traders, Cleaners, Laborers, petty trader Students, housewives, Unemployed Dependents

Table 1: Modified socioeconomic class (SES) classification

Table 2: Ages of the infants, mothers and fathers

	Infants	Mothers	Fathers
Mean age	1.5 (SD±1.3) months	29.2 (SD±5.8) years	37.5 (SD±6.8) years
Median	1 year	29 years	37 years
Range	3 days to 5 months	18 to 41 years	23 to 56 years

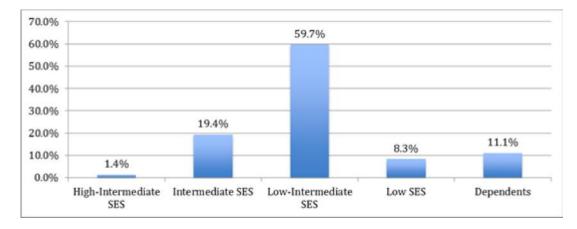


Figure 1: Frequency distribution of socioeconomic status (SES) amongst mothers

Type of cleft:	Cleft of primary palate with or				
	without secondary palate ( $CL\pm P$ )	77.8% (56)			
	Cleft of secondary palate (CP)	16.7% (12)			
	Rare craniofacial clefts	5.6% (4)			
Laterality	Left	36.1% (26)			
	Right	30.6% (22)			
	Bilateral	20.8% (15)			
	Midline	6.9% (5)			
	NA	5.6% (4)			
Extent	Complete	69.4% (50)			
	Incomplete	25.0% (18)			
	NA	5.6% (4)			
Cases with Associated	Yes	18.1% (13)			
anomalies	No	81.9% (59)			

Table 3: Characteristic	s of the cleft anomali	es
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Table	4:	Pattern	of	antenatal	practices
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Antenatal Practices		Frequency in percentage (number)		
Antenatal consultation	Yes	97.2% (70)		
	No	2.8% (2)		
Age of pregnancy at commencement of antenatal	Mean	4.1 (SD±1.6) months		
	Range	1 to 7 months		
Ultrasound during pregnancy	Yes	95.8% (69)		
	No	4.2% (3)		
When ultrasound was done	First ultrasound	5.1 (SD±1.9) months		
	Second ultrasound	$6.9$ (SD $\pm 2.0$ ) months		
	Third ultrasound	$7.5$ (SD $\pm 2.7$ ) months		
Identification of the cleft anomaly at ultrasound*	Yes	2.8% (2)		
	No	93.1% (67)		
	NA	4.2% (3)		
Smoking during pregnancy	Yes	0.0%		
0 01 0 2	No	100.0%		
Alcohol consumption during pregnancy	Yes	0.0%		
	No	100.0%		
Drugs taken during pregnancy	None	8.3% (6)		
0 01 0 .	Haematinics alone	36.1% (26)		
	'Abiwere'	20.8% (15)		
	Antimalaria	16.7% (12)		
	Analgesics	8.3% (6)		
	Others	9.7% (7)		
Age of pregnancy when drug was taken		3.6 (SD±1.4) months		
Trauma	Fall (3)	5.6% (4)		
	Motorbike accident (1)			
Illness	Febrile illness (24)	38.8% (28)		
	Diabetes (1)			
	Hypertension (1)			
	GIT disturbances (2)			
Mean age of pregnancy when other events occurred	Illness	$3.9 \text{ (SD}\pm 1.4) \text{ months}$		
0 1 0 7	Trauma	$4.9$ (SD $\pm 0.4$ ) months		

(Table 3). The clefts were commoner on the left side, 26 (36.1%), majorly 50, (69.4%) complete in extent and less than a quarter was associated with other congenital anomalies,13 (18.1%).

Majority, 70 (97.2%) of the mothers gave positive history of attending antenatal clinics, which commenced when the pregnancies were at a mean age of four months (Table 4). Almost all (95.8%) the

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		Socioeconomic status							Mothers age $\geq 35$		
		High-	Intermediate	Low-	Low	Dependent	P-value	Yes	No	P-	
		intermediate		intermediate		-				value	
Type of	CL±P*	0.0%	23.2% (13)	632.5% (35)	7.1% (4)	7.1% (4)	0.002!	12.5% (7)	85.7% (48)	0.059	
cleft	CP	8.3% (1)	8.3% (1)	58.3% (7)	16.7% (2)	8.3% (1)		50.0% (6)	50.0% (6)		
	Rare clefts	0.0%	0.0%	25.0% (1)	0.0%	75.0% (3)		25.0% (1)	75.0% (3)		
Extent	Incomplete	5.6% (1)	0.0%	72.2% (13)	11.1% (2)	11.1% (2)	0.001!	16.7% (3)	77.8% (14)	0.531	
	Complete	0.0%	28.0% (14)	58.0% (29)	8.0% (4)	6.0% (3)		20.0% (10)	80.0% (40)		
	NA	0.0%	0.0%	25.0% (1)	0.0%	75.0 (8)		25.0% (1)	75.0% (3)		

