

Risk Factors of cleft malformation in Children

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Abstract

Introduction: Most children born with cleft malformation (CM) are unable to be breastfed and require several surgical procedures and complex medical treatments. Therefore, this study was conducted to determine the risk factors of cleft malformation (CM).

Methods: The study used case-control design. Children with CM attending at Morang Co-operative Hospital were taken as cases, and controls included age ($\pm$ six months) and sex matched children for each case from Koshi Zonal Hospital. All cases and controls included were aged below ten years. A semi-structured interview schedule was used to collect information regarding exposure status.

Results: Majority (80.5% of the case and 78.6% control) children belonged to less than five years of age and CM was more common in males (71.4%) than in female (37.5%) with cleft lip and palate being the most common type of CM. One-fourth (25.0%) of the case children had positive family history of CM. Similarly, 10.7% mothers of case children had consumed alcohol during the first trimester of pregnancy. Analysis using chi-square and odds ratio identified positive family history (Odds Ratio 3.4) and maternal alcohol consumption during first trimester (Odds Ratio 4.8) to be significantly associated with CM in the offspring.

Conclusions: Study concludes that positive family history of CM and maternal alcohol consumption during the first trimester tends to be the significant risk factors of CM. Children born to the family with positive history of CM are three times more likely to develop CM and mothers who consume alcohol during first trimester are five times at greater risk of delivering offspring with CM. Burden of complex and expensive cleft treatment can be prevented by minimizing exposure to the identified risk factor.

Key Words: Cleft malformations, risk factors and case control study,

Introduction

Cleft malformation (CM) is the most common congenital abnormalities of the orofacial structures in children. Children with CM face numerous problems. Feeding and swallowing difficulties are the commonest problems. Along with these, speech and hearing impairment and dental problems like absence of teeth in the area of cleft lip or delayed eruption of teeth can also be seen¹. Children who have CM require several surgical procedures and complex medical treatments. Also, these children and their families often experience serious psychological problems².

A multidisciplinary approach is required to assist these children including a team of pediatricians, plastic surgeons, otolaryngologist, pedodontist, orthodontist, nurse, speech therapist, audiologist, and social worker³. Though the reconstructive surgery is possible, little is in the country for the rehabilitation of children with CM. Thus, the need for identifying the risk factors of CM and planning for the preventive programs at national level is noteworthy.

The situation of CM can be considered as the “hidden catastrophe” with inequalities in access to cleft care and the accumulation of unrepaired clefts of the lip and palate. No study has been known to be conducted so far in the developing countries like Nepal. Therefore, this study was conducted with overall objective of determining the risk factors of CM. The specific objectives of the study were to identify the association of CM with family history of CM, maternal age, smoking and use of alcohol.

In this study, CM includes “cleft lip with cleft palate”, “cleft lip only” or “cleft palate only”. Family history of CM was defined as the presence of CM either in the siblings, parents or maternal or paternal relative of the child. Maternal age was defined as the age of the mother at the time of birth of the child. Smoking includes active tobacco smoking (cigarette/ bidi/ cigar) by the mother any time from conception to completion of the first trimester of pregnancy. Alcohol use was operationally defined as the consumption of any type of alcohol (beer, jaad, home-made raksi) by the mother from conception to completion of the first trimester of pregnancy.

Methods

This study used a case-control design for assessing the risk factors of CM. Cases included the children with cleft malformation aged below 10 years and attending Morang Co-operative Hospital, Biratnagar for reconstructive surgery, speech therapy or counseling. Controls included age and sex matched children attending Koshi Zonal Hospital for general health problem with no CM, seizure or neuro-developmental disorders. Presence of maternal risk factors and positive family history of CM were the exposures of concern.

Altogether 56 children attending the Morang Cooperative Hospital during data collection period were taken as cases for the study. One control child was taken for each case child. Thus the total sample size was 112. Mothers of case children who were willing to participate were included in the study. However, two of the mothers of control children showed unwillingness to participate in the study so they were replaced by the next consecutive mothers meeting the inclusion criteria.

A semi-structured interview schedule as per the objectives

of the study was developed to measure the study variables. Validity of the instrument was established by consultation with experts in the area of research, paediatrics and statistics. Instrument was translated into Nepali by the Nepali language expert, which was back translated into English by an English language expert to check whether the meanings of questions were retained. Pretesting of the Nepali version instrument was conducted in 6 mothers of children with CM attending Kathmandu Model Hospital, Baghbazar for reconstructive surgery.

Prior to data collection, approval of the research proposal was obtained from the Institutional Review Board of Institute of Medicine. The permission for data collection was obtained from the selected settings through written request letters. Informed verbal consent was obtained from all subjects prior to including them in the study. Confidentiality of the information was ensured by maintaining privacy while collecting data and by using code numbers while entering the data in computer.

