Original article

Hemolytic uremic syndrome in children: some predictive findings on the disease outcome

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Abstract

Objective: To decrease or delay the major un-wanted clinical consequences to improve the quality of life in the involved patients. **Methods**: A retrospective case series study has been made on the forty five pediatric patients admitted to nephrology department of Ali-Asghar Hospital during a period of nearly 10 years. The patients have been divided into two groups of good and poor prognoses according to their clinical outcomes. The routine laboratory records and clinical manifestations extracted and statistically analyzed as independent variables both by univariate and multivariate methods. **Results**: Forty three patients have been managed successfully with only two deaths occurred. According to clinical findings, nineteen patients were classified as poor prognosis and the rest were categorized as good prognosis. Multivariate statistical analyses showed that lesser age at the time of admission (age < 46 months, $P<0.015$) and the higher initial WBC count (count > 15 000, $P<0.226$) were well-interrelated to ominous clinical consequences like convulsion, coma and peritonitis and statistically different between the two groups of patients. **Conclusion**: Despite the importance of predictive variables in the course of Hemolytic uremic syndrome (HUS) in children and their critical influence on the clinical outcome, many aspects of these parameters have been remained to be elucidated comprehensively. Our study showed that simultaneous low age of child at the time of admission with simultaneous high WBC count will result in the poorer prognoses of the patients. This may warn the clinicians to provide more supportive cares for this group of patients.

Keywords: Hemolytic uremic syndrome (HUS); Prognostic factor

INTRODUCTION

The hemolytic uremic syndrome (HUS) is a disease with serious clinical outcomes among young children. Although renal function recovers in up to 70% of patients but some may develop un-wanted clinical outcomes in body systems such as impaired consciousness, convulsion, hypertension, stroke, coma, peritonitis, end stage renal disease and even death which consists the poor prognoses patients [1].

To prevent, decrease or significantly postpone the serious clinical complications of the illness is a major concern of the practitioners and many studies have been designed to identify and control the major and minor influencing factors which determine the

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prognosis of involved patients [2, 3].

Hemolytic uremic syndrome associated with *Escherichia coli O157:H7* is the most common cause of acute renal failure in childhood and production of Vero toxin by the organism is pivotal in the pathogenesis of the disease[4, 5]. Some previous studies have shown that the mortality rate among the young patients is 5% – 15% while older children and adults have poorer prognoses. Some authors also have shown that the clinical or laboratory features are different between the two groups of enteropathica (typical or diarrhea associated disease which is mediated by toxin) and non-enteropathica HUS. The predict disease severity and the short-term outcome in patients with non-enteropathica disease are different too[6-8].

In the present study, we analyzed the outcome of 45 children and adolescents who involved with HUS and hospitalized in Ali-ashghar pediatric nephrology department. Our purpose of the study was to identify variables which could be predictors of poor prognosis among these children.

MATERIALS AND METHODS

Over a definite period of time (July 1993 up to the August 2004) a group of forty five pediatric patients involved with the HUS recruited to the emergency department of the Ali-ashghar hospital has been followed up in our study. These patients have been admitted to the emergency room mainly for their oliguria or anuria. HUS was confirmed after laboratory investigations showing features of hemolytic anemia, thrombocytopenia and renal insufficiency, then the patients were classified according to the clinical outcomes of the disease into two distinct groups of poor prognosis and good prognosis [5, 9, 10].

The clinical status at the time of admission and also during the period of treatment and follow ups were classified according to previous studies [11, 12] with the variables in two sets of clinical findings and para-clinical measures. The patients with one of major and ominous consequences such as impaired consciousness, convulsion, hypertension, stroke, coma, peritonitis, end stage renal disease and death have been classified as the poor prognosis patients and the remainders categorized as the good prognosis ones[3,13,14].

The recorded data included gender, age, and vital signs such as blood pressure and also presence or absence of fever, diarrhea, and neurological signs which analyzed for each group of the patients. The etiological context and the usual treatment of patients including drugs known as responsible for HUS were also analyzed[2, 15].

Retrospectively, the patients´ documents and history were evaluated and confirmed as established cases according to the sub-specialist assessment and by renal biopsy[16, 17].

All patients were treated according to standard guidelines. The symptomatic treatment consisted of the restoration of vital signs, the management of deranged water and electrolytic balances, and the control of hypertension. The laboratory measurements in all cases recorded from the first day of hospitalization These measurements were hemoglobin, hematocrit, RBC and WBC counts with platelets, the ESR, Cr and BUN measurements and also serum electrolytes (Na^+, K^+, and Ca^{2+}). The urinalysis has been requested for all patients and the results were recorded exactly.

All the raw data have been analyzed through a series of statistical analyses using the Box plots in two groups, one way ANOVA and *t*-test and in next step non-parametrical Mann-Whitney and Wilcox tests.

