

# Clinical and Hematological profile of Paediatric Patients with Cleft Lip and Palate in a Tertiary Care Hospital of Haryana, India

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## ABSTRACT

**Introduction:** Cleft lip and/ or cleft palate are the most common visible craniofacial anomalies. These patients often have feeding difficulties and recurrent infections leading to an altered immune system which can be assessed by the variations in hematological parameters. We intended to assess the clinical profile and the hematological parameters in patients with cleft lip and palate.

**Methods:** This is a three-year cross-sectional study conducted at SGT Medical College, Gurugram, Haryana, India from January 2017 to December 2019 involving assessment of patients with cleft lip and palate who visited the paediatric unit for complete evaluation before surgery. Syndromic children or those with associated deformities were excluded. A total of 115 patients were enrolled in the study and the following information was recorded: Age, Gender and type of cleft (Cleft lip and alveolus, cleft lip, alveolus and palate, and isolated cleft palate). Hematological parameters including hemoglobin, total leukocyte count, differential leukocyte count, absolute eosinophil count, and red cell indices were evaluated and compared amongst the anatomical subtypes.

**Results:** A total of 115 patients were included in the study, of which 66 (57.4%) were males and 49 (42.6%) were females. 57 (49.6%) had a cleft lip, alveolus, and palate, 36 (31.3%) had a cleft lip and alveolus and 22 (19.1%) had cleft palate only. Anaemia was present in 71.1% of cases. 83.4% cases of cleft lip and alveolus while 81.8% of isolated cleft palate were anaemic. Microcytic hypochromic anaemia was present in 63.4% of cases while 36.6% had normocytic normochromic anaemia. The total leukocyte count was elevated in 60 children (52.2%) which was highest in cleft lip and alveolus (66%). Absolute neutrophil count was significantly high in the lip and alveolus groups. (13.9%) Absolute lymphocyte count was highest in lip and alveolus (30.56%). Absolute monocyte count and the absolute eosinophil count was low in the majority of cases.

**Conclusions:** A large number of children with cleft lip and/ or palate are not exclusively breastfed due to anatomical deficits. They need supplemental iron to meet the demands. A standard policy to provide auxiliary iron by health care professionals should be made at the first visit to the health centre because nutritional anaemia negatively affects the physical and cognitive development of a child. It also unnecessarily prolongs the date for optimum and safe surgery.

**Keywords:** Cleft lip; Cleft palate; Infections; Nutritional anaemia



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## INTRODUCTION

Cleft lip and / or cleft palate are the most common visible cranio-facial anomalies throughout the world. The affected individual may have an isolated defect or a combination of both. The incidence of cleft lip and/ or palate worldwide is 1:600 while in India, one out of every 500 to 800 live births suffer from the defect.<sup>1,2</sup> Isolated cleft palate is more frequently observed in females while the cleft lip is common in males.<sup>3</sup> The etiology is complex involving both genetic and environmental influences. The etiological factors include heredity with polygenic inheritance, consanguinity, fetal environment and other factors such as maternal drug exposure, alcohol consumption, and smoking.<sup>4</sup>

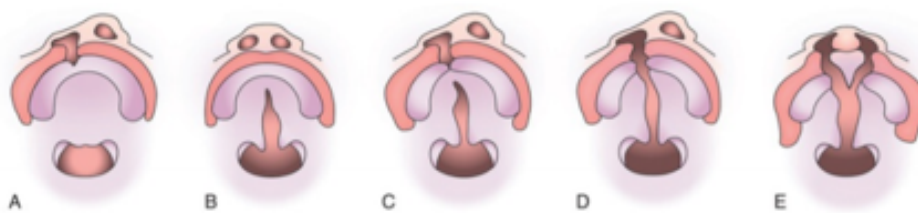
The embryonic development of the lip occurs between the 4th and the 7th week of intrauterine life whereas the palate develops between the 6th and the 9th week. It is observed that cleft of the lip appears because of hypoplasia of the mesenchymal layer, failing the medial nasal and maxillary processes to join whereas cleft of the palate occurs due to failure of fusion of palatal shelves. A cleft lip can have varied presentations from a small notch in the vermilion border to a complete separation involving skin, mucosa, tooth and bone. They may be unilateral (more often on the left side) or bilateral and can involve the alveolar ridge. An isolated cleft palate occurs in the midline and might involve only the uvula or can extend into or through the palates to the incisive foramen.<sup>5</sup> When associated with cleft lip, the defect can involve the midline of the soft palate and extend into the hard palate on one or both sides, exposing one or both of the nasal cavities as a unilateral or bilateral cleft palate [Fig 1].

