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MATERNAL RISK FACTORS ASSOCIATED WITH THE DEVELOPMENT OF CLEFT LIP AND/OR PALATE IN SUDAN

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ABSTRACT:

Background: Orofacial clefts (OFC) are considered as one of the common congenital anomalies that affect the health, impact negatively on patient, family and society as a whole .This anomaly has complex etiology, resulting from interaction of both environmental and genetic factors.

Objective of the Study: To identify the most common maternal risk factors of orofacial clefts in patients attending pediatric hospitals and plastic surgery clinics in Sudan, Khartoum State.

Methods: The research design for this study was a case descriptive cross-sectional hospital based study. The study was conducted in Khartoum state targeting three hospitals: Khartoum Denture teaching Hospital, Ahmed Gasim Specialized Hospital for children and Soba University Hospital. The study was conducted during the period from 1st of January to 15th of November 2018. It included all mothers of children with orofacial clefts (cleft lip and/or palate), who attended the above mentioned hospitals during the study period and fulfill the inclusion criteria. Data was collected by a standardized, close -ended Questionnaire through direct interview to the mother. The data collected was entered and descriptively analyzed using Statistical Packages for Social Sciences (SPSS) for windows version 20.

Results: The Study sample constituted 280 mothers of children with orofacial clefts. The most common age group of the studied children with OFCs was 1- 5 years (41.8 %) followed by 5- <10 years (30.7 %). Half of children143 (51.1%) had cleft lip with cleft palate (CLP), and more than one third 110 (39.3%) had cleft lip only (CLO). Cleft palate only (CPO) was the least common 27(9.6%). Male patients were more dominant with a ratio of 1.5:1 .Regarding the birth order of the index, 60 (21.2 %) cases were the first baby. The frequency of cleft lip only and cleft lip with palate were more common in males than females (23.1%) (32.1%) respectively, However cleft palate only (CPO) was near equal in both sexes. Most of the families were residing outside Khartoum state (٧٣,٢٪)and mostly from Kordofan state and rural areas. Regarding socioeconomic status of the families, more than one third of them were under the upper lower social class. Positive family history of OFCs was found in near half of the patients (44.6%), more on the paternal side 49 (39.2%). Most of the children belong to Aljaleen tribe 27(9.6 %).Passive smoking at home or at work place was experienced by 70 mothers (25%), of whom almost half 29 (41.5%) mothers were exposed to about 1-2 pocket per day. 17 (6.1%) of mothers had chronic diseases during their pregnancy course, of which Hypertension was the commonest one (30%). Drugs intake during pregnancy was reported in 55 mothers (19.6 %) and the commonly used drugs were Antibiotics (38.2%). Folic acid supplementation during pregnancy was received by only 110(40%) of mothers, however only 3.6 % received the recommended dose.

Conclusion: OFC are congenital defect, not uncommon in Sudan .So recognition of the etiological factors and the education of the females will help to decrease its occurrence.

1.1. INTRODUCTION:

The greatest asset of any country is its next generation of healthy, wise, intelligent, and creative children. Congenital malformations are a major factor making such a great asset inefficient.

Orofacial clefts (OFCs) are among the most common congenital facial anomalies. They result from a failed fusion of the medial, lateral, and maxillary processes, which normally occurs between the 6th and 10th weeks of intrauterine life. OFCs can appear as an isolated anomaly or as a part of a multiple congenital anomaly accompanied by other non-cleft malformations.–

The oral, nasal and pharyngeal structures are important not only to speech but also to normal swallowing and development of the face. These structures are the most commonly affected by facialanomalies, including cleft palate and cleft lip. Asians are at higher risk for orofacial clefts, followed by Caucasians and African Americans.

The etiology involves complex interactions between genetic and environmental factors. Genetic factors appear to create the most susceptibility for clefts. When environmental factors (i.e., triggers) interact with a genetically susceptible genotype, a cleft develops during an early stage of development.

Numerous studies have construed that the etiology of nonsyndromic cleft clip and or palate (NSOFC) may be multifactorial in origin with both genetic and environmental causative factors. Environmental factors which are of greater preponderance mentioned in various studies are associated with lower SES, maternal exposures to environmental factors like prescription of drugs which include (aspirin, ibuprofen, amphetamine, cocaine or ecstasy) and cigarettes smoking alcohol and nutritional deficiency particularly folic acid and certain illnesses of mother like epilepsy during critical early period of pregnancy.

The recognition of these conditions is very important because of the comorbidities that are usually associated with them, Several problems can be observed in the cleft-affected patients including dental abnormalities, malocclusion, malformations of the face and nose, feeding, respiratory, hearing, and speech problems.

The effects on an individual's speech, hearing, appearance, and

psychology can lead to long-lasting adverse outcomes for health and wellbeing. Even when repaired, complications such as persistent ear infections, speech impairments, facial deformities, and dental problems often remain.

The corrective surgery for cleft lip can be performed at any time after the child is born. Ingeneral, providers follow the "Rule of 10". That is, babies are operated on at about 10 weeks old, with body weight about10lb (4.5kg) andhemoglobinlevelofabout10.0g/dL. The risks in general anesthesia are much reduced when these parameters are attained. Cleft palates are customarily repaired at about 12 months of age.–

2. MATERIALS & METHODOS

2.1 Study Design:

The research design for this study was case descriptive cross-sectional hospital based study.

2.2 Study Area:

The study was conducted in Khartoum locality, which is the capital city of Sudan. Located at the confluence point of the White Nile flowing north from Lake Victoria, Uganda, and the Blue Nile flowing west from Ethiopia.The location where the two Niles meet is known as (al-Mogran). Khartoum – Although it is the smallest state by area, it is the most populous 2.274.321 inhabitants according to population census of (2008) and land survey of 22.142 Kilometer2. It is the national center of commerce and forms the cultural and industrial heart of the Sudan.

The study was carried out in the Khartoum state targeting three hospitals:

Khartoum Denture teaching Hospital: the only public hospital in Sudan specialized in all aspects of dental care. There is a special referred clinic for cleft patients for providing care and reconstructive surgery when needed. As well as a society targeting cleft patients, taking care of all aspects of their management. Preoperative and postoperative care are offered free of charge. The hospital constitutes of 35 beds, with average patients seen and / or admitted according to the last census in 2017 were 17.740 per months, coming from different parts of Sudan.

Ahmed Gasim Specialized Hospital for children: Constitutes of 98 beds for inpatient admission. As well as an emergency department including a total of 40 beds, in addition to a High Dependency Unit and a Pediatric Intensive Care Unit. The number of patients admitted last year according to the last census in 2017 were 60.138, coming from different parts of Sudan.

Soba University Hospital: This is University of Khartoum's teaching hospital. The samples of patients were collected from the referred clinic of cosmetic surgery carried out every Monday.

2.3 Study duration:

The study was conducted during the period from 1stof January to 15th of November 2018.

2.4 Study population:

Mothers of children with orofacial clefts (cleft lip and/or palate), who attended the above mentioned hospitals during the study period.

2.4.1 Inclusion criteria:

All Sudanese mothers of children with orofacial cleft (OFCs), who were willing to participate.

2.4.2 Exclusion criteria:

I. Mothers of Syndromic children with cleft lip or/and palate.
II. Non Sudanese mothers.
III. Mothers who refused to participate in this study.

2.5. Sample Size:

The sample size was determined by statistical equation
N=Z2PQ/D2
Where: Z= Statistical certainty= 1.96.
P= Prevalence. (.9 according to study in Sudan)
Q= Probability of failure at 95%.
D= Designed margin of error = 5%.

By application of the above equation, the sample size was 15. But for accuracy and to increase the strength of the study, 280 patients were included during the study duration. 245 patients were from Khartoum Denture Teaching Hospital, 17 patients from Soba University hospital and 18 patients from Ahmed Gasim Teaching Hospital.

