ANNUAL INCIDENCE AND CLINICO-LABORATORY STUDY OF HEMOLYTIC UREMIC SYNDROME AMONG ATTENDANTS OF PEDIATRIC ZAGAZIG UNIVERSITY HOSPITAL.

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ABSTRACT

Background: Hemolytic uremic syndrome (HUS) is the most common cause of acute renal failure in young children. It is characterized by microangiopathic hemolytic anemia (MAHA), acute renal failure, and thrombocytopenia.

Objective: This work aims to study causes, clinical presentation, annual incidence, and outcome of hemolytic uremic syndrome in children admitted to Pediatric Zagazig University Hospital.

Subjects and methods: This is a descriptive study, carried out at Children hospital, faculty of medicine, Zagazig University during the period from January 2012 to January 2014.This study included 42 patients younger than 15 years with diagnosis of hemolytic uremic syndrome.

Results: Most of cases were younger than 2 years of age (57%). Males (74%) were more affected than females (26%) and most of patients were detected during summer. The overall incidence in pediatric age group (<15 years) was 1.2 per 100,000 children. Incidence was highest below 5 years old (2.69 per 100,000 children). Most of patients were presented clinically by bloody diarrhea, pallor, oliguria & anuria. Laboratory abnormalities included hemolytic anemia, thrombocytopenia, leukocytosis, hyponatremia, hypokalemia or hyperkalemia, metabolic acidosis, elevated blood urea and serum creatinine. Stool culture was positive in only 7 cases (17%).The mortality rate was 21.4%.

Conclusion: Unfavorable outcome was associated with young age, anuria, intractable seizures, high WBC count more than 30,000 per mm3 ,and hyperkalemia above 5 m mol/ L.

Key words: Hemolytic Uremic Syndrome, Shiga-toxin, Acute Kidney Injury, Hemodialysis, Complement, TMA, MAHA.

INTRODUCTION

Hemolytic uremic syndrome (HUS) is diagnosed by combination of microangiopathic hemolytic anemia (MAHA), acute renal failure, and thrombocytopenia. It is the most common cause of acute renal failure in children [1]. The main histopathological feature is thrombotic microangiopathy (TMA), characterized by endothelial damage and formation of plugs containing platelet and fibrin. This induces ischemia, RBCs damage, and c thrombocytopenia [2]. HUS is classified into two types according to presence or absence preceding diarrhea. Diarrhea positive (typical) HUS and diarrhea negative (atypical) HUS [3]. Typical HUS (tHUS) is mainly caused by enterohemorrhagic E-coli (EHEC) infection or shigella desentriae type 1 infection [4]. Atypical HUS (aHUS) is mainly caused by other infections, complement factor abnormalities, drug exposure, malignancy, irradiation, or systemic lupus erythematosus [5].

The main features of HUS include microangiopathic hemolytic anemia (MAHA), thrombocytopenia, and acute renal failure. Peripheral blood smears reveal the presence of MAHA by fragmented RBCs (schistocytes, burr cells and helmet cells). The degree of renal involvement varies and determines the increase in blood urea, creatinine, potassium and phosphate [6] . The aim of this work is to study causes, clinical presentation, annual incidence, and outcome of hemolytic uremic syndrome in children admitted to Pediatric Zagazig University Hospital.

SUBJECTS AND METHODS

This is a descriptive study, carried out at Children hospital, faculty of medicine, Zagazig University during the period from January 2012 to January 2014.This study included 42 patients younger than 15 years with diagnosis of hemolytic uremic

syndrome. Informed consent was taken from parents or care-givers of children to be enrolled in the study. The study was approved by the ethical committee of faculty medicine, Zagazig University.

Inclusion criteria: Any patient who was presented with three or more of the following:
1. Anuria or oliguria lasting for more than 24 hours with elevated urea and creatinine level.
2. Features of hemolytic anemia with hemoglobin less than10 g/dl.
3. Low platelet count less than100000/mm3.
4. Past history of preceding bloody diarrhea.

