Assessment of Renal and Liver Function Tests Before and After Induction of Chemotherapy in Newly Diagnosed Acute Lymphoblastic Leukemia in Children

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Abstract

A prospective study was done in the Department of Paediatric Hematology & Oncology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, between January and June of 2012, to observe the renal and liver function status in children suffering from acute lymphoblastic leukemia (ALL) before and after induction of chemotherapy. A total of 30 diagnosed patients of acute lymphoblastic leukemia were enrolled in the study. Renal and liver function tests were done before and after induction of chemotherapy. All the patients of the study were within 2-11 years range. Mean age was 5.12±2.53 years. Maximum 43.3% patients were within 3-6 years of age followed by 33.3% up to 3 years of age,13.3% within 6-9 year of age range and 10% above 9-year age range. 73.3% were male and 26.7% were female. Among the liver functions tests, mean bilirubin level of the patients before induction of chemotherapy was 2.31±4.71 mg/dl and after induction of chemotherapy was 1.12±2.15 mg/dl (P=0.122). Mean SGPT levels were 35.33±15.82 IU/L and 75±57.12 IU/l respectively (P=0.001). Mean total protein levels were 67.05±6.99 gm/dl and 64.47±7.51 gm/dl respectively (P=0.06). All the patients were HBsAg negative. Among the renal function tests, mean blood urea level of the respondents before induction was 28.89±7.95 mg/dl and after induction was 30.67±9.39 mg/dl (P=0.429). Mean serum uric acid levels were 4.63±1.18 mg/dl and 5.12±0.44 mg/dl respectively (P=0.044). Mean serum creatinine levels were 0.74±0.27 mg/dl and 0.67±0.22 mg/dl respectively (P=0.168). Mean GFR was 99.77±37.38 ml/1.732/min. before induction of chemotherapy and 108.57±37.29 ml/1.732/min. following chemotherapy (P=0.177). Kidney and liver functions may be affected in ALL in children. Recognition of hepatic and renal impairment at the onset of illness helps judicious chemotherapy in management of ALL.

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Introduction

Leukemia is the most common type of cancer in children, which is approximately 31% of all malignancies. Its peak incidence is 2 to 6 years; however, it may occur up to 15 years of age.[1,2] Leukemia is a disease resulting from proliferation of hematopoietic precursor cells. It can be broadly divided into two types: Acute and chronic.[3] The acute leukemia was demonstrated in 80% of the children suffering from leukemia in the developed countries with the incidence ratio of 34.3:1000000 people.[4] Acute lymphocytic leukemia (ALL) occurs approximately five times

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more frequently than acute myeloid leukemia (AML) and accounts for approximately 78% of all childhood leukemia diagnoses.[5,6] There are about 13000 new cases of childhood cancer, among them near about 2600 ALL in the Bangladesh each year.[7] The incidence of ALL has been rising for the last 25 years. Hopefully survival rates for ALL have improved dramatically since 1980s with a current five-year overall survival rates greater than 85%.[8,9] Renal complications are frequent in acute leukemia and treatment and prevention of renal complications are also important in the management of acute leukemia.[10,11] Liver involvement in ALL is a frequent phenomenon, but hyperbilirubinemia is not a frequently presenting symptom in ALL.[12] Liver involvement in leukemic patient due to chemotherapy is very crucial. Some studies have shown that drug-induced liver injury due to chemotherapy is an important cause of morbidity in cancer patients.[12-14]

Acute lymphoblastic leukemia can affect many organs as well as liver and kidney by infiltration of leukemic cells into the organs or by chemotherapeutic drugs which are used for the treatment of ALL.[10-14] In Acute Lymphoblastic Leukemia there may be electrolyte and metabolic derangement, which also affect liver and kidney.[15,16] Treatment of Acute Lymphoblastic Leukemia depends on the status of kidney and liver.[10,12,14] If abnormalities of liver and renal function can be detected earlier and appropriate management can be given prior to introduction or remission therapy, outcome of treatment will be good. Hence, we proposed this study to observe renal and liver function status in patient suffering from ALL before and after induction of chemotherapy.