2.6. Sample techniques :-

The author had visited the above hospitals. Regarding Khartoum Denture Teaching Hospital the authors visited the hospital on daily base during the Campaign project from first of January to last of April. While the other two hospitals once per week. All mothers of children with orofacial clefts who fulfilled the inclusion criteria were included in this study. Data was collected directly from the mothers. Mother was given a coding number.

2.7. Data Collection tools and methods:-

A standardized, face-to-face structured questionnaire was used to obtain the required information from the mothers. The questionnaire was conducted by the researcher and a volunteer pediatric resident. It included the following points:

- Sociodemographfic factors of the parents and family:(Age, sex, types and position of OFC, Age of the parents, level of education and occupation of parents, and parity of the mothers (consider lady of high parity if she had 5 and more child) ,residency and family socioeconomic status (SES) using Kuppuswamy's scale taking into consideration fathers education and occupation, Mothers education, and number of children in the family).

- Genetic factors (consanguinity and its degree, family history of similar condition and the level of relation).

- Behavioral and environmental factors (Smoking, Alcohol intake during pregnancy.

- Maternal chronic diseases in the pregnancy.

- History of drugs intake during pregnancy.

- Folic acid and Multivitamins supplementation: Accordingly, we categorized perinatal folic acid intake into three groups: none, less than the current recommended daily dose (<400 µg), and the recommended daily dose (≥400 µg) . To be consistent with previous clefts studies ,we defined a three month exposure window for folate intake comprising the month before the last menstrual period and the first two months of pregnancy. We counted women as exposed if they took folic acid for at least one month during this window as the other study did. Women who reported using folic acid supplements were asked in which specific months they took them and how often they took them. We were able to confirm intake for by using the product name or pill bottle label. Women were asked similar questions about multivitamins; we again collected brand names, empty bottles, and labels for documentation. We estimated each woman's total folic acid intake from folic acid supplements and multivitamins based on the folic acid dosage (known or imputed) and the frequency of intake. The standard recommendation is 400µg folic acid a day in the periconceptional period. – Accordingly, we categorized perinatal folic acid intake into three groups: none, less than the current recommended daily dose (<400 µg), and the recommended daily dose (≥400 µg). For dichotomous analyses,

we assessed folic acid as <400 µg or ≥400 µg a day, consistent with previous studies .

Data had been sorted, cleaned, categorized, coded, and summarized on the master sheet to be ready for final data analysis.

2.8. Study variables:

2.8.1. Independent variables:

- Socio-demographic characteristics: (age of the parents, ethnicity, gender of the child, education, occupation, husband's education and occupation., residency and family socioeconomic status (SES))
- Parity of the mothers.
- Maternal health status during pregnancy
- Maternal drugs intake during pregnancy.
- Maternal behaviors during pregnancy.
- Genetic factors.
- Maternal folic acid and multivitamins intake.

2.8.2. Dependent (Outcome) variables:

Cleft lip, Cleft palate, Cleft lip and palate

2.8.3. Operational definition:

Operational definition of the variables and its scale of measurement.

- Age: age of participants at time of data collection in years, continuous variable measured on ratio scale.
- Education: level of education for both the mother and father measure as: illiterate, basic school and secondary school education. Measured on ordinal scale.
- SES: upper, upper middle, lower middle, upper lower and lower. Measured on ordinal scale.
- Occupation: occupation of the participant and her husband include jobless (none), employer and laborer. Measured on ordinal scale.
- Passive smoking status also measured as Yes or No. Measured on nominal scale.
- Genetic factors: positive history of similar condition in the family, as Yes or No. Then the degree of relativity in the family, as father, mother, sibling ….. Measured on nominal scale.
- Gender of the child: male or female measured on nominal scale.
- Parity of the mother: high parity and low parity.Measured on ordinal scale.

2.9. Data analysis and presentations:-

The data and Sociodemographic characteristics of the study participants were reported with absolute numbers and relative percentages corresponding to each category (n, (%)). The association between maternal risk factors and developments of orofacial clefts in offspring was assessed using Chi-square test.

A two-sided P-value of ≤ 0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 20. Data was presented in the form of simple frequency, tables and graphs.

2.10. Ethical Considerations:-

The study was approved bythe ethics review committee of the Sudan Medical Specialization Board, Pediatrics and Child Health Council. Furthermore written consents and permissions to conduct the study were obtained from hospitals administrators.

Verbal and written consent were obtained from participants after the nature and aim were explained to each by the investigators.

No experimental drugs were used.
Confidentiality of the data was maintained during the study and it will be continued in the future.

RESULTS

This study was a case descriptive cross-sectional hospital based study, conducted from January to November 2018, aimed to identify the most common maternal risk factors of orofacial clefts in the patients attendingKhartoum Denture teaching Hospital, Ahmed Gasim Specialized Hospital for children and Soba University Hospital. It included280 mothers of children with cleft lip and/or palate, the result showed:

3.1 Sociodemographic features of children with OFCs and their families:

The mean age of the studied children with OFCs was 5.6 years. The most common age group was 1- <5 years, which was present in 117 (41.8 %) children, followed by 5- <10 years which was present in 86 (30.7 %) of cases (Figure 1).

Male patients were more dominant 170 (60, 7%) than females 110(39.3%) with a ratio of 1.5:1 (Figure 2). This difference of gender and occurrence of OFCs was found to be statistically significant (P=.001) (Table 1).

Regarding the birth order of the index, 60 (21.2 %) cases were the first baby, followed by the third birth order in 55 (19.6 %) cases (Figure 3).

Of our studied children, it was observed that, the frequency of cleft lip only (CLO) and cleft lip with palate (CLP) was more common in males than females, 65(23.1%) and 90 (32.1%) respectively. However cleft palate only (CPO) was near equal in both sexes (Figure 4).

Most of cases 105(73.2%)were from outside Khartoum state, 53 of the families (18.9 %) reside in Kordofan state, those who reside in Darfour and AlGezera states account for 16.8 %, 16.1 % respectively (Figure5).

The mean age of the mothers was 28.7 years.About two third of studied mothers were in age group 20 - <35, accounting for 195(69.7%) mothers (Figure6).In all other groups of maternal age, the risk for cleft occurrence compared with the age 25-29 was reduced (Table 2).

Regarding the mother education and occupation, two third of mothers were illiterate or had basic school level, 183(65.4%) (Figure 7).The majority of mothers were housewife 256(91.4) (Figure8).

About one third of studied mothers 86 (30.7%) had high parity (5 children and above) at birth of child (Table 3).

The association between the parity of the mothers and types of OFC was not statistically significant (Table 4).

According to our results, the mean age of the fathers was 39.3 years. About two third of studied fathers was between 30-<45 years, accounting for 172(61.4%) fathers (Figure 9).

With all other groups of paternal age, the risk for OFC compared with the age group35 -<40 was reduced (Table 5).

Regarding father's education and occupation, two third 186 (66.4 %) of fathers, were educated till basic and secondary school level (Figure 10). While more than two third 235(83.9 %) fathers were laborer (Figure11).

Regarding SES of the family, more than one third of families 109(38.9%) were under the upper lower social class followed by one third 92 (32.9%) under the lower middle social class (Table 6).

3.2 Clinical features of children with OFCs:

Of the 280 patients, there were 143(51.1%) cases had cleft lip with cleft palate (CLP), 110 (39.3%) cases had cleft lip only (CLO). Cleft palate only (CPO) was present in 27(9.6%) (Figure12).

About half of children with cleft lip only 137(51.1%) had the cleft in

the left side, while right sides cleft lip was present in 66(26.1 %) cases. Bilateral cleft lip was found in 50(19.8 %) children (Figure13). The difference between types of clefts (CLO, CPO, CLP) according to child sex was not found to be statistically significant (P= 0.327, 0.282, 0.218 respectively) (Table 7).

