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A Retrospective Audit of Treatment Outcomes of Paediatric Hodgkin Lymphomas in A Tertiary Care Centre.

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I. Introduction

Hodgkin lymphoma (HL) has a dramatic response in terms of survival outcome since it was first described by Thomas hodgkin in 1832 [1]. Survival outcomeof paediatric HL may differ between developed and developing countries due to various reasons particularly the socio economic factors. The recurrence of the disease was also widely reported in backward regions. In developing countries, HL usually presents with a higher-stage of disease and generally has mixed cellularity histologically[2-5]. HL is by and large treated on the basis of the stage of disease and risk profile, which provide the basis for different treatment strategies such as chemotherapy, radiotherapy, or a combined modality approach. The optimal treatment approach still remains controversial, especially in the advanced disease stage. Initially, high-dose extended-field radiation proved to be effective in adults with early-stage disease, whereas chemotherapy combinations of mechlorethamine, vincristine, procarbazine, and prednisone as well as doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) or combined-modality treatment were reserved for advanced disease [6].

These treatments were modified for children by reducing radiation dose and field size and relying on chemotherapy across all disease stages. With increasing concerns about agieng survivors of paediatric cancer, general treatment approaches for the disease have changed. The use of alkylators has been reduced and the number and composition of chemotherapy cycles have been adapted to individual risk factors [7,8] Radiotherapy (RT) has been limited to involved fields and doses adapted to disease risk [9]. The concept of using early response to tailor therapy in dose-dense regimens has been refined[10]. Procarbazine has been gradually eliminated to reduce the risk of infertility, and etoposide and doxorubicin substituted to reduce the cumulative alkylating agent dose. Treatment for pediatric HL has focused on minimizing toxicity and late effects and preserving high cure rates. We report outcomes at our centre in poor socio economic background scenario.

II. Methodology

All children <15 years of age diagnosed with HL on biopsy and presenting to our centre during the study period (2010-2015) were included in the study. This was a retrospective design and analysis at follow up was evaluated. A total of 86 patients were diagnosed with Hodgkin lymphoma (HL) during this period. Clinical information including gender, age and sites of involvement was obtained from case records. All the patients were confirmed with histopathology and IHC. Immunohistochemistry (IHC) was done using the HPR polymer method. All cases were classified according to the 2008 WHO classification, based on both morphology and immunohistochemistry.After staging workup, all patients with early stage disease (I-II) were started into favourable and unfavourable groups, based on B-symptoms and bulky disease. Early stage favourable patients (IA, IIA) received 2-4 cycles of ABVD, and early stage unfavourable patients (IB, IIB) were treated as advanced disease and received 4 cycles of ABVD. All patients with late stage disease (stage III and higher) received 6 cycles of ABVD. Severity of disease was defined to include those of early stage unfavourable disease (stage IB, IIB) and late stage disease (stage (III to IV).When a patient was lost to follow-up, the time of most recent follow-up examination was used. Variables assessed were – complete response (CR) after four cycles, Partial Response (PR) or relapse (REL), development of secondary malignancy, and death. Measurements of growth and development, assessment of cardiac, pulmonary, and thyroid functions were performed.

III. Results

A total of 86 children were included in the study. The male to female ratio was 8.5:1. The mean age was 9.3 ± 2.2 (range, 3 to 15) years. Boys presented at a younger age of 7.2 ± 2.1 years as compared with girls for whom the mean age was 9.9 ± 3.1 years, the difference being statistically significant (P = 0.02). There were 17 children younger than 5 years (20%). Cervical lymphadenopathy was the most common primary site of disease, followed by axillary and inguinal sites. Advanced- stage disease was present in 59% of children. Treatment regimen give to the study population is charted in table 1.

Table 1 : Treatment Regimen In The Study Group

Chemotherapy Regimen	Early	Advanced	Total
ABVD +COPP	13	20	33
MOPP / COPP	10	11	21
VAEP	12	7	19
ABVD	**6**	**7**	**13**
Total	**41**	**45**	**86**

MOPP: nitrogen mustard 6mg/m2, vincristine 1.5mg/m2, procarbazine 100mg/m2, prednisone 60mg/m2, nitrogen mustard and vincristine IV days1 and 8 , prednisone 60mg/m2. Nitrogen mustard and vincristine IV : days 1 and 8, prednisolone and procarbazine PO for 14 days
COPP: cyclophosphamide 600mg/m2, vincristine 1.5 mg/m2, procarbazine 100mg/m2, prednisone 60 mg/m2, cyclophosphamide and vincristine IV days 1 and 8, prednisone and procarbazine PO for 14 days
VAEP: vincristine 1.4 mg/m2, etoposide 200mg/m2, adriamycine 25mg/m2, prednisolone 60mg/m2
ABVD: adriamycin 25mg/m2, bleomycine 10mg/m2, dacarbazine 375mg/m2, vinblastine 6mg/m2.

Table 2 : Staging of disease in study population

STAGE	No of patients
i	28
ii	12
iii	33
iv	13

Table 3 : Study distribution based on histopathology :

Type	No of patients
Mixed cellularity	55 (65%)
Nodular sclerosis	11 (13%)
Lymphocytic predominant	7 (8%)
Lymphocytic depleted	1 (1%)
unspecified	12 (13%)

The OS in early-stage disease was statistically higher at 95.7% as compared with 88.2% in late-stage disease (P = 0.05).The EFS rates were 93.2% and 78.2% in children with early-stage and advanced-stage disease, respectively (P = 0.0081). The EFS rates in various regimens were as follows: ABVD 83.5%; ABVD/ COPP 81%; VEEP 79.7%; and COPP/MOPP 65.5%. The differences were not significant. There were 14 cases of relapse and mean duration of relapse was 9.4 months. 6 cases had relapse within one year of therapy and the rest 8 after one year.

IV. Discussion

We reviewed patients treated in a single tertiary care institution with multiagent chemotherapy for identifying epidemiologic and prognostic features that might be specific to this patient population. Multiagent chemotherapy was the mainstay of treatment.Success of combination Chemotherapy in late stages of HL and delayed side effects of RT in children directed us to initiate chemotherapy in all the stages of the disease. Despite advances in therapy, 10% to 20% of children relapse. Cases of relapse were documented in 14 (16.2%) patients. Most of the relapses occurred in patients with advanced-stage disease (63.6%). There was no signifiant difference in relapse rate with different histologic subtypes (P=0.65).

Treatment modalities in low-income countries have to be tailored to the resources of the local health teams. Protocols have to be easily adaptable as low-income countries do not have all the facilities available in the developed world. We have achieved an OS and EFS comparable to those of developed nations using chemotherapy alone in our setup.Small sample size precluded derivation of prognostic factors in our study.

Larger populations with longer follow up would better derive the prognostic factors in low socio economic group affected with hodgkins disease.

V. Conclusion

Although the present group could get away with chemotherapyy alone, a larger analysis would better delineate the role of radiation in this paediatric presentation. The ultimate goal would always be the reduction of treatment burden and the maintaining of high cure rates with fewer systemic toxicity in paediatric age group.

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