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EDUCATIONAL REVIEW

Long-term outcomes of Shiga toxin hemolytic uremic syndrome

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Abstract Shiga toxin-producing *Escherichia coli* (STEC) hemolytic uremic syndrome (HUS) is an important cause of acute kidney injury (AKI). The outcomes of STEC HUS have improved, and the acute mortality rate in children is 1–4 %. About 70 % of patients recover completely from the acute episode and the remainder have varying degrees of sequelae. Only a few retrospective studies have reviewed these patients over long periods. Methodological flaws include a lack of strict definitions, changing modes of treatment, ascertainment bias and loss of subjects to follow-up. The kidneys bear the brunt of the long-term damage: proteinuria (15–30 % of cases); hypertension (5–15 %); chronic kidney disease (CKD; 9–18 %); and end-stage kidney disease (ESKD; 3 %). A smaller number have extra-renal sequelae: colonic strictures, cholelithiasis, diabetes mellitus or brain injury. Most renal sequelae are minor abnormalities, such as treatable hypertension and/or variable proteinuria. Most of the patients who progress to ESKD do not recover normal renal function after the acute episode. Length of anuria (more than 10 days) and prolonged dialysis are the most important risk factors for a poor acute and long-term renal outcome. After the acute episode all patients must be followed for at least 5 years, and severely affected patients should be followed indefinitely if there is proteinuria, hypertension or a reduced glomerular filtration rate (GFR).

Keywords Hemolytic uremic syndrome · Long-term outcomes · Prognosis STEC HUS · D+HUS

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Introduction

The hemolytic uremic syndromes (HUS) are a major cause of acute kidney injury (AKI) in childhood and adults [1]. Before any causes were known, HUS was divided into diarrhea-associated (D+, typical HUS) and non-diarrheal (D-, atypical HUS). The term atypical HUS (aHUS) now refers to a group of cases with defined or suspected inherited or acquired abnormalities in the alternative complement cascade. Patients with aHUS, *S. pneumoniae* HUS, and secondary causes of HUS are excluded from this analysis. Major problems regarding studies on the long-term outcomes of HUS involve the inclusion of all types of HUS in early studies, short follow-up periods, loss to follow-up, varied treatment regimens, and different outcomes from different parts of the world [2]. These limitations especially affect the interpretation of meta-analyses, which aggregate data from heterogeneous studies [3]. Because the purpose of this review is to focus on the long-term outcomes of Shiga toxin-producing *Escherichia coli* (STEC) HUS, we included studies that focused only on D+HUS, assuming that most of these patients had STEC HUS. We tried to separate out long-term from acute outcomes and have attempted to present an overview in which long-term complications are dealt with separately; neither of these two objectives was always possible.

Pathophysiology of kidney injury

Shiga toxin causes combinations of thrombotic occlusion of glomerular and afferent arteriolar capillary lumens, glomerular cell swelling, apoptosis of glomerular and tubular cells, acute tubular necrosis, and cortical necrosis [3]. Kidney biopsies are rarely performed in the early acute phase, and much of what is known about the renal pathology was derived from biopsies of severely affected cases later in the course and post-mortem studies. However, the more

severe the histopathological changes, in particular cortical necrosis or significant thrombotic microangiopathy (TMA), the greater the likelihood of unfavorable long-term outcomes [4].

Acute mortality

When patients were classified into mildly affected (no anuria) and severely affected (anuric), the mild cases did extremely well (zero mortality rate), whereas the severely affected cases had a high acute mortality rate of about 80 % [5]. Historically, the overall acute mortality rate of about 30 % declined dramatically with the introduction of early dialysis for severely affected oligo-anuric patients [5–7]. The acute mortality rate has improved to between 1 and 4 %, with most deaths occurring during the acute phase [8–10]. Brain involvement is the most common cause of death, and less frequent causes are congestive heart failure, pulmonary hemorrhage, hyperkalemia/arrhythmia, and bowel perforation/hemorrhagic colitis [11]. Older age at presentation in adults is associated with increased morbidity and mortality [12].

