

HEMOLYTIC UREMIC SYNDROME EPIDEMIOLOGICAL AND CLINICAL STUDY

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Abstract

This study carried out on 55 recorded cases of hemolytic uremic syndrome in children admitted during a period of eight years (1991 – 1998) to Al-Mansour children teaching hospital in Baghdad . I found that :-

The age range was (4 month – 11 years) and the mean was 3.4 years . The male constitute (58.2 %) from the total . There is seasonal variation and annual increment on the admission range. (87.3 %) had diarrheal prodrome . During the acute phase of the disease, eighteen patients (32.7 %) died (children younger than 2 years , absence of diarrheal prodrome , white blood cell count above $20 \times 10^9 / L$ on admission) were statistically significant risk factor for death . The result of this study come with the result of other studies in the world except that the result of stool culture for E-Coli in this study was only (10.4%) while Siegler – RL study⁽¹⁰⁾ was (62.%) and this difference was due to lack of specific laboratory facilities in our country .

الخلاصة

هذه الدراسة اجريت على (55) حالة طفل مصاب بالمتلازمة اليوريمية الانتحالية خلال فترة ثماني سنوات من (1991 – 1998) في مستشفى المنصور التعليمي للأطفال . كان متوسط العمر (3.4) سنة ضمن مدى 4 أشهر – 11 سنة . وكان الأطفال الذكور يولفون نسبة (58.2 %) من المجموع . وجدت اختلافات فصلية وزيادة سنوية على معدلات الدخول . على (87.3 %) من الأطفال من بادرة اسهالية توفى ثمانية عشر مريض (33 %) اثناء الفترة الحادة للمرض . وجدنا ان عوامل مثل العمر اقل من الستين . العدم البادرة الاسهالية . ارتفاع عدد كريات الدم البيضاء اكثر من (20×10^9 / لتر) لها علاقة احصائية مهمة بزيادة نسبة الوفيات وكانت نتائج هذه الدراسة مشابهة مع نتائج دراسات اخرى في العالم الا انه هناك اختلاف واضح في نتائج زرع الخروج لـ الاشركية السقولونية حيث كانت (10.4 %) في هذه الدراسة و (62 %) في دراسة (Siegler – RL) 10 ويعزى ذلك الى قلة الإمكانيات المتوفرة في مختبراتنا .

Introduction

Hemolytic uremic syndrome compromises a heterogeneous group of disorders in which a triad of features; microangiopathic hemolytic anemia, thrombocytopenia and acute renal failure occurs together. Hemolytic uremic syndrome is the most frequent cause of acute renal failure in children and the incidence is increasing. It becomes an important pediatric and public health problem. Martian – DL and his colleagues⁽⁶⁾ showed increased annual incidence of cases in Minnesota from 0.5 – 2 cases / 100 000 child in the period from 1979 – 1988 respectively the main target is the gut and the kidney but nearly every organ system

can be involved . the most common extra renal involvement is damage to the central nervous system . Hemolytic uremic syndrome usually affects children less than 4 years . a recent reports refutes gender predisposition. Hemolytic uremic syndrome can be classified into categories :- The typical (post diarrheal) and atypical (non diarrheal) . The typical form account for 90 % of cases , affect younger children and in association with prodromal illness usually of bloody diarrhea . The commonest etiological agent being the verocytotoxin (shiga like toxin ₁ , shiga like toxin ₂) producing Entero hemorrhagic E – coil strain (O157 : H7) . The reservoir of this organism is the intestinal tract of the domestic animals , it is usually transmitted by under cooked meat and unpasteurized milk . And this type occurs most commonly in summer months and there is no seasonal incidence of non diarrheal cases. Young age and infection with strains that produce (Stx2) regarding as a risk factor for the progressing from colitis to hemolytic uremic syndrome . The atypical form account for only 10 % of the total number of cases , it is not associated with prodromal illness

Aim of the study

The incidence of the hemolytic uremic syndrome is increasing and it becomes an important pediatric and public health problem in the world . This study was aimed to compare hemolytic uremic syndrome cases in the center in which the study was conducted with other studies in the world .