The statistical analyses were conducted in two successive stages. Firstly a univariate analysis has been applied to the recorded data to identify variables which associated with the ominous consequences significantly. In this condition, the differences between two groups of poor and good prognoses were evaluated through a two-sided log-rank test[4,16]. On the other hand continuous variables have been dichotomized through maximum likelihood estimation in which the higher measures correspond to the cut-off point and differentiate the poor prognostic patients from the good prognostic ones, in the best way.

On the second stage of the statistical analysis, the non-parametrical tests such as Mann-Whitney and Wilcox´s regression model have been applied to identify the independently associated variables with the poor prognostic states in the case of necessity.

RESULTS

There were a total of 45 (10 female and 35 male)

patients with an average age of 62 months (range from 2 to 168 months) and 19 patients out of them (with average age of 82 months, range from 7 months to 156, male to female ratio of 15 to 4) were classified as good prognosis while the remained 26 (with the average age of 49 months, range from 2 to 168 months, male to female ratio of 20 to 6) were considered as poor prognosis patients.

The measurements of the main variables of the two groups of the patients are summarized in Table 1 associated with the test for equal variances for age of the two groups. In the first step it has been assumed that age from the clinical variables and Hb, RBC and WBC count analyzed to find any interference with the clinical outcome. In the next step multivariate analyses showed statistically significant inter-relationships of these variables.

According to the first step statistical analyses, there is statistically significant difference between the mean ages of the two groups of patients with the poor prognostic cases of much lower age (Table 2).

The next step analyses confirmed the findings ($P < 0.015$).

Table 1 Some important variables which presumed to be of predictive value

Variables	Good Prognosis Patients	Poor Prognosis Patients
Age	81 (7 – 156) months	46 (2 – 168) months
Hemoglobin	8.9 (5.7 – 14) g/dL	7.85 (4.3 – 13.8) g/dL
RBC count	3.1 (1.89 – 5.41) 10^6/μL	3 (1.3 – 4.55) 10^6/μL
WBC count	11 600 (5500 – 40 000) cell/mm^3	15 000 (4100 – 46 900) cell/mm^3
Hematocrit	26 (16 – 40) %	23 (12.5 – 42) %
Platelet count	106 000 (10 000 – 285 000) cell/μL	137 000 (10 000 – 651 000) cell/μL
ESR	56 (13 – 120) mm/h	44 (16 – 84) mm/h
Cr	3 (0 – 7.9) mg/dL	3.4 (0.8 – 10.9) mg/dL
BUN	47.1 (10 – 108) mg/dL	51 (10 – 110) mg/dL
Urea	8.57 (7 – 10) mg/dL	49 (4 – 154) mg/dL

Table 2 Poor prognosis and good prognosis groups´age statistics

	M	N	Mean	Std. Deviation	Std. Error Mean
Age	0	19.00	81.42	47.68	10.94
	1.00	26.00	46.56	44.15	8.66

The same statistical analyses then applied to the other selected laboratory measurements but the results for these laboratory measurements analyses showed to be somewhat different. Only in the case of WBC count (DF = 43) a statistically significant difference were detected between the two groups of patients.

Further analyses of the other two important laboratory measurements, i.e. RBC count (DF = 38) and also the hemoglobin value (DF = 43) showed no statistically significant differences between poor and good prognosis patients.

It should be noted that 41 patients achieved complete remission, two had a partial response, and two had no response and died because of progressive disease. One death was a female of two months old with severe diarrhea and electrolyte loss and the other was a male in the third month of his life who admitted to the hospital in deep coma.

DISCUSSION

Many clinical and laboratory aspects of predictive variables in the prognosis of hemolytic uremic syn-

drome in children are not exactly shown up to this time despite their importance in the management of the patients. The data from the literature are difficult to interpret because of the large heterogeneity of the studies concerning the definition of the disease, the diversity of its etiologies, and also the heterogeneity of treatment in retrospective studies [16].

This study is a report on analysis of the different variables influencing prognosis of hemolytic uremic syndrome in children as a retrospective mono-centric study which concerns a recent cohort of HUS in children for whom the treatment was homogenous.

Concerning the prognostic factors influencing the clinical consequences during the period of admission and hospitalization, our study indicates that age at the first hospitalization time would be significant independent risk factor for the patients. At this point one may conclude from the in depth statistical analyses that the lower the age at the first hospitalization time, the worse would be the outcomes and clinical consequences. Specifically, these worse clinical findings correlated well with the age under. 46 month of life at the time of admission. This may warn the clinicians and pediatricians of the importance of more urgent and intense supportive and monitoring measures for this group of patients at the preliminary steps of clinical treatments to prevent the unwillingly ominous preventable consequences.

By univariate and multivariate analyses, higher WBC counts were also significantly associated with late ominous clinical manifestation such as impaired consciousness and convulsion. The other laboratory variables such as RBC counts, and also Hb and Hct measures were not found as independent predictors of poor prognosis in the next step analyses. This suggests that the clinical apparent differences between these measurements may rather relate to some other conditions rather than the disease itself. We observed a mortality rate of 4.4% and an excellent improvement outcome for these primary forms of HUS.

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