Prognostic factors for long-term sequelae

The most important risk factor for long-term renal sequelae is the severity of renal injury during the acute episode, as manifested by the duration of anuria, with anuria for 5–14 days associated with worse renal outcomes [9, 13–17]. By averaging the reports in the literature, we believe that patients who have anuria for more than 10 days are more likely to have a poorer renal outcome [17]. The need for dialysis [3, 16, 18–20], severity of injury on kidney biopsy [4] or decrease in effective renal plasma flow [14] are also risk factors. Although dialysis for more than 7 days is associated with worse long-term renal outcomes, the indications for starting or continuing dialysis vary and are not established [3, 16]. Patients rarely recover renal function if dialysis exceeds 4 weeks [3]. Severe AKI can be associated with long-term hypertension, proteinuria, decreased glomerular filtration rate (GFR), and neurological sequelae [13, 15, 18]. Criteria in the acute phase that are not consistently associated with a poor long-term renal prognosis are hypertension [16, 18, 19, 21], central nervous system (CNS) symptoms [16, 21, 22], gastrointestinal (GI) complications [18], or the severity of anemia or thrombocytopenia [9, 18, 23, 24]. High hematocrit levels, high white blood cell counts, and dehydration have been associated with poor prognosis in some, but not all studies [11, 25–27]. While some authors found a worse outcome in younger patients [9, 28], others found the opposite [20] or no association (Table 1).

In the 1990s, Siegler et al. [29] reviewed the outcomes of 157 HUS patients followed for 16–18 years. A diarrheal prodrome was identified in 89 % of patients and only these 140 patients were included in the analyses of outcomes. *E.*

Table 1 Updated clinical features at onset related/not related to poor prognosis in studies reported in the literature (adapted from Gianviti et al. [25], used with permission)

Reference	Related	Not related
[20]		Younger age, diarrhea +, onset in summer
[64]	Oligo-anuria >8 days, age <3 years	Diarrhea +
[65]	High polymorphonuclear leukocyte count	
[26]	Onset in winter	Central nervous system involvement, hypertension, leukocyte count
[13, 29, 66]	Oliguria >15 days, anuria >8 days, age <2 years, high white blood count	Diarrhea + or diarrhea −
[67]	Severe colitis and prolapse	Diarrhea +, high white blood cell count
[15]	Anuria >10 days	
[21]		Diarrhea+or diarrhea −, age <2 years, anuria, central nervous system involvement
[16]	Oliguria >14 days, anuria >7 days, age <1 year	Leukocyte count, diarrhea
[68]	Diarrhea −, normal urine output, hypertension	Age
[30]	Anuria >10 days, dialysis >10 days, proteinuria at 1 year	Age at onset, polymorphonuclear leukocyte count, diarrhea + or diarrhea −
[14]	Anuria >7 days, hypertension	Central nervous system involvement
[1]	Leukocytosis, cerebral involvement, serotype O157:H7	
[18]	Plasma therapy, bloody diarrhea, hypertension, leukocytosis, and dialysis duration	Antibiotic therapy, Shiga toxin *E. coli* serotypes, age

coli O157:H7 was isolated from 62 % of specimens. Adverse outcomes (death, ESKD or stroke) occurred in 11 %. Most of the 5 % who died did so in the acute phase. Chronic renal sequelae were usually mild and were found on follow-up (median 6.5 years) in 51 % of survivors. Patients who were not oliguric or anuric generally had excellent long-term outcomes [17]. The incidence of chronic renal sequelae increased markedly in those who had anuria for more than 5 days or 10 days, with anuria being a stronger predictor than oliguria of most sequelae. These findings were confirmed by many other studies and help to identify children who need periodic and extended follow-up after hospital discharge.

Clinical findings at 1-year follow-up have been evaluated to see if they are associated with long-term sequelae. The development of proteinuria at 1 year may be associated with future adverse effects [30–33]. In particular, an Argentinian study showed that proteinuria at 1 year was a particularly poor prognostic factor for chronic kidney disease (CKD) [30]. Occasionally, patients who recover normal serum creatinine and creatinine clearance, but who have persistent proteinuria, are at risk of progressing to CKD and ESKD after more than 5 years, and sometimes as late as 20 years, after the acute disease [34].

Small et al. [33] concluded that renal function at 1 year cannot be predicted with certainty from the initial illness. They concluded that if renal function were normal at 1 year, it would remain stable between 1 and 5 years following HUS in most children; and that longer-term follow-up can be restricted to those with proteinuria, hypertension, abnormal renal ultrasound, and/or impaired GFR at 1 year. However, Rosales et al. [18] suggested that it may take 2–5 years before any clinical changes are evident and that all patients with STEC HUS should have long-term follow-up to detect late-emerging sequelae.