Materials and methods

In this retrospective study , medical records of fifty – five patient admitted to Al- Mansour teaching hospital in Baghdad from the first of January , 1991 till the 31 st of December 1998 (eight years period) were reviewed and all cases met the definition of Hvs . (i.e. Microangiopathic hemolytic anemia, acute renal failure and thrombocytopenia). Renal failure was considered whenever there is increase in the serum creatinine level above the normal range for age. The following data for patient were obtained. The age , sex , seasonal and annual variation , presence or absence of diarrheal prodrome , important clinical features at presentation include (pallor , Jaundice , edema , petechiae , hepatomegaly) The important laboratory data are : hemoglobin , white blood cell count , platelet count , blood urea , serum creatinine , stool examination and stool culture) . Finally the significant risk factors for death in Hvs cases. Statistical analysis were done by using the usual statistical method were used in order to analyze and assess my result, include mean, rate, range, ratio line chart, Bar chart, z- test and p- value)

Results

Epidemiology of Hvs

Age distribution

(Table 1) shows the distribution of patients according to the age groups . It clearly shows that most of the patient 35 (63 %) were less than 4 years and 26 patient (47.3 %) of them were less than 2 years of age . Smaller peak 9 patient (16.4%) at the age group 6 – 8 years . The age range was 7 month – 11 years and the

mean was 3.4 years. (Figure I) shows that the incidence of the disease will decrease with the age.

Sex distribution (Figure II)

32 Patient (58.2 %) were males while 23 patients (41.8 %) were females. With male to female ratio of (1.4:1).

Annual variation

Figure III shows increasing frequency of cases of HUS admitted from January 1991 - December 1998.

Seasonal variation

(Figure IV) shows that out of 48 cases of HUS with diarrheal prodrome there were 18 cases (37.5 %) occurred during autumn, 16 cases (33.3 %) occurred during summer , while 9 cases (18.8 %) occurred during spring and only 5 cases (10.4 %) occurred during winter .

Clinical course of Hvs

Prodromal illness

(Table II) shows that diarrheal prodrome was present in 48 cases (87.3 %) , it is duration from 2 days - 21 days with a mean value of (11.5 days) . Patients without diarrheal prodrome were only 7 cases (12.7%) ; 3 cases (5.5 %) were preceded by respiratory prodrome ; 2 cases (3.6 %) with no prodrome and 2 cases (3.6 %) were familial .

Clinical features of Hvs

Table III shows the important clinical features . Pallor and acute renal failure which were present in all cases 55 (100 %) ; edema was present in 23 cases (41 %) ; hepatomegally in 15 cases (27 %) ; petechiae in 10 cases (18 %) ; and jaundice was present only in 4 cases (7 %) .

Laboratory findings

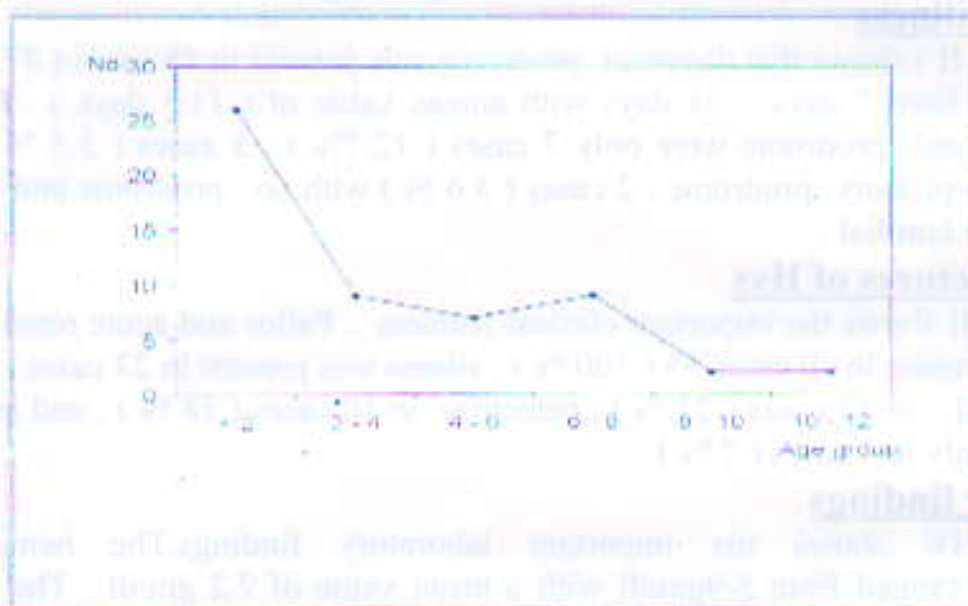
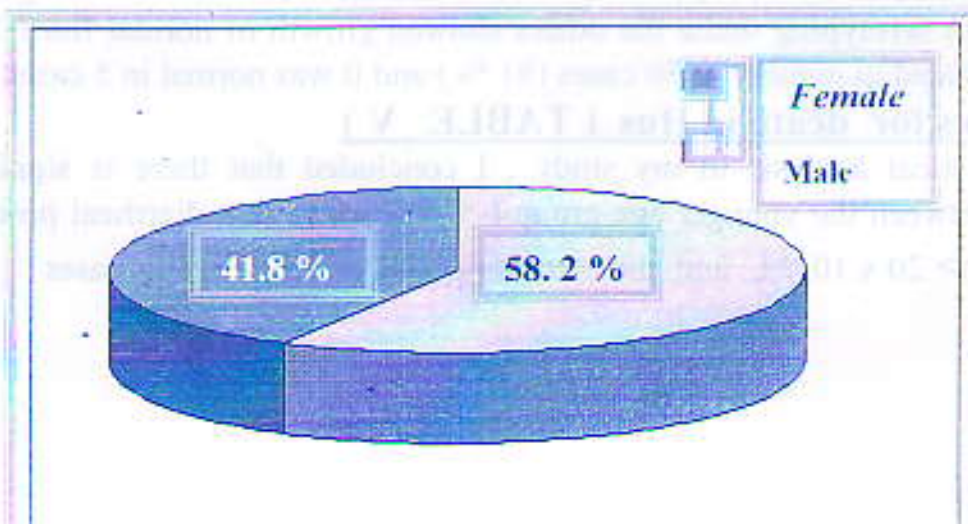
Table IV shows the important laboratory findings. The hemoglobin concentration ranged from 5-9gm/dl with a mean value of 7.2 gm/dl . The W.B.C count ranged from $4 - 40 \times 10^9 / L$ with a mean value of $16.2 \times 10^9 / L$. B.urea ranged from 80 - 350 mg / dl with a mean value of 200 mg/dl, and s.creatinine 0.5 - 6 mg / dl with a mean value of 2.9 . Five (10.4 %) out of 48 stool cultures showed growth of E. coil without serotyping while the others showed growth of normal flora .Platelet count was reduced in number in 50 cases (91 %) and it was normal in 5 cases (9 %)

