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RESEARCH ARTICLE

ASSESSMENT AND CO-RELATION OF OROFACIAL MANIFESTATIONS WITH EXISTING MALIGNANT CONDITIONS IN CHILDREN

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ABSTRACT

Introduction: Indian Cancer Register reports the proportion of childhood cancers relative to all cancers as 0.8-5.8% in boys and 0.5-3.4% in girls. It's imperative that dentists be familiar with the medical history and oral manifestations of Pediatric Malignancies in order to detect, diagnose and plan for effective intervention.

Objective: To enumerate the types of Pediatric Malignancies as seen at Regional Cancer Center, Bengaluru, and to correlate it with their dental findings.

Materials and Methods: This was a cross-sectional hospital- based study, involving in and outpatients aged 15 yrs. and below. Case history was recorded and retrospective analysis of medical files was undertaken. Relevant data was tabulated and subjected to statistical analysis.

Result: Leukemia's accounted for the most common type of malignancy reported. Significant reduction in constitutional symptoms was seen after chemotherapy, but oral complications like mucositis and ulceration were present. Dmft was significantly higher in cases group compared to control group.

Conclusion: History taking, inspection and palpation should be mandatory in a dental setup. Also, once therapy is initiated appropriate treatment modalities should be employed to reduce the oral complications, so as to reduce discomfort and not hamper the progress of treatment.

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INTRODUCTION

The last decades of the 20th century and this early millennium, have shown an increased incidence of cancer, and has achieved relatively greater importance in pediatric practice (Terracini, 2011). In the global scenario, the annual number of new cases of pediatric malignancies exceeds 200,000 and the developing world constitutes more than 80% of these cases. (Barr *et al*., 2006) The overall incidence of 38 to 124 per million children, per year, in India is lower than that in the developed world, (Arora *et al*., 2009) though its incidence seems to be increasing. (Satyanarayana *et al*., 2014) Considering the low knowledge penetration in low and middle income group countries regarding pediatric cancer, it becomes imperative that we as Pedodontists be familiar with the medical history as well as oral manifestations of Pediatric Malignancies in order to detect, diagnose and plan for effective intervention, thereby improving child's quality of life. Orofacial manifestations, which are not uncommon findings in haemotological malignancies may be clinical indicators of oncological disorders in apparently healthy, undiagnosed individuals. (Adeyemo *et al*., 2011) In children with known diagnosis, the objective is to prevent infections, maintain oral hygiene and minimize the adverse effects of anticancer therapies. (Carrillo *et al*., 2010) The purpose of this study was to enumerate the different types of Pediatric Malignancies as seen at Regional Cancer Center, Bangalore (i.e the KIDWAI Institute Of Memorial Sciences), and to investigate the occurrence of oral complications in these children.

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MATERIALS AND METHODS

This was a descriptive cross-sectional hospital based study, involving in and out patients aged 15 years and below, visiting the OPD of Pediatric Oncology Department, as well as patients admitted to the Pediatric Oncology Ward of the Regional Cancer Centre, Bengaluru. The oral and perioral examination was done using latex gloves and plain mouth mirrors. None of the children had undergone any special dental prophylactic treatment [fluoride application, scaling of teeth] before examination. Case history including demographic details and details pertaining to medical history and oro-facial manifestations of 104 patients were recorded. Retrospective analysis of medical files was done to obtain information regarding the diagnosis and treatment plan. The DMFT and

deft scores were recorded in accordance to WHO recommendations. The OHI-S index was used to evaluate the oral hygiene status in these children. 104 children, with no pathology, were age matched and served as control group. The relevant data was subjected to statistical analysis using Chi-square test and Mc Nemar tests. p value of less than 0.005 is taken to be significant.

