Kathmandu University Medical Journal (2004) Vol. 2, No. 4, Issue 8, 291-296

Original Article

Prognostic indicators in Haemolytic Uraemic Syndrome

Malla K[1], Malla T[1], Md Hanif[2]
[1]Formerly Lecturer Kathmandu Medical College, Sinamangal, [2]Professor, paediatric nephrology Dhaka Shishu Hospital, Bangladesh

Abstract
Objective: This study aims to review the clinical presentations of Haemolytic Uraemic Syndrome (HUS) and to compare the poor prognostic indicators with mortality. **Methods and Materials:** Prospective study carried out in Renal Dialysis ward of Dhaka Shishu Hospital, Bangladesh from September 2001- November 2003 for a period of 26 months. All children admitted to renal dialysis ward with oliguria or anuria with pallor was included in this study. HUS was confirmed after laboratory investigations showing features of hemolytic anaemia, thrombocytopenia and renal insufficiency. Various clinical presentations were reviewed. Then bad prognostic factors were compared with mortality. **Results:** There were total 25 cases of HUS in 26 months.17 (68%) were males and 8(32%) females.21 (84%) children were <5 years. Only 4(16%) were >5 years. Before onset of HUS 40% children had bloody diarrhoea, 36% had acute watery diarrhoea and 24% had others symptoms. The other presentations noted were fever 88%, respiratory distress and convulsion 52% and oliguria 40%, anuria 60%, reluctant to feed 40% and cough 28%. The main physical findings noted were irritability 40%, pallor 100%, dehydration 28%, puffy face with oedema 32%, high blood pressure 16%, hepatomegaly 28%, jaundice, sclerema and petechial rashes 8%, lethargic 16%, acidotic breathing 48% and rectal prolapse 12%. 44% children died after HUS and 56% recovered from the illness. Mortality was 66% when duration of illness before onset of HUS was >14 days. With duration of anuria <3 days there was no mortality but it was 91% and 100% with anuria >3-8days and >8 days respectively. Mortality was 78% when age was<18months and it was 75% when age was >5years.Diarrhoea associated HUS had 27% and non diarrhoea associated HUS had 85% mortality. Mortality was 77% and 100% respectively when HUS was associated with convulsion and hypertension. WBC >30,000 had mortality 100% and decreased platelet count <30,000 had mortality 80%. With creatinine level >700µmol/L mortality was 80% and with Serum potassium level 5.6-7.5mmol/L mortality was 67%.**Conclusion:** HUS comprised of varieties of presentations. Diarrhoea was the commonest preceding illness before onset of HUS. The bad prognostic indicators carrying high mortality was duration of illness before onset of HUS >14 days, anuria >3days, age < 18 months and >5 years, Non diarrhoea associated HUS, HUS associated with convulsion and hypertension, WBC >30,000/cumm, platelets <30,000/cumm, creatinine level >700µmol/L and serum potassium level 5.6-7.5mmol/L. Since bad prognostic factors may progress rapidly to mortality, consultation with paediatrician and transfer to a tertiary care centre should be done when HUS is diagnosed so that it can be managed appropriately in time.
Key words: Haemolytic Uraemic Syndrome-clinical presentation-mortality.

Introduction

The term Haemolytic Uraemic Syndrome (HUS) was first introduced to describe a heterogeneous group of diseases characterized by microangiopathic haemolytic anaemia, thrombocytopenia and acute renal failure.[1]It is uncommon but significant childhood illness and is the most common cause of acute renal failure in some regions of the world.[2] 90% of HUS is preceded by acute gastroenteritis, often with bloody stool.[3]Others may have prodrome of upper respiratory symptoms.[4] Most cases occur in patients <5 years.[5]HUS is associated with mortality which may reach upto15-35% and residual disabilities as hypertension, chronic renal failure neurological deficit like irritability ataxia, coma, seizures may develop in 25% of patients.[6] The child may also have cramping abdominal pain, fever, restlessness, irritability, pallor, petechiae, purpura.[7] Poor prognostic factors include elevated WBC>20,000/cumm,anuria>8days,age>3years,atypical form of HUS, Hypertension and prominent CNS symptoms.[7] This study was undertaken to review the clinical features of HUS and also to relate prognostic factors, both clinical and biochemical with mortality.

