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RESEARCH ARTICLE

ANALYSIS OF HAEMATOLOGICAL VALUES IN PATIENTS WITH CLEFT LIP AND/OR CLEFT PALATE

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ABSTRACT

Aim: To analyse the haematological values in patients with cleft lip and palate and compare it with normal values.
Methods: Patient case records (N=821) were accessed to collect the data. The following information was collected from patient records: Age, Gender, type of cleft, Haematological values like Total leukocyte count, Differential leukocyte count, Haemoglobin, Packed cell volume, Erythrocyte sedimentation rate. Pearson's chi-square test was performed for data analysis.
Results: Compared to normal values, in cleft individuals there was increase in parameters like total leukocyte count (in 41.4% cases), neutrophil count (in 7.4% cases), lymphocyte count (in 17.4% cases), Erythrocyte Sedimentation Rate (in 73.4% cases) which were statistically significant and there was a decreased monocyte count (in 99.1% cases), haemoglobin (in 55.5% cases), Packed Cell Volume (in 15.8% cases) which also showed statistical significance.
Conclusion: Increased infections and compromised nutrition occurring in the cleft patients due to anatomical deficit may reflect on the haematological values.

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INTRODUCTION

Craniofacial anomalies like Cleft Lip Palate (CLP), Cleft Lip alone (CL) and Cleft Palate alone (CP) affect about 1.09 for every 1000 live births in India (Reddy *et al*., 2010). The cleft patients have a plethora of etiologic risk factors, psychological and physiological problems, complications and also the treatment modalities which the families are not aware of. It is estimated that there are about 10 lakh cases of untreated oral clefts in India (Singh, 2009). Cleft lip and palate may give rise to many complications in affected individuals including the feeding problems and recurrent infections like otitis media, cholesteatoma (Sheahan *et al*., 2003), maxillary sinusitis (Jaffe, 1971) and bronchopneumonia (Christensen *et al*., 2004). The parents of such children are more concerned about craniofacial anomaly rather than the complications that may arise from the clefts in those patients. Children born with cleft lip and palate and no other known malformations appear to have an increased risk of mortality not only in the first year of life but throughout childhood and adulthood (Christensen *et al*., 2004).

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The cleft patients are known to have difficulty in breastfeeding due to the various contributing factors like anatomic factors where in the baby fails to create negative intraoral pressure [(6)] and also sometimes there is negligence by families to feed their children. Gil-Da-Silva-Lopes *et al*. (2013) carried out a study that showed around 78% of families had neglected breastfeeding the cleft child and hence feeding in cleft babies is a robust challenge. Breastfeeding may, in addition to the well-known passive protection against infections during lactation, have a unique capacity to stimulate the immune system of the offspring perhaps with numerous long-term positive effects (Hanson, 1998). Any alternations in the immune system can bring about variations in hematological values, especially the total leukocyte count, erythrocyte sedimentation rate and specifically the differential leukocyte counts. Anemia can affect the child both physically and psychologically thereby disturbing the total body function. In India, about three quarters of children showed that they were having some degree of anemia (IIPS, 2000).

METHODOLOGY

This retrospective study involved accessing medical records of cleft patients admitted to Craniofacial Unit at SDM College of Dental Sciences, Dharwad for a 24-month period between

January 2011 and December 2012. Total of 821 patient records were accessed. The study chiefly involved assessing the case data which involved the case history and laboratory reports. The following information was collected from the patient records: Age, Gender, (Education, Occupation and Income) of the parent, Hematological values like Total leukocyte count, Differential leukocyte count, Erythrocyte sedimentation rate, Hemoglobin and Packed Cell Volume in cleft patients

The inclusion criteria for the patients who were diagnosed with cleft lip and/or palate has been mentioned below

- Patients between the age ranges from birth to 12 years.
- Patients who were not operated for the clefts/not on any treatment/medication.
- Patients not associated with any syndromes.
- Patients not suffering from any chronic systemic illness like immunocompromising conditions, bleeding/clotting disorders, leukemia, juvenile diabetes etc.