The association between types of OFC occurrence and the mother age at birth of the child was not found to be statistically significant (P= 0.084) (Table 8).

There was no significant statistical association between types of OFC occurrence, and each of father's age at birth of the child. (P=0.373) (Table 9)

There was significant statistical` association (P=0.003) between family socioeconomic status and the types of OFCs. Risk for CLO was more increased in lower SES, while risk for CPO was more in upper SES. Risk for CLP was increased in middle SES (Table10).

3.3 Family history of children with OFCs:

Most of studied parents were belong to same tribe 228 (81.6 %) (Figure14).The association between genetic factors and the tribe of the parents was found to be statistically significant (p= 0.028) (Table 11).

Majority of our studied parents 204 (72.9 %), had consanguineous marriage (Figure15), of whom about two third 139(68.1%) reported first degree cousin relationship to their spouse (Figure16).

Positive family history of OFCs was found in 125 (44.6%) cases compared to a negative family history 155(55.4%) (Figure17).

Positive family history of OFC (n=125) was more common in the father side 49(39.2%) than the mother side 26(27.2%) of cases. 26(20.8%) of cases had positive history in their siblings (Table12).

Of the 280 studied populations, 27(9.6 %) children belong to Aljaleen tribe, followed by Rizegat 17 (6.1%) and Koahla 16 (5.7%) tribes (Table13).

There was significant statistical association (p = 0.025) between genetic factor (positive family history) and types of OFCs (CL, CP, CLP). The risk was increased in cleft lip only (CLO) (Table 14).

The association between genetic factors and position of cleft lip only (either Rt or Lt) was not found to be statistically significant (P=0.080) (Table 15).

There was significant statistical association (P=0.004) between genetic factor (positive family history) and the family residences, and it was more in Khartoum state (Table 16).

3.4 Maternal behavior and risk of OFCs in study population:

Regular antenatal care was reported in 144 (51.4%) mothers (Figure 18).

Awareness of pregnancy at 4-5 weeks by mothers was reported in 162(57.9%) mothers, 84 (30%) mothers were aware at 6-8 weeks, Only 34(12%) mothers were aware after the 8th week gestation (figure 19).

Passive smoking at home or at work place was experienced by 70(25%) mothers (figure 20), of whom almost half, 29 (41.5%) mothers exposed to about 1-2 pocket per day (Table17).

The association between passive smoking and types of OFCs was not statistically significant (Table 18).

None of our studied mothers had history of alcohol intake during their pregnancy.

3.5 Maternal history of chronic disease and risk of OFCs in study population:

17 (6.1%) of mothers had a positive history of chronic diseases during their pregnancy course (figure 21). of which Hypertension was the commonest one,7 (41.2%), followed by similar cases of Hypothyroidism and Asthma (11.8%) (Table19).

The association between mother chronic disease and types of OFCs wasstatisticalsignificant (Table 20).

Positive history of urinary tract infections was reported in 18 (6.4 %) of cases (Figure 22).

3.6 Drugs intake during pregnancy and risk of OFCs in study population):

Drugs intake during pregnancy was reported in 55 (19.6 %) mothers(Figure 23).

Commonly used drugs were Antibiotic (38.2%) and Antimalarial (16.4%) (Table21).

There was significant statistical association (P=0.007) observed between the intakes of drugs during early pregnancy and types of clefts (CLP), risk was more increased with cleft palate only (CPO) (Table 22).

3.7 Maternal Folic acid, multivitamins and iron supplementations and risk of OFCs in study population:

Folic acid supplementation during pregnancy was received by only 110(39.3%) of mothers (Figure 24), however only 3.6 % took the recommended dose (Table 23).

There was significant statistical association (P=0.042) between supplementation of Folic acid and types of OFCs (CL, CP, CLP). Mothers with no folic acid supplementation (n=170) had more risk for cleft lip only (CLO), while the risk remained the same in both cleft lip (CLP) and palate (CPO) (Table 24).

The association between the time of starting folic acid and types of clefts was not found to be statistically significant (P=0.431) (Table 25).

Only 2 mothers (0.7 %) of our studied population received multivitamins supplementation during pregnancy.

About two third 191 (68.2 %) of the mothers received iron supplementation during pregnancy (figure 25). The majority of them (58.1%) took it during the second trimester of pregnancy.(figure 26).

3.8 Surgical Treatment received by our study population :

The majority 227 (81.1%) of cases didn't receive surgical treatment, only 53(18.9 %) of cases had been received surgical treatment before and most of them came again due to the failures of surgical treatment (Figure 27).

Table 1: Correlation between development of cleft lip and palate and child sex (n=280)

Child sex	Frequency	Calculated Chi Value	df	Sig. (one-sided)	Statistical Inference
Male	170	12.857	1	.001	Difference is significant
Female	110				

Table 2: Distribution of children with OFCs according to mother's age at birth of child (n=280)

Mother's age at birth of child	Frequency	Percentage	Confidence Interval (95%)		
			Standard Error	Lower Limit	Upper Limit

< 20 years	23	8.2	0.016	5.51	10.92
20 -< 25	61	21.8	0.025	17.72	25.86
25 -< 30	68	24.3	0.026	20.06	28.51
30 -< 35	66	23.6	0.025	19.39	27.76
35 -< 40	46	16.4	0.022	12.77	20.08
≥40	16	5.7	0.014	3.43	8.00

Table3: Distribution of children with OFCs according to index child birth order (n=280)

Variables	Levels	Frequency	Percentage	Confidence Interval (95%)		
				Standard Error	Lower Limit	Upper Limit
Child's Birth order	First	60	21.4	0.025	17.38	25.47
	Second	41	14.6	0.021	11.16	18.13
	Third	55	19.6	0.024	15.73	23.56
	Forth	38	13.6	0.02	10.19	16.95
	Fifth	29	10.4	0.018	7.35	13.36
	Sixth	24	8.6	0.017	5.81	11.33
	Seventh	18	6.4	0.015	4.01	8.85
	8th	11	3.9	0.012	2.01	5.84
	9th & above	4	1.4	0.007	0.26	2.60

Table 4:Correlation between types of OFCs and Mother parity

Variables	Type of clefts			Calculated Chi Value	df	Sig. (one-sided)	Statistical Inference
	Lip only	Palate only	Both				
Mother with Low parity	78	19	97	.293	2	.432	Association is not significant
Mother with High parity	32	8	46				

Table 5: Distribution of children with OFCs according to father's age at birth of child (n=280)

Father's age at birth of child s	Frequency	Percentage	Confidence Interval (95%)		
			Standard Error	Lower Limit	Upper Limit
< 30 years	31	11.1	0.019	8.00	14.17
30 - <35	54	19.3	0.024	15.40	23.18
35 -< 40	65	23.2	0.025	19.05	27.38
40 -< 45	53	18.9	0.023	15.07	22.79
45 -< 50	38	13.6	0.021	10.19	16.95
≥50	39	13.9	0.021	10.51	17.34

Table 6: Families' socioeconomic status of children with OFCs (n=280)

Families' SES	Frequency	Percentage	Confidence Interval (95%)		
			Standard Error	Lower Limit	Upper Limit
Lower	34	12.1	0.020	8.92	15.36
Upper Lower	109	38.9	0.029	34.12	43.74
Lower Middle	92	32.9	0.028	28.23	37.49
Upper Middle	32	11.4	0.019	8.29	14.57
Upper	13	4.6	0.013	2.57	6.72

Table 7: Correlation between child sex and types of OFCs (n=280)

Types of OFCs	Child sex	Observed (n)	Ratio	Calculated Z Value	Sig. (one-side)	Statistical Inference
Lip only	Male	65	0.3824	0.447	0.327	Difference is not significant
	Female	45	0.4091			
Palate only	Male	15	0.0882	0.577	0.282	Difference is not significant
	Female	12	0.1091			
Both (Lip & Palate)	Male	90	0.5294	0.778	0.218	Difference is not significant
	Female	53	0.4818			

