

Antenatal Risk Factors and Orofacial Clefts in Children

Riaz Ahmad, Rizwana Nawaz and Hussain Humayun

ABSTRACT

Objective: To determine the association of various antenatal risk factors in the mothers and the occurrence of orofacial clefts in the offspring's.

Study Design: Observational / descriptive Study.

Place and Duration of study: This study was conducted at Ayesha Bashir Hospital (Cleft hospital) and Govt. Aziz Bhatti Hospital /NSMC, Gujrat from June to December 2016.

Materials and Methods: This study was done at Ayesha Bashir trust (Cleft hospital) which caters for the diagnosis, treatment and rehabilitation of the children with orofacial clefts. A particular Performa was made for the identification of association of various antenatal risk factors in the mothers and orofacial clefts in the off springs. The children with minor defects were excluded from the study.

Results: The total no. of the patients was eighty one. There was a little association (1.25%) between the family history and orofacial clefts. Consanguineous marriages was the most important factor, about 85% of the parents of the affected children had consanguineous marriages. Regarding the family history only 5% of the siblings were affected. About 3.75% of the affected children were twins. About 2.5% of the mothers had UTI and abdominal pain. No particular association with any medical disorder was observed in this study. The important association was observed regarding the use of folic acid. About 60% of the parents did not take folic acid during the current pregnancy.

Conclusion: It is concluded in this study that in addition to the other risk factors consanguinity among the parents and lack of intake of folic acid in early pregnancy are the factors increasing the incidence of orofacial clefts in the offspring's.

Key Words: Orofacial clefts, Antenatal, Cleft lip and Palate, Consanguineous, Folic acid.

Citation of articles: Ahmad R, Nawaz R, Humayun H. Antenatal Risk Factors and Orofacial Clefts in Children. Med Forum 2017;28(9):28-31.

INTRODUCTION

Orofacial clefts are one of the most common anomalies. The incidence of the defects is 1 in 500-550 births. This is a heterogeneous group of anomalies, these may be classified into the typical orofacial clefts (cleft lip CL; Cleft lip and palate CLP and cleft palates only CP) and atypical clefts (median, transversal, oblique and other Tessier, s type of the facial clefts.

These could be an isolated anomaly as a part of the primary sequence defect or as a multiple congenital anomaly (MCA). In this group, it could be part of a known genetic syndrome or part of a chromosomal aberration^{1,2}.

There are many demographic, social, familial and antenatal risk factors which can affect the occurrence of the orofacial clefts independently or in association with

each other. There are many antenatal risk factors which are associated with the occurrence of the orofacial clefts ranging from the paternal age, parity of the mother, parents affected or not, history in siblings, consanguineous marriage, The other variables could be whether it was a spontaneous or induced, single or multiple pregnancy, any drugs taken during the first trimester, parents smoker or not, either some multivitamin or folic acid taken during the first trimester or not, what type of the food she consumed, or exposure to any chemicals or gasses. There are certain myths associated with the occurrence of these defects. An important myth is the exposure of the pregnant lady to Sun and Moon Eclipse, which was also studied.

Consanguinity and family history is very important in the recurrence of orofacial clefts. In a met analysis³ it was concluded that there is a greater genetic component in the etiology of CL (cleft lip) based on the observation that there is an excess of individuals with CL over CLP in the offspring of consanguine parents. It was also found in another population study that anatomical severity does have an effect on recurrence in the first degree relatives and type of the cleft is predictive of the recurrence type. There are also increased chances of recurrence in the third degree relatives as compared to the background population. This particular fact was also supported in another study⁴ that multiple risk

Department of Obstet & Gynae, Govt. Nawaz Sharif Medical College, University of Gujrat.

Correspondence: Dr. Riaz Ahmad, Assistant Professor, Department of Obstet & Gynae, Govt. Nawaz Sharif Medical College, University of Gujrat.

Contact No: 0300-4389976

Email: riazmughal111@outlook.com, farariaz@ymail.com

Received: June 10, 2017;

Accepted: July 19, 2017

factors contribute to the development of a CLP ,including genetics ,advanced age, family history, antiepileptic drugs, consanguineous marriage and smoking, and history of the previous child. Isabel Cristina and associates provided evidence for strong association between oral cleft and a family history of malformations and parental consanguinity. It also provided statistically significant association between maternal smoking and alcohol use.⁵

In another study⁶, it was found that the use of folic acid containing prenatal vitamins is associated with decreased risk of several congenital anomalies, not only neural tube defects. This approach may be considered.