Risk factors for death in Hus (TABLE V)

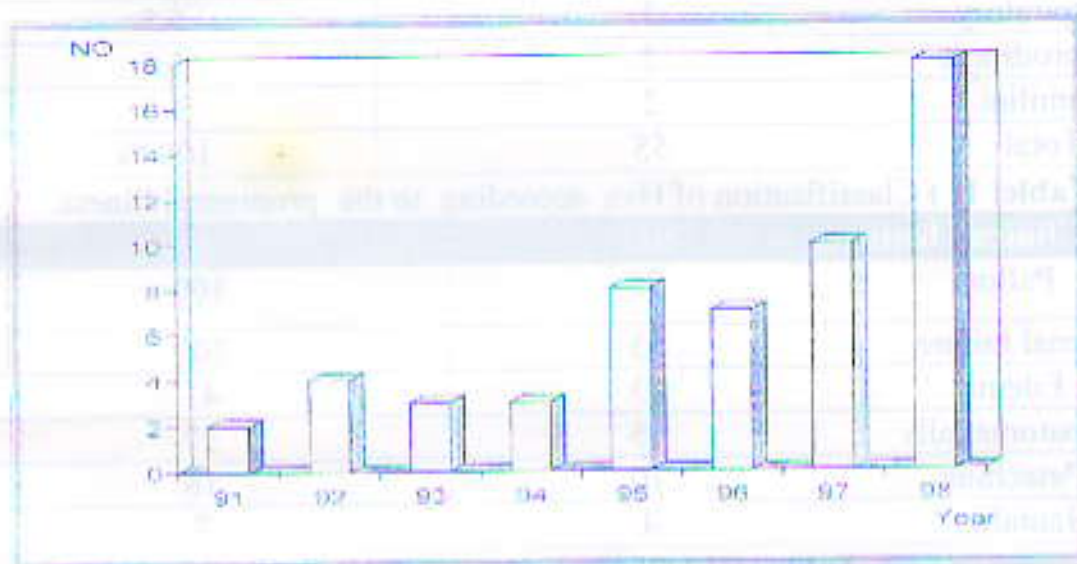
After statistical analysis in my study , I concluded that there is significance association between the younger age group (≤ 2 years) ; non diarrheal prodrome ; W.B.C. count $> 20 \times 10^9 / L$ and the increasing risk of death in Hvs cases .

Table(I) Age distribution of patients with Hvs .