Table 8: Correlation between types of OFC and mothers' age at birth of children with OFCs (n=280)

Mothers' age at birth of child	Type of clefts			Calculated Chi Value	Df	Sig. (one-sided)	Statistical Inference
	Lip only	Palate only	Both				
< 20 years	8	2	13	14.141	10	.084	Association isn't significant
20 -< 25	25	2	34				
25 -< 30	20	6	42				
30 -< 35	31	10	25				
35 -< 40	21	4	21				
≥40	5	3	8				

Table 9: Correlation between types of OFC and fathers' age at birth of children with OFCs (n=280)

Fathers' age at birth of child	Type of clefts			Calculated Chi Value	Df	Sig. (one-sided)	Statistical Inference
	Lip	Palate	Both				
< 30 years	11	2	18	6.787	10	.373	Association isn't significant
30 -< 35	23	4	27				
35 -< 40	31	4	30				
40 -< 45	19	8	26				
45 -< 50	12	4	22				
≥ 50	14	5	20				

Table 10: Correlation between types of OFC and family SES of children with OFCs (n=280)

Family SES	Type of clefts			Calculated Chi Value	df	Sig. (one-sided)	Statistical Inference
	Lip only	Palate only	Both				
Lower	20	1	13	23.441	8	.003	Association is significant
Upper Lower	44	8	57				
Lower Middle	28	9	55				
Upper Middle	13	4	15				
Upper	5	5	3				

Table 11: Correlation between genetic factors of OFCs and parents' tribe of children with OFCs (n=280)

Parent's tribes	Family history (genetic)		Calculated Chi Value	Df	Sig. (one-sided)	Statistical Inference
	No	Yes				
Different	35	17	3.690	1	.028	Association is significant
Same	120	108				

Table12: Distribution of children with OFCs according to positive family history of similar condition (n=280)

Genetic factors (If Similar Family Problem Yes)	Frequency	Percentage	Confidence Interval (95%)

			Standard Error	Lower Limit	Upper Limit
Father	3	2.4	0.014	0.14	4.66
Mother	2	1.6	0.011	0.00	3.45
Sibling	26	20.8	0.036	14.81	26.79
Father Family	49	39.2	0.044	32.00	46.40
Mother Family	34	27.2	0.040	20.63	33.77
Both father and mothers families	11	8.8	0.025	4.62	12.98

Table 13: Distribution of parents of children with OFCs according to their tribes (n=280)

No	Tribe Name	Mothers		Fathers	
		Frequency	Percentage	Frequency	Percentage
1	Aljaleen	21	7.5	27	9.6
2	Badriya	17	6.1	10	3.6
3	Hassanieh	17	6.1	13	4.6
4	Koahla	17	6.1	16	5.7
5	Rizeigat	15	5.4	17	6.1
6	Nubians	13	4.6	9	3.2
7	For	8	2.9	11	3.9
8	Joamaa	8	2.9	8	2.9
9	Btahin	7	2.5	5	1.8
10	Dnaqla	7	2.5	9	3.2
11	Jamoia	7	2.5	9	3.2
12	Rufaian	7	2.5	6	2.1
13	Shukriya	6	2.1	6	2.1
14	Barti	6	2.1	5	1.8
15	Magarba	6	2.1	6	2.1
16	Zaghawa	6	2.1	5	1.8
17	Tama	6	2.1	6	2.1
18	Muslamia	5	1.8	6	2.1
19	Bargo	5	1.8	5	1.8
20	Barno	5	1.8	5	1.8
21	Alhamar	5	1.8	3	1.1
22	Malia	5	1.8	6	2.1
23	Abdalab	4	1.4	4	1.4
24	BaniAmer	4	1.4	4	1.4
25	Shaigia	4	1.4	4	1.4
26	Halawin	4	1.4	4	1.4
27	Msaleit	4	1.4	5	1.8
28	Mahas	4	1.4	3	1.1
29	Salamat	3	1.1	2	0.7
30	Missiriya	3	1.1	1	0.4
31	Falata	3	1.1	4	1.4
32	Medoab	3	1.1	3	1.1
33	Abadi	2	0.7	1	0.4
34	Kebabish	2	0.7	2	0.7
35	Maalga	2	0.7	2	0.7
36	Kinaanah	2	0.7	2	0.7
37	Aoamra	2	0.7	2	0.7
38	Zidia	2	0.7	1	0.4
No	Tribe Name	Mothers		Fathers	
		Frequency	Percentage	Frequency	Percentage
39	Hoamda	2	0.7	3	1.1
40	Gulfan	2	0.7	2	0.7
41	Fadniyah	2	0.7	2	0.7
42	Grar	2	0.7	2	0.7
43	Mjaneen	2	0.7	3	1.1
44	Haosa	2	0.7	1	0.4
45	Alhoazma	1	0.4	2	0.7
46	Shuakhat	1	0.4	2	0.7
47	Bnihalba	1	0.4	2	0.7
48	Moby	1	0.4	1	0.4
49	Alkinoz	1	0.4	1	0.4
50	Rashaida	1	0.4	1	0.4
51	Tungd	1	0.4	1	0.4
52	Araky	1	0.4	1	0.4
53	Dinka	1	0.4	1	0.4
54	Trajma	1	0.4	1	0.4
55	Slihab	1	0.4	1	0.4
56	Gorania	1	0.4	1	0.4
57	Ashraf	1	0.4	1	0.4
58	Sibiaia	1	0.4	1	0.4
59	Buzai	1	0.4	1	0.4
60	Beja	1	0.4	1	0.4
61	Ahamada	1	0.4	1	0.4
62	Kabashia	1	0.4	1	0.4
63	Mahadi	1	0.4	1	0.4
64	Krjam	1	0.4	0	-
65	Daish	1	0.4	0	-
66	Rikabia	0	-	1	0.4
67	Baggara	0	-	1	0.4
68	Jmiaab	0	-	1	0.4
69	Bnihusien	0	-	1	0.4
70	Jlaba	0	-	1	0.4
71	Dngr	0	-	1	0.4
72	Musbaat	0	-	1	0.4
73	Dubasein	0	-	1	0.4

Table 14: Correlation between genetic factors and OFCs types in children with OFCs (n=280)

Type of clefts	Family history (genetic)		Calculated Chi Value	df	Sig. (one-sided)	Statistical Inference
	No	Yes				
Lip only	52	58	6.034	2	.025	Association is significant
Palate only	19	8				
Both (Lip & Palate)	84	59				

Table 15: Correlation between genetic factors and position of cleft lip (n=280)

Position of cleft	Family history (genetic)		Calculated Chi Value	Df	Sig. (one-sided)	Statistical Inference
	No	Yes				
Unilateral Right	29	37	3.673	2	.080	Association isn't significant
Unilateral Left	77	60				
Bilateral	30	20				

Table 16: Correlation between genetic factors of orofacial clefts and the family initial home (residence) (n=280)

Family Initial Home	Family history (genetic)		Calculated Chi Value	df	Sig. (one-sided)	Statistical Inference
	No	Yes				
Southern East States	14	13	17.554	6	.004	Association is significant
Kordofanian States	31	22				

Darfur States	33	14				
Northern States	9	11				
East States	12	1				
Khartoum State	23	43				
Al-Gazira State	24	21				

Table 17: Distribution of mothers of children with OFCs according to number of cigarette pockets exposures per day (n= 70).

