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Periodic trends in the incidence of cleft palate in a cohort of Sri Lankan cleft palate patients

Abstract

Background: Over the last few decades the incidence of cleft palate has been increasing across the world. There are several genetic and environmental factors are reported to be among the causative agents of cleft palate. Theres scarcity of data with regards to the seasonality and the occurance of cleft palate among sri Lankans. Hence, the purpose of this study was to identify periodic changes in the incidence of cleft palate in a cohort of Sri Lankan population

Material & methods: Subjects (n=323) with cleft palate registered at the Regional Cleft Centre & Maxillo-Facial Department, Teaching Hospital, Karapitiya, Galle, from the 1st of January 2001 to 31st of December 2020 were included in the study. Structured interviewer based questionnaire was used to collect the information after obtaining the informed written consent.

Results: Significantly higher number of cleft palate cases in this study were born in March ($p = 0.008$) compared with the national birth incidence while significantly lower numbers were born in October ($p = 0.01$). The sex ratio in the study sample was 0.71.

Conclusions: The periodic trends in the incidence of cleft palate found in this preliminary study reinstated that environmental factors may have accounted for the reported seasonal variations observed in the incidence of cleft palate. Future studies are warranted to investigate the putative harmful seasonal factors that can influence the occurance of cleft palate.

Keywords: Cleft palate, Incidence, Birth month, Sri Lankan

(Word count = 227)

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Introduction

Cleft palate (CP) is a congenital fissure in the roof of the oral cavity, resulting from incomplete fusion of the two palatine shelves during embryonic development (1). Extreme variability of this condition can be seen varying from a subtle submucous cleft to an overt cleft palate involving the whole of the soft and hard palate.

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Cleft palate is one of the commonest congenital anomaly of the craniofacial region and it is reported to be associated with orofacial clefts and other congenital malformations. Orofacial clefting occurs in all races, both sexes and all socio-economic groups (2,3). Oro-facial clefts contribute to long-term disability in children which ultimately affects social and psychological burden to the affected families. The management is a long term process and will be initiated soon after the birth and continues to the end of the second decade of life according to the complexity of the cleft. Modification of feeding methods, respiratory assessments, surgical repair of the defect, speech therapy, orthodontic management, autolaryngological and audiological assessment and management and, paediatric follow up and continuous psychological counseling is required on these patients (2,3).

Over the last few decades the incidence of cleft palate has been increasing across the world. In fact, the incidence of cleft palate has doubled during the last fifty years and tripled during the last one hundred years (4).

There are several causative factors including disruption of the palatal mesenchyme and failure of medial edge epithelial cell death have been recognized in the aetiology of cleft palate (3,5,6,7). Abnormalities in palatal shelf movements with growth of the tongue also lead to widening of the gap between the two palatine shelves and failure of meeting in the midline. Cleft palate that is seen in Pierre Robin sequence is an example (3,5,6,7).

There are several genetic and environmental factors involved in the process of morphogenesis of the primary and secondary palates. Shifting of this complex process toward a threshold of abnormality by adverse genetic and environmental conditions, can initiate the process of clefting of the lip and/ or palate (3,8,9)**.**

Genetic studies on human populations have demonstrated that non syndromic cleft lip with or without cleft palate (CL+/-P) and isolated cleft palate (ICP) have distinct genetic backgrounds (6,10). There are ten loci that have been linked to orofacial clefting (OFCl) with loci 1 to 4, being mapped to chromosomes 6p24, 2p13, 19q13.2 and 4q respectively. A further gene, T-box 22 (TBX22), has been implicated in the etiology of cleft palate, with the severity varying from a complete cleft palate to submucous cleft palate (3,6,7,10). There are many genes expressed during palatal growth including the fibroblast growth factor (FGF-1), FGF-10, FGF receptor 2b (FGFR2B) and Sonic Hedgehog gene (SHH) (3,6,11,12).

Taken together, cleft palate is considered as a multifactorial genetic condition where gene-environment linkage shows variation in its occurrence in different geographical regions. The objective of the study was to evaluate the periodic trends in the incidence of cleft palate in a cohort of Sri Lankan cleft palate patients.

Materials and methods

The subjects were identified among those who are under review in the Regional Cleft Centre & Maxillo-Facial Department, Teaching Hospital, Karapitiya, Galle. Subjects with cleft palate without cleft lip (i.e. isolated cleft palate) registered at the clinic from the 1st of January 2001 to 31st of December 2020 were included in the study. Structured interviewer based questionnaire was used to collect the information after obtaining the informed written consent. Ethical approval was granted to the study from the Ethics Review Committee, Faculty of Medicine, University of Kelaniya.

