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Original Research Article

Small steps towards bigger goals: A study of demography and outcome of paediatric cancers in a peripheral resource limited paediatric oncology centre

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ABSTRACT

Background: The aim of this study was to analyze the demography, clinical profile and outcome of pediatric cancer cases from a peripheral resource limited center.
Methods: We retrospectively analysed demography, clinical details and outcomes of 227 cases of paediatric cancer up to nineteen years of age, from August 2009 to May 2019. Their status of treatment was categorised as completed, ongoing, abandoned and expired. We generated Kaplan-Meier curves (KM) and calculated three-year event free survival (EFS) and overall survival (OS).
Results: Out of 227 children, 139 (61.2%) were boys and the rest were girls. Maximum number of children 108 (47.6%) were aged zero to four years. The socioeconomic status of 70 patients using the Kuppuswammy scale showed that 55 patients (78.57%) belonged to a lower socio-economic stratum. The commonest malignancy was leukaemia 119(52.4%) followed by solid tumours constituting 84 (37%) patients, of which 25 (11.01%) were renal tumours. Out of total 227 patients, 107 (47.13%) have completed treatment, 45 (19.8%) were on treatment, 24 (10.6%) have abandoned and 51 (22.5%) had expired. The median duration of follow up was 18 months. The three-year EFS and OS were 71.9% and 74.8% respectively for the entire COHORT, 74.4% and 75.5% for ALL (Acute Lymphocytic Leukemia), 38.4% and 46.1% for AML (Acute Myeloid Leukemia) and 74.3% and 76.6% for solid tumours. Among solid tumours, three-year EFS and OS was of renal tumours 86.9% and of neuroblastoma was 77.7%.
Conclusions: We achieved outcomes similar to those from well-established Indian single institute studies. The survival of our paediatric cancer patients can be improved with collaborative effort and establishment of new centres in the periphery.

Keywords: Event free survival, Overall survival, Outcome, Epidemiology of paediatric cancers

INTRODUCTION

Paediatric oncology in India accounts for 1.6-4.8% of the total burden of cancer.[1,2] Incidence of paediatric cancer in India was 18 to 235.3 per million for boys and 11 to 152.3 for girls during the period 2012-14.[3] Approximately 45,000 children are diagnosed with cancer every year; comprising a major cause of mortality after infectious diseases and malnutrition.[3] Survival outcome in paediatric oncology in the developed world is 75-79%.[4] Similar outcomes have been achieved in India also, at dedicated tertiary oncology institutes. However, one cannot extrapolate these results to the whole population as institutes like these are very few in number and concentrated in urban areas of the country hence inadequate to cater to our huge population.[5] The population-based cancer registry (PBCR) survival data, which is a better representation of cancer outcomes across India has reported a five-year overall survival for all childhood cancers to be a dismal 37-40%.[6] This can be attributed mainly to poor infrastructure, lack of access to tertiary cancer hospitals, lack of trained staff, limited financial resources, ignorance and cancer illiteracy.

Our institute was a tertiary care centre in the western India, catering to patients from rural areas and lower socioeconomic strata. The paediatric oncology department was started in 2009. The objective of this study was to assess demography, clinical profile and outcomes of paediatric cancer patients over the last ten years.

METHODS

This was a retrospective study done at the oncology unit of the paediatric department of a regional hospital in western India. The study period was from May 2019 to May 2020. The study was approved by the institutional review board. The data was collected from records maintained in the department. All histopathologically confirmed cases of paediatric cancer from zero to nineteen years of age, registered from August 2009 to May 2019 were included in the study. These cases were analysed for demographic and clinical variables like age, sex, diagnosis, treatment plan and outcomes. The socioeconomic status of 70 patients was analysed using Kuppuswammy scale.[7]

After reviewing departmental records, the treatment status for each patient was categorised as completed treatment; on treatment; abandoned treatment and expired. Abandonment of treatment was defined as the termination of care by the parent/caregiver and/or not presenting for scheduled treatment for four or more weeks at the time of data record. The record of the last follow up for each patient was noted and survival was estimated from the date of diagnosis to generate KM survival curves.

The three-year EFS and OS were calculated and the corresponding KM curves were generated. An event was considered to be either a relapse or death of the patient. A mortality analysis of the patients was performed and cause of death was categorized into disease related (for example-relapsed/refractory disease or its complications) and treatment related (chemotherapy toxicity, infections). Relapsed patients were analysed with respect to their diagnosis, treatment status and outcome.