The data of cleft type was documented according to the Kernahan and Stark's classification [10]. For ease of comparison and statistical analysis the subjects were grouped into Neonate, Infancy, Toddler and Childhood [11]. The cleft types were also further grouped into Cleft lip and Alveolus, Cleft Palate, Cleft lip and Palate. The data was collected and added into Microsoft Excel sheets. In the process, all the patient records were coded and patient's identity was concealed. The waiver of consent was taken from the Institutional Ethics Committee before conducting the research. The SPSS software was used for the statistical analysis to do the chi-square test and significance level adopted was 5% ($P < 0.05$).

RESULTS

A total of 821 cases were assessed and statistically analysed using the SPSS software to correlate the values for statistical significance by doing Pearson's Chi-Square test (P-value=0.05). 41.4% of the total cases showed a raise in Total Leukocyte count (Table 2).

The parameter is statistically significant (p=0.049). 7.4% of the total cases showed an increase in the Neutrophil count and is statistically significant (p=0.010). 4.9% of the total cases showed an increase in the Eosinophil count. 17.9% of the total cases showed an increase in Lymphocyte count out of which 8.9% were Cleft palate only and is statistically significant (p=0.043). 99.1% of the total cases showed reduced Monocyte count levels and is statistically significant (p=0.005). 55.5% of the total cleft cases showed decrease in Haemoglobin levels and is statistically significant (p=0.000). 15.8% of the cases showed sub-optimal PCV and the parameter is statistically significant (p=0.000). 73.4% of the total cases showed raise in Erythrocyte Sedimentation Rate. 17.7% of the cases had a history of recurrent infections and the parameter is statistically significant (p=0.006).

DISCUSSION

The intention behind assessing the haematological values in cleft patients was to see if there was a difference in the values and try to correlate that with the problems and complications that would usually arise in patients because of the anatomical deficit. Although it is obvious that the haematological values would be raised in cleft patients due to infections or any complications, our study may thrive to show the importance of assessing the haematological values of non-operated cleft patients time and time again so that the patient's systemic health status is maintained right from the beginning till surgery. Since haematological analysis is highly sensitive against any infections/inflammatory reactions the clinician can rely on the data and proceed for further investigations. The total leukocyte count was found to be increased in 41.4% of the total cases and was found to statistically significant (Table 2). Our study also showed that 17.7% of the total cleft cases gave a history of recurrent infections (Table 10) but the details of infection (type, site, degree) were not available but it reflected the raise in total leukocyte count mentioned above. This finding was seen less pronounced in other study conducted by Fadeyibi *et al.* (2010) which showed only 9.8% increase of total leukocyte count in cleft patients.

Table 1. Prevalence pattern of Cleft types among both Genders

Gender		Cleft type			Total
		Cleft Lip and Alveolus	Cleft Palate	Cleft Lip, Alveolus and Palate	
FEMALE	Count	93	156	101	350
	% of Total	11.3%	19.0%	12.3%	42.6%
MALE	Count	153	177	141	471
	% of Total	18.6%	21.6%	17.2%	57.4%
Total	Count	246	333	242	821
	% of Total	30.0%	40.6%	29.5%	100.0%
Pearson Chi-Square	Value	Degree of Freedom		P-value	
	4.842	2		.089	

Table 2. Comparison of Total Leukocyte Count in cleft patients with Normal values

Cleft type		Total Leukocyte Count			Total
		HIGH	LOW	NORMAL	
Cleft Lip and Alveolus	Count	113	12	121	246
	% of Total	13.8%	1.5%	14.7%	30.0%
Cleft Palate	Count	138	6	189	333
	% of Total	16.8%	0.7%	23.0%	40.6%
Cleft Lip, Alveolus and Palate	Count	89	11	142	242
	% of Total	10.8%	1.3%	17.3%	29.5%
Total	Count	340	29	452	821
	% of Total	41.4%	3.5%	55.1%	100.0%
Pearson Chi – Square	Value	Degree of Freedom		P-value	
	9.549	4		.049	