Methods

This prospective study was done in the Department of Paediatric Hematology & Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, between January and June of 2012. A total of 30 patients with acute lymphoblastic leukemia were enrolled in this study.

Inclusion Criteria:

1. New cases of Acute Lymphoblastic Leukemia (ALL) diagnosed based on history, physical examination, comments on peripheral blood film and confirmed through bone marrow examination;
2. Patients who were selected for induction of remission therapy and completed induction therapy;
3. Patients aged 1-15 years.

Exclusion Criteria:

1. Partially treated acute lymphoblastic leukemia (ALL);
2. Relapse case of acute lymphoblastic leukemia (ALL);
3. Children suffering from any active kidney or liver disease;
4. Children having any known congenital anomalies of kidney or liver.

Patients were selected randomly who were newly diagnosed with ALL and admitted into Bangabandhu Sheikh Mujib Medical University (BSMMU) Hospital, Dhaka, Bangladesh. Initially 45 cases were included but 15 cases were excluded, as because 5 had history of previous renal and liver disease, 6 had relapse, 4 were partially treated patients. Finally, 30 cases fulfilled the inclusion criteria. Cases were diagnosed from

history, through physical examination, comments on peripheral blood film and confirmed through bone marrow examination. In all the cases, parents were the informants. Renal and liver function tests were done before and after induction of chemotherapy. Renal function tests included measurements of blood urea, serum creatinine, serum uric acid, and GFR, while liver function tests included measurements of serum bilirubin, SGPT, total protein, and HBsAg antigen test. Besides, serum electrolytes were done before and after induction of chemotherapy. Glomerular filtration rate (GFR) was estimated by using Schwartz formula. All data were collected in a structured questionnaire after having consent from the parents. Comparisons were done using Paired 't' tests and Chi-square tests. P value <0.05 was considered as statistically significant. Statistical analyses were done by using SPSS version 22.0. This study was approved by the Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.

Results

All the patients of the study were within 2-11 years range. Mean age of the respondents was 5.12±2.53 years. Maximum 43.3% patients were within 3-6 years of age followed by 33.3% up to 3 years of age, 13.3% within 6-9 year of age range and 10% above 9-year age range. 73.3% were male and 26.7% were female (Table-I).

Among the liver functions tests, mean bilirubin level of the respondents before induction of chemotherapy was 2.31±4.71 mg/dl and after induction of chemotherapy was 1.12±2.15 mg/dl; however, the difference was not statistically significant (P=0.122). Mean SGPT levels were 35.33±15.82 IU/L and 75±57.12 IU/l respectively and the difference was statistically significant (P=0.001). Mean total protein levels were 67.05±6.99 gm/dl and 64.47±7.51 gm/dl respectively and the difference was not statistically significant (P=0.06) (Table-II). All the patients were HBsAg negative.

Among the renal function tests, mean blood urea level of the respondents before induction was 28.89±7.95 mg/dl and after induction was 30.67±9.39 mg/dl; however, the difference was not statistically significant (P=0.429). Mean serum uric acid levels were 4.63±1.18 mg/dl and 5.12±0.44 mg/dl respectively and the difference was statistically significant (P=0.044). Mean serum creatinine levels were 0.74±0.27 mg/dl and 0.67±0.22 mg/dl respectively, the difference was not statistically significant though (P=0.168). Mean GFR was 99.77±37.38 ml/1.732/min. before induction of chemotherapy and 108.57±37.29 ml/1.732/min. following chemotherapy; however, the difference was not statistically significant (P=0.177) (Table-III).