No. of Pockets exposed Per day	Frequency	Percentage	Confidence Interval (95%)		
			Standard Error	Lower Limit	Upper Limit
<1	22	31.4	0.055	22.27	40.58
1-2	29	41.4	0.059	31.71	51.14
3-4	14	20.0	0.048	12.11	27.89
> 5	5	7.1	0.031	2.06	12.22

Table 18:Correlation between types of orofacial clefts and Mother smoking during pregnancy

Mother Smoking during pregnancy	Type of clefts			Calculated Chi Value	df	Sig. (one-sided)	Statistical Inference
	Lip only	Palate only	Both				
No	88	18	104	2.861	2	.120	Association isnot significant
Yes	22	9	39				

Table 19: Distribution of mothers of children with OFCs according to presence of chronic diseases during pregnancy (n=17)

Maternal chronic diseases	Frequency	Percentage	Confidence Interval (95%)		
			Standard Error	Lower Limit	Upper Limit
Diabetes	2	11.8	0.057	0.00	15.3
Hypertension	7	41.2	0.111	11.18	47.65
Ischemic heart	2	11.8	0.057	0.00	15.3
Asthma	3	17.6	0.078	0.00	24.66
Hypothyroidism	3	17.6	0.078	0.00	24.66

Table 20:Correlation between types of orofacial clefts and Maternal history of chronic disease

Maternal history of chronic disease	Type of clefts			Calculated Chi Value	df	Sig. (one-sided)	Statistical Inference
	Lip only	Palate only	Both				
No	101	24	139	4.961	2	.042	Association issignificant
Yes	9	3	4				

Table 21: Distribution of mothers of children with OFCs according to types of drugs received during pregnancy (n=55)

Names of drugs	Frequency	Percentage	Confidence Interval (95%)		
			Standard Error	Lower Limit	Upper Limit
Neomarcazole.	2	3.6	0.025	0.00	7.80
Antibiotic.	21	38.2	0.066	27.37	48.99
Antihypertensive.	1	1.8	0.018	0.00	4.79
Paracetemol.	1	1.8	0.018	0.00	4.79
Anti-histamine.	1	1.8	0.018	0.00	4.79
Carbamezapine .	1	1.8	0.018	0.00	4.79
NSAID.	3	5.5	0.031	0.4	10.51
Metranidazole.	1	1.8	0.018	0.00	4.79
Thyroxine.	3	5.5	0.031	0.4	10.51
Anti-acid.	1	1.8	0.018	0.00	4.79
OCP.	4	7.3	0.035	1.50	13.05
Anti-malaria.	9	16.4	0.050	8.13	24.59
Aspirin.	2	3.6	0.025	0.00	7.80
Antibiotic+Anti-malaria.	2	3.6	0.025	0.00	7.80
Heparin+ Aspirin+OCP.	1	1.8	0.018	0.00	4.79
Antibiotic+OCP.	1	1.8	0.018	0.00	4.79
Antibiotic + NSAID+ Paracetamol.	1	1.8	0.018	0.00	4.79

Table 22: Correlation between types of OFCs and drugs intake by mothers during pregnancy (n= 280)

Drugs intakes	Type of clefts			Calculated Chi Value	df	Sig. (one-sided)	Statistical Inference
	Lip only	Palate only	Both				
No	95	17	112	8.718	2	.007	Association is significant
Yes	14	10	31				

Table 23: Distribution of mothers with children of OFCs according to doses of folic acid supplementation during pregnancy (n=110)

Levels Nutritional supplements	Frequency	Percentage	Confidence Interval (95%)		
			Standard Error	Lower Limit	Upper Limit
One month before LMP and first 2 months of pregnancy	4	3.6	0.018	0.69	6.58
After the mother knows she is pregnant (4-5 week)	64	58.2	0.047	50.42	65.94
After first trimester	42	38.2	0.046	30.54	45.82

Table 24: Correlation between types of OFCs and folic acid intakes during pregnancy (n=280)

Folic intakes	Type of clefts			Calculated Chi Value	df	Sig. (one-sided)	Statistical Inference
	Lip only	Palate only	Both				
No	74	12	86	4.973	2	.042	Association is significant
Yes	36	15	57				

Table 25: Correlation between types OFCs and time of folic acid intake during pregnancy (n=110)

Time of starts folic acid	Type of clefts			Calculated Chi Value	Df	Sig. (one-sided)	Statistical Inference
	Lip only	Palate only	Both				
One month before LMP and first 2 months of pregnancy	1	1	2	1.298	4	.431	Association isn't significant
After the mother knows she is pregnant (4-5 weeks).	19	9	36				

After first trimester	16	5	21				

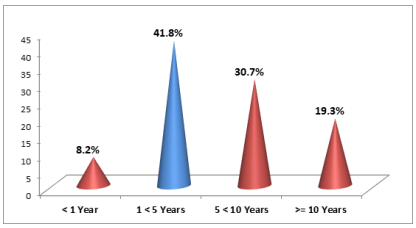


Figure 1:Age distribution of children with OFCs

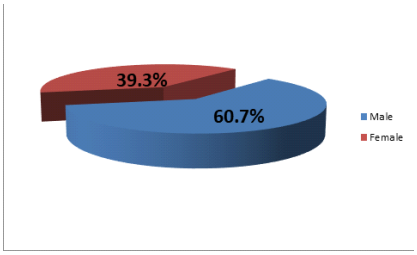


Figure2: Gender distribution of children with OFCs

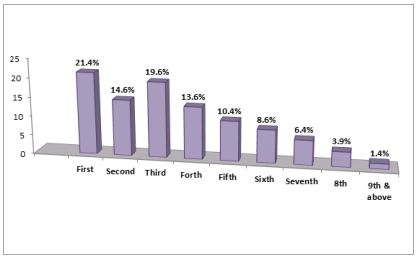


Figure 3: Distribution of children with OFCs according to Child's Birth order

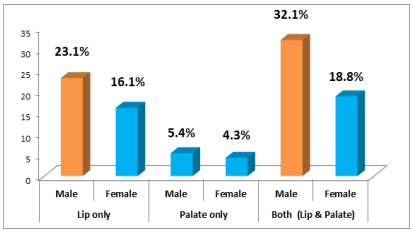


Figure 4: Distribution of types of OFCs according to child sex

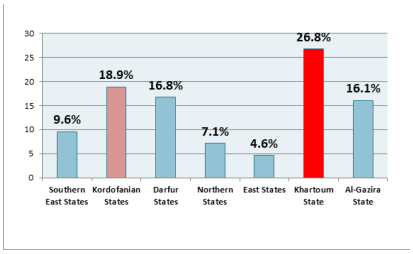
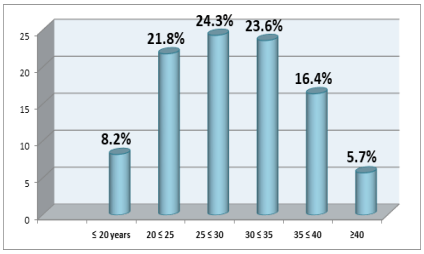


Figure 5: Distribution of children with OFC according to residence of Initial home



Figures 6: Distribution of children with OFCs according to mother's age at child birth

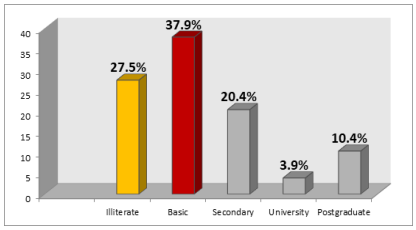


Figure 7: Distribution of mothers of children with OFCs according educational level.

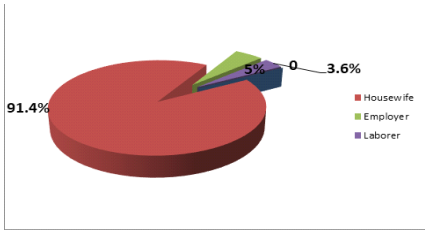


Figure 8: Distribution of mothers of children with OFCs according to occupation.

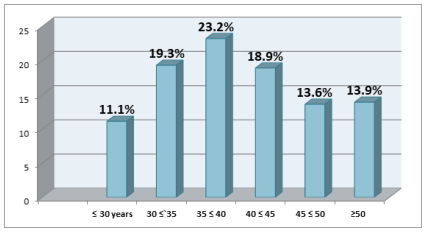


Figure9: Distribution of children with OFCs according to father's age at child birth.