Statistical analysis

Data was statistically described as frequencies (number of cases) and percentages where appropriate. Descriptive statistics were used to calculate the relative frequencies of age, sex, diagnosis. Survival curves were plotted using the KM method and comparison was made using the log-rank test. The entire data is statistically analysed using statistical package for social sciences (SPSS version 21.0, IBM Corporation, USA) for MS windows.

RESULTS

A total of 227 children were analysed and their demographic data has been depicted in Table 1. The analysis of the socioeconomic status of 70 patients using the Kuppuswammy scale showed that 55 patients (78.57%) belonged to a lower socio-economic stratum.

Our paediatric oncology unit was started in 2009, the following line graph depicts the rise in the number of patients over the last 10 years (Figure 1).

The breakup of the cases according to the diagnosis is given in Table 2.

Out of total 227 patients, 107 (47.13%) have completed treatment, 45 (19.8%) were on treatment, 24 (10.6%) had abandoned treatment and 51 patients (22.5%) had expired (Figure 2). These abandoned patients were excluded from further analysis.

The median duration of follow up of these patients was 18 months.

The estimated three-year EFS of the entire COHORT was 71.9% and OS was 74.8%.

On analysing the individual malignancies, three-year EFS of ALL (BCP and T cell ALL) was found to be 74.4% and OS was 75.5%. The best three-year EFS and OS was found to be 100% in LCH followed by 87.5% and 100% in HL and 80% in APML. The three-year EFS and OS of NHL was 58.3% and 66.7% and of AML was 38.4% and 46% respectively. The three-year EFS and OS of solid tumours was 74.3% and 75.6%. Among solid tumours, highest three-year EFS and OS was of renal tumours 86.9% and of neuroblastoma was 77.7% (Figure 3 and 4).

Table 1: Demographic details.

Parameters	Number	Percentage
Gender		
Male	139	61.2
Female	88	38.8
Age groups (in years)		
0- 4	108	47.6
5-9	69	30.4
10-14	34	15
15-19	16	7

Table 2: Distribution of cases according to diagnosis.

Diagnosis	No. of cases (%)
Leukaemia	119 (52.4)
ALL	
Pre-B cell ALL	82 (36.1)
T-cell ALL	15 (6.6)
AML	14 (6.2)
APML	5 (2.2)
CML	2 (0.9)
Juvenile myelomonocytic leukaemia	1 (0.4)
Non-Hodgkin's lymphoma	12 (5.3)
Hodgkin's lymphoma	8 (3.5)
Langerhans cell histiocytosis	4 (1.8)
Solid tumours	87 (37)
Renal tumours	25 (11.01)
Germ cell tumours	12 (5.3)
Neuroblastoma	11 (4.8)
Retinoblastoma	6 (2.6)
Rhabdomyosarcoma	9 (4)
Liver and pancreatic tumours	5 (2.2)
Nasopharyngeal carcinoma	1 (0.4)
Bone tumours	7 (3.08)
Brain tumours	8 (3.5)
Total	227