Long-term sequelae

Long-term renal outcomes include proteinuria, microalbuminuria, hypertension, CKD, and ESKD. Clearly, the most important of these are CKD and ESKD. Adverse extrarenal outcomes include colonic strictures, gall bladder disease, diabetes mellitus, and CNS and cognitive sequelae [22, 23, 35–39]. Between 20 % and 40 % of patients have long-term sequelae, with the majority having renal disease [3, 4, 13, 18, 25, 30, 40]. The percentages of adverse outcomes tend to be lower in more recent studies, possibly because of advancements in critical care medicine, improvements in dialysis, better understanding of HUS, newer treatment modalities, and perhaps better follow up [2, 3, 25].

Siegler et al. [29] found that death, ESKD or brain damage occurred in 11 % of 140 HUS patients. Seven patients (5.0 %) had severe problems when last evaluated. It is important to emphasize that the chronic sequelae were usually mild and that follow-up data were available for only 51 % of survivors. It is therefore possible that no follow-up data were available for the other 49 % of survivors because they had recovered completely. Of the 51 % with one or more abnormalities when last evaluated, four (5.6 %) had hypertension controlled with antihypertensive medication; 22 (31 %) had proteinuria, and 22 had a decreased GFR (< 90 mL/min/1.73 m2); GFR was <60 mL/min in only one patient. Nine (12.5 %) had both proteinuria and a low GFR. Although 22 (31 %) had proteinuria, there was no information on the severity of proteinuria, nor whether benign postural proteinuria was ruled out.

Siegler et al. [29] speculated that the later emergence of proteinuria and/or declining renal function might be the result of hyperfiltration and subsequent, further sclerosis of remaining glomeruli [41]. There is indirect support for this theory from studies of glomerular renal functional reserve, in which acute protein loading did not result in an expected increase in GFR in a percentage of patients who had recovered completely from HUS [32, 33]. However, the clinical relevance of these findings remains to be determined.

Proteinuria/microalbuminuria

Microalbuminuria and/or proteinuria may be detected years after the acute phase of HUS [13] with incidences of 20–40 % more than 5 years after diagnosis [40, 42, 43]; this is substantially higher than the background rate of 7–12 % in adults. The clinical importance of microalbuminuria in these patients is unknown [42, 43].

In general, 15–30 % of HUS patients developed proteinuria [3, 13, 15, 18, 21, 30]. Proteinuria may be present after recovery and improve, it may persist, or it may first be detected 5 years after recovery [15, 18]. Patients with a more severe acute illness are more likely to develop proteinuria [44].

In an Argentinian cohort of 130 patients with HUS who were followed for 5 years, 20.8 % had microalbuminuria and 11.5 % had proteinuria [45]. However, this study excluded 529 patients from the original cohort who were lost to follow-up. Assuming that patients lost to follow-up had complete recovery, the true prevalence of microalbuminuria and proteinuria may be lower.

On the basis of these studies, we conclude that proteinuria per se is neither a universally poor prognostic factor nor an indication of a poor outcome. Furthermore, patients may have mild, moderate or severe proteinuria, and not all levels are necessarily associated with the same outcomes.

Angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) may improve the outcomes of patients with proteinuria [21, 46]. Caletti et al. [46]

performed a double-blind randomized controlled trial to evaluate the effects of diet, enalapril (and losartan) in patients with HUS. A low protein diet alone eliminated proteinuria in 66 % of patients. The patients who continued to have proteinuria were randomized to treatment and control groups. Importantly, 82 % of losartan- and 66 % of enalapril-treated patients no longer had proteinuria compared with 30 % in the placebo group. There is, therefore, a role for protein restriction and ACE inhibitors/ARBs to play. To date, there have been no studies evaluating the benefits of treating microalbuminuria with ACE inhibitors/ARBs in this context.

Chronic kidney disease

The GFR in long-term follow-up studies has been estimated using various calculations based on serum creatinine or cystatin C, or measured by nuclear medicine clearance studies. Most studies define abnormal kidney function as a GFR<80 ml/min/1.73 m^2. However, because the current KDOQI classification defines abnormal kidney function as a GFR<90 (CKD stage 2), many of these studies may underestimate the incidence of CKD after HUS [47].