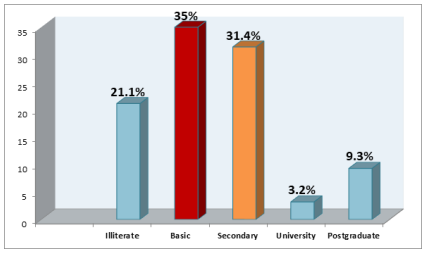


Figure 10:Distribution of fathers of children with OFCs according to educational level.

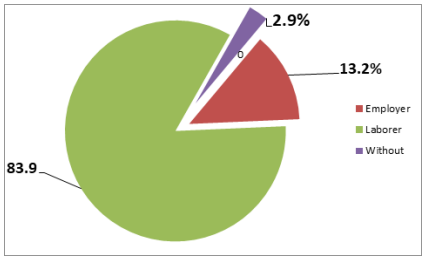


Figure11: Distribution of fathers of children with OFCs according to occupational level.

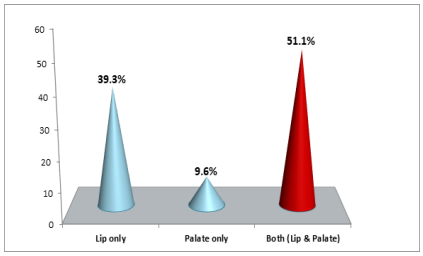


Figure 12: Distribution of children with OFC according to types of clefts

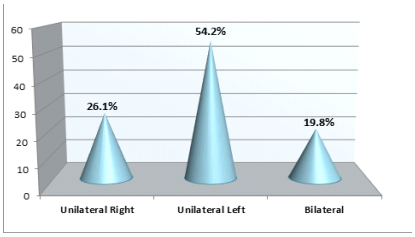


Figure 13: Distribution of children with OFC according to position of cleft lip

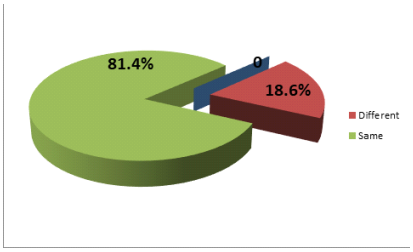
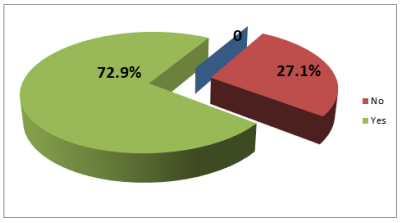


Figure 14: Distribution of children with OFCs according to parent's tribes



Figures 15: Distribution of children with OFCs according to parent'sConsanguinity

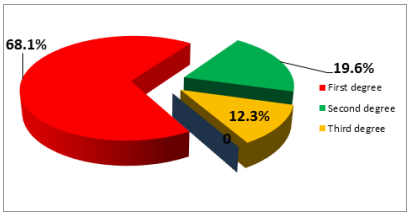


Figure 16: Distribution of children with OFCs according to degrees of Consanguinity

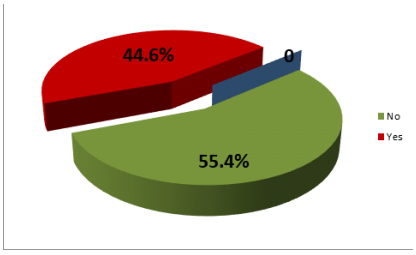


Figure17: Distribution of children with OFCs according to positive family history.

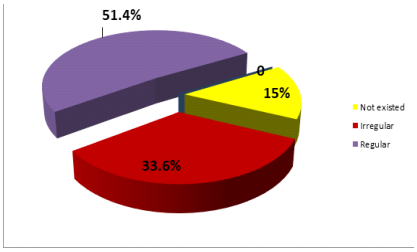


Figure 18: Distribution of children with OFCs according to maternal antenatal visit

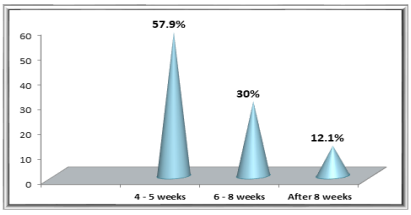


Figure 19: Distribution of mothers of children with OFCs according to time of awareness of pregnancy.

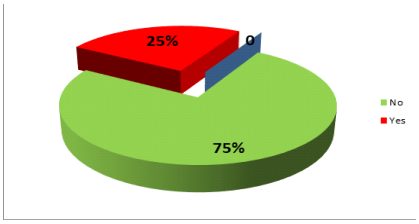


Figure 20: Distribution of mothers of children with OFCs according to exposures to passive smoking

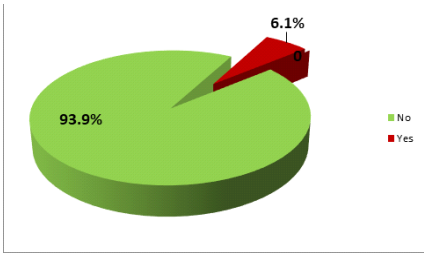


Figure 21: Distribution of children with OFCs according to maternal chronic diseases.

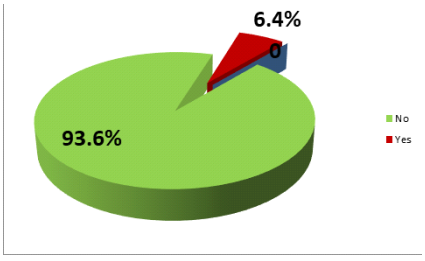


Figure 22: Distribution of mothers of children with OFCs according history of UTI during pregnancy.

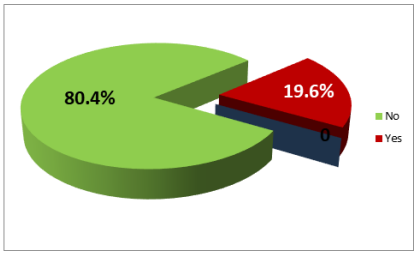


Figure 23: Distribution of mothers of children with OFCs according to history of drugs intake during pregnancy.

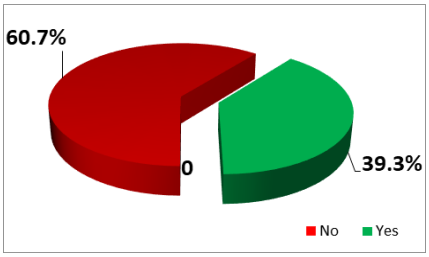


Figure 24: Distribution of mothers with children with OFCs according to folic acid supplementation during pregnancy

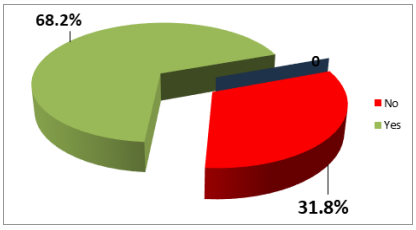


Figure 25:Distribution of mothers of children with OFCs according to iron supplementation during pregnancy

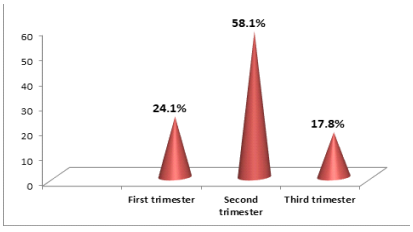


Figure 26: Distribution of mothers of children with OFCs according to time of iron supplementation during pregnancy

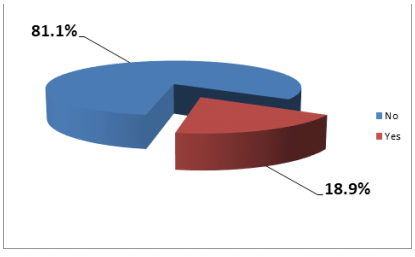


Figure 27: Distribution of children with OFC according to previous surgical treatment.