Table 3. Comparison of Neutrophil count in cleft patients with Normal values

Cleft type		Neutrophil Count			Total
		HIGH	LOW	NORMAL	
Cleft Lip and Alveolus	Count	15	6	225	246
	% of Total	1.8%	0.7%	27.4%	30.0%
Cleft Palate	Count	24	21	288	333
	% of Total	2.9%	2.6%	35.1%	40.6%
Cleft Lip, Alveolus and Palate	Count	22	3	217	242
	% of Total	2.7%	0.4%	26.4%	29.5%
Total	Count	61	30	730	821
	% of Total	7.4%	3.7%	88.9%	100.0%
Pearson Chi – Square	Value	Degree of Freedom		P-value	
	13.190	4		.010	

Table 4. Comparison of Eosinophil Count values in cleft patients with Normal values

Cleft type		Eosinophil Count		Total
		HIGH	NORMAL	
Cleft Lip and Alveolus	Count	13	233	246
	% of Total	1.6%	28.4%	30.0%
Cleft Palate	Count	15	318	333
	% of Total	1.8%	38.7%	40.6%
Cleft Lip, Alveolus and Palate	Count	12	230	242
	% of Total	1.5%	28.0%	29.5%
Total	Count	40	781	821
	% of Total	4.9%	95.1%	100.0%
Pearson Chi – Square	Value	Degree of Freedom	P-value	
	.191	2	.909	

Table 5. Comparison of Lymphocyte count in cleft patients with Normal values

Cleft type		Lymphocyte Count		Total
		HIGH	NORMAL	
Cleft Lip and Alveolus	Count	39	207	246
	% of Total	4.8%	25.2%	30.0%
Cleft Palate	Count	73	260	333
	% of Total	8.9%	31.7%	40.6%
Cleft Lip, Alveolus and Palate	Count	35	207	242
	% of Total	4.3%	25.2%	29.5%
Total	Count	147	674	821
	% of Total	17.9%	82.1%	100.0%
Pearson Chi – Square	Value	Degree of Freedom	P-value	
	6.310	2	.043	

Table 6. Comparison of Monocyte Count in cleft patients with Normal values

Cleft type		Monocyte Count		Total
		LOW	NORMAL	
Cleft Lip and Alveolus	Count	240	6	246
	% of Total	29.2%	0.7%	30.0%
Cleft Palate	Count	333	0	333
	% of Total	40.6%	0.0%	40.6%
Cleft Lip, Alveolus and Palate	Count	241	1	242
	% of Total	29.4%	0.1%	29.5%
Total	Count	814	7	821
	% of Total	99.1%	0.9%	100.0%
Pearson Chi – Square	Value	Degree of Freedom	P-value	
	10.740	2	.005	

Table 7. Comparison of Haemoglobin Levels in cleft patients with Normal values

Cleft type		Haemoglobin Level		Total
		LOW	NORMAL	
Cleft Lip and Alveolus	Count	138	108	246
	% of Total	16.8%	13.2%	30.0%
Cleft Palate	Count	208	125	333
	% of Total	25.3%	15.2%	40.6%
Cleft Lip, Alveolus and Palate	Count	110	132	242
	% of Total	13.4%	16.1%	29.5%
Total	Count	456	365	821
	% of Total	55.5%	44.5%	100.0%
Pearson Chi – Square	Value	Degree of Freedom	P-value	
	16.462	2	.000	

Table 8. Comparison of Packed Cell Volume values in cleft patients with Normal values

Cleft type		Packed Cell Volume			Total
		HIGH	LOW	NORMAL	
Cleft Lip and Alveolus	Count	41	23	182	246
	% of Total	5.0%	2.8%	22.2%	30.0%
Cleft Palate	Count	31	64	238	333
	% of Total	3.8%	7.8%	29.0%	40.6%
Cleft Lip, Alveolus and Palate	Count	15	43	184	242
	% of Total	1.8%	5.2%	22.4%	29.5%
Total	Count	87	130	604	821
	% of Total	10.6%	15.8%	73.6%	100.0%
Pearson Chi – Square	Value	Degree of Freedom		P-value	
	23.411	4		.000	

Table 9. Comparison of Erythrocyte Sedimentation Rate values in cleft patients with Normal values