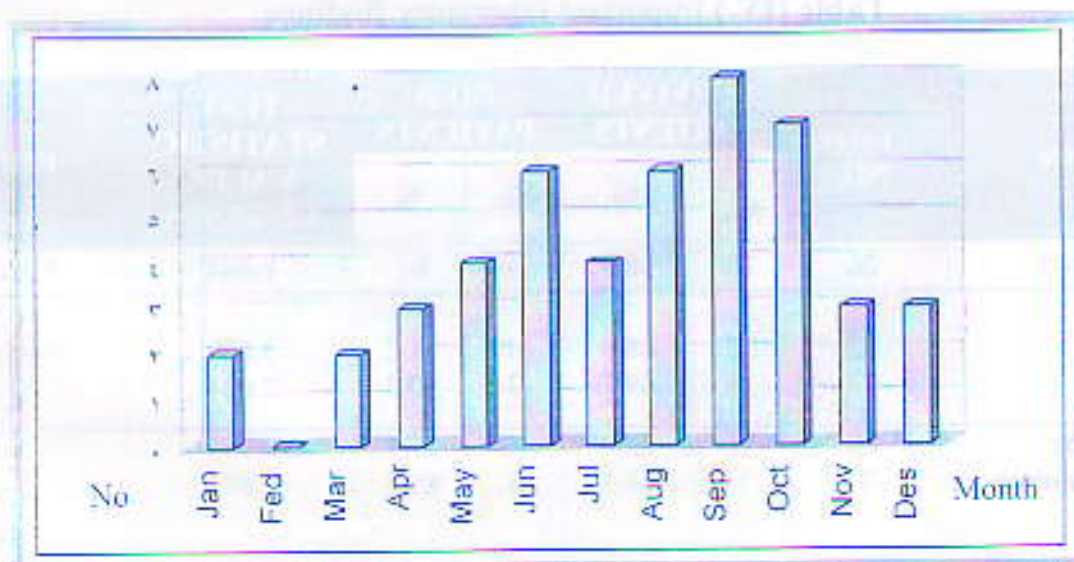
AGE GROUP(YEAR)	NO.	%
< 2	26	47.3
2 - 4	9	16.4
4 - 6	7	12.7
6 - 8	9	16.4
8 - 10	2	3.6
10 - 12	2	3.6
Total	55	100 %

Figure(I) Line chart representation of incidence number among age group**Figure (II)** Sex distribution of patients with HVS

Figure(III) Annual variation of HVS cases



Figure(IV) Seasonal Variation of HVS cases



PRODROME	NO.	%
Diarrhea	48	87.3
Non diarrhea		
Respiratory	3	5.5
No. prodrome	2	3.6
Familial	2	3.6
Total	55	100 %

Table (II) Classification of IIVs according to the prodromal illness

Clinical features	NO.	%
Pallor	55	100
Renal failure	55	100
Edema	23	41
Hepatomegally	15	27
Petechiae	10	18
Jaundice	4	7

Table (III) Clinical feature of IIVS

Laboratory Findings	Range	Mean
Hb gm .dl	5 - 9	7.2
W.B.C. (10^9 / L)	4 - 40	16.2
B. urea (mg / dl)	80 - 350	200
S. creatinine (mg / dL)	0.5 - 6	2.9

Table (IV) Important laboratory findings

Risk Factors	Total NO.	SURVIVED PATIENTS		DIED PATIENTS		TEST STATISTIC VALUE (Z-TEST)	P. VALUE
		No.	%	No.	%		
Age \leq 2 years	26	10	38.5	16	61	1.664	< 0.05 (S)
Sex							(NS)
Male	32	22	68.8	10	31.2	3.000	< 0.05
Female	23	16	69.7	7	30.3	2.654	< 0.05
Diarrheal prodrome	48	35	72.9	13	27.1	0.939	> 0.05
Non diarrheal prodrome	7	1	14.3	6	85.7	2.673	(NS)
							< 0.05
							(S)
W.B.C. count $> 20 \times 10^9/L$	20	7	35	13	65	1.897	< 0.05 (S)