Exclusion criteria: Exclusion criteria included infants and children with any condition or disease state which may cause impaired kidney function and anemia without fulfilling the diagnostic criteria of hemolytic uremic syndrome including

- Disseminated intravascular coagulopathy (DIC).
- Septicemia.
- Bilateral renal vein thrombosis.
- Chronic renal failure**.**
- Chronic hemolytic anemia.
- Tumor lysis syndrome.
- Children taking nephrotoxic drugs

Methods:

All children included in this study were subjected to full history taking, thorough clinical examination, laboratory investigations in the form of CBC (complete blood count), reticulocytic count, peripheral blood smear for features of hemolysis, Coombs' test, kidney and liver function tests, PT (prothrombin time), PTT (partial thromboblastin time), routine stool analysis (physical and microscopic examination), stool culture, routine urine analysis urine culture, arterial blood gas analysis (ABG), blood glucose level, serum sodium, and serum potassium, blood culture, complement (C3) concentration, anti-nuclear antibody (ANA) titre, Anti-ds-DNA antibody titre, hepatitis B

surface antigen (HBs Ag), hepatitis C virus antibody (HCV-Ab). Radiological investigations in the form of plain chest radiography and pelvi-abdominal ultrasonography were done also for all patients. As regard treatment given to our patients, 37 patients (88%) received packed RBCs transfusion. Plasma infusion 10 mg/kg twice daily was given to 41 patients (98%) for 5-14 days. 36 patients (86%) were subjected to hemodialysis for 2 – 14 sessions. Antibiotics were avoided specially in patients with history of diarrhea.

STATISTICAL ANALYSIS

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into **Statistical Package for the Social Sciences (SPSS version 20.0)** software for analysis. According to the type of data qualitative represent as number and percentage , quantitative continous group represent by mean $\pm$ SD , the following tests were used to test differences for significance. Differences between frequencies (qualitative variables) and percentages in groups were compared by **Chi-square test. P value** was set at <0.05 for statistically significant (s) results & P value <0.001 for highly statistically significant (HS) result. P value > 0.05 was considered as non-statistically significant (NS). Data were collected and submitted to statistical analysis .

RESULTS

The study was performed at the nephrology unit and intensive care unit, Children hospital, Pediatrics and Clinical Pathology departments, faculty of medicine, Zagazig University during the period from January 2012 to January 2014 . Forty two children who were diagnosed as HUS were included in the present study.

Table (1) shows the annual incidence and age specific incidence of hemolytic uremic syndrome of children.

Age	Number of cases per year	Number of children at risk	Incidence per 100000 children
< 15 years	21	1755674	1.2
< 5 years	16	594568	2.69
5 – 10 years	3	581689	0.516
10 – 15 years	2	579417	0.35

The overall incidence of hemolytic uremic syndrome of children in pediatric age group (<15 years) was 1.2 per 100000 children. The annual incidence of HUS was highest below 5 years old (2.69 per 100000 children).

Table (2) Demographic picture of Hemolytic uremic syndrome (N=42)

Parameter	Frequency	Percent (%)
Age (years)		
<1 year	3	7
From 1 year to < 2 years	21	50
From 2 years to < 5 years	8	19
From 5 years to < 10 years	6	14
From 10 years to < 15 years	4	10
Sex		
Male	31	74
Female	11	26
Season		
From April to June	21	50
From July to September	12	29
From October to December	3	7
From January to March	6	14

Most of cases were younger than 2 years of age (57%). Males (74%) were more affected than females (26%) and most of patients were detected during summer.

Table (3) Clinical manifestations of hemolytic uremic syndrome (N=42).

Sign and symptoms	Frequency	Percent(%)
Diarrhea		
Absent	7	17
Bloody	30	71
Non bloody	5	12
Fever		
Absent	16	38
≤ 10 days	23	55
> 10 days	3	7
Urine Output		
Oliguria	29	69
Anuria	13	31
Intractable seizures	3	7
Pallor Moderate	32	76
Severe	10	24
Edema	16	38
Ascites	3	7
Hepatomegaly	5	12
Absent bowel sound	2	5
Neurological manifestations	10	24
CVS manifestations	3	7
Cardiomegaly	1	2
Symptoms & signs congestive heart failure	2	5
Chest manifestations	3	7

The majority of patients (83%) presented with history of diarrhea. Bloody diarrhea was described in 71% of patients while non-bloody diarrhea was described in 12% of cases. However 17% of patients presented without history of diarrhea. Decreased urine output was found in all patients (100%), and 31% of patients had complete anuria.

About 7% of patients presented with intractable generalized convulsions. All the patients presented with pallor which was severe in 10 (24%) patients. 38% of patients presented with edema. We noticed ascites in 7% patients, hepatomegaly in 12% of cases and absent bowel sounds in 5% of patients.

Neurological manifestations as headache, convulsions, disturbed conscious level and irritability were present in 10 (24%) patients. Chest examination revealed diminished air entry and crepitations in 3 (7%) patients. Cardiovascular system manifestations were found in 3 (7%) cases. One patient showed cardiomegaly and two patients showed signs and symptoms of congestive cardiac failure.