Spizzirri et al. [30] followed a group of HUS patients for a mean period of 13 years (range 10–19.8 years) from 1968 to 1984. At follow-up, 62.7 % of patients had complete recovery, but 19.4 % had some decrease in GFR and 3.4 % developed ESKD. Among patients who were anuric for more than 11 days during the acute illness, 69.2 % developed low GFR, proteinuria, and/or hypertension. O'Regan et al. [48] found that 85 % of patients with HUS had decreased GFR 6–11 years after recovery. A majority had a GFR<80 ml/min/1.73 m^2 (plasma slope clearance using 99MTc DTPA), despite only mild increases in the average serum creatinine concentration (0.65 mg/dl). However, there may be ascertainment bias in this study, and the long-term clinical significance of a normal serum creatinine and limited follow-up is unclear. It is important to note that subtle decreases in GFR might be missed, because, in most studies, only serum creatinine concentrations were measured [42].

Small et al. [33] studied 114 patients: 1 patient remained on chronic peritoneal dialysis, 5 (5 %) had moderate to severe CKD (GFR 25–50 ml/min/1.73 m^2), 20 (22 %) had mild CKD (GFR 50–80), and 66 (72 %) had normal renal function (> or = 80 ml/min/1.73 m^2). GFR was measured in 40 patients at 1 and 5 years. Of the 28 patients with a normal GFR at 1 year, 3 progressed to mild CKD at 5 years. There was a negative correlation between the number of days of dialysis and GFR at 1 year. Siegler et al. [13] found that 28 % of HUS patients had a GFR<90 ml/min/1.73 m^2, but only 10 % had a GFR<70 ml/min/1.73 m^2 a mean of 9 years after diagnosis. A lower GFR at presentation and a more severe clinical course are associated with lower GFRs at follow-up [18, 44]. The GFR may also decline over time even if normal after 1 year [33]. In summary, the percentage of patients with an estimated GFR<80 ml/min/1.73 m^2 ranges from 9 % to 18 % [3, 18, 21, 40].

End-stage kidney disease

The incidence of ESKD in HUS patients is around 3 % [3, 25, 30]. In a study described above, Siegler et al. [29] noted that characteristics of the acute illness were predictive of ESKD. In their cohort of 72 surviving patients, one child developed ESKD at the outset, and 4 others developed ESKD over a period of years. All 4 had severe persistent hypertension before ESKD. Neither death nor ESKD occurred in those with milder HUS (P=<0.0001). Seizures or any other neurological findings during the acute illness were also strongly associated with death or ESKD (24 % vs 2 %; P =0 .0002).

Patients with STEC or D+HUS rarely require renal transplant or chronic dialysis. North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) data show that only 2.6 % of all pediatric renal transplants were performed with a diagnosis of HUS and 3.1 % with a prior diagnosis of HUS were on dialysis [49]. Furthermore, this may overestimate the numbers for STEC HUS because the type of HUS was not indicated.

Hypertension

Hypertension can persist after recovery or develop later; it may be an isolated finding, but often occurs with proteinuria and/or elevated serum creatinine concentrations [13, 40]. Although up to 25 % of patients can be hypertensive during the acute phase, persistent hypertension occurs in only 5–15 % of patients [3, 13, 18]. However, because the severity of the hypertension or the methods of detection are not always defined, it is difficult to determine its significance in long-term outcomes [3, 13, 18]. In one study, children with a history of HUS were three times more likely to develop pre-hypertension or hypertension compared with controls, but this difference was not statistically significant [42]. The average systolic blood pressure percentile in the HUS patients was 2 % greater than that in the controls, but this may be an underestimation of the degree of hypertension as 16 % of patients with HUS were on ACE inhibitors.

Hypertension can also be masked in HUS patients [50, 51]. Krmar et al. [50] performed conventional and 24-h ambulatory blood pressure monitoring on 28 patients a median of 8.4 years after diagnosis. Only 1 patient had hypertension (>95th percentile) based on conventional measurements. However, based on 24-h ambulatory blood pressure monitoring, 2 additional patients were diagnosed

with hypertension and another 5 patients had at least one abnormality on ambulatory study, such as isolated daytime hypertension. In a similar study of 24 patients with a median follow-up of 5.8 years, all the patients had normal blood pressure according to conventional measurements, but 24-h ambulatory studies identified 11 with hypertension [51]. Both of these studies suggest that conventional blood pressure monitoring might not be adequate in this group of patients and might underestimate the prevalence of hypertension.