Methods and materials

Prospective study carried out for a period of 26 months from September 2001-November 2003 in Renal dialysis ward of Dhaka Shishu Hospital, Bangladesh. All children referred or directly admitted with C/F and laboratory investigations consistent with HUS were included. The exclusion criteria was cases of acute renal failure due to other causes.

Correspondence:
Dr. Kalpana K Malla
Email: Kalpana17@hotmail.com

Detail history and variable clinical presentations were noted in a pre-designed questionnaire. HUS was confirmed after Laboratory support. The investigations included Complete blood count with peripheral blood film (especially for RBC morphology and Platelets count), Blood urea, Serum creatinine, S. electrolytes-Sodium& Potassium. Then bad prognostic factors were compared with mortality. Statistical analysis- SPSS computer package.

Results

There were total 25 cases of HUS in 26 months.17(68%) were males and 8(32%) females with male: female ratio 2:1(fig 1).18 children were ≤18months among them 12 were males and 6 females (Table 1).3 were between 19 months-5 years. 4 were >5 years with males 3 and females 1in number. Before onset of HUS 40% children had bloody diarrhea, 36%had acute watery diarrhoea and 24% had other symptoms. (Fig.2)

Fig. 1: Sex distribution of cases

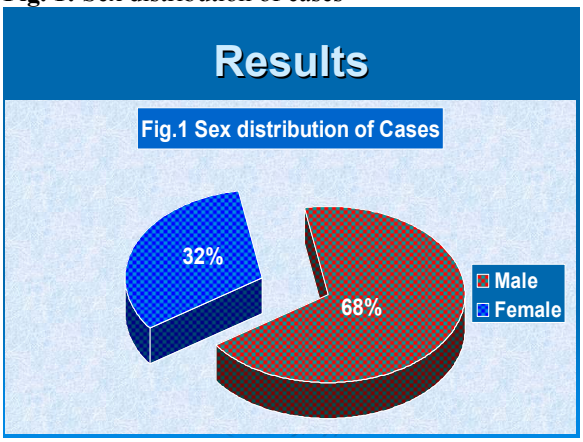
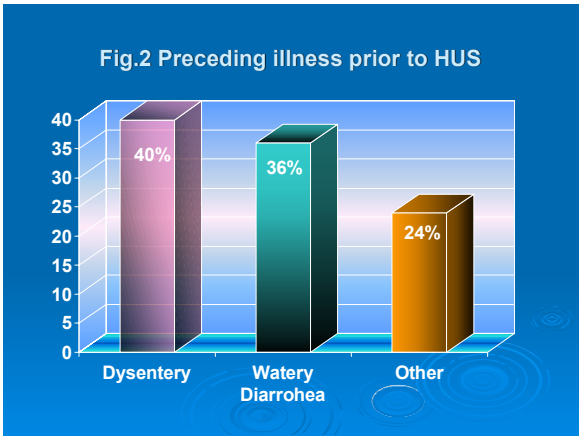


Table 1: Age and sex distribution

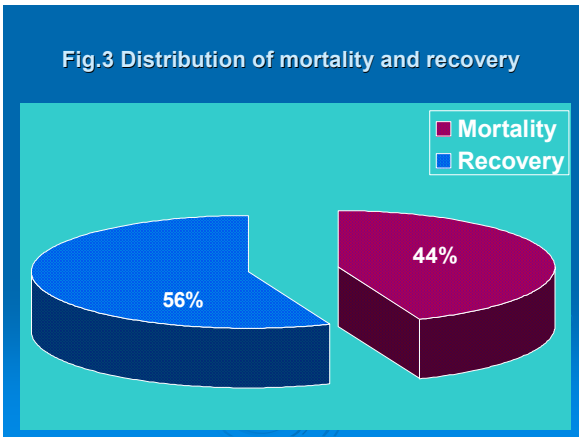
Age	Male No.	Female No.	Total
≤18months	12	6	18
19mo-5yrs	2	1	3
>5yrs	3	1	4
Total	17	8	25