Table (4) Hematological Abnormalities of HUS patients (N=42).

Parameter	Frequency	Percent (%)	Mean ± 1 SD (Range)
TLC			18021 ± 13050 (4100 -35000)
<15000/mm3	14	33	
15000 - 30000/mm3	18	43	
>30000/mm3	10	24	
Platelet count			84600± 51600 (13500-30400)
<50000/mm3	9	21	
50000-100000/mm3	24	57	
>100000/mm3	9	21	
Hemoglobin (g/dL)			6.7 ± 1.9 (4.3-9.2)
< 5	9	21	
5-8	28	67	
>8	5	12	
Reticulocytosis	42	100	2.25 ± 1.3 (0.7-7.2)
Features of hemolysis in blood film	42	100	
Negative direct Coombs test	42	100	
Positive blood culture	3	7	
Normal prothrombin time (PT) and partial thromboplastin time (PTT).	42	100	

Leukocytosis (> 15000/mm3) was found in 67% cases. The platelet count range from 13500 to 30400 with mean count as 84600 per mm3. Nine patients (21%) had platelet count less than 50000 per mm3. Nine patients (21%) had severe anemia (< 5 g/dL) and the mean hemoglobin was 6.7 g/dL and range of hemoglobin level was from 4.3 to 9.2 g/dL. The mean reticulocytic count was 2.25%. Direct Coombs test was negative in all cases (100%) and blood film showed fragmented RBCs in all cases (100%). Positive blood culture was noticed only in three patients (7%); pseudomonas aeruginosa in one case, Streptococcus pneumoniae in the second, and klebsilla pneumoniae in the third case. All patients had normal PT (prothrombin time) and PTT (partial thromboplastin time).

Table (5) Biochemical abnormalities of HUS patients (N=42).

Parameter	Frequency	Percent (%)	Mean ± SD (range)
Sodium (m mol/L)			126.6 ± 9.5 (107-161)
<135	38	91	
135-145	3	7	
>145	1	2	
Potassium (m mol/L)			4.12 ± 1.58 (2.1-8.7)
<3.5	19	45	
3.5-5	12	29	
>5	11	26	
Low bicarbonate level (m mol/L)	28	67	12.45 ± 3.97 (6.5-20.6)
Low PH	28	67	7.31 ± 0.06 (7.21-7.42)
Creatinine (mg/dL)			2.51 ± 1.59 (1.1-5.8)
1 - 3	12	29	
3 – 5	19	45	
>5	11	26	
Urea (mg/dL)			113.7 ± 45.2 (56-187)
50 - 100	6	14	
100 - 150	10	24	
>150	26	62	

91% of patients had hyponatremia and only 2% of patients had hypernatremia . Also, 45% of cases had hypokalemia and 26% of cases had hyperkalemia. Metabolic acidosis with low PH and low bicarbonate was observed in 28 cases (67%). High serum creatinine level above 1 mg/dL was noticed in all cases (100%) and was higher than 5 mg/dl in 26% of cases. All patients (100%) showed high blood urea level, and in 62% cases, the blood urea was above 150 mg/dL.

Table (6) Stool examination of Hemolytic Uremic Syndrome patients (N=42).

Parameter	Frequency	Percent(%)
Routine examination		
Normal stool exam.	20	47
RBCs > 5/HPF	4	9
Pus cells > 5/HPF	6	14
Entamaeba Histolytica cysts	5	12
Giardia Lamblia cysts	7	17
Positive stool culure	7	17
Klebsilla pneumoniae	2	5
Shigella	1	2.4
Pseudomonas aeruginosa	1	2.4
Enterobacter	1	2.4
Acenitobacter baumanii	1	2.4
Candida.	1	2.4

In routine stool examination, RBCs were found in 4 cases (9%), and pus cells were detected in 6 cases (14%). We noticed entamaeba histolytica cysts in 5 patients (12%) and giardia lamblia cysts in 7 patient (16%). Routine stool examination was normal in 20 patients (47%). Stool culture was positive in only 7 cases (17%); Klebsilla pneumoniae in 2 cases, Shigella in one case, Pseudomonas aeruginosa in one case,

Enterobacter in one case, Acenitobacter baumanii in one case, and in one case Candida was grown.