Clefts may be associated with various syndromes and other congenital malformations of the body. Frequent complications observed in affected individuals include feeding difficulties and recurrent infections like otitis media, cholesteatoma, maxillary sinusitis and bronchopneumonia.<sup>6-8</sup> Breastfeeding a child is a tough challenge and there are various contributing factors like the inability to create negative intraoral pressure and occasionally negligence by the family members to feed their child.<sup>9</sup> Hence these children are not only devoid of nutrient benefits of breast milk but also altered immune system leading to various infections.

The suppressed immune system brings about variations in hematological parameters, especially the erythrocytes (leads to anemia), total and differential leukocyte counts. This study aimed to assess the clinical profile and hematological parameters of patients with cleft lip and palate.

## METHODS

This is a three year cross sectional study conducted at SGT Medical College, Gurugram, a tertiary care centre in Haryana, India between January 2017 to December 2019 involving assessment of patients with cleft lip and palate between age three months to 18 years of either gender who visited paediatric unit for complete evaluation before surgery. Syndromic children or those with associated deformities were excluded. Patients were enrolled in the study after taking informed consent from parents/guardians. Approval was taken from the Institutional ethical committee before starting the study. The following information of the patients enrolled in the study during this period was

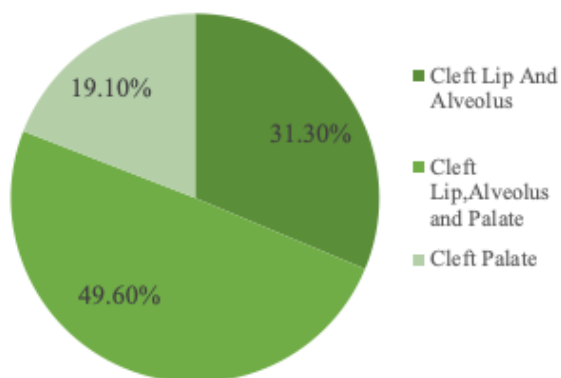


**Figure 1.** A, Cleft lip and alveolus. B, Cleft palate. C, Incomplete unilateral cleft lip and palate. D, Complete unilateral cleft lip and palate. E, Complete bilateral cleft lip and palate. (From Shaw WC: Orthodontics and occlusal management. Oxford, UK, 1993, Butterworth - Heinemann)

recorded: age, gender and type of cleft which was either an isolated cleft lip with alveolus, cleft palate or a combination of both. These patients underwent complete blood count analysis and the hematological parameters assessed in the study included hemoglobin, total leukocyte count, differential leukocyte count with analysis of absolute neutrophil count and absolute eosinophil count, platelets, red cell indices and peripheral blood smear. These were compared amongst the anatomical subtypes. Patients were enrolled in the study after taking informed consent from parents/guardians. Approval was taken from the Institutional ethical committee before starting the study. All hematological tests were done by an automatic analyzer (Sysmex XN-550, Kobe, Japan). Further cross-checking of these results were done manually using light microscopy. All the age-dependent standard references of hematological parameters were drawn from standard references.<sup>10</sup> Anaemia was classified as mild (10.0-10.9g/dl), moderate (7.0-9.9 g/dl) and severe (< 7.0g/dl). The data was compiled, entered, and analysed. SPSS version 20 was used for the statistical analysis to do the chi-square test and the significance level was set at 0.05.