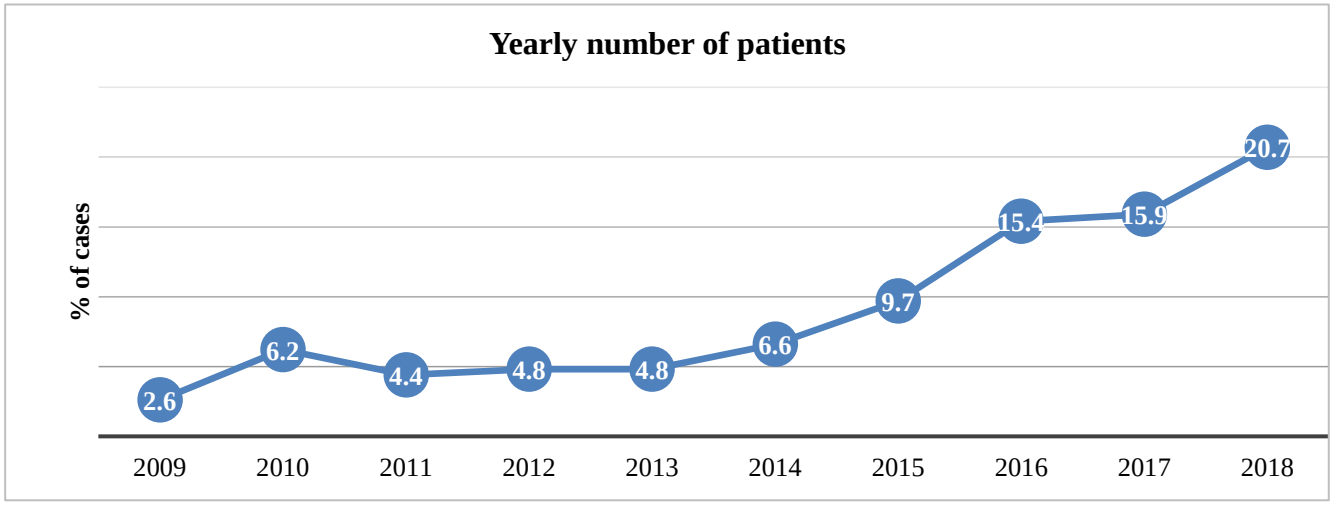

Figure 1: Distribution of new paediatric cancer cases (2009-2018).

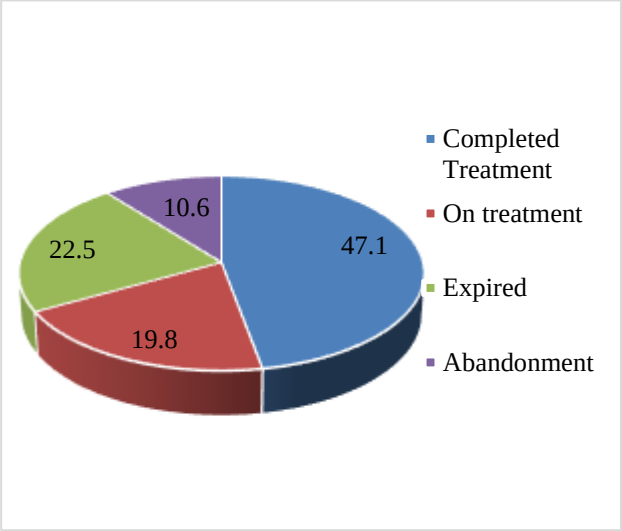

Figure 2: Treatment status of patients.

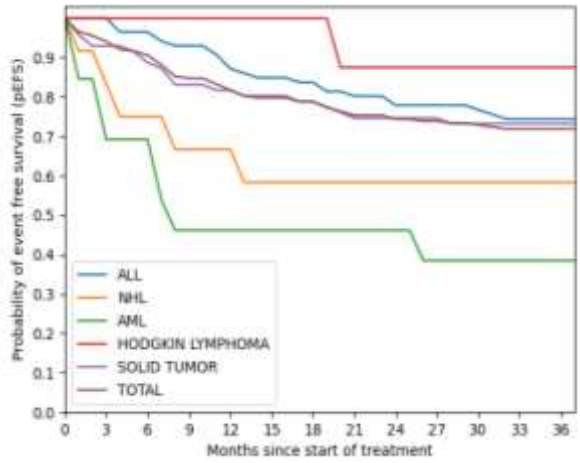

Figure 3: The distribution of three-year event free survival of the cases studied according to diagnosis.

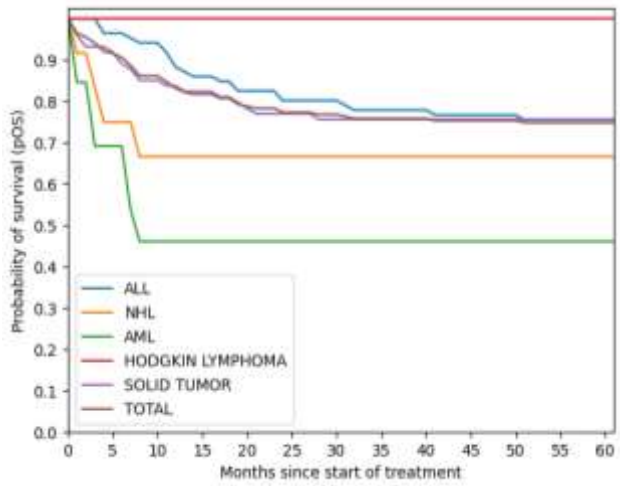

Figure 4: The distribution of overall survival of the cases studied according to diagnosis

Out of 227 patients 51 (22.5%) expired. Forty three patients expired due to disease related causes which included relapse (N=23), refractory disease (N=15) and complications in the induction phase (N=5). Eight patients expired due to treatment related causes (chemotherapy toxicity, infections).

A total of 34 patients relapsed, out of which, 23 patients expired, three patients were salvaged, six patients were on treatment and two patients abandoned treatment.

DISCUSSION

Survival outcome in paediatric oncology is one of the biggest success stories of developed world in the last millennium.[5] This was through the adoption of uniform guidelines, risk stratification, multicentric clinical trials and supportive care leading to a five-year relative survival rate from less than 58% in 1970 to more than 80% in 2014.[8,9] Our medical fraternity can deliver similar excellent results as seen in dedicated tertiary oncology centres around the country in spite of huge challenges peculiar to our country.