VW Omo-Aghoja et al found in their study that following risk factors were associated with the risk of development of cleft lip and palate: Paternal age>40 years. Maternal age>35 years, genetic, family history, low socio economic status, alcohol consumption and indulgence in the intake of herbal medications in pregnancy.⁷

Family history is very important in the occurrence of orofacial clefts. Jane .C et al. Concluded in their study that family history was strongly associated with increased risk. Advanced maternal age, pre gestational hypertension and gestational seizures, Low maternal, paternal education and tobacco smoking were associated with increased risk⁸.

MATERIALS AND METHODS

This Study is a descriptive observational type which was done for a period of six months from June to December 2016 at Ayesha Bashir Trust (Cleft Hospital Gujrat) and Aziz Bhatti Teaching Hospital (NSMC).Ayesha Bashir Trust is a multi-disciplinary Hospital especially catering for the diagnosis, research, treatment and rehabilitation of the children with orofacial clefts and defects. A particular Performa was made for the identification of association of various antenatal risk factors and orofacial clefts. The parents and attendants were interviewed for the data. The children with minor degrees of clefts were excluded from the study. The study was not funded and the data was analyzed on SPSS 16.

RESULTS

The total number of the patients was 81. There was a little association (1.25%) between the family history and orofacial clefts, only one mother was affected in this study.

There was a strong association between the consanguineous marriages and the children affected, the frequency was 85%. Regarding the family history only 5% of the siblings were affected.

About 3.75% of the affected children were twins, rest were singleton pregnancies. The association of a particular food and orofacial clefts may be there, but in this study almost all the patient were consuming the

same food like Roti (bread), meat, vegetables.

Table No.1: Family history as a determinant

Fathers affected	1	1.25%
Mothers affected	0	0
Family history	1	1.25%

**Table No. 2: Consanguinity And Siblings affected
Consanguine marriages=68 Percentage=85%
Association of siblings affected/not affected**

Total no .of the patients=81		
Siblings affected/not affected	No of Patients	Percentage
Affected	4	5
Not affected	76	95

Table No.3: number of fetuses in relation with orofacial clefts

Type of the pregnancy	Frequency	Percentage
Singleton	77	96.25
Twins	3	3.75
Multiples	0	0

Table No.4: Type of the food consumed in the affected (parents)

Type of the food	Frequency	Percentage
Roti saalan (gravy food)	81	
Rice	70	
Meat	81	
Vegetable	81	
Organic	80	
Non Organic	80	

Table No.5: Maternal illness in the current pregnancy and orofacial defects

Maternal illness	Numbers affected	Percentage
Malaria	0	0
UTI	2	2.5
Abdominal pain	2	2.5
PV Bleeding	1	1.25
Diarrhea	1	1.25
Miscarriage	1	1.25
Exposure to agriculture spray	0	0

Table No.6: Medical disorders in current pregnancy and occurrence of orofacial clefts

Medical disorder	Frequency	Percentage
HTN	2	2.5
Anemia	2	2.5
Thyroid	2	2.5
Allergy	1	1.25
Asthma	0	0
Steroids-anesthesia	0	0
Addiction	0	0

And it included organic and inorganic as well. About 2.5% of the mothers had a history of UTI and

abdominal pain in early pregnancy and 1.25% each mothers had an episode of PV bleeding, diarrhea and miscarriage.

Regarding the medical disorders in such pregnancies about 2.5% each were diabetic, hypertensive and anemic.

There are certain myths about the orofacial clefts in association with moon and sun eclipse, none of the patients had moon eclipse during their pregnancy ,however about 13.75% had sun eclipse during the current pregnancy.

Regarding the conception about 86.25% had spontaneous conception, and 11.25% had induced and 2.5% had others method for conception

DISCUSSION

Family history may predict the occurrence of orofacial clefts. In this study only one father and mother were affected and no other family member was affected. Sami Slieihu⁹ and associates concluded in their study that heredity with a family history of clefts was the most important risk factor in addition to the other risk factors e.g. maternal age, drugs and smoking.

In this study a very important finding was observed that about 85% of the parents of the children having a consanguineous marriage which is alarming. Sultani MK and colleagues found in their study that consanguinity was there in about 31% of the cases. And about 38% had other abnormalities and the incidence was 1.09/1000 live births¹⁰.