In urine examination, significant albuminuria (>++) was found in 5 cases (12%), while mild proteinuria was detected in 16 cases (38%). We found microscopic hematuria (> 5 RBCs/HPF) in 20 cases (48%) and pyuria (> 5 pus cells/ HPF) in 6 cases (14%). In 3 patients (7%), we detected epithelial cells and in 2 patients (5%), we observed granular casts. Positive urine culture was found in 2 cases (5%); E. coli in one case, and klebsilla pneumoniae in the other.

C3 level was low in 9 cases (21%), while C3 level was normal in 33 cases (79%). Antinuclear antibody level (ANA) and Anti-ds-DNA titre were negative in all patients (100%). Hepatitis markers (HBs Ag and HCV Ab) were also negative in all patients(100%).

As regard treatment given to our patients, 37 patients (88%) received packed RBCs transfusion. Also, plasma infusion 10 mg/kg twice daily was given to 41 patients (98%) for 5-14 days. Only one case that was suspected to have pneumococcal HUS did not receive plasma infusion. 36 patients (86%) were subjected to hemodialysis for 2 – 14 sessions. Five patients (12%) improved without the need for dialysis and one patient (2%) died before initiation of dialysis. Antibiotics were avoided specially in patients with history of diarrhea. However, 26 cases (62%) had history of antibiotic treatment before admission to our hospital either in outpatient clinic or in secondary hospital before diagnosis and referral.

Table (7) Outcome distribution among studied group of hemolytic uremic syndrome patients.

			Frequency	Percent
Outcome	Complete recovery		30	71.4
	Chronic kidney disease (CKD)	Necessitating dialysis (ESRD)	1	2.4
		Not necessitating dialysis	2	4.8
	Death		9	21.4
Outcome	Bad		12	28.6
	Favorable		30	71.4
Survival	Survived		33	78.6
	Died		9	21.4
	Total		42	100.0

Out of 42 patients, 30 patients (71.4%) improved completely However, recurrence was documented in two cases who had complete recovery. Three patients (7.2%) developed chronic kidney disease (CKD). One of them (2.4%) developed end stage renal disease (ESRD) and became dialysis dependent, while two patients (4.8%) developed mild impairment of kidney functions with hypertension and persistent microscopic hematuria (not necessitating dialysis). Mortality rate was 21.4% (nine patients).

Table (8) showing comparison between favorable and unfavorable outcome of hemolytic uremic syndrome patients.

	Outcome	N	Mean	Std. Deviation	t/ MW	P
Age	Favorable	30	4.6747	3.42568	2.394	0.021*
	Unfavorable	12	2.1667	1.81175		
HB	Favorable	30	6.3533	.97900	1.527	0.135
	Unfavorable	12	5.7333	1.61546		
WBC	Favorable	30	13.9600	3.42220	-14.384	0.00**
	Unfavorable	12	31.4417	3.89369		
Platelet	Favorable	30	93.1667	20.43000	6.909	0.00**
	Unfavorable	12	47.2500	16.62487		
Reticulocytic count	Favorable	30	5.8867	4.36473	-0.375	0.710
	Unfavorable	12	6.4417	4.24038		
Urea	Favorable	30	160.6000	48.62425	-7.082	0.00**
	Unfavorable	12	267.4167	29.28685		
Creatinine	Favorable	30	3.5933	1.18494	-6.013	0.00**
	Unfavorable	12	6.0167	1.16684		
PT	Favorable	30	11.6833	.70078	-0.735	0.466
	Unfavorable	12	11.8500	.55350		
PTT	Favorable	30	34.2667	2.24274	0.681	0.500
	Unfavorable	12	33.5833	4.25245		
C3	Favorable	30	107.2333	21.23381	0.246	0.807
	Unfavorable	12	105.4167	22.73347		
PH	Favorable	30	7.3027	.07017	6.405	0.00**
	Unfavorable	12	7.1542	.06142		
NA	Favorable	30	132.4667	4.79751	0.604	0.550
	Unfavorable	12	130.8333	12.94628		
K	Favorable	30	3.4633	.73835	-6.824	0.00**
	Unfavorable	12	5.2083	.77513		

Unfavorable outcome was associated with young age (P value <0.05), high WBC count more than 30000 per mm3 (P value < 0.001), low platelet count less than 50000/mm3 (P value < 0.001), high blood urea above 250 mg/dl (P value < 0.001), high serum creatinine above 5mg/dl (P value < 0.001), low PH of the blood < 7.2 (P value < 0.001), and hyperkalemia above 5 m mol/ L (P value < 0.001).