Our institute had a well-developed paediatric unit catering to children referred from a wide radius of semi-urban and rural areas, the majority of which hail from a low socioeconomic class. The paediatric cancer unit was started in 2009 with very humble beginnings and since then has gradually developed in multifaceted ways which include better diagnostic services, transfusion services, supportive care and trained staff like dedicated medical professionals, nurses, nutritionists and social workers. We presented the results of a retrospective study of the demography and outcomes of our children with cancer from 2009 to 2019.

We analysed a total of 227 children in our study. We found the three-year EFS and OS of the entire COHORT to be 71.9% and 74.8% respectively. There was a scarcity of publications from India about overall incidence and survival of childhood malignancies, however, the Madras metropolitan tumour registry (MMTR), PBCR, reported the absolute OS of all childhood cancers as 46% at three years.[10-12]

The data from the SEER registry from the USA showed the five-year OS for childhood cancer had improved markedly over the past three decades from 58% in mid 1970s to 83.4% in 2014, due to new and improved treatment modalities.[9]

In our study the commonest childhood malignancy was found to be leukaemia, affecting 119 patients out of 227 (52.4%). This was corroborated by larger studies conducted in India and data from the SEER registries, which also reported the commonest childhood malignancy to be leukaemia.[4,13]

On analysing the individual malignancies, we found the three-year EFS and OS of ALL (BCP ALL and T cell ALL) to be 74.4% and 75.5% respectively. An important effort at multicentre collaboration in India led to the development of the MCP-841 protocol for paediatric ALL, which then resulted in the long-term survival figures improving from 20 to 60%.[14] This was due to implementation of a uniform treatment regime, well-organized data collection and access to experts.[15]

As compared to our data, advanced countries perform better regarding survival outcomes. The long-term results of four consecutive trials in childhood ALL performed by the ALL-BFM study group from 1981 to 1995 showed significant improvement; the five-year EFS and OS were roughly 78% and 85% respectively using ALL-BFM 95 protocol.[16] We also reviewed the SEER registry, which recorded OS as 83.1% for ALL.9

The three-year EFS and OS of HL was 87.5% and 100%, which were relatively high figures, probably due to the small number of cases over which these were calculated. Data from a tertiary centre in North India showed the five-year EFS and OS to be 77.75% and 92.7% respectively.[17]

Similarly, children with Wilms tumour also had a good outcome with three-year EFS and OS of 94.5%. Retrospective analysis from a single centre in South India showed the EFS and OS to be 73% was 80% and the data from SEER up to 2014 showed OS to be 90.4%.[9,18]

The three-year EFS and OS of NHL was 58.3% and 66.7%. These results were poorer compared to a retrospective study done in All India Institute of Medical Sciences, New Delhi, which reported the three-year EFS to be 82.6% until 2014.[19]

The three-year EFS and OS of neuroblastoma was 77.7% in our study. This was higher than a retrospective analysis from a tertiary care centre in India, which reported a three-year EFS and OS to be 36% and 47% respectively.[20] This can again probably be attributed to smaller number of cases in our study.

The three-year EFS and OS of AML was 38.4% and 46.1%. This was similar to the results of a retrospective study done in Chennai showing OS to be 36% as well as a number of other single Indian institute studies.[21] The SEER data showed 67.1% OS for AML.[9]

In our study the rate of abandonment was 10.6%. In low and middle-income countries treatment abandonment had been reported up to 15%.[22] Even though our abandonment rate was lower, efforts were needed to reduce it further. Interestingly, we found that of the total 24 (10.6%) patients who abandoned treatment, 17 (7.4%) patients abandoned treatment in the first 5 years of a newly opened centre, whereas only 8 (3.5%) patients did so in the last five years. This was probably due to improved social services support, governmental financial schemes and collaboration with non-governmental organizations working specifically for children with cancer.

The limitation of our study was the small number of cases in its purview and a short median follow up from a single institute to comment on the standard outcomes of the individual cancer studies.

CONCLUSION

In conclusion, our study shows that, survival outcomes at par with those of established centres are achievable in a newly established paediatric oncology unit in spite of limited resources and multiple challenges. It also supports decentralization of paediatric oncology care to tertiary hospitals with necessary facilities in suburban and rural areas of India, so that maximum number of children with cancer have access to the treatment leading to improvement in the overall outcomes of paediatric cancer in our country.

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