Original Article-I

Paediatric Hodgkin's Disease - A study of 232 Cases Seen at Gujarat Cancer & Research Institute, Ahmedabad.

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ABSTRACT

Background : We reviewed case records of two hundred and thirty two children diagnosed to have Hodgkin's disease between June, 1992 and may, 2002 in the division of paediatric oncology at the Gujrat Cancer & Research Institute. Ahmedabad.

Design: Retrospective study.

Results: Patients mean age was 8.5 years, ranging from 3 to 14 years. Male to female ratio was 5:1. All patients had evidence of lymphadenopathy at presentation, 43% had organomegaly. B symptoms were present in 37% of patients. Mixed cellular histology was the most common subtype (80%) followed by lymphocytic predominant (15%) and nodular sclerosis (5%) subtype. 52.5% of patients had stage I-II disease at diagnosis and 43.5% had stage III & IV disease. 67.2% of children received ABVD and 16.3% received COPP combination chemotherapy. Remaining patients received either hybrid COPP/ABV or other combinations. Involved field radiotherapy was added to the site of bulky disease.

Conclusions: Mean age of 8.5 years, marked male preponderance, presence of B symptoms in 37% of patients, mixed cellular histology and stage III-IV in half of the patients is similar to reports from other centres in India and other developing countries.

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INTRODUCTION

Childhood Hodgkin's disease is a rare and a highly curable disease.[1,2] The incidence of Hodgkin's disease in children in India comprises 21% of all patients with Hodgkin's disease,[6] in contrast to much lower incidence in western hemisphere.[20]

Correa and O' Conner[15] described a typical pattern of Hodgkin's disease in tropical and subtropical areas characterized by high rate in young children, marked male preponderance, poor prognostic subtypes and advanced clinical stage at presentation. This pattern has also been substantiated in relation to environmental factors and socioeconomic status as reported by Gutensohn et al with similarity of the clinical picture as seen in Portugal, Turkey, Africa[5] and Israel.[6] While Hodgkin's disease occurs in various age group, children with the disease need special attention as the problems that arises in treatment and follow up can differ from those in adults and a speciality care can best deal with these problems.

A separate division for paediatric oncology was started first time in India in 1992 at Gujarat Cancer & Research Institute, Ahmedabad. It is the aim of this paper to present a review of paediatric Hodgkin's disease in respect to clinical and epidemiology at this institute during the last decade.

PATIENTS AND METHODS

Two hundred and thirty two children, (14 years and younger) histologically confirmed to have Hodgkin's disease according to Rye classification[2,3] have been evaluated. The record

of the patient, the complaints, presenting symptoms and their duration, the haematological and biochemical investigations results as well as histology report of all patients who were diagnosed as having Hodgkin's disease were reviewed for the study.

Clinical staging was determined according to Ann-Arbour classification.[4] Chest X-ray was done routinely for all cases and this provided evidence for intrathoracic involvement. Ultrasonography of abdomen was done in all cases, which provided evidence for intra abdominal disease. Exploratory staging laparotomy, lymphan-giography and intravenous pyelography etc. were not performed in any patient. Hisopathological classification was according to Lukes & Buttler scheme.[4]

giving ratio of 5:1. Mixed cellularity was the commonest histologic subtype observed in 185 (80%) patients. Only 11(4.8%) patients had lymphocyte predominant histology. Forty-one (17.6%) had stage 1, 81(34.9%) stage II, 78 (33.6%) had stage III and 32 (13.7%) patients had stage IV disease. However patients with B symptoms were not separately analyzed, that may still add to advanced disease Various patient characteristics shown in Table-1.

A literature search of Hodgkin's disease (across all age group) in Indian population revealed various studies done by Shah P.M. et al[5], Tavalkar G.V. et al[6], Dinshaw K. et al[7] and Mehrotra R.M.L., et al[8] While the disease pattern and response to treatment in children from western hemisphere have been widely reported

Table 1: Patients Characteristics: (N=232)

Characteristics	**Particulars**	**Number %**
Age	Mean	8.5 years
	Range	3-14 years
Gender	Male	194 (83.6%)
	Female	38 (16.3%)
	M: F	5:1
Presentation	Lymphadenopathy	232 (100%)
	Visceromegaly	100 (43.1%)
Stage	I	41 (17.6%)
	II	81 (34.9%)
	III	78 (33.6%)
	IV	32 (13.7%)
Histology	Mixed cellularity	185 (80%)
	Lymphocyte predominant	36 (15.2%)
	Nodular sclerosis	11 (4.8%)
	Lymphocyte depleted	00 (0.0%)

RESULTS AND COMMENTS

In our experience, 13.3% of childhood malignancy is due to lymphoma. Hodgkin's disease comprises 6.6% of pediatric malignancy at CGRI, that is 42.6% of total lymphoma cases.