Table (9) showing association between outcome and other parameters

			Outcome		Total	X²	P
			Unfavorable	Favorable			
Diarrhea	NO	Count	0	7	7	3.36	0.06
		%	0.0%	23.3%	16.7%		
	YES	Count	12	23	35		
		%	100.0%	76.7%	83.3%		
Anuria	NO	Count	2	27	29	21.5	0.00**
		%	16.7%	90.0%	69.0%		
	YES	Count	10	3	13		
		%	83.3%	10.0%	31.0%		
Intractable seizures	-VE	Count	9	30	39	8.07	0.004*
		%	75.0%	100.0%	92.9%		
	+VE	Count	3	0	3		
		%	25.0%	0.0%	7.1%		
Urine culture	-VE	Count	12	28	40	0.84	0.35
		%	100.0%	93.3%	95.2%		
	+VE	Count	0	2	2		
		%	0.0%	6.7%	4.8%		
Stool analysis	+VE	Count	4	14	18	0.62	0.43
		%	33.3%	46.7%	42.9%		
	-VE	Count	8	16	24		
		%	66.7%	53.3%	57.1%		
Stool culture	-VE	Count	11	24	35	0.84	0.35
		%	91.7%	80.0%	83.3%		
	+VE	Count	1	6	7		
		%	8.3%	20.0%	16.7%		
Blood culture	-VE	Count	9	30	39	8.07	0.004*
		%	75.0%	100.0%	92.9%		
	+VE	Count	3	0	3		
		%	25.0%	0.0%	7.1%		
Low C3	NO	Count	10	23	33	0.22	0.63
		%	83.3%	76.7%	78.6%		
	YES	Count	2	7	9		
		%	16.7%	23.3%	21.4%		
Packed RBCs transfusion	-VE	Count	1	4	5	0.2	0.65
		%	8.3%	13.3%	11.9%		
	+VE	Count	11	26	37		
		%	91.7%	86.7%	88.1%		
Plasma infusion	-VE	Count	1	0	1	2.56	0.11
		%	8.3%	0.0%	2.4%		
	+VE	Count	11	30	41		
		%	91.7%	100.0%	97.6%		
Dialysis	NO	Count	1	5	6	0.48	0.47
		%	8.3%	16.7%	14.3%		
	YES	Count	11	25	36		
		%	91.7%	83.3%	85.7%		

This table shows highly significant association between unfavorable outcome and anuria (P value < 0.001). Also, there is significant association between unfavorable outcome and intractable seizures (P value < 0.05) and there is significant association between unfavorable outcome and positive blood culture (P value < 0.05). However there is no significant association with other parameters.

Table (10) showing association between diarrhea and positive stool culture.

			Diarrhea		Total	X^2	P
			No	Yes			
Stool culture	-VE	Count	7	28	35	1.68	0.19
		% within diarrhea	100.0%	80.0%	83.3%		
	+VE	Count	0	7	7		
		% within diarrhea	0.0%	20.0%	16.7%		
Total		Count	7	35	42		
		% within diarrhea	100.0%	100.0%	100.0%		

This table shows that there is **no** significant association between diarrhea and positive stool culture (P value > 0.05).

DISCUSSION

Hemolytic uremic syndrome (HUS) is the most common cause of acute renal failure in young children . The present study aimed to calculate the annual incidence of HUS and to observe variable clinical manifestations, laboratory abnormalities and the outcome of HUS patients. The present study was performed in a tertiary care centre at nephrology unit and intensive care unit, Children hospital, Pediatrics and Clinical Pathology departments, faculty of medicine, Zagazig University over a period of 2 years.

In the present study, we noticed that the overall incidence of hemolytic uremic syndrome of children in pediatric age group (<15 years) was 1.2 per 100,000 children. Similar to our results, **Noris and remuzzi** observed that the overall annual incidence of HUS was 1- 2 cases per 100,000 children [7] .

In our study, the annual incidence of HUS was highest below 5 years old (2.69 per 100,000 children). However HUS incidence was 0.516 per 100,000 children between 5 – 10 years and 0.35 per 100,000 children between 10-15 years.

Similar to our results, **Tarr et al.,** noticed that the annual incidence of HUS was higher in young children and that age specific incidence was 3.1 per 100,000 children for Canadian children younger than five years [8].

Tozzi et al., also reported higher incidence of hemolytic uremic syndrome in Italian children below five years (1.68 cases per 100,000 population) [9].

Also, Elliott et al., reported HUS in Australian children younger than five years as 1.35 per 100,000 population [10].