Table 5: Comparison SES of mothers to the characteristics of the craniofacial clefts

\*Age was not available for one mother, ! 73.3% had less than the required cell count.

mothers had ultrasonographic scanning done, first of which was at pregnancy age of 5.1 months and only in 2.8% was the cleft anomaly detected (Table 4). None of the mothers gave a positive history of either smoking or alcohol intake but 91.7% gave positive history of some form of drug intake during pregnancy, majority (36.1%) of which were haematinics alone without associated anomalies. Thus, the population of babies in this report is similar to the pattern of previously reported for orofacial cleft populations.<sup>6,10,11</sup> Therefore the participants of this study are considered to be representative of mothers of the population of babies with orofacial cleft anomalies. On this background, the antenatal events and practices were assessed.

Table 6: Comparison of antenatal practices of mothers to the characteristics of the craniofacial clefts

		Use of medication			Trauma			Illness		
		Yes No		Р-	Yes	No	Р-	Yes	No	P-
				value			value			value
Type	CL±P	91.1% (51)	8.9% (5)	0.823	5.4% (3)	94.6% (53)	0.812	46.4% (26)	53.6% (30)	0.534
of cleft	CP	91.7% (11)	8.3% (1)		8.3% (1)	91.7% (11)		33.3% (4)	66.7% (8)	
	Rare clefts	100.0% (4)	0.0%		0.0% (0)	100.0% (4)		25.0% (1)	75.0% (3)	
Extent	Incomplete	88.9% (16)	11.1%(2)	0.759	5.6% (1)	94.4% (17)	0.881	33.3% (6)	66.7% (12)	0.422
	Complete	92.0% (46)	8.0% (4)		6.0% (3)	94.0% (47)		48.0% (24)	52.0% (26)	
	NA	100.0% (4)	0.0% (0)		0.0% (0)	100.0% (4)		25.0% (1)	75.0% (3)	

(Table 4). The mean age of pregnancy at which these drugs were taken was 3.6 months. Traumatic events were reported in 5.6% at a mean pregnancy age of 4.9 months and 38.8% gave a positive history of illness at a mean pregnancy age of 3.9 months (Table 4).

Comparison of the mother's age, use of medication, history of trauma and illness with the type and extent of the cleft anomaly did not reveal any significant differences between the younger and older mothers and between those who gave a positive history and those who did not (Table 4). However, there were significant differences between the SES classes in terms of the type and extent of cleft anomaly (Table 5).

# DISCUSSION

This study has described the events and practices of a population of Nigerian mothers of babies with orofacial cleft anomalies during the antenatal period. The commonest anomaly type was the  $CL\pm P$  and CP had the least frequency. The anomaly was more on the left side, a larger proportion of the cases were complete in extent and majority were isolated cases

The uptake of antenatal services was common among the mothers however the age of pregnancy at the time of commencement of antenatal services was delayed to the second trimester; a stage at which the anomaly would have occurred. This precludes any form of preventive measures against congenital anomalies (such as the use of folic acid especially preconception) during antenatal period as the formation of the face occurs between the 4<sup>th</sup> and 8<sup>th</sup> week of intra-uterine life.<sup>6</sup>

The birth of a child with congenital anomaly can be devastating to parents.<sup>12</sup> A prenatal diagnosis is helpful in the acceptance of a baby born with congenital anomaly as it provides the time for the would-be parents to prepare for the arrival of such a child.<sup>12</sup> Perinatal ultrasound scanning has been a routine component of antenatal care in many countries.<sup>13</sup> A prenatal diagnosis of cleft anomaly using ultrasonography was first described in 1981.<sup>12</sup> Over ninety percent of pregnant women usually take up this service.<sup>13</sup> The first ultrasound has been documented to be done in less than four months of gestational age in about seventy percent of the cases.<sup>13</sup> The detection

rate for cleft anomaly appears to be low but higher when the cleft anomaly occurs with other congenital malformations.<sup>13,14</sup> As far back as 1995 in a study of over 180,000 pregnancies of known outcomes, 178 were cleft anomalies and only 17.5% were detected prenatally by ultrasound scanning.<sup>13</sup> In the year 2000, from the analysis of 20 European registries of congenital anomalies, the detection rates for orofacial clefts in general, CL±P and CP were 21.4%, 26.8% and 6.6% respectively.15 However, the detection rate for orofacial clefts has improved over the years to about 85% since the introduction of the routine transabdominal 20-week fetal anomaly scan in 2007 in the Netherlands.<sup>16</sup> This notwithstanding, the detection of cleft palate alone still remains a considerable challenge.17 Ultrasound scanning was also found to be a common practice among the mothers in this study. This was usually done once, when the pregnancy was just over 5 months. However the reported detection rate was extremely poor as only a very small percentage of the anomaly was detected before birth. The reason for this was not explored in this study but may be due to lack of available expertise in the field of radiological prenatal diagnosis<sup>13,17</sup> and/ or lack of adequate facilities.18