In a study in in Brazil¹¹ there was evidence of strong association between oral clefts and a family history of malformations and parental consanguinity. It also provided a moderate but consistent association between the alcohol use and orofacial clefts. In a hospital based study in Riyadh Ravichandran K and associates¹² found that consanguine relationships were seen in 56.8% of our patient's parents. Family history was more likely to be positive for patients whose parents were consanguineous than those who were non consanguineous (34.2% vs. 25.8% p=0.003) both for the CL and palate and C P groups. Recurrence among siblings did not differ between those born to consanguine versus non consanguineous parents. Sushmitah Basker in her study found that (13) in most cases, parents of the affected children had consanguineous marriages. It was also concluded in this study that females were more affected than male siblings.

In another study consanguinity¹⁴ Rajeev and colleagues concluded that nearly half of the population in their study had a positive history of consanguinity, statistically a significant association was seen between CP and consanguinity. Cleft lip and Palate cases were the most common type identified, followed by CL and CP.

Males predominated in all types of the clefts. The prevalence of O.F.C is high and there is a potential of congenital disabilities from consanguinity.

It was also found in this study that about 5% of the siblings of these children was also affected which was higher as compared to the general population.

It has been found, and generally that the congenital anomalies, and deformities are more in multiple pregnancies than in singleton. In this study there were no multiple pregnancies however 3.75% were twins as compared to 96.25% which were singleton. In another it was found¹⁵ that the prevalence of oral clefts was 15.8/10,000 Twins and 16.6/10,000 singletons (Prevalence proportion ratio=0.9).Twins prevalence was similar for monozygotic and dizygotic twins. No excess risk of oral cleft could be demonstrated for twins compared with singletons. The concordance rate heritability estimates for both types of clefts show a strong genetic component.

Maternal illness may affect the fetus in utero especially in the embryonic period, so it may be one of the reasons of orofacial defects. It was found in this study that 2.5% of patients had UTI and abdominal pain and 1.25% each had pv bleeding, diarrhea and miscarriage Almost similar results were found In a study by Ana Thereza de Saboia Campos Neves and associates that maternal and paternal smoking in the first trimester of pregnancy and parity were significantly associated with the occurrence of CLP. Parents age, educational level and occupation did not interfere in occurrence of oral clefts. There was also no significant association between maternal illness, medication use, alcohol consumption and maternal exposure to chemicals in the first trimester of pregnancy and occurrence of clefts in the population.

A particular type of the food is consumed in certain societies, which may be associated with certain congenital anomalies. In this particular study all of the parents of the children were using the same type of the food, being most of the Punjabi population. All of them were using Roti (Bread) Saalan (gravy food), meat, vegetables, organic and non-organic type of the food, so no particular association with any food was observed. However in a review study¹⁶ it was found that use of maternal western diet, high in the meat, pizza, legumes and potatoes and low in fruits and vegetables increases the risk of offspring with a cleft lip or cleft palate approximately two fold. Bille C and associates in their case control study that first trimester maternal smoking was associated with an increased risk of oral clefts. Although not statistically significant, we also saw associations with first trimester consumption of alcohol and drinking more than one liter of cola per week.¹⁷

There are certain congenital anomalies which may be associated with certain medical disorders in the mother. In this study the mothers had 2.5% each diabetes, hypertension and anemia and 1.25% thyroid disorder, but none of them had asthma, use of steroids, any surgery and addiction of any drug. In a similar study¹⁸ it was found that family history of clefts was strongly associated with increased risk of these defects. Advanced maternal age, pregestational hypertension, and gestational seizures were statistically significant factors. Similarly some environmental factors e.g. rural

background, indoor cooking with food appeared to be associated with increases risk adjusted models.

The intake of folic acid and multivitamins is considered to be preventive for the occurrence of various congenital anomalies in the children of these mothers. About 60% of the mothers did not take folic acid in this particular pregnancy but rest of the mothers took it. Lynn B bailey and Robert J .Berry in their study^{19,20} concluded that there was 50% reduction in the occurrence of orofacial clefts which was same as was found in earlier studies that the preconception use of folic acid and multivitamins reducing the risk of various birth defects and especially the orofacial clefts.

CONCLUSION

Antenatal risk factors certainly do affect the occurrence of various congenital anomalies in the offspring's. By the results of this study and other National and international studies, it is concluded that in addition to other factors consanguineous marriages and lack of intake of folic acid in early pregnancy are the factors increasing the incidence of orofacial clefts in the newborns. Further studies are required to prove the association of consanguineous marriages and folic acid intake in early pregnancy by keeping the other variables constant.