## RESULTS

A total of 115 patients were included in the study, of which 66 (57.4%) were males and 49 (42.6%) were females.



**Figure 2.** Distribution based on primary diagnosis

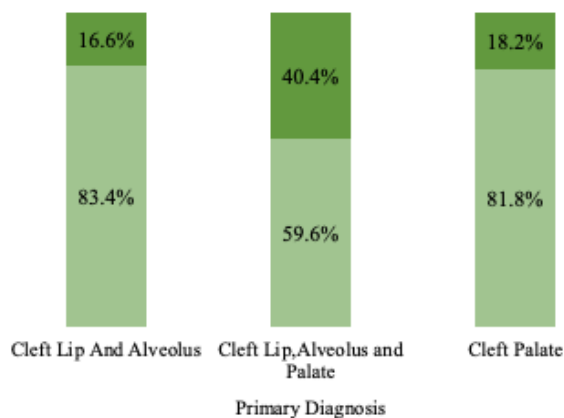
Based on the primary diagnosis, 57 (49.6%) had a cleft lip, alveolus, and palate, 36 (31.3%) had a cleft lip and alveolus and 22 (19.1%) had isolated cleft palate (Figure 2). The combination of cleft lip, alveolus, and palate was more common in males.

Anaemia was present in 71.1% of cases, of which 83.4% cases belonged to cleft lip and alveolus whereas 81.8% of isolated cleft palate were anaemic which was statistically significant (p-value 0.023). [Fig 3] It was more common in females (41/49, 83.7%) in comparison to males (41/66, 62%). Mild anaemia was seen in 44 cases (53.7%), moderate in 31(37.8%), and severe in seven cases (8.5%). Microcytic hypochromic anaemia was present in 63.4% of cases while 36.6% had normocytic normochromic anaemia.

The total leukocyte count was elevated in 60 cases (52.2%) which was highest in the cleft lip and alveolus (66%) group which was statistically significant. (P -value 0.041) [Table 1]

Absolute neutrophil count was significantly high in the lip and alveolus (13.9%) group (P-value 0.018). (Figure 4)

Absolute lymphocyte count was highest in lip and alveolus (30.56%) followed by 29.83% of lip, alveolus and palate while it was raised only in 4.5% cases of isolated cleft palate. (p-value 0.046). (Figure 5)



**Figure 3.** Distribution of hemoglobin in relation to primary diagnosis

**Table 2.** Bacterial pathogens of neonatal sepsis, distribution, MDR and associated mortality

		Total Leucocyte Count			Total	P value
		Low	Normal	High		
Primary Diagnosis	Cleft lip and alveolus	0	12	24	36	0.041
	Cleft lip, alveolus and palate	7	22	28	57	
	Cleft palate	1	13	8	22	
Total		8	47	60	115	

Absolute monocyte count was low in the majority (88.7%) of cases(p-value 0.296).[Table 2]

The absolute eosinophil count was high in 15.7% of cases (P-value 0.067). [Table 3]

History of recurrent infections was present in 20.80% of cases. [Fig 6] It was not statistically significant in any group. However, it was high in cleft lip, alveolus, and palate. It did not reflect the rise in total leukocyte count as mentioned above.

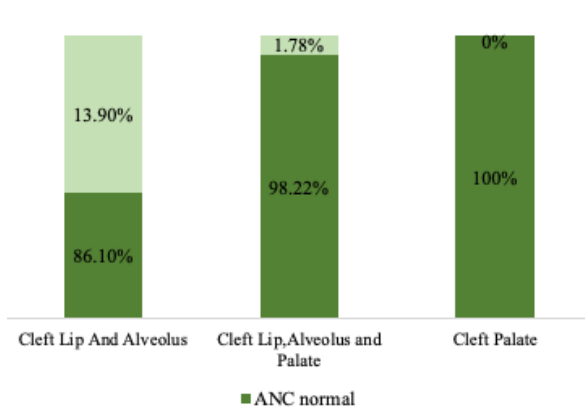
Platelet count was high in 52.2% cases (p value 0.067). [Table4 ]