Table-I: Distribution of patients by age group and sex (n=30)

Variables	Frequency	Percentage
Age (years)		
<3	10	33.33
3-6	13	43.33
6-9	4	13.33
9-11	3	10
Mean±SD	5.12±2.53	
Sex		
Male	22	73.3
Female	8	36.7
Male**:** Female	2.77**:**1	

Table-II: Distribution of liver function test before and after induction

Variables	Before induction	After induction	P value
Bilirubin(mg/dl)	2.31±4.71	1.12±2.15	0.122
SGPT(IU/L)	35.33±15.82	75±57.12	0.001
Total protein (gm/dl)	67.05±6.99	64.47±7.51	0.06

Table-III: Distribution of renal function tests before and after induction of chemotherapy

Variables	Before induction	After induction	P value
Blood urea (mg/dl)	28.89±7.95	30.67±9.39	0.429
Serum Uric acid (mg/dl)	4.63±1.18	5.12±0.44	0.044
Serum creatinine (mg/dl)	0.74±0.27	0.67±0.22	0.168
GFR (ml/1.73^2/min)	99.77±37.38	108.57±37.29	0.177

Discussion

In this study, the mean age of the patients was 5.12(±2.53) years. The peak incidence of ALL is reported at the age of 5 years, which is similar to our study.[17] In our study, 73.3% patients were male. Males are predominantly affected in acute lymphoblastic leukemia which is about 65%, as reported in a previous study.[18]

Serum bilirubin level may be raised at diagnosis of acute lymphoblastic leukemia in children.[12] In the present study, 13.3% patient had raised serum bilirubin level before induction of chemotherapy. Before induction it was raised probably due to hepatic infiltration of leukemic cells.[19] After induction of chemotherapy 29.8% patient had raised serum bilirubin level. Another study from our country also showed that serum bilirubin was significantly raised after chemotherapy, and after induction it was raised due to toxicity of anticancer drugs which were used during induction of remission.[20] It was reported that more than two-thirds of the patients suffered from increased levels of SGPT after induction therapy.[21,22] In this study, 66.6% patients had raised SGPT level after induction of chemotherapy. The present study findings are in congruence with that of those previous studies. Decreased serum total protein was observed in 10% cases, which is also supported by the evidence from Pakistan.[23]

In our series, blood urea level was found normal in 96.7% and 86.7% patient before and after induction respectively, i.e. only 3.3% and 13.3% had increased blood urea level before and after chemotherapy. However, several other studies showed significantly raised serum urea levels both before and after chemotherapy.[24,25] In this study, 13.3% patients had hyperuricemia at diagnosis. Hyperuricemia was also observed in ALL patients at diagnosis and after chemotherapy.[24-26] In the present study, due to proper hydration, alkalization and use of uricosuric agents like allopurinol, the uric acid level became normal. Hyperuricemia is an unusual presenting feature of acute lymphoblastic leukemia (ALL) and is generally associated with a large leukemic cell burden.[10,11,27] In ALL, acute renal failure is rare, but some of the patients may present with raised serum creatinine level at diagnosis.[26,27] In our series, only 3.3% patient had increased serum creatinine level at diagnosis and subsequently that became normal after induction of chemotherapy. The explanation is probably the leukemic cells that infiltrated in the kidney removed by chemotherapeutic effect. We found that 36.6% patient had decreased GFR before induction of chemotherapy. Among them, around half improved after induction of chemotherapy. Several studies showed that GFR may be normal or slightly decreased during diagnosis, but highly variable after induction of chemotherapy in children with leukemia.[25-27]

Our study has several limitations. Small sample size and short duration of the study resulted from the budget constraint. Facilities for biochemical tests were limited. Infection screening and assessment of prothrombin time was not included in the study. Moreover, uses of some antibiotics like gentamicin, ceftriaxone, ceftazidime,

trimethoprim sulphamethoxazole, Amphotericin-B, Vancomycin and their effects on renal and liver function could not be ascertained.

Conclusion

Kidney and liver can be affected in children having acute lymphoblastic leukemia. Recognition of hepatic and renal dysfunction at the onset of disease is important. With proper and judicious management of these abnormalities it can overcome. On the other hand, a higher number of patients may have raised serum SGPT level after induction of chemotherapy. But only raised SGPT level is not a reliable predictor of extended hepatocellular injury. With raised SGPT level chemotherapy can be continued safely. Further studies with larger samples and longer duration on multi-centre approach are recommended.

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