Data on socio-demographic characteristics and exposure status of case children were collected by interviewing the mothers of the case children using pretested instrument from December, 2012 to January, 2013 in a separate room of Morang Cooperative Hospital. The corresponding matched controls were selected from Koshi Zonal Hospital and the mothers of the control children were interviewed in the same way using the same instrument.

On an average 5-6 mothers were interviewed per day and the average time required for an interview was 20-35 minutes. Collected data was edited, organized, coded and entered in SPSS software program for analysis. Frequency, percentage, means, SD, chi square and odds ratio were used for data analysis.

Results

Findings obtained from mothers of 56 cases and 56 controls are displayed in table 1 to 4. Demographic characteristic of the mothers of case and control children is presented in table 1. Table 2 presents the demographic information of the case and control children and table 3 presents the type of CM according to the sex in case children. Univariate analysis of the risk factors of cleft malformation among the case and control children is presented in table 4.

Table 1. Demographic Characteristics of the Mothers of Case and Control Children

Characteristics	Cases (n=56) Percent	Controls (n=56) Percent	Total (n=112) Percent
Age of mothers (in years)			
at delivery of child	17.9	26.8	22.3
Below 20	78.6	67.9	73.2
20-30	3.5	5.3	4.5
Above 30	22.5±3.8	22.2±4.0	
Mean ±S.D.	(yrs)	(yrs)	
Education of mother			
None	14.3	32.1	23.2
Primary	30.3	16.1	23.2
Secondary	44.6	26.8	35.7
Higher secondary and above	10.7	25.0	17.9
Occupation of mother			
Housework	66.1	76.8	71.4
Farmer	21.4	5.4	13.4
Service	7.1	10.7	8.9
Others	5.4	7.2	6.3

Table 1 depicts that the majority of mothers of case (78.6%) and control (67.9%) children were in the age group of 20-30 years when the child was born with the mean age 22.5±3.8 and 22.2±4.0 respectively. In regards to education, 55.3% of the mothers of cases and 51.8% of the mothers of controls had secondary and higher level education. Majority of the mothers of cases (66.1%) as well as controls (76.8%) were housewives.

Table 2. Demographic Information of the Case and Control Children

Characteristics	Cases (n=56) Percent	Controls (n=56) Percent	Total (n=112) Percent
Age of child (in months)			
12 and below	25.0	19.6	22.3
13-60	55.4	59.0	57.2
61 and above	19.6	21.4	20.5
Birth order of child			
First	51.8	58.9	55.4
Second	23.2	26.8	25.0
Third and above	25.0	14.3	19.6

Table 2 reveals that 80.4% of case children and 78.6% of control children were in the age group of under five years. Majority (51.8%) of the case children and 58.9% of the control children were similar in birth order i.e. first born children.

Table 3. Type of CM according to Sex of Case Children

Sex of case children	Cleft lip No. (%)	Cleft palate No. (%)	Cleft lip and palate No. (%)	Total No. (%)
Male	2 (5.7)	8 (22.9)	25 (71.4)	35 (62.5)
Female	1 (4.8)	7 (33.3)	13 (61.9)	21 (37.5)
Total	3 (5.4)	15 (26.8)	38 (67.8)	56 (100.0)

Table 3 reveals that cleft lip and palate was the most common (67.8%) type of CM and in total comparatively higher proportion of children with CM were male children (62.5%).

Risk Factors of Cleft Malformation among the Case and Control Children:

Table 4 reveals that higher proportion (i.e. 25.0%) of case children had family history of CM in compare to control children (i.e. 8.9%). In relation to age of mother 17.9% and 28.6% of mothers of cases and controls respectively were young mothers (i.e. less than 20 years of age) when the child was born. Equal but small proportion (i.e. 3.6 %) of mothers were elderly mother i.e. above 30 years of age) when the child was born in both cases and controls. Comparatively a higher proportion of mothers of case children had a positive history of alcohol consumption and smoking during the first trimester of pregnancy than the mother of control children as depicted in table 4.

Table 4 also presents the result of univariate analysis of risk factors of CM, which confirms the association of positive family history of CM ($p=0.023$, Odds Ratio (OR) =3.4; CI, 1.1-10.02) and maternal alcohol consumption during the first trimester of pregnancy ($p=0.013$, OR=4.8, CI, 1.27-18.16) with Cleft Malformation. Table also reveals that children who had positive history of CM in the family were 3.4 times more likely to be born with cleft than those who did not have. Similarly, the risk of delivering an infant with CM was 4.8 times higher among mothers who consumed alcohol during first trimester than those who did not consume alcohol. No significant association of maternal age and maternal smoking was seen with CM in the offspring.