Results and Discussion

Gender variation

There were three hundred and twenty-three (n=323) subjects with cleft palate (without cleft lip), who were attending the Regional Cleft Centre & Maxillo-Facial Department, Teaching Hospital Karapitiya,

Sri Lanka. Out of which one hundred and eighty-seven (n=187; 57.9%) were females and one hundred and thirty-six (n=136; 42.1%) were males. The male to female ratio (sex ratio) in the study sample was 0.71. According to the department of census and statistics in Sri Lanka the sex ratio in the southern province of Sri Lanka is 0.96[13]. There was a significant different (p = 0.0148) in sex ratio of the study sample and the national figure for the southern province. It shows that the cleft palate (without cleft lip) is more common in females than males in the Southern part of Sri Lanka.

Geographical distribution

Two hundred and ninety-one (n=291; 90.1%) subjects who participated for the study were residents in the Southern part of Sri Lanka. One hundred and sixty-one (n=161; 55.3%) were from the Galle district, Sixty-four (n=64; 22%) and Sixty-six (n=66; 22.7%) respectively were from the Matara and Hambantota districts. There were also twenty (n=20; 6.2%) subjects from the Western province. Twelve subjects (n=12; 3.7%) were from the Sabaragamuwa province.

Incidence of cleft palate according to the birth month

The birth months of all subjects were evaluated (Figure1) and compared according to the gender and the frequency of births of each month. Forty-six (n=46; 14.20%) and thirty-eight (n=38; 11.73%) births in the study population were in the months of March and February respectively. There were ten (n=10; 3.10%) and thirteen (n=13; 4%) births in October and September respectively (Figure 1).

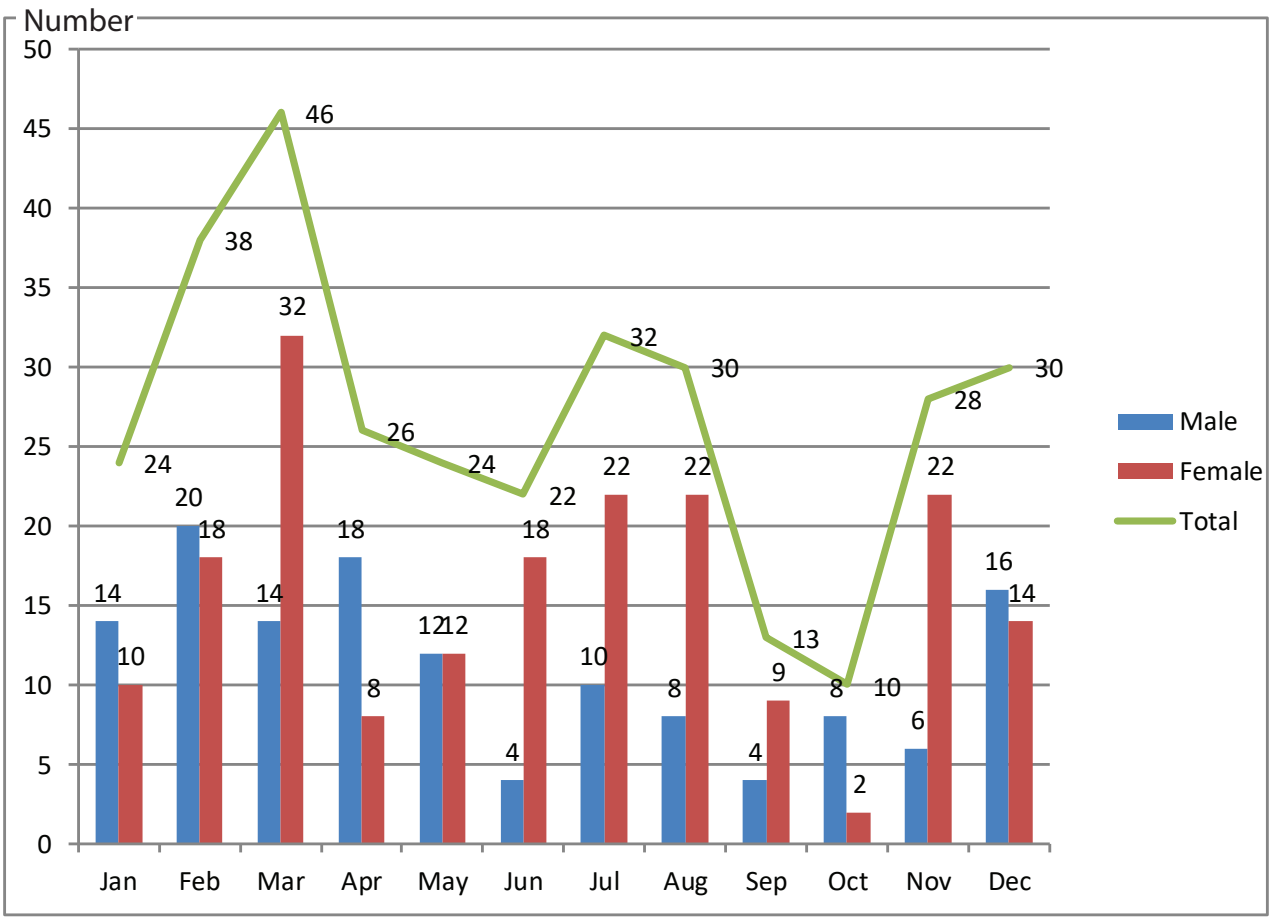

Figure 1: Periodic trends in the incidence of cleft palate according to the birth months.