The socioeconomic status (SES) stratification employed for this study was a modification of the SES classification by Oyedeji as described by Ogunlesi.9,19 The Ogunlesi's classification considered in addition the income of the individual. However, some modifications were made to this classification as individuals considered in our society to belong to very high socioeconomic class (as identified in Table 1) do not appear to be represented under the Ogunlesi's classification and were therefore included as 'High' SES in this study. Also, it was challenging to place dependants in a particular class, as they do not necessarily belong to the class of the individual on whom they were dependent. For instance a housewife may be married to a father in Intermediate SES but may not have the full benefits of that class as access to these benefits are assumed to be dependent on the judgment of whom she is depending on. The conventional middle class was split into three categories; the high-intermediate, intermediate and the low-intermediate as there exist significant income disparity between these categories of middle classes.9 Majority of the mothers were in the Low-Intermediate SES class in this study. The possibility of nutritional deficiency as an aetiological factor in the occurrence of orofacial cleft in our environment is entertained because of the predominance of low-intermediate SES class in this category of mothers. However further investigation will be required to analyze the effect of nutrition on the prevalence of cleft anomalies in our environment as the distribution of the classes of SES observed in the study may be a reflection of what obtains in our general population.

The role of advanced parental age on the prevalence of congenital anomalies is not consistent in literature.<sup>11,20</sup> The influence of maternal age on pregnancy outcomes has been documented severally, while data on the effect of paternal age is sparse.<sup>20</sup> Some studies found associations between advanced parental age<sup>20</sup> while some did not.<sup>21</sup> Some found associations between advanced maternal age and CLP6, some found between increasing paternal age and CLP<sup>22</sup> while some reported increased incidence with both maternal and paternal ages.23 Hay et al reported higher prevalence of cleft palate in mothers older than 35 years and fathers older than 40 years.<sup>24</sup> The mean ages of the fathers and mothers were both lower than these (29 years for mothers and 37 years for fathers). These age values were strikingly similar to the findings of a similar study in a different part of the country that reported mean age of 37.1 years for fathers and 29.2 years for the mothers.<sup>25</sup> The role of parental age on the prevalence of orofacial clefts is not clear in literature and therefore requires further investigation.

Maternal smoking has been found to be associated with increased risk of having babies with orofacial clefts.6 Relationship between maternal alcohol consumption and orofacial clefts on the other hand is not well understood.<sup>26</sup> A number of studies have found no relationship (Bell) while some have documented increased risk of having babies with orofacial clefts with consumption of high quantities of alcohol.<sup>5,27</sup> This risk was observed for CL±P and syndromic clefts in women who consumed 5 or more drinks at a time on at least a weekly basis.<sup>6,27</sup> However the roles of these possible teratogens are uncertain.<sup>6,26</sup> In our study smoking and alcohol consumption do not appear to be a practice among mothers having babies with cleft lip and palate anomalies in our environment. This negative history of smoking was similarly reported from some other part of our country.25

Medication during pregnancy does not appear to be a common practice in this report including the use of herbal concoctions locally termed 'abiwere'. Abiwere, literally translated from the local Yoruba language means to be delivered of a baby without complications. Less than a quarter, 15 (20.8%) of the participants in this study gave a positive history of taking this concoction during pregnancy. This number of respondents was also similar to a previous study that reported 22.1% of the mothers gave a positive history of taking herbal concoctions during pregnancy.<sup>25</sup> Admittance to taking any form of medications; orthodox or traditional was at the beginning of the second trimester a period at which the face was expected to have been formed.<sup>6</sup> Thus the practice of taking medication during pregnancy in this study does not appear to have influenced the occurrence of the cleft anomaly.

Fever during the first trimester of pregnancy has been associated with increased risk of orofacial clefts when antipyretic is not taken to alleviate the fever.<sup>28</sup> The prevalence of trauma was low and almost one third was ill during pregnancy, majorly febrile illness. These were similar to the findings of a previous study although the age of pregnancy at the time of occurrence of the events were not stated.<sup>25</sup> However the age of pregnancy at the time of occurrence of these events was reported to be within the second semester therefore is not considered to be influential in the occurrence of the cleft.

# CONCLUSION

Although uptake of antenatal service was common practice among mothers of babies with orafacial clefts in this study, detection of orofacial cleft anomaly via ultrasound was very low. No antenatal aetiological predisposing factor was identified in this study.

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