The clinical presentation and physical findings of the patient is shown in table 2.The clinical presentations were fever 88%, anuria 60%, respiratory distress, convulsion 52%, oliguria 40% reluctant to feed 40%,cough 28%.Physical findings pallor 100%,acidotic breathing 48% irritability 40%,edema/puffy face 32%,dehydration and hepatomegaly 28% each, ronchi/crepts 20%,high blood pressure and lethargy 16% each, Rectal prolapse 12%,petechial rash and jaundice 8% each. The mortality was 44 % after HUS and 56% recovered from the Illness (Fig .3).Table 3 illustrates the comparison of bad prognostic indicators with mortality. It was seen that mortality was 33% with duration of illness <7 days. When duration of illness was 7-14 days and > 14 days mortality was 60% and 66% respectively. All children with period of anuria < 3 days recovered but when anuria was 3-8 days mortality was 91% and with anuria >8 days mortality was 100%.Age l ≤18 months mortality was 78% and with age 19 months-5 years mortality was 17%and with age > 5years mortality was 75%.Diarrhoea associated HUS had 27% and non diarrhoea associated HUS had 85% mortality. Mortality was 77% with those presenting with convulsion and this was 100% in those presenting with hypertension.

Table2.Clinical presentations and physical findings:

Presentations	Number(n=25)	Percentage
Fever	22	88%
Anuria	15	60%
Convulsion	13	52%
Resp distress	13	52%
Oliguria	10	40%
Reluctant to feed	10	40%
cough		28%
Physical findings		
Pallor	25	100%
Acidotic breathing	12	48%
Irritability	10	40%
Oedema/puffy face	8	32%
Dehydration	7	28%
Hepatomegaly	7	28%
Crepts /Ronchi	5	20%
High BP	4	16%
Lethargy	4	16%
Rectal prolapse	3	12%
Petechial rash	2	8%
Jaundice	2	8%



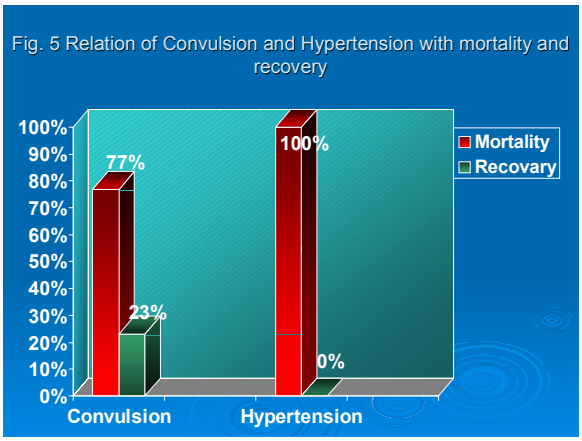


Table 3.Comparison of bad prognostic factors with mortality:

Table 3. Relation of Poor prognostic factors with mortality

Poor prognostic factors	Mortality No.	Mortality %	Recovery No.	Recovery %	Total	Grand Total
Duration of illness						
<7 days	4	33%	8	66%	12	25
7-14 days	6	60%	4	40%	10	
>14 days	2	66%	1	33%	3	
Period of anuria						
<3 days	0	0%	3	100%	3	15
3-8 days	10	91%	1	9%	11	
>8 days	1	100%	0	0%	1	
Age						
≤18months	7	78%	2	22%	9	25
19mo-5yrs	2	17%	10	83%	12	
>5years	3	75%	1	25%	4	

Table 5 provides the relation of some biochemical parameters with mortality. Mortality was 100% when WBC was elevated >30,000/cumm and it was 66%,50% and 0% with count <29,000,<22,000 and <15,000.when platelet decreased <30,000/cumm mortality was 80% and This was 62%,13% & 25% respectively when platelet was between>30,000-50,000, >50,000-80,000 & >80,000-1lakh.With creatinine level >700µmol/L 300µmol/Lmortality was 75% & between 501-700µmol/L and 301-500µmol/L it was 50% and 67% respectively. But there was no mortality with level<300µmol/L.It was noted that mortality was 67% with potassium level 5.6-7.5mmol/L.when potassium level was 3.5-5.5mmol/l and <3.5mmol/L mortality was 50% and 27% respectively. The mortality was 50%, 44% and 43% with haemoglobin levels<4gm/dl, 4-7 gm/dl and 7-9gm/dl respectively.

