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Hemolytic Uremic Syndrom In Children

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Abstract:

Background: Hemolytic – uremic syndrome may be sporadic, epidemic, and in some countries e.g Argentina endemic. The disease occurs between the ages of 4 months and 4 years. The incidence of disease is increasing. Most but not all studies have shown that white children more susceptible to HUS than black children. Classic (post diarrheal) the disease occurs frequently during warmer months.

Objective: To assess the epidemiology, clinical presentation, laboratory studies, and important risk factor that affect the outcome.

Patients and method: A prospective cross-sectional study included thirty-six consecutive patients with Hemolytic – uremic syndrome in this study who fulfil the criteria of the diagnosis of HUS (microangiopathic hemolytic anemia, acute renal failure and Thrombocytopenia.Patients who need dialysis referred to the renal unit AL- Yarmouk Teaching Hospital for peritoneal dialysis.

Results: prodromal diarrheal was present in 32 cases (89%), 26 patients (72%) had dialysis; 10 patients required peritoneal dialysis once. significant association between; the younger age group (<2Years); non diarrheal prodrome; number of dialysis increasing risk of death in H.U.S cases.

Conclusion: there is an association between Hemolytic – uremic syndrome with substantial morbidity and the incidence of the syndrome is increasing particularly in young age child.

Keyword: Hemolytic – uremic syndrome, prodromal diarrheal, acute renal failure, children.

Introduction:

Hemolytic – uremic syndrome (HUS) is characterized by a microangiopathic hemolytic anemia renal cortical injury (sometimes progressing to renal cortical necrosis), and thrombocytopenia HUS is a major cause of acuts renal failure in children and it increasing in frequency [(1)]. It was initially believed to be a renal disorder with secondary hematologicmanifestation, but recent studies indicate that the syndrome should be regarded as a systemic disease [(2)]. With aggressive management of the acute renal failure, more than 90% of the patients survive the acute phas , and the majority of these recover normal renal function[(3)].

EPIDEMIPLOGY:

HUS may be sporadic,epidemic, and in some countries e.g Argentina endemic. The disease occurs between the ages of 4 months and 4 years [(4)]. The incidence of HUS is increasing [(1)]. Most but not all studies have shown that white children more susceptible to HUS than black children [(5)]. Classic (post diarrheal) HUS occur frequently during warmer months[(6)].

ETIOLOGY:

The disease most frequently follows an episode of gastroenteritis caused by an enterohemorrhagic strain of Escherichia coli (O157:H7) [(3)]. E. coli O157:H7 refers to the somatic antigen and H to the flagellarantigen) is the prototypic EHEC and is the E. coli serotype responsible for more than 90% of EHEC infections in USA [(7)]. HUS has been associated with other bacterial (shigella,salmonella, campylobacter, S.Pneumoniae),Bartonella, and viral coxackie, ECHO, influenza,varicella, HIV,Epstein, Bar infections and with endotoxemia. It has been reported also to follow use of oral contraceptives and pyrancopolymer, an inducer of interferon.It has been associated with SLE. malignant hypotension pre – eclampsiapost-partum renal failure and radiation nephritis. There are several reports for occurrence in more than member of a family, but the role of genetic factor in predisposition to the disease is unknown [(2)]. The idiopathic (familial) cases which is inherited either as AD or AR or may occur as sporadic cases [(7)].

PATHOGENESIS:

Only a small inoculum of EHEC is needed to allow enteric colonization [(9,8)].Microvascular injury with endothelial cell damage is characteristic of all forms of TMA, including HUS. In the diarrhea-associated form of HUS, enteropathic organisms produce either Shiga toxin or the highly homologous Shiga-like verotoxin. These toxins are easily absorbed from the colonic mucosa into the systemic circulation, bind to endothelial cells in the glomerulus and elsewhere, and directly cause endothelial cell damage.

