RESEARCH COMMUNICATION

Pattern and Implications of Therapy Abandonment in Childhood Acute Lymphoblastic Leukemia

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Abstract

Abandonment of therapy is cited as an important factor contributory to inferior survival outcome in developing nations. In this communication we describe the pattern of therapy abandonment and its impact on survival of childhood acute lymphoblastic leukemia at a large tertiary care center in Northern India and discuss remedial measures.

Keywords: Acute lymphoblastic leukemia - abandonment - pattern - survival - mortality

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Introduction

Therapy abandonment is often cited as an important reason for inferior survival outcome in childhood cancers in resource constrained nations (Arora et al,.2007, Bonilla et al., 2009). However, there is extremely scanty data addressing the pattern and impact of abandonment on outcome of childhood acute lymphoblastic leukemia (ALL) from India and other Asian developing countries (Arora et al., 2007). Hence, in this communication we describe the pattern of abandonment of therapy in our institute over a period of 18 years in childhood ALL.

Materials and Methods

A total of 532 patients treated with United Kingdom ALL (UKALL) X/XI protocols at Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India from January 1990 to December 2005 and followed until December 2008 were analyzed. There is variability on definitions of abandonment, default, refusal and loss to follow up, all of which are rampant in developing nations. Herein we used the definitions suggested by Arora et al (2007) where abandonment is defined as initiation but not completion of treatment.

Results

Some 96 (18.1%) out of 532 patients abandoned therapy. Their mean age at presentation was 5.04 years. The male:female ratio was 2.69:1 as against 3.2:1 in the entire cohort suggesting that more female children tended to abandon therapy although differences were not statistically significant (p=0.212). Almost 70% (against 53% in the remainder, p=0.121) of these patients belonged to lower lower and upper lower socioeconomic strata as defined by Kuppuswami scale (Mishra and Singh, 2003). We analyzed if any of the clinical-demographic and laboratory parameters impacted abandonment. None of age (p=0.456), parental literacy status (p=0.094), geographic location and distance from our center (p=0.08), symptom diagnosis interval (p=0.202), lymphadenopathy (p=0.082), hepatomegaly (p=0.642), splenomegaly (p=0.911), bulky disease (p=0.167), mediastinal adenopathy (p=0.348), central nervous system disease at diagnosis (p=0.365), white cell count (p=0.662), platelet count (p=0.293), hemoglobin (p=0.409) were significantly associated with therapy abandonment when compared to 436 patients who did not abandon therapy.

There was steep increase in abandonment in the induction phase of therapy (1 month) followed by more gradual phenomenon (see Figure 1). The Kaplan-Meier

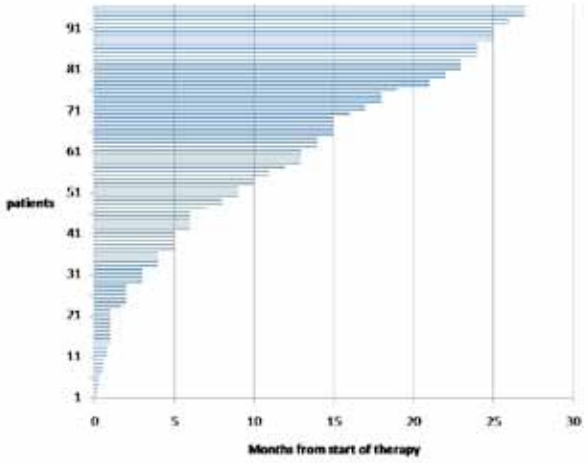

Figure 1. Incidence of Therapy Abandonment from 0 (Start of Therapy) to 27 (Completion) Months of Therapy