Significantly higher number of cleft palate cases in this study were born in March (p = 0.008) compared with the national birth incidence while significantly lower numbers were born in October (p = 0.01) (Table 1).

Table1: Comparison of monthly incidence of births of cleft palate cases with data from the general population (14)

Month	Sri Lankan population* (% of births per month)	Current study**	p value
January	7.8%	7.4% (n=24)	0.98
February	7.75%	11.73% (n=38)	0.08
March	8.14%	14.2% (n=46)	0.008
April	7.7%	8.02% (n=26)	0.99
May	7.92%	7.41% (n=24)	0.92
June	8.74%	6.79% (n=22)	0.46
July	8.67%	9.88% (n=32)	0.68
August	8.29%	9.26% (n=30)	0.76
September	8.57%	4.32% (n=13)	0.07
October	8.92%	3.09% (n=10)	0.01
November	8.77%	8.64% (n=28)	0.93
December	8.71%	9.26% (n=30)	0.91

(*Extracted from population and housing statistics, 2010)

(**Expressed as a percentage of the total number of subjects, n=323)

Gender variation of the incidence of cleft palate in different months

The periodic trends in the incidence of cleft palate cases in different birth months in the study sample were analyzed according to their gender. Out of one hundred and thirty-six (n=136) male subjects, twenty (n=20; 14.7%) subjects were born in January and four (n=4; 2.9%) subjects each were born in June and September. Out of one hundred and eighty-seven (n=187) female subjects, thirty-two (n=32; 17.1%) subjects were born in March and two (n=2; 1.05%) female subjects were born in October (Figure 2).

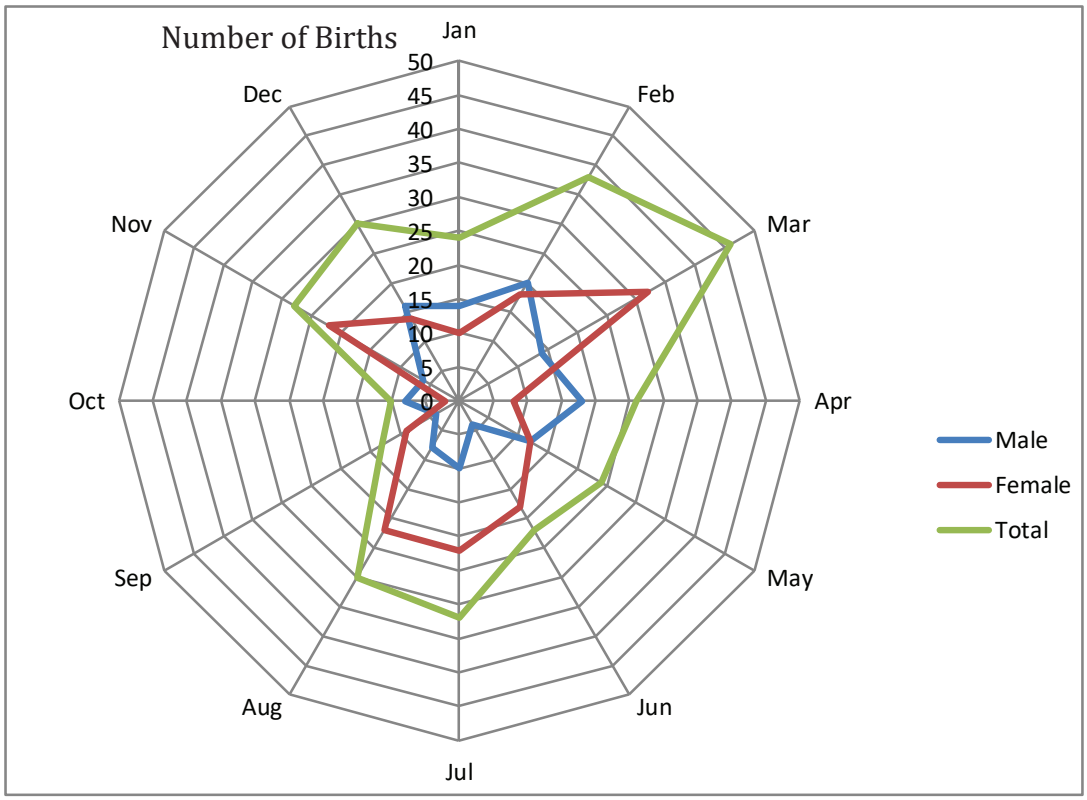

Figure 2: Monthly variation of births according to the gender

Table 2: Comparison of monthly variation of cleft palate births of the study sample according to the gender

