

## IV. SUMMARY

The survival rate of childhood acute lymphoblastic leukemia (ALL), the most common cancer in children, is as high as 80% in developed countries but frequently is <35% in developing nations. This difference is believed to be attributable primarily to refusal or abandonment of treatment, both of which are almost unknown in developed countries.

Treatment refusal or abandonment constitutes one end of the non-compliance spectrum, which ranges from occasional lapses to total withdrawal. Failure to adhere to treatment is not restricted to patients and parents, but can also concern physicians.

Aims of this study are:

- 1) To examine the influence of socio-economic status on childhood ALL treatment and treatment refusal or abandonment in a developing country.
- 2) To investigate parental experiences during childhood ALL treatment and their reasons to refuse or abandon treatment.
- 3) To determine whether a structured parental education program increases the access to donated chemotherapy and decreases treatment refusal or abandonment.

A major reason for poor survival of childhood acute lymphoblastic leukemia in developing countries is treatment refusal or abandonment. This can be associated with parental socioeconomic status and attitudes of health care providers. In **Chapter 1** we examined the influence of 2 socioeconomic status determinants, parental income and education, on treatment in an Indonesian academic hospital. Medical charts of 164 patients who received a diagnosis of acute lymphoblastic leukemia between January 1997 and August 2002 were abstracted retrospectively. Data on treatment results and parental financial and educational background were collected. Open interviews were conducted with 17 parents and 21 health care providers. Of all patients, 35% refused or abandoned treatment, 23% experienced treatment-related death, 22% had progressive or relapsed leukemia, and 20% had an overall event-free survival. Treatment results differed significantly between patients with different socioeconomic status; 47% of poor and 2% of prosperous patients refused or abandoned treatment. Although poor and prosperous patients used the same protocol, the provided treatment differed. Poor patients received less individualized attention from oncologists and less structured parental education. Strong social hierarchical structures hindered communication with doctors, resulting in a lack of parental understanding of the necessity to continue treatment. Most poor patients could not afford treatment. Access to donated chemotherapy also was inadequate. Treatment refusal or abandonment frequently resulted. There was no follow-up system to detect and contact dropouts. Health care providers were not fully aware that their own attitude and communication skills were important for ensuring compliance of patients and parents.

Based on these findings a structured parental education program about leukemia, its therapy, donated chemotherapy and compliance was designed. Starting from January

2004 this program has been provided to all parents. The program contained: a video-presentation in hospital, information booklet, audiocassette, DVD, procedures for informed-consent, statement of understanding for donated chemotherapy and a complaints-mechanism.

Chapter 1 illustrated that treatment results differed significantly between poor and prosperous children with leukemia in Indonesia. In **Chapter 2** we determined whether parental socio-economic status influences beliefs, attitude and behavior of health-care providers treating childhood leukemia in Indonesia. A self-administered semi-structured questionnaire was filled in by 102 health care providers (69 doctors, 28 nurses, 2 psychologists, 2 hematology technicians, 1 administrator) from November 2004 till August 2005. We found that most health care providers (98%) asked parents about their financial situation. The decision to start treatment was influenced by parental socio-economic status (86%), motivation of parents (80%), and motivation of doctors (76%). Health care providers stated that prosperous patients comply better with treatment (64%), doctors comply better with treatment for the prosperous (53%), most patients cannot afford to complete treatment (58%), less extensive explanations are given toward poor families (60%), and communication is impeded by differences in status (67%). When dealing with prosperous families a minority of health care providers stated that they pay more attention (27%), work with greater accuracy (24%), take more interest (23%), and devote more time per visit (22%). Most health care providers denied differences in the quality of medical care (93%) and the chances of cure (58%) between poor and prosperous patients. We concluded that beliefs, attitude and behavior of health care providers toward poor versus prosperous patients appeared to differ. These differences may contribute to the immense drop-out rate and slight chances of survival among poor leukemia patients in developing countries.