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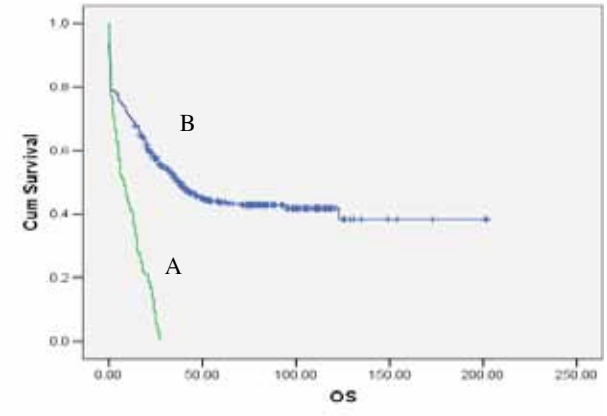

Figure 2. The Kaplan-Meier Survival Estimates for Patients Abandoning (A) and Compliant with Therapy (B)

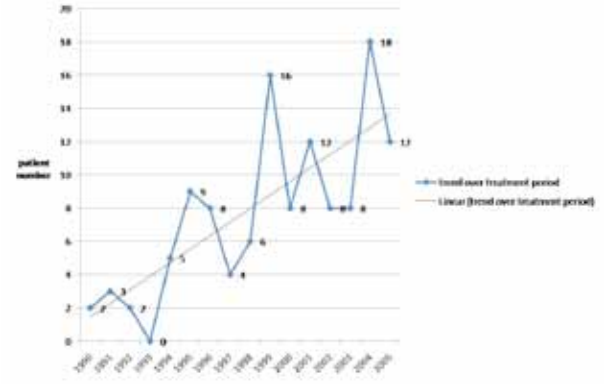

Figure 3. Trends and Absolute Number of Patients Abandoning Therapy Over the Entire Treatment Period

survival estimates for patients abandoning and compliant with therapy depicted in Figure 2 show a sharp drop in survival in both the groups during induction. Thus, abandonment is an important competing risk during induction to early mortality,

Over the entire time era, cumulatively, approximately 3 patients abandoned therapy during each post-induction month of therapy, providing an almost linear correlation during second to 27th month of therapy. There was a steady increase in the absolute number of patients (from 2 to 12) abandoning therapy over the treatments era (Figure 3). Mean percentage of annual abandonment was 22.5±2.3. Despite its periodicity, the percentage of patients abandoning therapy was roughly constant over the study period despite increase in absolute numbers. This could be explained by an approximately 10% annual increase in number of patients managed at our institute.

Discussion

To the best of our knowledge, this is the first study from India addressing the pattern of abandonment in childhood ALL. We observed a very high overall percentage of abandonment (especially during induction and throughout the treatment period) similar to figures stemming from other developing nations which thereby contributes significantly to treatment failure and inferior survival outcome (Kulkarni et al., 2009; Sitaresmi et al., 2010). No clinicodemographic or laboratory parameters correlated, in contrast to data reported from Honduras where travel time and age correlated with abandonment, other unpublished Indian series and a study from El Salvador (Arora et al., 2007; Bonilla et al., 2009). Rampant illiteracy (over 20% patients are totally illiterate) and high percentage of patients from lower socioeconomic strata and below poverty line presenting to our institute may explain the lack of statistical association of these parameters with abandonment. A constant percentage of patients abandoning therapy despite improvements in supportive care and overall survival indicates need of urgent interventions to reduce abandonment, especially during induction therapy with a constant surveillance thereafter to prevent dropouts.

Our observations and lack of correlation of clinicodemographic factors with abandonment indicate need of further prospective and detailed studies assessing objective parameters associated with socioeconomic status, parental psychological perceptions, fears and beliefs about disease, treatment and cure, literacy, community rituals faiths and practices, methods and quality of communication of diagnosis and treatment related information, quality of health care provided, interaction of these factors and interventions based on identified problems (Israels et al., 2008; Sitaresmi et al., 2010). Assessment of dynamics of abandonment and further and detailed exploration of the factors and pattern of therapy default at larger scale are necessary for introduction of remedial measures. Since abandonment is an important phenomenon in developing nations, efforts including financial, educational initiatives, social support measures and twinning for its prevention are imperative in improving cure rates of ALL in developing countries.

Acknowledgments

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