Author's Contribution:

Concept & Design of Study: Riaz Ahmad
 Drafting: Rizwana Nawaz
 Data Analysis: Hussain Humayun
 Revisiting Critically: Rizwana Nawaz & Riaz Ahmad
 Final Approval of version: Riaz Ahmad

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Kawalec A, Nelke K, Pawlas K, Gerber H. Risk factors involved in orofacial clefts predisposition; Review Open Med 2015;10:163-175.
2. Marie M. Tularova Jaroslav Cervenka. Classification and Birth Prevalence of orofacial clefts. Am J Med Genet 1998;75:126-137.
3. Vera Lucia Gil-da-Silva-Lopes, Monello IL. Risk factors and the prevention of oral clefts. Braz oral Res 2014;(spec issue):1-5.
4. Ucar MG, et al. Cleft lip and cleft palate, a disease with multiple risk factors in a pregnant woman, Int J Reprod Contracept obstet Gynecol 2015;4(6): 2044-2046.
5. Cristina I, Leite G, Koifman S. Oral clefts, Consanguinity, Parental tobacco smoking and alcohol use: A case control study in Rio de Janeiro, Brazil. Braz Oral Res 2009;23(1):31-37.
6. Goh I, Bollano E, Einarson TR, Koren G. Prenatal multivitamin supplementation and rates of

congenital Anomalies. Ameta-analysis Obstet Gynecol Can 2006; 28(8):680-689.

7. V W Omo-Aghoja, et al. Antenatal determinants of orofacial clefts in Southern Nigeria. Afr Health Sci 2010;10(1): 31-39.
8. Jane C, et al. Parental risk factors for oral clefts among central Africans, Southeast Asians, and Central Americans. Clin Molecul Teratol 2015; 103(10):863-879.
9. Sami Sleihu etal. Analysis of potential oral cleft risk factors in the Kosovo population. Int Surg 2014;99(2):161-165.
10. Soltani MK, Mohammadi Z, Nasab AZ, Golfashan F. The incidence of cleft lip and palate in a Kurd population; A prospective study, community dental health 2014;31(10):50.
11. Jia ZL, et al. Maternal malnutrition, environmental exposure during pregnancy and risk of non syndromic orofacial clefts. 2011;17(6):584-589.
12. Ravichandran K, Shoukri M, Al Johar A, Shazia NS, Al-Twaijri Y, Al Jarba I. Consanguinity and occurrence of cleft lip/Palate: A hospital based registry study in Riyadh. Am J Med Genet Part A 2012;158 A: 541- 546.
13. Basker S. Prevalence of orofacial defects due to familial aggregation, at tertiary care Centre in Chennai. A cross sectional study. J Med Sci Clin Res 2014;2(6):1428-1437.
14. Rajeev BR, Prasad K, Shetty PJ, Preet R. The relationship between orofacial clefts and consanguineous marriages. A hospital based study in Dhārwad, South India Cleft LIP Palate craniofac Anomal 2017;4:3-8.
15. Ana Thereza de Saboia Campos Neves, Luiz Evaristo Ricci Volpato, Mariano Martinez Epinosa, Andreza Maria Fabio Arahana and Alvaro Harrigue Borges. Environmental factors related to the occurrence of oral clefts in a Brazilian subpopulation. Niger Med J 2016;57(3): 167-172.
16. Diaz GH. Casado GJ, Gravalos Diaz. Orofacial closure defects: Cleft lip and palate. A literature review 2013;39(5):267-271.
17. Bille C. Olsen J, Vach W, et al. Oral clefts and life style factors. A case cohort study based on prospective Danish data. Epidemiol 2007;22:173.
18. Yun C, Wang Z, He P, Chao GUO, Chen G, Zheng X. Prevalence and parental risk factors for speech disability associated with cleft palate in Chinese children-A National Survey. Int J Enviorn Res Public Health 2016;13(11):1168.
19. Baily LB, Berry RJ. Folic acid supplementation and the occurrences of congenital heart defects, orofacial clefts, multiplebirths and miscaariage.AM J Clin Nutr 2005;81(suppl):121(3s-7s).
20. Gorlin RJ, Cervenka J, Pruzansky S. Facial clefting and its syndrome. Birth Defects Orig Artic Ser 1971;7(7):3-49.