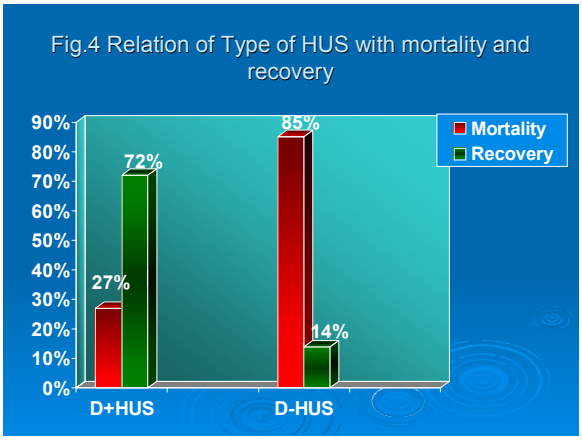


Table 5.Relation of biochemical parameters with mortality:

Biochemical parameters	Mortality No.	%	Recovery No.	%	Total No
WBC/cu. mm:					
>30,000	5	100%	0	0%	5
<29,000	2	66%	1	33%	3
<22000	4	50%	4	50%	8
<15,000	0	0%	9	100%	9
Platelet/Cu. mm:					
<30,000/cumm	4	80%	1	20%	5
30,000-50,000	5	63%	3	37%	8
>50,000-80,000	2	29%	5	71%	7
>80,000-1lakh	1	20%	4	80%	5
Creatinine					
>700µmol/L	4	80%	1	20%	5
501-700µmol/L	3	75%	1	25%	4
301-500µmol/L	6	67%	3	33%	9
≤300µmol/L	0	0%	7	100%	7
Potassium:					
<3.5mmol/L	3	27%	8	72%	11
3.5-5.5mmol/L	4	50%	4	50%	8
5.6-7.5mmol/L	4	67%	2	33%	6
Haemoglobin:					
<4gm/dl	1	50%	1	50%	2
4-7gm/dl	7	44%	9	56%	16
7-9gm/dl	3	43%	4	57%	7

Discussion

HUS though uncommon has its highest incidence in children and is the leading cause of Acute renal failure in some regions of the world.[3, 5] There is a close relationship between severity of acute illness, extent of renal involvement & ultimate mortality.[8] Present study was also designed to see the variable presentations of HUS and to the relation of some factors mainly the bad prognostic factors with mortality.

In the present study there were 25 cases of HUS over a period of 26 months. In a series 67 patients in 6 year were reported in Jahannesburg.[9] 40 cases were also reported in Vellore medical college over a period of 32 months.[10]The occurrence of HUS in male were double compared to females with ratio 2:1 and percentage 68% and 32% but Stephanie M. Jernigan and F. Bryson waldo had found HUS more common in females.[11]This study supports other studies that HUS is more common in children<5 years. In this study 81% children were <5 years. In another study Median age of the patient was 5.7 years.[12]

Majority of children with HUS have previously been entirely healthy and develop gastroenteritis as initial event. In this study 76% children had gastroenteritis before onset of HUS.40% had bloody diarrhoea and 36% had acute watery diarrhoea. This was also noted by other workers where they noted diarrhoeal illness in 87%.[13] In another study 34 of 39 patients had gastroenteritis as antecedent illness.[14] 28 % cases had other symptoms like fever and cough. Respiratory tract infection is less common but it preceded development of HUS in 5 of 39 patients in a study by Ellin Lieberman,M.D.[14] Frequency of fever in this study was 88%.This high frequency of fever was also noted by Gianantonio and associates(43%)[15] and Mathieu and associates (>50%).[16] They had also noted seizures ,stupor, coma, decerebrate rigidity and hemiperesis as prominent neurological findings .These were not noted in this study except 52% children had convulsion and 40% children were irritable. The combination of gastroenteritis, bleeding manifestations, pallor, oliuria may be present to varying degrees in majority of patients. In this study oliguria was present in 40%,and 60% had anuria, respiratory distress was present in 52%,40 % were reluctant to feed,48% had acidotic breathing,100% were pale,32% had oedema ,28% were dehydrated,16% had high blood pressure and 12% had rectal prolapse. In another study it was noted that 19 patients had bleeding manifestations,11 entered the hospital because of pallor ,9 patients presented with renal shutdown.[14] The most typical abnormalities were pallor 75% and hypertension 46% by some other workers.[13]