4.1 Discussion:

Our study was case descriptive cross-sectional hospital based study, conducted from January to November 2018. The purpose of this study was to identify the most common maternal risk factors associate with orofacial clefts in the patients attending Khartoum Denture Teaching Hospital, Ahmed Gasim Specialized Hospital for children and Soba University Hospitalin Khartoum state; it included 280 mothers of children with OFCs.

Orofacial defects are the most common developmental deformities seen worldwide and they are undoubtedly an important oral health issue due to their impact on the quality of life, function and also clinical impacts over many years.

4.1.1 The relation between Sociodemographicfeatures of family and risk of OFCs:

In our study populationthe most common age group of the children with OFCs was 1- <5 years, followed by 5- <10 years.This older age presentation is due to low socioeconomic status of the families,which limit their access to timely and adequate health care. Most of the families reside outside Khartoum and there is only one hospital that offers free surgical repair, Khartoum denture hospital, meaning that families have to come all the way to Khartoum and a long waiting list of patients.

This finding is in the contrary to a study done in Nigeria where they found the most common age was < 1 year (58%), followed by 1-<5 year (20%) and 5-<10 (10%).(47)

In this study the overall prevalence of OFCs has been reported to be commoner in males than female, what is similar to thestudy done in Pakistan by Elahi MM in 2004. (16)

We found that first child in the family has higher risk, that was in match to Iran study 2015, in university hospitalized patients at Mashhad.(87)and dissimilar to a meta-analysis study in countriesin which the prevalence of these disorders is higher in the mothers' next labours; in this regard, age is considered as confounding factor.(88)I recommend future research to control for it at the study design since we couldn't do that in our cross section study.

While there has been no consensus on the most common type of cleft lip and palate (16), we found that combined cleft lip and palate (CLP) is the commonest type of cleft in Sudan and this is similar to study in Southern Nigeria 2010(47) and Iran 2012.(89)

Cleft palate only(CPO) was least common in present study and this in contrary to what was found in Southern Nigeria(47) and what reported from West Scotland.(90)As well as in a study done in Mashhad - Iran 2015 by MortezaNoorollahian, over 10 years in university hospitalised patients about the Cleft lip and palate and related factors and they reported that CPO had the highest prevalence of cleft anomalies.(87)

In terms of gender, the incidence rate of different types of the cleft was different between the two genders; in local studies, the overall prevalence of OFC was higher in males. In terms of the frequency of cleft types according to gender, CLO and CLP were commoner in males than females, these results are consistent with those reported in Southern Nigeria.(54)and dissimilar to what widely reported(84)(85) and that reported in Iran by MortezaNoorollahian, in which CLO was more prevalent in males while CPO was more common amongst females.(87)

In the study by Kim et al. in South of North Korea, the prevalence of CLO and CLP were more common in male than female which is similar to our results. The only difference between the two studies is that frequency of cleft palate is more in female than male which is inconsistent to our study which is rather near equal in the two genders.(91)

Left side position of cleft lip was more common than right sidedposition in present study, that was opposite to what found in Nigeria (unilateral clefts were equally distributed on the right and left sides of the face but had more male distribution) .(47)

The majority of our cases 105(73.2%) reside outside Khartoum state and living in rural areas and it can be concluded that the prevalence of this congenital anomaly is more observed in this group, which has an economically lower status. In similarity to study of Iran 2015 in university hospitalized patients at Mashhad.(87)

In 2010, Messer et al. performed a study on the incidence of cleft lip and palate in urban and rural areas of Texas and they concluded that living in rural areas is associated with an increased risk of cleft lip and palate, though it is not related to the incidence of cleft palate only. This may be due to the fact that women living in rural areas have less access to insurance, health services and medical care, similarly in the present study, the highest prevalence was observed in the group who were living in rural areas. (92)

Maternal factors:

By comparing the risk for cleft occurrence in mothers in the age groups, we found the age group between 25-<35 yearswas more related to have child with OFCs.And this is consistent with a study done in Tehran, Iran 2012 , in which a(89)low maternal age (24-<34) is the risk factor.And that in contrary to Sipak et al who confirmed that women older than 35 were prone to a higher risk for orofacial clefts.(93)Whereas, Shaw et al concluded that the risk for women older than 39 of having children with orofacial clefts is 3 times higher compared with women aged 25 to 29.(94)

High parity (HP) refers to having 5 or more pregnancies.While HP is rarely seen in developed countries, it is still common in many developing countries. HP is especially common in Arab countries where having a big family is the common preference.(95)About one

third of the studied motherswere high parity at birth of child 86 (30.7%). Unlike the study in China 2015,(96) they found the low parity was more common in their studied mothers (78.1%),Para 1, para2 and para3and more was 45.3%,31,9%,.9% respectively.

Most of studied mothers (91%) had no occupation, and that reflect there was no occupational maternalfactors related to have offspring with OFCs. In contrary to study done in China 2015 (96)the study was done in Heilongjiang Province is an industrial base area and agricultural province which in northern China. Its industry mainly focus on coal, petroleum, machinery, and pesticides in the province, they report that , maternal occupational exposure to toxic agents seemed a priori to have a more direct effect on development of OFC in offspring , and was previously found to be associated with an increased risk of NSOFC in offspring .

More than 50% of studied mothers had low education level, thismay reflect that low educational levelis risk to have child with OFCs.Similar to previous study in China (96)they found that: (in compared with parents of the children in control group, parents of the children in the case group were more likely to be poorly educated (primary or junior high school) . Also other result in Tehran 2012, they report that : low maternal education seemed to be risk factors for having a child with orofacial clefts similar to our study .(89)

Paternal factors:

According to our results, the highest risk for cleft occurrence was with paternal age 35-<40 years (23.2%) and the fathers age more than 40 years represents almost 46.1 % of the studied fathers, and this result is consistent with study of southern Nigeria ,(47)where they stated : paternal ages greater than 40 years were observed as significant risk factors for the development of specific cleft types.

Socioeconomic status of the families:

Low socioeconomic status as a risk factor should be considered because it can be a marker of parental health and life style. Individuals with low education tend to smoke more and have less healthy diets and nutrients. The life style factors, either alone or combination with occupational activities and genetic background, play a role in the etiology of orofacial cleft.(89)

Regarding SES of the family, more than one third of our study population were coming at upper lower class (about 40 %) and one third at lower middle class (about 33%).and this results were similar to what found in India 2017 by(Goveas and Savitha:Role of Environmental Factors in the Etiology of Non-syndromic Cleft Lip Palate) in which the majority of families were under the upper lower and lower middle classes. Their results for this were statistically significant (P = 0.000) showing that there is a strong tendency for lower SES group toward CLP.(10)

India March 2017	SES classes	Sudan November 2018	Comparisons
	Upper	4.6 %	
2.4 %	Upper middle	11.4 %	
28.4 %	Lower middle	32.9 %	Similar finding in the two study
57.6 %	Upper lower	38.9 %	Our level is less than that reported in India
1.6 %	Lower	12 %	

In Iran, also the Low socioeconomic status seemed to be risk factors for having a child with orofacial clefts similar to our study where more than one third at upper lower .(89) and that is again similar to Kraples et al. study (98)and also in same side of other study done in Ireland 2011.(40)

4.1.2Genetic factors and OFCs:

Our findings confirmed that positive family clefts history increased therisk to have a child with OFCs compared with those cases with a negative family history.