Five cases of lymphoma were present and one case of naso-pharyngeal carcinoma was recorded. (Table 1) Malignancies showed a higher incidence in boys than girls (85.5% /14.4%) (Graph 1) and was most common in children aged between 3 to 6 yrs (31.7%). The least incidence of cancer was seen between the age group of 0-2 yrs (16.3%). (Table 2)

Table 1. Frequency and percentage distribution of different types of malignancies reported

		Frequency	Percent	Cumulative Percent
Leukemia	ALL-B	70	67.3	67.3
	ALL-T	15	14.4	81.7
	AL Mixed	2	1.92	83.7
	AML	2	1.92	85.6
Others	Lymphoma	5	4.8	90.4
	Nasopharyngeal carcinoma	1	0.96	91.3
	Neuroblastoma	2	1.92	93.3
	Hepatoblastoma	1	0.96	94.2
	Medulloblastoma	1	0.96	95.2
	Ewings sarcoma	1	0.96	96.2
	Osteosarcoma	1	0.96	97.1
	Yolk sac tumour	1	0.96	98.1
	Rhabdomyosaarcoma	2	1.92	100
	Total	104	100	

Table 2. Distribution of study subjects according to Age group and cancers

	Leukaemia	Others	Total	Chi square test
0-2 years	11 (12.36)	6 (40)	17 (16.35)	P =0.062
3-6 years	31 (34.83)	2 (13.33)	33 (31.73)	
7-10 years	24 (26.97)	4 (26.67)	28 (26.92)	
11-15 years	23 (25.84)	3 (20)	26 (25)	
Total	89 (100)	15 (100)	104 (100)	

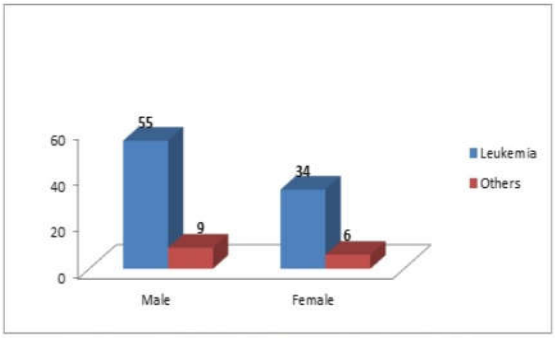
Table 3. Data at baseline and post chemotherapy (Leukemia, n= 89; Other malignancies, n =15) Significant difference in scores between the two groups, p< 0.05

	Leukemia			Other malignancies		
	Before*	After *	Significance	Before*	After*	Significance
Fever	88(98.8)	0(0)	P<0.001	14(93.3)	1(6.6)	P<0.001
Pallor	83(93.2)	0(0)	P<0.001	12(80)	1(6.6)	p=0.001
Anorexia	46(51.6)	0(0)	P<0.001	6(40)	0(0)	P=0.031
Cervical lymphadenopathy	42(47.1)	2(2.2)	P<0.001	5(33.3)	0(0)	P=0.063
Epitaxis	10(11.2)	0(0)	P = 0.002	1(6.6)	0(0)	P=1.00
Gingivitis	60(67.4)	78(87.6)	P<0.001	9(60)	12(80)	P=0.250
Gingival bleeding	8(8.9)	3(3.3)	P = 0.125	0(0)	0(0)	P=1.00
Mucositis	1(1.1)	32(35.9)	P <0.001	0(0)	3(20)	P=0.250
Ulceration	0(0)	20(22.4)	P <0.001	1(6.6)	4(26.6)	p=0.250

*Present before intervention
*Present after intervention

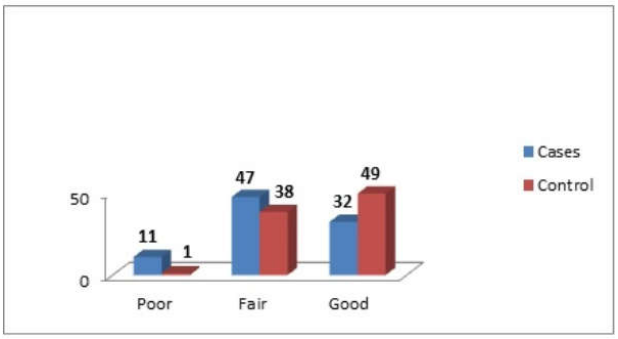
RESULTS

81.7% of the reported malignancies were Acute Lymphoblastic Leukemia. 1.9% of the cases showed Acute Myeloid Leukemia and the same percentage of cases showed mixed phenotypic leukemia.