In the present study, we found that the majority (57%) of the cases were younger than two years, and most of them (76%) were below the age of five years. Similar to our results, **Srivastava et al.,** also found that most of their patients (59%) were younger than the age of two years and 92% of their patients were younger than five years. We also found that males patients (74%) were more than females patients (26%) and male to female ratio was 2.8: 1. Similar to our results, **Srivastava et al.,** also noticed that males (72.6%) were more affected than females and observed that male to female ratio was 2.5: 1[11].

However, **Jodele et al.,** observed equal affection of males and females and reported more severe disease in female patients[12].

In the present study, we found that the most of our cases(79%) were detected in summer (from April to September), which is similar to other studies where the authors noticed that hemolytic uremic syndrome occurred more frequently during summer months. For example, **Taylor et al.,** in their study reported that the incidence of HUS was higher in warmer months, especially from June to September [13].

However, **Brandt et al.,** reported that North West epidemic did not occur in summer[14].

Siegler and Oakes also noticed that most of their patients had oliguria and that about 50%

of them had anuria. They also reported that convulsions occurred in 10% of patients[15].

Chang et al., also reported that bloody stool occurred in 82% of their patients [16].

Similar to our results, **Watanabe** reported severe CNS manifestations occurred in less than 20% of cases in the form of Seizures and significant encephalopathy resulting from focal ischemia due to microvascular CNS thrombosis [17].

Weitz et al., in their study reported that 5 % all HUS cases were associated with streptococcus pneumoniae infection and was manifested with pneumonia and empyema [18].

Mannucci reported congestive heart failure in 5% of hemolytic uremic syndrome patients and stated that and severe anemia, volume overload and hypertension can together precipitate heart failure [19].

However, in contrast to our study, **Brilliant et al.,** reported that hemolytic uremic syndrome was found without evidence of microangiopathic hemolytic anemia on blood film (peripheral blood smear) [20].

Similar to our results, **Kavanagh et al.,** reported hyponatremia in 86% of their patients, hypokalemia in 57% of patients and hyperkalemia 23% of patients [21].

Tarr also reported that dilutional hyponatremia is common in HUS patients (89%), hyperkalemia may occur (20%) due to acute renal failure, however, unexplained significant hypokalemia is more common in most (50%) of HUS patients (paradoxical finding in a case of acute renal failure [22].

Similar to our results, **Jha et al.,** in their study found positive stool culture in only 17% of their patients. The most common organisms were E coli and shigella were. However, other authors reported in their study that out of 73 patients, 27 (37%) patients had positive stool culture positive and that the main organisms were E. coli and Shigella [23].

Lei et al., reported that most of HUS patients (85%) required packed RBCs transfusion [24].

Ariceta et al., in their study, reported that daily plasma infusions have been effective in treatment of atypical HUS [25].

Licht et al., reported that plasma therapy remains the most important line of treatment for most patients of atypical hemolytic-uremic syndrome because plasma products can replace the deficient or abnormal von Willbrand factor (vWF) metalloproteinase or complement factors [26].

Loirat et al., recommended peritoneal dialysis for infants and young children because it is technically easier, and usually well tolerated especially in small infants [27].

Harrison reported that hemodialysis is also suitable for children and for cases with severe abdominal pain [28].

Some authors reported high mortality rate as 60 % of cases while **Siegler** observed that mortality rate was between 4-10% [29].

In the present study, unfavorable outcome and mortality were associated with young age, high WBC count, hyperkalemia, anuria, and intractable seizures.

Similar to our results, **Walters et al., (2012)** observed that polymorph nuclear cell count was significantly higher in their diarrhea associated HUS patients who had a poor outcome [30].

Also, **D'Souza et al., (2009)** reviewed literature and reported **bad prognostic factors** as younger age at presentation, leukocytosis, hyperkalemia, systemic involvement, anuria or prolonged oliguria, and prolonged convulsions [31].

CONCLUSION

The overall incidence of hemolytic uremic syndrome of children in pediatric age group (<15 years) was 1.2 per 100000 children. The annual incidence of HUS was highest below 5 years old (2.69 per 100000 children). Unfavorable outcome was associated with young age , anuria, intractable seizures, high WBC count more than 30,000 per mm3 ,and hyperkalemia above 5 m mol/ L. The presence or absence of enteropathic organisms on stool culture has is not essential for diagnosis of diarrhea-associated HUS. This is because only a small number of patients infected with those organisms develops HUS, and also the organisms that cause HUS may be rapidly eliminated. Therefore the stool culture is often negative in patients who have diarrhea-associated HUS.

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