### DISCUSSION

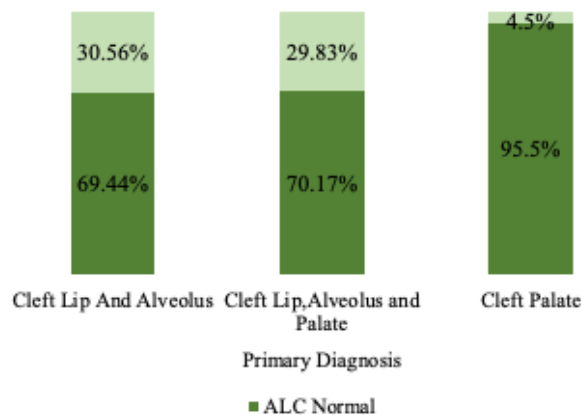
Orofacial clefts are the most common congenital malformations of the lip, palate or both. Due to considerable variation in geographic location, ethnicity and socioeconomic status, the prevalence and clinico-hematological profile of the patients vary in different populations across the world.<sup>11</sup> This study highlights the clinical and hematological

profile of patients with such anatomical deficits attending a tertiary care institute of rural Haryana which likely represents a trend in a predominantly rural population. As the majority of the population in India resides in a rural area, the understanding of such trends is essential. However, there is a paucity of data from other parts of the country to make any generalization.

The purpose to assess the haematological values in cleft patients was to compare the differences in the various types in an attempt to correlate with the problems and complications appearing in patients due to the anatomical deficit. Despite the fact, it is quite evident that the hematological values would be raised in cleft patients due to infections or any complications, our study shows the significance of estimating the hematological values and accordingly treating the unoperated cleft patients. This would achieve a normal systemic health status of patients till surgery.



**Figure 4.** Distribution of absolute neutrophil count in relation to primary diagnosis

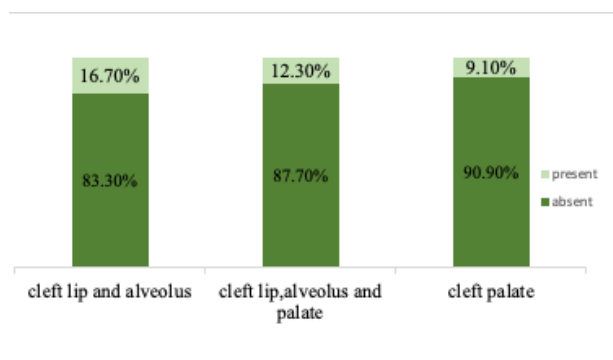


**Figure 5.** Distribution of absolute lymphocyte count in relation to primary diagnosis

**Table 2.** Primary Diagnosis \* Absolute Monocyte Count

	Primary Diagnosis	Absolute Monocyte Count		Total	P value
		Low	Normal		
	Cleft lip and alveolus	34	2	36	0.296
	Cleft lip, alveolus and palate	48	9	57	
	Cleft palate	20	2	22	
Total		102	13	115	

In the present study, male to female ratio was 1.3:1. However, studies conducted by Dwivedi et al and Singhal et al observed a male-to-female ratio of 2:1.<sup>12,13</sup> Studies conducted in various parts of the world including Brazil, Kenya, Iran and Saudi Arabia<sup>14-18</sup> showed a male predominance while a study conducted in Dharan, Nepal, presented that clefts were more common among females (56% females and 44% males).<sup>19</sup> In our study, the majority of cases (49.6%) had a combination of cleft lip, palate, and alveolus. This was contrary to a study by Swami et al where isolated cleft palate was the most common type (40.6%).<sup>20</sup> These findings were similar from the findings of studies conducted in Brazil, Iran, Jordan.<sup>14,17,21</sup> In a study conducted in Japan<sup>22</sup> it was revealed that the order of decreasing frequency of the clefts was cleft lip with alveolus and palate followed by cleft palate and cleft lip. This was in contrast to a study published by Swami et al (40.6%)<sup>20</sup> where isolated