Cleft type		Erythrocyte Sedimentation Rate		Total
		HIGH	NORMAL	
Cleft Lip and Alveolus	Count	173	73	246
	% of Total	21.1%	8.9%	30.0%
Cleft Palate	Count	255	78	333
	% of Total	31.1%	9.5%	40.6%
Cleft Lip, Alveolus and Palate	Count	175	67	242
	% of Total	21.3%	8.2%	29.5%
Total	Count	603	218	821
	% of Total	73.4%	26.6%	100.0%
Pearson Chi – Square	Value	Degree of Freedom	P-value	
	3.061	2	.216	

Table 10. Comparison of Cleft types with History of Recurrent Infections

Cleft type		H/O Recurrent Infections		Total
		ABSENT	PRESENT	
Cleft Lip and Alveolus	Count	218	28	246
	% of Total	26.6%	3.4%	30.0%
Cleft Palate	Count	269	64	333
	% of Total	32.8%	7.8%	40.6%
Cleft Lip, Alveolus and Palate	Count	189	53	242
	% of Total	23.0%	6.5%	29.5%
Total	Count	676	145	821
	% of Total	82.3%	17.7%	100.0%
Pearson Chi – Square	Value	Degree of Freedom	P-value	
	10.217	2	.006	

Eosinophilia has always been associated with cleft lip and palate (Greer et al., 2014). The eosinophil counts were raised in 4.9% cases (Table 4) and the parameter was not statistically significant. Singhal *et al.* (2014) conducted a study to show and correlate the eosinophilia in cleft patients which revealed eosinophilia in 20.6% cases. Kumari *et al*. (2009) also correlated eosinophilia in cleft cases. The other differential counts like Neutrophil counts, Lymphocyte counts showed uniform increase in the values and were statistically significant (Table 3, Table 5). The erythrocyte sedimentation rate was seen to be increased in 73.4% of the total cases (Table 9). Since ESR is a non-specific indicator of inflammation it implicates the presence of underlying infections in the body and can be used as a diagnostic marker by the clinician to detect any secondary infections or inflammations in cleft patients. Patients with Cleft Palate are known to have Eustachian tube dysfunction [(16)] which may cause food particles to lodge in the tube leading to middle ear infections like otitis media, cholesteatoma (Jaffe, 1971). They can also aspirate food particles into the upper airway through the palatine defects leading to respiratory tract infections like bronchopneumonia (Clarren, 1987). Since breast milk is known to protect against the underlying infections in the cleft child (Hanson, 1998), the pediatrician should pay special attention to the immune status of the child born with cleft lip and palate by ensuring the feeding of colostrum and further breastfeeding to the optimal level so that further complications may be avoided to a certain extent and provide appropriate therapy for the infections. The hemoglobin assessment showed that 55.5% of the total cases were anemic (Table 7). Studies conducted by Fadeyibi *et al.* (2010), Singhal *et al.* (2014) showed the presence of anemia in cleft lip and palate patients. A low preconceptional iron status increases the risk for anaemia in offsprings (Casanueva, 2003), Krapels *et al.* (2004) showed that the dietary intake of iron in mothers who gave birth to cleft children was lower than the recommended daily intake. An awareness can be created in cleft afflicted families (genetic tendency) about the iron intake so that the anaemic condition can be avoided in cleft off springs. The occurrence of cleft palate in offspring of mice has been correlated to the presence of anemia [(19)]. The hypothesis of correlating history of maternal anemia to orofacial clefting is not conclusive, but an implication for further research in this regard would pave the way for a new etiologic risk factor. The Packed Cell Volume was suboptimal in 15.8% cases and the parameter was statistically significant (Table 8). Adenekan (2012) conducted a study which showed that 18.6% of the cleft cases had sup-optimal PCV, which is well within the observed range of our study. The data presented in our study about anaemia and packed cell volume in cleft patients should create an awareness

among the organizations and clinicians for a more holistic approach towards treating the cleft patients.

Conclusion

Children with untreated orofacial clefts show considerable alteration in haematological values compared to the normal values. Anatomical defect leading to increased risk of infections and difficulty in feeding may act as the contributing factors for such variation.

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