There are no compelling data to support the suggestion that surviving women may be at increased risk of developing pre-eclampsia.

Gastrointestinal

Patients with HUS are at increased risk of the development of GI complications. Brandt et al. [23] found that 21 % of patients had GI sequelae after a short period of follow-up. Three had cholelithiasis and cholecystectomy, 2 had persistent pancreatitis, and 1 each had late colon stricture. Cholelithiasis may be related to hemolysis or the use of parenteral nutrition.

Hemorrhagic colitis (HC) is a severe manifestation of HUS with a presentation rate of 5.5 % among 987 patients, with nearly half requiring bowel resection [52]. The transverse and ascending colon were most frequently affected. Macroscopic evaluation showed bowel necrosis and perforation. A leukocyte count >20,000/mm^3 and hematocrit >30 % were more common in HC patients than in patients without HC ($p<0.001$ and $p<0.0001$ respectively). The mortality rate was higher in HC patients (33.3 %) than in patients without HC (1.4 %; $P<0.0001$). Dialysis >10 days, seizures, and coma were more frequent in HC patients ($P<0.0001$). There are no studies that specifically evaluate the long-term sequelae of colectomies in these patients.

Diabetes mellitus

Pancreatic microthrombi can cause exocrine and/or islet cell death with extensive pancreatic arteriolar thrombosis, necrosis of islet cells, pancreatic inflammation, and fibrosis [35]. In a meta-analysis, the pooled incidence of diabetes mellitus during the acute phase of HUS was 3.2 % (range 0–16) [53], although only 1.7 % of patients in an Argentinian study developed diabetes [30]. HUS patients with severe disease including need for dialysis and CNS symptoms were more likely to develop diabetes. In those who survived, one third had permanent diabetes at a follow-up of 0.5–15 years. Relapse of diabetes has occurred, albeit rarely, years after the acute illness [35]. There is no relationship between glucose intolerance and other late pancreatic sequelae [23].

Neurological sequelae

Neurological involvement in STEC HUS is associated with severe renal disease, but does not always result in death or severe long-term disability [37]. However, despite the serious nature and possible dire consequences of CNS involvement, there are only a few case reports of neurological outcomes [38, 39]. Nathanson et al. [37] studied this in 52 patients with STEC or D+HUS and only included patients with severe initial neurological involvement. Fifty had AKI requiring dialysis. Plasma exchanges were done in 25 patients: 7 died, 7 survived with severe CNS sequelae, and 11 survived without neurological deficits. Of the 11 who were treated with plasma exchanges within the first 24 h, 4 died, 2 survived with severe sequelae, and 5 survived without neurological deficits. Severe hypertension was noted in 7 out of 45 patients; 48 out of 48 patients had leukocytosis (median 31,965; range 15,220 to 83,000/mm^3), and 23 patients had hyponatremia. Magnetic resonance imaging (MRI) showed that every structure in the central nervous system could be involved, and there were no focal lesions in 3 patients. There was no correlation between a specific profile of localization on early MRI and the final outcome. Neurological complications of HUS led to death in 17 % of patients and to severe sequelae in 23 %. Twenty-six patients (50 %) recovered fully.

Loos et al. [54] reviewed 90 children in Germany from the 2011 HUS outbreak. Twenty-six percent of patients (23 out of 90) had severe neurological symptoms, including seizures, visual impairment or impaired consciousness. After a short follow-up of 4 months, 18 of the 23 had complete neurological recovery. Only 1 patient had residual major impairment with dyskinesia after cerebral edema. However, all patients with residual neurological deficits improved.

Cardiovascular sequelae

Cardiovascular complications in HUS are secondary to fluid overload, electrolyte abnormalities, and hypertension, as well as myocarditis and cardiac TMA [55]. Additional cardiac complications include dilated cardiomyopathy [56], cardiac tamponade [57], and ischemic myocardial involvement [58]. Owing to the risk of myocardial injury, monitoring troponins in patients with HUS may have a role to play [58]. The long-term outcome of these cardiac complications is not known.

Behavioral and cognitive sequelae

There is scanty information on the long-term behavioral and cognitive effects of HUS. In a small Canadian study of 22

patients who recovered from an acute episode of HUS [36], the children tended to have lower cognitive and achievement scores, as well as higher behavioral problem ratings. Statistically significant differences (P=0.01–0.1) were found on the Wechsler Full Intelligence Scale, Verbal Intelligent Quotient score, and on both achievement measures and behavioral ratings. There was no correlation between the acute episode severity and degree of CNS dysfunction, perhaps because of the small sample size. More studies are needed to replicate and/or expand on these findings.