**Figure 6.** History of recurrent infections in relation to primary diagnosis

**Table 3.** Primary Diagnosis \* Absolute Eosinophil Count

	Primary Diagnosis	Absolute Eosinophil Count		Total	P value
		high	normal		
	Cleft lip and alveolus	8	28	36	0.067
	Cleft lip, alveolus and palate	10	47	57	
	Cleft palate	0	22	22	
Total		18	97	115	

cleft palate was the most common type. Another study by Neela et al suggested cleft lip as the most common variety.<sup>23</sup> These findings reveal that there is a demographic variation in the frequency of different phenotypes.

Anaemia was prevalent in 71.1% of cases in the current study. Females had a higher preponderance. This was similar to studies conducted by Singhal et al and Fadyeyibi et al.<sup>13,24</sup> The prevalence of anaemia was higher than the national average in our study which was indistinguishable from a study done by Chattopadhyay et al.<sup>25</sup> 63.3% of cases in our study had microcytic anaemia which has been noted in various similar studies conducted in India. A low amount of stored iron in the body due to poor oral intake leads to nutritional anemia while various complications like recurrent or persistent infections associated in these patients further aggravates anemia requiring blood transfusions and

**Table 4.** Primary Diagnosis \* Platelet Count

	Primary Diagnosis	Platelet Count		Total	P value
		normal	High		
	Cleft lip and alveolus	16	20	36	0.067
	Cleft lip, alveolus and palate	31	26	57	
	Cleft palate	8	14	22	
Total		55	60	115	

hematinics. Total leucocyte count was elevated in 52.2% cases and it was statistically significant in the cleft lip group. However, Fadeyibi et al showed only a 9.8% rise in leukocytes in cleft patients while a study by Singhal et al revealed leucocytosis only in 20.63% of cases. Greer et al in his study had suggested an association of eosinophilia in patients with clefts. In the present study eosinophilia was seen in 15.7% of cases which was not statistically significant. Similar studies by Singhal et al showed eosinophilia in 20.6%.<sup>13</sup> The various contributory factors leading to high eosinophil count includes local climatic factors, worm infestation and allergies. Hence these patients may require treatment with anti-helminthics and anti-histaminics prior to surgery. Another study conducted by Swami et al suggested that only 4.9% of the cases had eosinophilia.<sup>20</sup>

Patients with cleft palate are known to have complications like otitis media and cholesteatoma due to eustachian tube dysfunction. The food particles get lodged in the tube causing middle ear infections. Similarly they can aspirate food particles into the upper airway through the palatine defects leading to lower respiratory tract infections like bronchopneumonia as described by Clarren et al.<sup>26</sup> Hence a special attention to improve the immune status of the child by providing breast milk and feeding the colostrum is required. However, in

the present study, 20.08% of cases had history of recurrent infection which was not statistically significant. Though platelet count was high in 52.2% cases, it was not statistically significant in any of the subgroups.

Although ours is a novel study in our region, it is a single-center study from a tertiary care institute. Hence, although the findings appear to be significant, caution needs to be exercised in generalizing the results and our findings need to be substantiated further in larger studies in the future.

## CONCLUSIONS

A large number of children with cleft lip and / or palate are not exclusively breastfed due to anatomical deficits. They need supplemental Iron to meet the demands. A standard policy to provide auxiliary iron by health care professionals and meticulous counseling of parents to provide breast milk and colostrum to the child should be made at the first visit to the health centre because nutritional anaemia and recurrent infections negatively affects the physical and cognitive development of a child. It also unnecessarily prolongs the date for optimum and safe surgery.

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