Prognosis worsens with presence of bad prognostic factors like duration of illness before onset of HUS, duration of anuria more than 8 days, age less than 3 years, non diarrhoeal associated HUS, presence of neurological deficit like irritability, convulsion. This study also tries to predict the prognosis in presence of bad prognostic factors which is illustrated in table 3.It is seen that relation of mortality is directly proportion to the duration of illness. In a study by Habib and associates ,[17] the findings indicating poor prognosis were age <18 months, anuria >3 days, Leukemoid reaction with WBC >50,000/cumm and longer duration of illness. In this study it was seen that when period of anuria was 3-8 days mortality was 91 % and with anuria >8days mortality was 100%. Supporting the above study this study also showed that mortality was highest 78% when age was <18 month. It is well known fact that non-diarrhoeal associated HUS has worse prognosis. In this study mortality was 57% in non diarrhoeal associated HUS compared to 31% in diarrhoea associated HUS.

Relation with some biochemical parameters with mortality was also observed. It was seen that WBC >20,000 indicated worse prognosis as mortality was 81%.Out of 25 patients platelet count was < 1 Lakh in 22 patients. In another study,[18] platelet was < 1lakh in all patient. Mortality was 80% when platelet was < 30,000/cumm.Between30,000-50,000/cumm it was 62%, between >50,000—80,000/cumm this was 25% and with >80,000/cumm mortality was 20%.Supporting literature was not available for this finding. Creatinine levels are elevated to varying degrees depending upon the severity of presentation. The degree of elevation of serum creatinine, blood urea, phosphate and potassium reflects the extent of renal damage and hence the prognosis. In the present study with rise of creatinine at presentation >700µmol/L had 80% mortality. Between 501-700 µmol/L mortality was 75% and between 301-500µmol/L it was 67%.There was no mortality with creatinine level ≤300µmol/L.This indicates that prognosis is worse with rising creatinine level. Relation with potassium revealed that with level ≤3.5mmol/L there was 27% mortality. With level 3.5-5.5mmol/L this was 50% and with range 5.6-7.5mmol/L there was 67%mortality.Hemoglobin level decreased in all cases. The range of haemoglobin level was 4-9gm/dl.This did not have any significance in the prognosis as mortality was 50% with haemoglobin level < 4gm/dl and it was 43% with 7-9gm/dl.

Conclusion

In conclusion, HUS presents with varieties of symptoms. Diarrhoea is the commonest preceding illness before onset of HUS. Bad prognostic indicators carrying high mortality in this study were duration of illness before onset of HUS > 14 days, anuria>3 days, age < 18 months, Nondiarrhoea associated HUS, HUS associated with convulsion and hypertension. Regarding the biochemical parameters prognosis was bad with WBC count >30,000/cumm, platelet count <30,000/cumm, creatinine level>700mmol/L, Serum potassium level 5.6 7.5mmol/L.Further studies are needed in a larger sample to determine the significance of these bad prognostic indicators. With bad prognostic factors mortality progresses rapidly, so close monitoring and appropriate management of HUS patient is very essential.

Acknowledgement

We thank all children and parents of Renal Dialysis ward, Dhaka Shishu hospital for their cooperation, Sisters of Renal dialysis ward for their excellent assistance to conduct this study. A special acknowledgement is extended to Mrs. Anjushree Pradhan for providing her brilliant idea on computer workup.