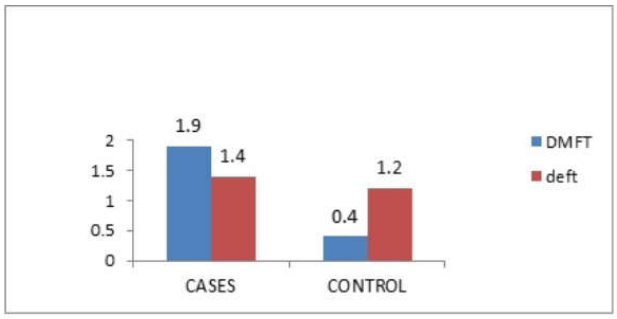


Graph 1. Distribution of study subjects according to Gender and cancers

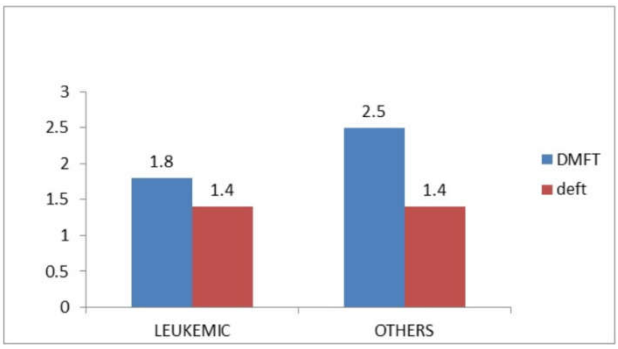
Constitutional symptoms like fever, pallor and anorexia, showed significant reduction in occurrence after medical intervention. (Table 3) Cervical lymphadenopathy was seen in 45.1% of the cases, with a significant decrease after intervention. Gingivitis was initially present in 69 (66.3%) patients with malignancies and after intervention present in 90(86.5%) patients, showing significant increase. At the time of diagnosis 8 cases of gingival bleeding were noticed, all of which were leukemic cases and this number decreased to 3 after intervention. (Table 3) 11 children under chemotherapy had poor OHIS score in contrast to one child in the control group. 45.1% of cases showed Fair OHIS score and only 30.7% of cases showed Good OHIS score, whereas 47.5%(i.e almost half) of children in the control group showed Good OHIS score. (Graph 2) Caries severity was lowest in controls, and the difference between DMFT in Cases and Controls was statistically significant. (Teeth with carious lesions were the highest DMFT component). (Graph 3) The DMFT score was significantly higher among non- leukemic malignancies,



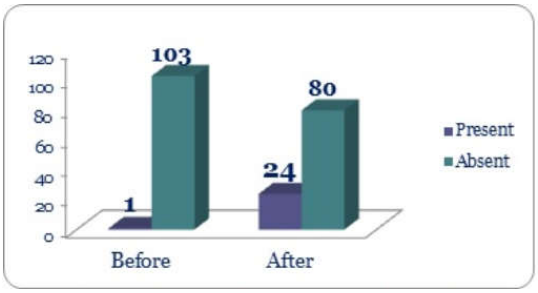
Graph 2. Distribution of Cases and Controls according to OHIS score categories



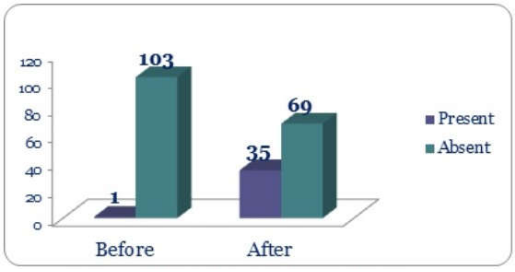
Graph 3. Mean DMFT and deft scorce of Cases and control grops



Graph 4. Mean DMFT and deft scores of leukemic and non-leukemic malignancies



Graph 5. Distribution of ulceration in cases before and after intervention



Graph 6. Distribution of mucositis in cases before and after intervention

compared to leukemic malignancies. Deft scores did not show any significant variation between the two groups. (Graph 4) Chemotherapeutic effects in oral cavity like mucositis and ulceration were observed in 35 and 24 of the cases respectively, with their incidence only one before chemotherapeutic intervention. (Graph 6 and 5)