The mean age was 8.5 years (range, 3 to 14 years). There were 194 males and 38 females

by Schnitzer et al,[21] Fuller et al,[22] Shrith et al,[23] and Donaldson et al,[24] there is great paucity of information regarding Hodgkin's disease in under developed and developing countries.

In the United states the incidence of paediatric Hodgkin's disase is 3.7% (range, 2-4%).[4] Overall crude age adjusted incidence rate

reported by Waterhouse et al[20] is low in developed country. In contrast, Talvarkar et al[6] reported the incidence in childhood Hodgkin's disease in western India to be quite high.

In a series of 2238 consecutive patients at Stanford University 4% were 10 years or younger and 11% were 11 to 16 years. Hodgkin's disease is rare before 5 years of age and in 10 years of age; the incidence is higher in boys. The median age of 8.4 years in our patients is younger than that reported from Uganda[12], the United States and Canada.[4] There is no obvious explanation for the difference.

Overall male preponderances in incidence of Hodgkin's disease, which is more marked in childhood form.[4] The incidence rate in the 0-9 years of age group in Bombay[6] male population is higher than United States rate but less than that reported from Cali, Colombia (South America).[16]

In present study, 194 (83.6%) were males and 38 (16.3%) were females giving male to female ratio of 5:1. Similar male preponderance for this disease have been observed at Ahmedabad (2.4:1)[5], Bombay (5:1)[6], Lucknow (5.6:1)[8] and Chandigarh (5:1)[9] as well as in Uganda[12] (7:1) and South Africa[11] (4.4:1).

Lymphadenopathy (100%), viscero-megaly (43.1%) and B symptoms (37%) were common mode of presentation. Involvement of extranodal site at presentation was not observed in our study.

Mixed cellularity was the predominant histopathology in 80% of patients followed by lymphocyte predominant subtypes in 15.2% of patients. The distribution of different histologic subtypes in some of the reported series is shown in Table II.

Table II: Distributions of histologic subtypes. (Including all age group).

Country	MC (%)	LP (%)	NS (%)	LD (%)	No. Of cases studied
India: Ahmedabad (Current Series)	80	15.2	4.8	00	232
Bombay (1)	54	23	09	14	979
Israel (7)	30	19	34	17	161
Lucknow (9)	80	08	03	09	300
Uganda (16)	50	18	12	20	128
Chandigarh (17)	54	04	15	27	100
Egypt (19)	44	29	13	14	86
Japan (22)	38	29	26	07	166

LP: Lymphocyte predominant; MC: Mixed cellularity; NS: Nodular sclerosis; LD: Lymphocyte depleted.

In paediatric age group, most reports from North America shows an excess of nodular sclerosis over other histologic subtypes. Pizzo et al[4] reported nodular sclerosis in 40%-70%, mixed cellularity in 30%; lymphocyte predominant in 10%-15% and lymphocyte depleted as very rare histology. Olweny et. al. (South Africa)[12] reported 70% of patients had mixed cellularity or lymphocyte predominant histology. In developing countries with suboptimal socio-economic conditions, histologic subtypes associated with poor prognosis are predominant. Histologic differences may be largely dependent on variable host response, which may in turn be influenced by genetic and environmental factors. Since it was hypothesized that disease progress from lymphocyte predominant through mixed celluarity to lymphocyte depleted and nodular sclerosis represent arrest of this progression due to host immunologic status.[15]

Donaldson S.S. et. al[4] reported stage at presentation of pediatric Hodgkin's disease as, stage I in 18%, stage II in 43%, stage III in 36% and stage IV in 3%. In present study distribution of stage is stage I in 41 (17.6%), stage II in 81 (34.9%), stage III in 78 (33.6%) and stage IV in 32 (13.7%) patients. Advanced disease at presentation was reported in 47.3% of our patients.

Combination chemotherapy was the mainstay of treatment. Various chemotherapeutic regimens used were ABVD, COPP (Cyclophosphamide, Vincristine, Procar-bazine, Prednisolone), COPP\EVA (Etoposide, Vinblastine, Adriamycin), ABV\COPP and BEACOPP.

Combination chemotherapy has dramatically changed the outlook in children with Hodgkin's disease. ABVD regimen is safe; effective and gold standard treatment for paediatric Hodgkin's disease.[1,2,3,4] In our center ABVD is the most preferred treatment regimen. Out of 232, 156(67.2%) patients were treated with ABVD regimen, 38(16.3%) patients received COPP and others were given COPP\ABV, EVA\COPP, BEACOPP etc. Involved field radiation therapy was added to site of bulky and/or residual disease.

CONCLUSION:

This series comprised 6.6% of all pediatric patients with Hodgkin's disease registered. Mean age was 8.5 years at presentation, marked male preponderance, clinically advanced stage, poor prognostic subtypes of Hodgkin's disease are typical patterns described by Correa and O'Connor and were observed here and seems to be the predominant presentation in developing countries.

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