Month	Male*	Female**	p value
January	10.3% (n=14)	5.3% (n=10)	0.34
February	14.7% (n=20)	9.6% (n=18)	0.11
March	10.3% (n=14)	17.1% (n=32)	0.35
April	13.2% (n=18)	4.3% (n=8)	0.06
May	8.8% (n=12)	6.4% (n=12)	0.76
June	2.9% (n=4)	9.6% (n=18)	0.15
July	7.4% (n=10)	11.8% (n=22)	0.6
August	5.9% (n=8)	11.8% (n=22)	0.28
September	2.9% (n=4)	4.8% (n=9)	0.8
October	5.9% (n=8)	1.1% (n=2)	0.18
November	4.4% (n=6)	11.8% (n=22)	0.2
December	11.8% (n=16)	7.5% (n=14)	0.30

(*Expressed as a percentage of the total number of male subjects, n=136)

(**Expressed as a percentage of the total number of female subjects, n=187)

According to the above figures there was no statistically significant gender variation of births months (Table 2).

Discussion and conclusion

In the study population, the peak incidence of cleft palate births was found in March and the lowest incidence in October. This difference was statistically significant in both the highest ($p=0.008$) and the lowest ($p=0.01$) incidence months compared with the general population data (14).

A total of four hundred and thirteen cleft subjects that were operated during the period from 2000 to 2006 in Zambia and a statistically significant ($p<0.01$) increase in cleft births was observed in April and May (15). There was also a higher proportion of births between March to August (57.2%) compared to between September to February (42.8%). Seven hundred and eighty one (n=781) cleft palate subjects for monthly incidence of cleft palate in Czech regions were studied and there was a significantly higher birth incidence of cleft palate in February when compared to the birth months of the general population (16). Coupland and Coupland, (1988) studied three hundred and eighty one (n=381) patients with cleft palate in the Trent region, UK. Number of cleft palate births in the period from February to June was shown to fall two standard deviations or more below the annual mean births while in the period from July to October, the number of cleft palate births was more than two standard deviations above the annual mean (17). These results suggested that there was a seasonal variation in the incidence of cleft palate births. Owens et al., (1985) analysed the epidemiology of facial clefting in patients with cleft lip and palate notified to the Liverpool Congenital Malformations Registry during a period of 1960 to 1982. There were one hundred and fifty three (n=153) subjects with cleft palate among whom a significant trend towards an increase in the frequency of conception in the second half of the year (July to December) (18). Qiao-Juan et al., (2006) investigated one thousand three hundred and thirty one (n=1331) cleft palate patients in China. The variation of birth months demonstrated a significant seasonal trend with a peak incidence of cleft palate births in the summer (June to August) and lower incidence in winter (November to March) (19). In a previous study among five hundred and one (n=501) cleft lip and palate subjects in Sri Lanka, a peak incidence of cleft palate was found in April (8,20).

On the contrary, following two studies shows no statistically significant association between the months of birth and the incidence of cleft palate. Wehrung, (1970) studied two thousand nine hundred and ninety seven (n=2997) United States subjects with isolated cleft palate for seasonal variation of incidence but found no significant differences compared to control (21). Knox and Braithwaite, (1963) studied one hundred and eighty eight (n=188) cleft palate patients UK and reported no statistically significant association between the months of birth and the incidence of cleft palate (22).

The variation in the incidence of cleft palate births in this study was also reported in six studies (8,15,16,17,18,19,21,22). There is no consistent month or season in which cleft palate births increase across different countries (Table 3). Taken together, there appears to be as yet unidentified seasonal factors that may be contributing to this observation. Different geographical regions show different seasonal variations and extrem environmental conditions. Gene environmental interactions leads to genetic mutations/polymorphic variations specially in the early embryonic development which may leads to development of cleft palate. An indepth understanding of the periodic trends in incidence of cleft palate is very important as it would, in turn, help in genetic counseling towards the prevention of genetic disorders especially cleft palate.

Table 3: Seasonal variation of births in different populations

Study/Population	Association of periodic variation of births	Period of peak incidence of births
Wehrung, (1970)	No association	
Knox and Braithwaite, (1963)	No association	
Elliot *et al.*, (2008)	Significant association	April and May
Cervenka *et al.*, (1969)	Significant association	February
Coupland and Coupland, (1988)	Significant association	July to October
Owens *et al.*, (1985)	Significant association	July to December
Qiao-Juan *et al.*, (2006)	Significant association	June to August
Amaratunga, (1989)	Significant association	April
Current study	Significant association	March higher than the average October lower than the average

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