DISCUSSION

Leukemia is the most common childhood cancer in India with relative proportion varying between 25 and 40%. Of all leukemia's 60-85% are acute lymphoblastic leukemia. (Arora *et al*., 2009) 81.7% of the reported malignancies in the present study were acute lymphoblastic leukemia. Malignancies in this study showed highest incidence among children aged between 3 to 6 yrs. (31.7%), and least incidence was seen between the age group of 0-2 yrs (16.3%), though Smith *et al* found high incidence in the first year of life, with another peak at 2 to 3 years of age, after which it declines until age 9 and then steadily increases through adolescence. (Smith and Ries, 2002) Inter-regional variance in incidence and mortality rates of childhood cancer across India especially in rural areas, proposes a probable deficit in ascertainment of cases and death notification, (Satyanarayana *et al*., 2014) which may ascertain for the decreased prevalence of childhood cancer in India compared to developing countries, particularly in the age group of 0-2yrs. Higher incidence was seen in boys than girls (60.5% /39.5%) The reported incidence of pediatric malignancies in India in males (39-150 per million children per year) is higher than in females (23-97 per million children per year) in all areas except the North East India, at a ratio that is much higher ratio than what is seen in the developed world.

A likely cause would be gender bias in pursuing healthcare, including treatment of cancer. (Arora *et al*., 2009) Less etiological connection is seen in childhood cancers, instead they develop from a broad range of different histological types of tumors, (Kerrod B Hallett, 2010) with the most common malignancy being leukemia. The general clinical manifestations of leukemia are weight loss, fever, infections, anorexia, hemorrhage, anemia, hepatosplenomegaly and lymphadenopathy. (Nemeyer and Sallan, 1993) Cervical lymphadenopathy was seen in 47.1% of leukemic and 33.33% of non -leukemic patients, in our study. In a study done by KV Vijay Kumar *et al* in Bengaluru they found that, barely 37% of the dentists palpate the lymph nodes, (Vijay Kumar and Suresan, 2012) which may lead to missed diagnosis. It should be noted that supraclavicular or posterior cervical lymphadenopathy carries a much higher risk for malignancies than, anterior cervical lymphadenopathy. (Leung and Robson, 2004) Leukemia among malignancies shows a high incidence of oral complications both at the time of diagnosis and resulting treatment. (Theodorpoulos-Papadimitriou *et al*., 1989) The most common intraoral manifestations of ALL at the time of diagnosis are sore throat, laryngeal pain, gingival bleeding, and oral ulceration. (Hou *et al*., 1997). Gingival bleeding as recorded at the time of diagnosis was seen in 8 leukemic patients. It is usually present in more acute cases, wherein the hyperplastic nature of the gingivitis may be inconspicuous, and instead evident free spontaneous hemorrhage from the gingiva may be present. Gingival bleeding might occur even during therapy, as seen in 3 cases of our study. Poor oral hygiene may predispose to gingival bleeding, particularly during myelosuppressive therapy because plaque forms readily and aggravates pre-existing periodontal disease.

(Peterson and D'ambrosio, 1992) Chemotherapy is the principal treatment modality utilized in childhood cancer and has brought about a tremendous change in survival rates. The major side effects of chemotherapy include alopecia, nausea and vomiting, mucositis and myelosuppression. (Albini *et al*., 2012) The occurrence of such complications in published data changes significantly, but they appear to be far more common in children, (Stafford *et al*., 1980) with no conclusive reason. Gingivitis initially present in 66.3% of the cases, increased to 86.5% during chemotherapeutic intervention. Hegde *et al*. found that gingival inflammation was directly associated with the duration of chemotherapy. (Hegde *et al*., 2011) 11(10.5%) children under chemotherapy had poor OHIS compared to one child (0.9%) in the control group. Also only 32 children (30.7%) undergoing chemotherapy showed Good OHIS score, compared to 49(47.1%) of children in the control group. A reduced salivary flow rate (SFR) (due to chemotherapy induced salivary gland hypoplasia) aids in dental plaque accumulation, which if untreated, may elicit periodontal inflammation in immunocompromised patients. (Hegde *et al*., 2011; Javed *et al*., 2009; Javed and Romanos, 2009) Oral prophylaxis and Oral hygiene instructions can efficaciously stall or lessen the severity of oral infections, by a reduction in both gingival inflammation and the level of colonization of the normal oral flora. (Cheng *et al*., 2001; Peterson and Sonis, 1982; Lindquist *et al*., 1978; Beck, I979; Peterson *et al*., 1980) Chemotherapeutic effects in oral cavity like mucositis and ulceration were obversed in 33.3% and 23.1% of cases respectively. In a study by Childers *et al*. (1993) they found the incidence of oral mucositis to be 65%, which was considerably higher than that obtained in our study. (Childers *et al*., 1993) This may be due to the improvement in chemotherapeutic agents employed over the years as well a shift in attitude towards oral health.