In Chapter 1 we described that the access to donated chemotherapy for childhood leukemia patients in Indonesia was limited from 1997 until 2004: only 16% of eligible families received donations. After the introduction of our structured parental education programme in January 2004, we examined in **Chapter 3** the access of parents of children with leukemia to donated chemotherapy. Of 72 new childhood ALL patients attending the Indonesian academic hospital from November 2004 till April 2006, 51 parents (71%) were interviewed by independent psychologists using semi-structured questionnaires. Parents of 21 patients (29%) did not participate because their children dropped-out (n = 10) or died (n = 11) before an interview took place. Four patients had health insurance and did not need donated chemotherapy. Access to donated chemotherapy was improved: 46/47 patients (98%) received donations. Structured parental education improved the access to donated chemotherapy. Outreach-programs may benefit from this approach. This may enable more patients from poor socio-economic backgrounds in the developing countries to receive aid and achieve cure.

Treatment refusal and abandonment are common causes of treatment failure in childhood acute lymphoblastic leukemia (ALL) in many developing countries. In most studies reasons for abandonment were based on the opinion of health care providers, very few studies have focused on the parental point-of-view. Aims of the study in **Chapter 4** were

to analyze the parents' reasons of abandonment and to ascertain the fate of children who abandoned treatment in a pediatric oncology center in Yogyakarta, Indonesia. We conducted home-visits to interview families of ALL patients, diagnosed between January 2004 and August 2007, who refused or abandoned treatment. During this period, 159 patients were diagnosed with ALL of which 40 children (25%) refused or abandoned therapy. Thirty-seven (93%) of these children were home-visited. Reasons for abandonment were complex. Most parents mentioned several reasons. Financial and transportation difficulties were not the only or main reasons for abandonment. Belief of ALL incurability, experience of severe side-effects and dissatisfaction with health care providers were also important considerations. Most patients (64%) abandoned treatment during the diagnostic-evaluation or remission-induction phase. Of the 37 patients who refused or abandoned treatment, 26 (70%) children died, and 11 (30%) children were still alive, 2 of them more than 2 years after abandonment. We concluded that reducing treatment abandonment of childhood ALL in developing countries requires not only financial and transportation support, but also parental education, counselling, psychosocial assistance, improvement of quality-of-care and adequate management of side-effects.

In **Chapter 5** we examined socio-economic, treatment-related, and psychological experiences of parents during the acute lymphoblastic leukemia treatment of their children in an academic hospital in Indonesia. Children were treated with the WK-ALL-2000 protocol and received donated chemotherapy. From November 2004 to April 2006, 51 parents were interviewed by psychologists using semi-structured questionnaires. The family income had decreased (69%) since the start of treatment. Parents lost their jobs (29% of fathers, 8% of mothers), most of whom stated that this loss of employment was caused by the leukemia of their child (87% of fathers, 100% of mothers). Treatment-costs resulted in financial difficulties (78%), debts (65%), and forced parents either to postpone or withdraw from parts of treatment (18%). Parents mentioned needing more information (86%) from and contact (77%) with doctors. The parent organization did not pay any visits (69%) during hospitalization, nor did they give information (59%) or emotional support (55%). We have concluded that the socio-economic impact of leukemia treatment was profound. Communication between parents and doctors requires improving. The role of the parent organization was insignificant and must be ameliorated.

In **Chapter 6** we compared childhood ALL treatment outcome before and after introduction of the parental education program. We reviewed medical records of 283 children with ALL diagnosed during two periods: before (January 1997- August 2002; n=164) and after (January 2004-December 2006; n=119) introduction of the education program. Data on treatment results and parental socioeconomic status were collected. After introduction of the education program, treatment refusal decreased significantly and event-free survival increased significantly in poor patients. Treatment abandonment increased significantly in prosperous patients. In the overall population toxic-death increased significantly and no significant difference in event-free survival was found. We concluded that after introduction of the education program, poor families received structured information about leukemia, treatment, and donated chemotherapy for the first time. Treatment refusal decreased and event-free survival increased significantly in poor

patients. To improve survival significantly in the overall population, it is important that toxic-death and treatment abandonment decrease as causes of treatment failure. Improvement of knowledge, skills and communication of doctors is required to manage treatment toxicity and prevent treatment abandonment. Treatment intensity should be matched with possibilities of supportive-care.