Table 4. Univariate Analysis of the Risk Factors of Cleft Malformation among the Case and Control Children

Risk factors	Cases (n=56) No. (%)	Controls (n=56) No. (%)	Odds Ratio (95% CI)	p-value
Family history of CM				
Present	14 (25.0)	5 (8.9)	3.4	0.023*
Absent	42 (75.0)	51 (91.1)	(1.1-10.2)	
Young mothers** (below 20 years)				
Yes	10 (17.9)	16 (28.6)	0.54	0.179
No	46 (82.1)	40 (71.4)	(0.22-1.33)	
Elderly mothers (Above 30 years)				
Yes	2 (3.6)	2 (3.6)	1.0	1.0a
No	54 (96.4)	54 (96.4)	(0.13-7.36)	
Alcohol consumption during first trimester				
Yes	12 (21.4)	3 (5.4)	4.8	0.013*a
No	44 (78.6)	53 (94.6)	(1.27-18.16)	
Smoking during first trimester				
Yes	5 (8.9)	1 (1.8)	5.4	0.208 a
No	51 (91.1)	55 (98.2)	(0.6-47.72)	

CI means confidence interval; *indicates association, and a indicates Yate's Corrected p-value

Discussion

Majority of the mothers in this study both in cases (78.6%) and controls (67.9%) were in the age group of 20-30 years when the child was born. This may be probably because 20-30 years age group is the most fertile age group. More than half (i.e. 55.3% and 51.8%) of the mothers of cases and controls respectively had the secondary and higher level of education and majority of the mothers both among cases (66.0%) and controls (76.8%) were housewives. Majority (80.5%) of the case and 78.6% of control children were in the age group of less than five years. This may be related to the awareness of parents about better outcome of early treatment. More than half of the case children (51.8%) and control children (58.9%) were first born children.

In consistence with the findings of DeRoo, Gaudino and Edmonds⁴ and Natsume, Kawai, Ogi and Yoshida⁵, the present study revealed that majority of the children with cleft malformation (62.5%) was male. Cleft lip and palate was the most common pattern of CM (67.9%) in this study

which is similar to the findings of Singh, Sharma, Roy and Roy⁶ and Tewfik³ who reported 41.1%, and 66.7% respectively.

The present study found a significant association of the positive family history of CM and the risk of delivering offspring with CM with p value as 0.023 which is supported by studies conducted by Buyu et al.⁷, Leite and Koifman⁸, and Natsume et al.⁵. Result of present study also indicated that the risk of developing CM was 3.4 times higher among children with positive family history of CM than those without it. The role of genetic factors in contributing the orofacial cleft deformity had been documented by DeRoo et al.⁴.

The results of previous studies on the association of maternal age and risk of oral clefts in the offspring have been inconsistent. Taghavi et al.⁹ and DeRoo et al.⁴ identified an increased risk of CM among younger mothers aged below 20 years at the time of delivery. Herkrath, Herkrath, Rebelo and Vettore¹⁰, and Bille et al.¹¹, on the other hand, documented an association of high maternal age at delivery with cleft anomalies in the offspring but no association between low maternal age with CM. Present study revealed no association of cleft malformed offspring and the maternal age at delivery (neither younger nor elderly mothers). Since few births occurred among women aged above 30 years, the ability to draw conclusions about high maternal age was weak in this study.

This study revealed that mothers who consumed alcohol in any amount during the first trimester of pregnancy were 4.8 times more likely to have an infant with CM compared to those who did not. This finding is similar to the findings of study conducted by Grewal, Carmichael, Ma, Lammer and Shaw¹² and Romotti et al.¹³. Inconsistent to the findings of the current study, Lebby, Tan and Brown¹⁴ and Natsume et al.⁵ reported no evidence of association between maternal alcohol uses with occurrence of oral clefts in the offspring.

The present study found no association between maternal smoking during pregnancy and CM in the offspring though the percentage of cleft malformed children was high among mothers who smoked during first trimester. Romitti et al.¹³ also reported similar finding. In contradiction, Chung, Kowalski, Kim and Buchman¹⁵, Lorente et al.¹⁶ and Mossey & Little¹⁷ had found significant association between maternal smoking during pregnancy and CM in the child. The absence of association in the present study can be attributed to small proportion of smokers in both cases and controls probably due to small sample size.

Conclusions

In light of the results obtained, it is concluded that positive family history of CM and alcohol intake by mothers during the first trimester of pregnancy are the potential risk factors of having offspring with cleft malformation. It is also concluded that children with positive family history of CM are 3.4 times more likely to have CM than those without positive family history. Similarly, alcohol intake by mothers during pregnancy increases the risk of having offspring with cleft malformation by 4.8 times. On the other hand, maternal age and smoking during first trimester have no association with having an offspring with CM.

Findings of the study are based on the information given by mothers. Since mothers of malformed children are likely to recall exposures more accurately than the mothers of healthy children, recall bias might have occurred in the study. Another possible limitation of the study is that researchers could not control for potential confounders such as nutrition, socio-economic status and maternal health during pregnancy. The significant risk factors of cleft malformation, identified in this study are potentially modifiable. So, parents with positive family history should be given preconceptional counseling and prophylactic treatment with folic acid which is known to prevent CM. Parental awareness raising programs should be planned regarding the teratogenic effect of alcohol on fetus in inhibiting the fusion of facial processes during embryonic development.

Conflict of interest: None declared

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