Mechanical injury to RBCs passing through the thrombotic microvasculature results in a severe nonimmune anemia with a negative direct Coombs test [(2)].

Moreover, leukocytosis is a consistent feature of post diarrheal HUS and magnitude of the W.B.C. elevation correlates with severity and outcome. Platelets activating factor a phospholipid produce by platelets and endothelial cells play a role in the activating platelet,Vero toxin has also been shown to cause platelets aggregation[(7)].

Thrombocytopenia is due intrarenal platelets adhesion or damage. Damaged red cell and platelet are reoved from the circulation by the liver and spleen [(8).]

Plasminogen activator inhibitor type I (PDS-1), the main plasma inhibition of both tissue plasminogen activator and urokinase, was identified as the inhibitor in the hemolytic uremic syndrome.

It appears that PDL-1 may be the circulating inhibitor of fibrinolysis that was previously noted in patients with HUS. When plasma PAL-1 Levels are normalized, for example, by peritoneal dialysis, renal function improves. IT was not proven that increased plasma PAL-1 level rather causes or result from the hemolytic uremic syndrome [(8)].

CLINICAL FEATURES:

The syndrome is most common in children, under age of 4 years. The onset is usually preceded by gastroenteritis (fever, vomiting, pain and diarrhea which is often bloody) [(2)] pain can be so severe andexamination[(9)].

Sometimes reveals extreme abdominal tenderness which can be mistaken for acute surgical abdomen or ulcerative colitis. The majority (60%) of patients experience oliguria that lasts on average approximately one week. Almost half are anuric for an average of 3 days [(7)].

The brain is most commonly involved, evidence of CNS dysfunction occurs in approximately one third of the cases. In 3% - 5% of children frank stroke or cerebral edema is present, and the CNS involvement is the most common cause death [(10)].

DIAGNOSIS AND LABORATORY STUDIES:

The diagnosis is made by the combination of microangiopathic hemolytic anemia with schistocytes, thrombocytopenia, and some degree of kidney involvement. The anemia can be mild at presentation, but it rapidly progresses. Thrombocytopenia is an invariable finding in the acute phase, with platelet

counts usually 20,000-100,000/mm3. Partial thromboplastin and prothrombin times are usually normal. The Coombs test is negative, with the exception of pneumococci-induced HUS, where the Coombs test is usually positive. Leukocytosis is often present and significant. Urinalysis typically shows microscopic hematuria and low-grade proteinuria. The renal insufficiency can vary from mild elevations in serum blood urea nitrogen and creatinine to acute, anuric kidney failure [(3)].

Urinalysis are consisted of low-grade microscopic hematuria and proteinuria [(2)], liver transaminase elevation is common, serum albumin concentration is low. Elevation serum amylase and lipase concentration are observed in approximately 20% of patients and hyperglycemia has been reported to occur in 4-15% of children [(10)].

AIM OF THE STUDY

To assess the epidemiology, clinical presentation, laboratory studies, and important risk factor that affect the outcome

PATIENTS AND METHODS

Thirty-six consecutive patients with H.U.S in this study were hospitalized either initially as diarrheal diseases and later on develop the picture of HUS or the patients referred directly to emergency unit for anuria or oliguria, we included patients who fulfil the criteria of the diagnosis of HUS (microangiopathic hemolytic anemia, acute renal failure and Thrombocytopenia.

Patients who need dialysis referred to the renal unit AL- Yarmouk Teaching Hospital for peritoneal dialysis.

Information obtained from each patient including the name <age,sex, socioeconomic state, duration of hospitalization, precipitating factor, family history of similar condition and preceding illness.

Active treatment given to each patient and almost all patients treated as A.R.F. Routine Investigations and especially those needed to evaluate the renal function are carried out from each patient.

Statistical analysis was done using.

- Descriptive statistics:percentage, rank and mean.
- Statistical significance was considered when even the Chi square X2 value 3.642 and P. value was equal or less than 0.05.
- Degree of freedom (d.f.) = 1.