Effects of treatment on long-term outcomes

The evidence supporting the notion that the type of treatment in the acute phase might influence long-term sequelae is weak. There have been conflicting reports of the use of antibiotics during the diarrheal prodromal phase. Antibiotics were thought to be associated with a poorer prognosis [24], but this may not be universally true [18]. In the German epidemic in 2011, bacteriostatic antibiotics were shown to reduce the duration of STEC carriage [59]. Among azithromycin-treated patients, long-term STEC carriage (defined as >28 days) was found in 1 out of 22 patients versus 35 out of 43 patients who never received antibiotics. None of the patients who received antibiotics had recurrence of STEC. Menne et al. [60] also showed that antibiotics given to HUS patients during the German epidemic significantly reduced the incidence of seizures, death, and duration of STEC carriage. However, the role of antibiotics needs to be further investigated to help clarify their risks and benefits in STEC HUS.

In the recent study of 619 patients from Austria and Germany, the use of plasma therapy was shown to be the strongest risk factor for development of renal or neurological complications [18]. This was compared with bloody diarrhea, hypertension, leukocytosis, and dialysis duration. However, plasma therapy was used in the most severely affected group of patients [24]. There is no evidence that patients with STEC HUS benefit from plasma therapy [25]. There are also many complications of plasma therapy.

Validation of the long-term use of renoprotection with ACE inhibitors also awaits further studies. Early volume expansion during the prodromal phase may decrease the incidence of oliguric renal failure [61]. Acute treatment of STEC HUS is mainly supportive (fluid and electrolyte management, judicious blood transfusions, blood pressure control); about 50 % require dialysis or hemodiafiltration.

Eculizumab has been used for the treatment of STEC-HUS [62], but the value of this treatment remains to be determined. Although Lapeyraque et al. [62] suggested that eculizumab was beneficial in patients with STEC, others found no benefit in larger numbers of patients in the German HUS epidemic [60, 63].

Conclusions

Shiga toxin-producing *Escherichia coli* hemolytic uremic syndrome is a common cause of AKI. The outcomes of HUS have improved over time, with current mortality rates less than 4 % during the acute illness. Almost all patients recover from the acute episode, but 20–40 % can develop long-term sequelae of variable significance. Initial morbidity and short-term outcome due to *E. coli* O104:H4 are comparable to outcomes reported in previous pediatric series of STEC HUS [54]. Prolonged anuria and the duration of dialysis during the acute episode are clearly associated with a poor long-term prognosis. Use of antibiotics needs to be reassessed and plasma therapy should be avoided. The most common long-term adverse outcomes involve the kidneys, with proteinuria the most common abnormality at follow-up. However, many of the long-term renal complications may be minor (microalbuminuria, slight but stable decrease in GFR, controllable hypertension) with unknown long-term clinical importance. Studies are needed that follow these patients into their 3rd and 4th decades to determine whether these minor clinical manifestations are associated with poor outcomes. STEC HUS can also lead to injury and long-term complications in the pancreas, gastrointestinal system, and central nervous system. Since adverse sequelae may rarely appear at variable time intervals after the acute episode, it is important to follow these patients for at least 5 years, and over longer periods if indicated.

Multiple choice questions (answers are provided following the reference list)

1. Long-term sequelae for STEC HUS include all of the following EXCEPT:
   a) Diabetes
   b) Hypertension
   c) Kidney stones
   d) Proteinuria
2. The percentage of patients who have long-term sequelae after STEC HUS is closest to:
   a) 50%
   b) 75%
   c) 30%
   d) 5%

3. Of the following, which risk factor is MOST predictive of long-term sequelae in STEC HUS?
   a) Leukocytosis
   b) Duration of anuria
   c) Age
   d) Anemia
   e) Use of antibiotics
4. The acute mortality rate of STEC HUS is closest to:
   a) Less than 1 %
   b) 1–4 %
   c) 5–10 %
   d) 10–15 %
5. Treatment of STEC HUS includes all of the following EXCEPT:
   a) Plasmapheresis
   b) Early volume expansion
   c) Dialysis
   d) Blood transfusions

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Answers

1. C
2. C
3. B
4. B
5. A