It is proposed that since the treatment modalities influence cells with a higher mitotic index, and younger persons have a high mucosal cell turnover rate, they encounter a higher incidence of this complication. (Sonis, 1983) Potentially, variations in resistance or the immunological status of children may also influence its incidence. (Sonis and Clark, 1991) Furthermore, the predominant type of childhood cancer is haematological, which is considered to lead to higher rates of oral mucositis than in patients with solid tumours. (Niscola *et al*., 2007) Literature on bacteraemia in cancer patients have indicated that patients with oral mucositis and neutropenia have a 4 times higher risk of septicaemia than those without oral mucositis. (Gonzalez-Barca *et al*., 1996; Eting *et al*., 1992) Data has also additionally demonstrated that viridans streptococci from the oral mucosal lesions are responsible for the notable increase in gram-positive bacteraemia in neutropenic cancer patients. (Gonzalez-Barca *et al*., 1996; Schimpff *et al*., 1994) Oral mucositis, in addition to its influence on morbidity and quality of life, may result in treatment interruptions and dose reductions with a direct effect on disease survival, including cure rates or durability of remission. (Wilkes, 1998; Graham *et al*., 1993; Kenny, 1990; National Institutes of Health, 1989; Dodd *et al*., 1996) The NIH (National Institute of Health) consensus conference in 1989 reiterated that in order to optimize cancer treatment, curtailing oral complications becomes necessary. (National Institutes of Health, 1989) The present study showed significant increase in caries severity in children undergoing chemotherapy. Under chemotherapy increased caries risk may result from altered salivary gland secretion and saliva properties, vomiting and potentially mucositis. (Krasuska-Sławińska *et al*., 2016) The association between mucositis, poor oral hygiene, and caries was confirmed by Cheng *et al*. in their study. (Cheng *et al*., 2001) Impact of chemotherapy on caries intensity, is still debatable in whether chemotherapy exerts a direct influence on caries, or a combination of deficient dental care, dietary habits, and hygienic negligence exert a more deciding influence on the development of caries. (Krasuska-Sławińska *et al*., 2016) Two patients had abscessed teeth. Studies have found that chronic infections of the dental pulp and the periodontal tissues may become a portal of systemic infection during periods of myelo-suppression. (Cheng *et al*., 2001; Greenberg *et al*., 1982; Peterson and Overholser, 1981) Hence, oral examination and preventive treatment have to be undertaken at periodic intervals. Significant association exists between dental findings and Pediatric malignancies and the onus lies on the dentist to best ascertain and utilize this information. Also, once therapy is initiated appropriate treatment modalities should be employed to reduce the oral complications, so as to reduce discomfort and not hamper the progress of treatment.

Conclusion

45.1% of children at the time of diagnosis had cervical lymphadenopathy, and 8 cases of gingival bleeding were present during diagnosis of all. Chemotherapeutic side effects like oral mucositis and ulceration were manifested in 33.3% and 23.1% of the cases respectively. In children undergoing chemotherapy, the Dmft score was significantly higher compared to the control group. Also, 0.9% of the control group showed poor OHIS score, in contrast to 10.5% of the children undergoing chemotherapeutic intervention. Knowledge regarding oro-facial manifestations should be gained and implemented by dentists, not only to improve the child's quality of life but also to detect the presence of any malignancy. Screening by a Pediatric dentist prior to commencement of chemotherapy should be mandatory, and when dental treatment is needed meticulous planning with the oncology team is essential. (Hickey *et al*., 1982; Hong and da Fonseca, 2008) The objective should be to maintain optimal oral health during cancer therapy and to handle any oral complications. (Hallbook *et al*., 2006; Levy-Polack *et al*., 1998; American Academy of Pediatric Dentistry Clinical Affairs Committee, 2005-2006; Melo de Brito *et al*., 2003)

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