- Meam X= ———
  n

  m2-m2 SD d2

  X2 = ————, SE = ———, SD = S2 = ————

  SE n n-1

  Where:

  m=mean.

  SE= standard Error.

  SD= standard Deviation.

  d= difference.

RESULTS

1. EPIDEMIOLOGY of HUS

Age Distribution:

Table (1) shows the distribution of patients according to group. It clearly shows the most of patients (78%) were less than 4 years and (56%) of them were less than 2 years of age.Moreover (Table1) show the distribution of patients according to socioeconomic state It. Clearly shows that most of patients (55%) of low socioeconomic state; (39%) of patients of moderate socioeconomic state, and only (6%) of high socio – economic state.

Family History of similar Condition:

the frequency of cases of HUS that occurred in the same family. There were 7 cases of patients had similar condition 4 patients. In one and 3 patients in another family, the 7 cases (19%) had similar condition 29 case (81%) had no similar illness. (Table 1)

Table I: Socio-demographic distribution of patients with HUS

	No.	%
Age Group (Year)		
<2	20	56
2-4	8	21

4-6	3	8
6-8	2	6
8-10	2	6
10-12	1	3
>12	0	0
Total	36	100%
Socio – economic state		
Low	20	56
Moderate	14	34
High	2	5
Total	36	100%
Family history of similar condition		
Present	7	19
Absent	29	81
Total	36	100%

CLINICAL COURSE OF HUS

(Table 2) shows that prodromal diarrheal was present in 32 cases (89%) ; its duration from 5 – 17 days , patients with non – diarrheal prodromal present in 4 cases (11%) , 3 cases (8%) were preceded by respiratory prodromal and (1) patient (3%) was preceded by measles.

Table 2: classification of HUS according to the prodromal illness

Prodrome	No.	%
Diarrheal	32	89
Non- Diarrheal		
Respiratory	3	8
Measles	1	3
Total	36	100%

Clinical features of Hus:

(Table 3) shows the important clinical features, Renal failure and pallor were present in all patients (100%) oliguria was present in (67%) edema in (55%) hepatomegaly in (22%); petechiae in (11%) and splenomegaly in (19%).

Table3: clinical features of HUS

Clinical Feature	No.	%
Renal Failure	36	100
Pallor	36	100
Oliguria	24	67
Oedema	20	55
Hepatomegaly	8	22
Splenomegaly	4	11
Petechiae	7	19

Laboratory findings:

(Table 4) shows the important laboratory findings. The hemoglobin concentration ranged from 5 – 9 gm/dL. The W.B.C. count ranged from 5 – 28 x 10^6/L. The blood urea ranged from 70 – 370 and platelet count ranged from 40.000 – 100.000.

Table 4: Important Laboratory Findings

Laboratory finding	Range	Mean
HB (gm/dL)	5-6	7
WBC (10^9/L)	5-28	14
B.urea (mg/dL)	70-370	214
Platelet count	40.000-100.000	60.000

Management of Hus:

(Table 5) shows the frequency and number of patients who required peritoneal dialysis, 26 patients (72%) had dialysis; 10 patients required peritoneal dialysis once; 13 patients had peritoneal dialysis twice; one case required peritoneal dialysis three times and 2 patients required four times.

Table 5: Dialysis needed among patients with HUS

No. of dialysis	No. of patients	%
No need	10	28

Once	10	28
Twice	13	36
Three	1	4
Four	2	5
Total	36	100%

RISK FACTORS FOR DEATH IN HUS

(Table 6) shows the risk factors for death in HUS. After statistical analysis we concluded that there is significant association between; the younger age group (<2Years); non diarrheal prodrome; number of dialysis increasing risk of death in H.U.S cases.

There is no statistical significance association between death and sex; diarrheal prodrome; dialysis (no need, one) and W.B.C count > 20.000 x 10/L.