Table (V) Risk factors for death in IIVs

Discussion

In my study I sheds light upon 55 cases of hemolytic uremic syndrome admitted during a period of eight years (1991 – 1998) to Al- Mansour teaching hospital in Baghdad in epidemiological and clinical aspects of the disease. The study shows that most of the patients 35 patients (63 %) were less than 4 years (table I) and this finding is similar to Bhimma – R et al ⁽²⁾ It also shows that 26 patients (47.3 %) were less than 2 year this finding is similar to Milford – DV et al ⁽⁷⁾ Another small peak 9 patients (16.4) % were related to 6 – 8 age group . It is found that the incidence of the disease will decrease with the age (figure I). This finding is similar to Bahimma – R et al study ⁽²⁾ . 32 patients (58.2 %) were males while 23 patients (41.8%) were females with male to female ratio of 1.4:1 (figure II) , this finding is similar to a recent study Bahimma – R et al . (2) Which showed that (61.7 %) of patient were males with males to female ratio of 1.6 : 1 but most of the previous studies showed a female predominance. . There is yearly increases in the frequency of cases in my study from January 1991 – December 1998 (Figure III) . this finding is consistent with siegler – RL et al ⁽¹⁰⁾ in Utah which showed increase annual incidence of hemolytic uremic syndrome from as low as 0.2 to as high as 3.4 / 100 000 child from 1971 – 1990 and this probably due to deterioration of primary health services as contaminated water supply increase use of unpasteurized milk and milk products . Non diarrheal hemolytic uremic syndrome is not associated with seasonal variation. This finding is similar to A.G.M Campbell ⁽¹⁾ and Douglas – AS ⁽⁴⁾ so only 48 cases were included in this section of the study . My study showed that there is increase in the number of the cases admitted during the warmer months. 18 cases (37.5 %) occurred during autumn and 16 cases (33.3) occurred during summer (Figure IV) . this finding is similar to the result of Milford DV . et al ⁽⁷⁾ . This finding may be due to the increase excretion of Enterohemorrhagic *E.coli* from the reservoirs (as cattle and poultry) during the warmer months . ^{(6) , (8)} . This study shows that 48 cases (87.3 %) of hemolytic uremic syndrome had diarrheal prodrome . (Table II) , this finding is similar to Siegler – RL et al ⁽¹⁰⁾ (90 %) of the cases had diarrheal prodrome . The majority of the patients 43 had bloody diarrhea while only 5 patients had watery diarrhea .this is similar to Milford DV et al ⁽⁷⁾ . Non diarrheal prodrome was present in 7 cases (12.7 %) , 3 cases (5.5 %) were preceded by respiratory prodrome (2 cases preceded by upper respiratory tract infection and one by pneumonia) . 2 cases (3.6 %) were familial , a girl of 3 years old and her brother of 5 years old both have first attack at the same time. familial cases also was reported in Argentinean (Voyer – I.E) . ⁽¹²⁾ The last 2 cases (3.6 %) of non diarrheal hemolytic uremic syndrome were not preceded by specific illness pallor and acute renal failure were present in all of our patients . edema occurs in about half of the patient , while hepatomegaly , petechiae and jaundice occurs infrequently as shown in (table III) . This finding is consistent with .Milford – DV. ⁽⁷⁾ . The laboratory findings in my study as shown in (table IV) and the platelet count are similar to A.G.M. Campbell

⁽¹¹⁾ and Richart L ⁽⁸⁾. Stool culture were positive for E – Coli without serotyping in only 5 cases (10.4 %) . This result was very low comparing with siegler – RI ⁽¹⁰⁾. A 20 years population – based study of post diarrheal hemolytic uremic syndrome in utah – E coil 0157 : H7 was isolated from the stool of (62 %) of children who had specimens submitted . This difference in the result is due to lack of specific laboratory facilities for Entero hemorrhagic *E . Coli* : as sorbitol , macconky agar , latex agglutination test and the indirect hemagglutination assay .18 patients (33 %) were died during the acute phase of the illness , this regard as a high figure in comparison with Tapper D et al ⁽¹¹⁾ study which is only (8 %) . Young age (< 2 years) ; presence of high whit blood cell count at admission (> 20 x 10⁹ / L) , non – diarrheal prodrome are statistically significant risk factors for death . These findings is caps with Rowe – Pe et al ⁽⁹⁾.

Conclusions

After having discussed the results of the work done on hemolytic uremic syndrome . The following points were concluded :-

- 1- hemolytic uremic syndrome is emerging as an important clinical and public health problem .
- 2- hemolytic uremic syndrome affects children mainly from 4 months to 4 years .
- 3- There is a seasonal variations in the occurrence of hemolytic uremic syndrome with peak rise during summer and autumn .
- 4- There is annual increment in the incidence of the disease .
- 5- Young age < 2 years ; absence of diarrheal prodrome , high W.B.C. count at admission were statistically significant risk factors for death .

Recommendations

- 1- Prevention of the disease caused by Entero – hemorrhagic E – Coli is best done by maintaining prolonged breast feeding , paying careful attention to personal hygiene , proper food handling, milk pasteurization , water supply , and health educational programs .
- 2- special attention paid by physician to patients with hemolytic uremic syndrome who have one of the risk factors include ; young age group (< 2 years) , absence of diarrheal prodrome , and high W.B.C. count above (20 x 10⁹ / L) on admission .
- 3- Improve the laboratory facilities to detect the pathogenic strains that cause hemolytic uremic syndrome in our community .

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