Leite and Koifman, in a case-control study, found that the history of oral clefts either in the father's or in the mother's family is strongly associated with both types of clefts(CLP), but paternal consanguinity was associated only with CLO and cleft palate (CPO).(99)

Also ,Zarante et al found that a positive family history of another craniofacial malformation (OR = 3.1, CI 95% 2.2–4.3) and cleft lip with or without cleft palate (CLP) (OR = 2.5, CI 95% 1.1–5.8) are important risk factors for orofacialclefting.(100)

In Korea, a positive family history is found in 7% of cleft cases, with the most common type being a CLO (10.8%) followed by CLP (6.7%), and the rarest type being a CPO (3.7%).(91) Natsume et al found that 15.4% (47 of 306) of cases of cleft in Japan had a positive family history for CLP, whereas in the control group only 1.6% (5 of 306) of cases had a positive family history for clefting.(101)

4.1.3Maternal behavioral factors and risk of OFCs:

Regarding Smoking:

However, in our study none of mothers had smoking habit which could be explained because of the Sudan culture where most of them do not indulge in smoking habits. Interestingly, however we found, passive smoking was common in 25%, and many of the women were exposed to passive smoking at home giving, suggesting a correlation between passive smoking and orofacial clefts development.

This result is in accordance with a study by Taghavi et al.,(89) and various other studies.(45)(102)(98)(103)

4.1.4Maternal chronic disease and risk of OFCs:

In our study chronic diseases was found in (6.1%), with (29.4%) being Hypertension, followed by Hypothyroidism and Asthma in (11.8%) of cases.

In study done in 2011 Ireland, they stated that Parental disease, did not correlate with cleft lip and/or palate.(40)

Other Study (10) have also shown that maternal diseases such as epilepsy, ulcerative colitis, and angina pectoris have been one of the contributing factors for CLP.

4.1.5 The relation of drugs intake and risk of OFCs in study population:

Another factor to be considered is the intake of drugs during the first trimester of pregnancy. In our study, a total of 55 mothers (20%) had taken drugs during their pregnancy, mainly antibiotic, antimalarial, Analgesics, Anticonvulsants, andNeomarcazole.

Our study confirmed that the intake of drugs during pregnancy, is a risk factor to have child with OFCs (P = 0.007).

Puhó et al evaluated the possible association between all kinds of drug treatments during pregnancy and isolated cleft lip with or without cleft palate and posterior cleft palate in the offspring. They found that children born to mothers treated with amoxicillin, phenytoin, Oxprenolol, and Thiethylperazine during the second and third months of pregnancy have an increased risk for isolated CLP.(104)

Sami Salihu did his study in 2014 a total of 27 mothers had taken drugs during their pregnancy, mainly Analgesics, Antiemetics, Sedatives, Corticosteroids, Anticonvulsants,and drugs containing iron and Folate. And his study confirmed that the intake of drugs during pregnancy as a potential risk factor has little influence on the prevalence of clefts (P = 0.19).(4)

4.1.6 Supplementation (Folic acid, Multivitamins and iron) and OFCs:

The vast majority of mothers interviewed in our study did not plan pregnancy and, as a result, started multivitamins or folic acid uptake during the 2nd or 3rd month of pregnancy, as soon as they found out that they were pregnant. Adequate folic acid levels are reached three months later. Consequently, multivitamins or folic acid treatment was null or inadequate during the first gestational trimester, which is the crucial period for craniofacial development.

4.1.6.1Folic acid:

To assess the protective role of vitamins supplement especially folic acid the history of folic acid supplement was interviewed and we found that the majority of studied mothers didn't take Folic acid supplements in pregnancy (about 61%), suggesting there might be anincreased riskof clefts among the ones who had not taken the supplements which agree with the studies about the protective role of vitamins supplement before or after conception.(5)(105)(106)(107)
(107)

4.1.6.2Iron:

While about two third (68.2 %) of studied mother took iron supplementation during pregnancy and of them more than half (58.1%) took it at the second trimester. And this isin contrary with analysis of data studied in Iran,(89) showed that folic acid and iron intake during pregnancy would decrease the risk for orofacial cleft .which is adjusted for most studies in this field.(108)

4.1.6.3 Multivitamins:

Very few mothers (0.7 %) took multivitamins supplementation during pregnancy,this maysuggest thatpreconception multivitamin use isassociated todecreased risk ofOFCs. Because multivitamins contained different vitamins and minerals and the composition and dose of vitamins and minerals in multivitamins vary, it was difficult to identify which component(s) of multivitamins possibly contributed to risk reduction.(105)(106)

4.1 Study strengths & limitation:

- The strengths of this study include ditsrelativelyhigh participation by study subjects, and its separate analysis of CPO, CLO, and CLP, which are likely to be unique etiologic entities. Nevertheless, our study had some potentially important limitation.

- The potential limitations of this study were the fact that part of the information/data collected were based on history from the parents and therefore there was the possibility of concealing facts or information and indeed may even have recall bias. However, efforts were made to overcome this difficulty by counseling the patients/parents appropriately. The importance of volunteering accurate information/data was emphasized by the patient's management and identifying preventive strategies that will avoid a recurrence in future conceptions in the family.

- Additionally, efforts were made to determine the associated environmental risk factors for the development of clefts and not genetic factors, which was only indirectly inferred from the family history due to lack of facilities for DNA testing in the current situation.

- Regarding the point of supplementation (Folic acid, Multivitamins and Iron), the mothers could not recall the exact prescription to differentiate between other vitamins and folic acid which could be due to a lack of education or lack of documentation and this remains a drawback of this study.

4.3 Conclusion:

From this study, it is concluded that, OFCs were not uncommon congenital anomalies in Sudan. OFCs were commoner in male and the combined CLP was the commonest entity in the study,with the common age observed in the children was 1-4years.

The study revealed that there are many factors that can be involved in OFCs predispositions. Many of them require additional research to confirm their significance in etiology of these orofacial malformations.

The main risk factors associated with the development of cleft lip and cleft palate in a Sudanese population at Khartoum Denture Teaching Hospital, Ahmed Gasim Specialized Hospital for children and Soba University Hospital were lack of folic acid intake during pregnancy, heredity with a positive family cleft history, high parity of the mothers, paternal age greater than 40 years and maternal age lower than 35 years.

Low education of the mothers and the low SES of the families are strongly related to development of OFCs.

Passive smoking and the use of drugs during pregnancy also increased the risk for cleft incidence but did not reach a significant level. On the other end of the scale, maternal chronic disease had the least relation with the development of these malformations.

Moreover, a statistically significant association was found between a lack of folic acid intake, hereditary factors, low SES, systemic diseases and drug intake during pregnancy and the types of OFCs.

Improving our knowledge about the potential risk factors leading to oral clefts can be very useful in their prevention.Very important to educate future mothers about behaviors before and during pregnancy that can increase the risk of oral clefts.

The parent's attitude in OFC patients and their response to prognosis and treatment is very important. Most parents do not perceive oral clefts as a severe condition .Because of a great but long term treatment of OFC the patient's quality of life can be greatly improved if treatment takes place just after childbirth and lasts almost their entire life

4.1 Recommendations:

- To conduct more advance researches, especially in the field of cleft genetics.

- We need observation researches with better study design like cohort study to identify causal relationship between OFCs and maternal chronic diseases or the drugs intake.

- To do more local studies concerning the role of folic acid and OFCs.

- To increase awareness of this anomaly, its prevalence, and the huge numbers of the complication so that affected persons may seek and receive early treatment.

- To increase awareness of the women in child bearing age through large media programs, health education program at different level in community, distribution of free photos about the etiological factors and the preventionto obviate the occurrence and reduce the burden.

- To increase awareness and knowledge of the community population about the risk of consanguineous marriage.

- There is an urgent need for an intensive worldwide education program for healthcare professionals to focus on the prevention of NSOC.

- To do information campaigns about prompt onset of multivitamins or folic acid supplementation (at least three

months before conception).

- There is a need for collaboration of all responsible stakeholders, including the Ministry of Health of Sudan and Non-Governmental Organizations involved in the management OFC management, to ensure that there is adequate management policy to produce an excellent outcome.

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