Table 6: Risk factors for Death HUS

Risk factor	Total No.	NO. of patients survived (%)	NO. of patients died (%)	P. value
Young age>2 years	20	12(60	8(40)	<0.05 S
Sex Male Female	 16 20	 10(62) 14(70)	 6(38) 6(30)	0.95 Ns
Diarrheal prodrome Non-diarrheal prodrome	32 4	22(69) 2(50)	10(31) 2(50)	< 0.001 S
WBC count > 20.000 x 10^9/L	13	10(77)	3(23)	<0.95 Ns
No. of dialysis - No need - One - Two - > two	 10 10 13 3	 10(100) 7(66) 6(50) 1(34)	 Zero (0%) 3(34) 7(50) 2(60)	0.02 S

Family history similar condition	7	4(57)	3(43)	< 0.05 S

DISCUSSION

Hemolytic uremic syndrome is now recognized as the most frequent class of acute renal failure in infants and young children, as an important cause of stroke and chronic renal failure in the young children, and as a substantial consumer of health care resources [(7)]. Our study throws a light on 46 cases of HUS admitted in the last year tour hospital evaluating different aspects of the disease. This study shows that (56%) of patients were less than 2 years. This Finding is similar to Milford DV et al [(13)];Palomeque – Rico .et al [(14)] and Rowe-pe et al [(15)].

This study shows that (89%) of cases of HUS had diarrhealprodrome, this finding is similar to;Glasgo study (89%);Siegler – RL et al,(90%) [(16)]; and Milford – DV et al.(95%) [(13)] of cases had diarrheal prodrome. This is similar to what was mentioned in Godjani – N [(3).]

Non-diarrheal prodrome was present in (11%) of the patients [(4)] cases), 3 cases were preceded by URTI and other one by measles observation was seen the 4 patients have HUS belong to one family, two of them died. The second family had 3 patients with HUS and one had history of death. Familial cases also seen in other studies, in USA (Pichette – V et al. [(17)] and Argentinean families (Voyer- Le et al.)[(18)]. Pallor and renal failure were present in all cases, other physical sign which include edema. hepatomegaly; splenomegaly and petechiae were present in considerable numbers of patients this finding is consistent with A.M.G Campbell [(1)].

Most of the laboratory findings in the are comparable to Glasgow study [(1)]. Thirty – three percent of patients died during the course of the disease. This regarded as high figures in comparison with Glasgow study (9%) [(2)]. Tapper – D et al (8%) [(12)], and Bhimma –R et al (17%) [(19)]. The fact that most of cases were dialysis and shortage of other medical supplies may contribute to increase death among our patients. Young age (<2years) is a significant risk factor for death (Table VIII). This is agreed with ROW – PC et al (15) which showed in addition the presence of high W.B.C. count at admission (>20.000) as not significant risk factor.

CONCLUSION

After having discussed the result of the work done on HUS, the following was concluded:

1- HUS and E. coli 0157: H7 infection are emerging as important clinical and public health problem.

2- HUS is associated with substantial morbidity and its incidence is increasing particularly in young children.

3- Prevention of some cases may be possible through early recognition of outbreaks of E. col: 0157: H7 infection and through consumer education (such as teaching adult not to serve raw milk or under cooked to young children).

RECOMMENDATIONS

1- Prevention of disease is best done by maintaining prolonged breast feeding; paying careful attention to personal hygiene, milk pasteurization ; water supply and health educational programs.

2- Early comprehensive management including fluid and electrolytes, normalization of blood pressure and aggressive nutritional support.

3- A pediatric dialysis unit may be the problems solving step for the misinterpretation between pediatrician and physicians regarding indication of dialysis in HUS.

4- Improve the laboratory facilities to detect the pathogenic strains of HUS in our community.

5- Special attention paid to patients with young ago group (<2years) and absence of diarrheal prodrome.

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