References

1. Ray PE, Liu XH. Pathogenesis of Shiga toxin-induced Haemolytic Uraemic Syndrome. Pediatr Nephrol.2002 Oct; 17(10): 271-2
2. A N Alam, N M Abdal, M A Wahed, B Rao, C A Kawser, M Hoque, M M Rahaman. Prostacyclin concentrations in Haemolytic Uraemic Syndrome after acute Shigellosis in children. Arch. Dis. child 1991; 66:1281-1284
3. Neild. G. The Haemolytic Uraemic Syndrome.Q.J.Med.1987 63: 367-76
4. Cleary. T. G. Cytotoxin producing E.Coli and the Haemolytic Uraemic Syndrome. Pediatr. clin. North Am.1988.35:485-501
5. Carter, A.O., Borezyk. A.A., Carison. J.A.K., Harvey. B., Hockin. J.C., et al. A severe outbreak of E.Coli 0157:H7-associated hemorrhagic colitis in a nursing home.N.Engl.J.Med.1987.317:1496-1500
6. Loirat. C., Sonsino. E., Varga Moreno, A, Pillon.G., Mereier J.C., et al. Haemolytic Uraemic Syndrome :an analysis of the natural history and prognostic features. Acta Pediatr Scand,1984.73:505-508
7. Michelle Bailey. Haemolytic Uraemic Syndrome.Archives.2003:1-5(http://www.the berries.ns.ca/Archives/HUS.html)
8. Anthony, P.P and Kaplan A.B, :Fatal haemolytic Uraemic Syndrome in two siblings, Arch.Dis.Child.1968.43:316
9. Avolas J.S., Vitacco M, Molinas, F., et al: Coagulateion studies in the Haemolytic Uraemic Syndrome,J.pediatr.1970.76:538
10. P Raghupathy, Anand Date, JCM Shastry, A sudarshanam, malati Jadhav. Haemolytic Uraemic Syndrome complicating Shigella dysentery in south Indian children. British Medical Journal,1978,1,1518-1521
11. Stephanie M. Jernigan and F. Bryson Waldo, Racial incidence of Hemolytic Uremic Syndrome, Pediatr Nephrol,1994.8: 545-547
12. Sandor Turi, Hona Nemeth, Hona Vargha and Bela Matkovies, Oxidative damage of red blood cells in Haemolytic Uraemic Syndrome, pediatr Nephrol 1994.8:26-29
13. Van Wieringen PMV, Monnens LAH, Sehrentlen EDAM. Haemolytic Uraemic Syndrome-Epidemiological and clinical study. Arch Dis child .1974.49:432-437
14. Ellin Lieberman, M.D. Haemolytic Uraemic Syndrome. The journal of Pediatrics. Jan 1972.Vol80.No1:1-16
15. Gianantonioc, Vitaceau M, Mendilabruza E.et al. The Haemolytic Uraemic Syndrome.J.Pediatr.1961:64:178-91

16. Mathieu IU, Walters MS, Kay R, Dillon MJ,Barrat TM. The Polymorphonuclear Leukocyte count in childhood H a emolytic Uraemic Syndrome. Pediatr Nephrol.1986.3:120-134
17. Habib R, Courtecuisse v, Leclere F, Royer P. Syndrome Hemolytique et Uremique de L'enfant. Arch Fr Pediatr.1969.26:391-416
18. Tesh, V.L, and A.D.O' Brien. The pathogenic mechanisms of Shiga toxin and the Shiga-like toxins. Mol. Microbiol.5:1817-1822

Title: Prognostic Indicators in Hemolytic Uremic Syndrome

Authors:

1. Dr. Kalpana K Malla, MBBS,MDpediatrics, Lecturer,Department of Pediatrics,Kathmandu Medical College Teaching Hospital, Sinamangal

2. Dr, Tejesh Malla , MBBS,MDpediatrics, Lecturer,Department of Pediatrics,Kathmandu Medical College Teaching Hospital, Sinamangal

3. Professor Md Hanif,MBBS,FCPS Professor,Dhaka Shishu Hospital,Sher-e-bangla nagar Bangladesh

Correspondence:
Dr. Kalpana K Malla
Email: Kalpana17@hotmail.com