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End-Stage Renal Disease from Hemolytic Uremic Syndrome in the United States, 1995 to 2010

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Abstract

Background—Management of hemolytic uremic syndrome (HUS) has evolved rapidly, and optimal treatment strategies are controversial. However, it is unknown whether the burden of end-stage renal disease (ESRD) from HUS has changed, and outcomes on dialysis in the US are not well described.

Methods—We retrospectively examined data for patients initiating maintenance renal replacement therapy (RRT) ($n = 1,557,117$), 1995–2010, to define standardized incidence ratios (SIRs) and outcomes of ESRD from HUS) ($n = 2241$).

Results—Overall ESRD rates from HUS in 2001–2002 were 0.5 cases/million per year; and were higher for patients characterized by age 40–64 years (0.6), 65 years (0.7), female sex (0.6), and non-Hispanic African American race (0.7). SIRs remained unchanged ($P = 0.05$) between 2001–2002 and 2009–2010 in the overall population. Compared with patients with ESRD from other causes, patients with HUS were more likely to be younger, female, white, and non-Hispanic. Over 5.4 years of follow-up, HUS patients differed from matched controls with ESRD from other causes by lower rates of death (8.3 per 100 person-years in cases vs. 10.4 in controls, $P < 0.001$), listing for renal transplant (7.6 vs. 8.6 per 100 person-years, $P = 0.04$), and undergoing transplant (6.9 vs. 9 per 100 person-years, $P < 0.001$).

Conclusions—The incidence of ESRD from HUS appears not to have risen substantially in the last decade. However, given that HUS subtypes could not be determined in this study, these findings should be interpreted with caution.

Keywords

Dialysis outcomes; hemolytic uremic syndrome; incidence

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Introduction

Hemolytic uremic syndrome (HUS) is characterized by microangiopathic hemolytic anemia, thrombocytopenia, and acute renal dysfunction.^{1,2} Shiga-toxin-producing *Escherichia coli* are thought to be responsible for 90% of cases, particularly in children, with the remaining cases attributable to a variety of disorders including, among others, genetic defects in complement proteins, pneumococcal or other systemic infections, disseminated intravascular coagulation, hematopoietic stem cell therapy, certain medications, and underlying autoimmune conditions.^{1–8} This heterogeneity should be noted when considering trends in ESRD from HUS.

The term atypical HUS (aHUS) generally refers to cases not caused by Shiga toxin.² Estimated annual incidence of HUS due to genetic defects in regulatory complement proteins is approximately 2 per million in the general population, and progression to ESRD is thought to occur in up to 50% of patients.^{3,8} In contrast, risk of subsequent ESRD development due to Shiga-toxin-associated HUS is thought to be below.⁹

The mainstay of therapy for HUS varies with cause; it consists of a combination of plasma exchange, plasma infusion, immunosuppression, liver-kidney transplant, and novel therapies such as Eculizumab.^{10–12}

For clinicians confronted with a management issue as thorny as that related to ESRD from HUS, information about the prognosis following institution of renal replacement therapy (RRT) could be informative. In addition, from a public health perspective, information about national trends in disease burden might also be relevant, not least because some treatment options are costly. Surprisingly, few if any current clinical epidemiological studies of ESRD from HUS in the United States are available. Hence, we primarily set out to describe the incidence and outcomes of ESRD from HUS between 2001 and 2010 and secondarily between 1995 and 2010.

Materials and Methods

Objectives

The principal objectives of this study were to evaluate trends in standardized incidence ratios, relative to rates in 2001–2002, of ESRD from HUS necessitating RRT in the US between 2001 and 2010. We were secondarily interested in studying standardized incidence ratios relative to rates in 1995–1996. Regarding clinical outcomes after RRT initiation, we set out to quantify rates of death, listing for renal transplant, and renal transplant.

Subjects

In this retrospective study, we examined data for patients initiating maintenance RRT ($n = 1,557,117$) between 1995 and 2010. Baseline characteristics at RRT initiation were determined from the Centers for Medicare & Medicaid (CMS) Medical Evidence Report (form CMS-2728). By federal requirement, this form must be submitted for all new patients starting RRT in the US, and resultant data are housed in the United States Renal Data System Medevid95 and Medevid05 files. The Medical Evidence Report form changed twice

in the past two decades, in 1995 and 2005. Unlike previous iterations, the 2005 version includes information about predialysis nephrologist care and vascular access for hemodialysis. On both versions, one of 82 causes is entered as the primary cause of ESRD, with identical options on the 1995 and 2005 versions. For this study, cases of ESRD from HUS were those with the primary cause of ESRD listed as “hemolytic uremic syndrome” in the Medical Evidence Report. Dates of death and first renal transplant were obtained from the Patients file, and first listing for transplant was determined from the Waitlist_ki and Waitlist_kp files.

Analysis

US census data were used for population denominators for the years examined, with age in 5-year increments. Hispanic ethnicity has been routinely incorporated in US census documentation only since 2000; therefore, we performed two separate race/ethnicity analyses. Using rates in the 2001–2002 biennium for standardization, we accounted for Hispanic ethnicity and designated four race/ethnicity categories: non-Hispanic white, non-Hispanic African American, Hispanic, and other. For the analysis standardized against rates in the 1995–1996 biennium, we included three race categories: white, African American, and other.^{13,14} The Poisson distribution was used to compute incidence rates of RRT-requiring ESRD from HUS. For computation of standardized incidence ratios, expected incidence rates were calculated by applying incidence rates in 2001–2002 and 1995–1996 separately for each individual permutation of age, sex, and race/ethnicity to the corresponding subgroup of the US population in subsequent 2-year periods. Chi-square analysis was used for unadjusted comparisons of patients with and without ESRD from HUS, and logistic regression was used for adjusted comparisons. The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used to estimate glomerular filtration rate at RRT initiation. For comparisons of clinical outcomes of patients with and without HUS, patients were matched according to year of RRT initiation (in 1-year intervals), age (in 1-year intervals), sex, race, and ethnicity. Poisson regression was used to compute incidence rates and proportional hazards regression to compute adjusted hazards ratios (AHRs) for events occurring after inception of RRT, with follow-up ending on June 30, 2011. SAS, v9.1.3 (SAS Institute, Inc., Cary, North Carolina) was used for data analysis.

Results

In 2001 and 2002, 287 patients began RRT because of ESRD from HUS, a rate of 0.5 cases per million per year (Table 1); similar or higher rates were seen with age younger than 5 years (0.5 per million per year), 40–64 years (0.6 per million per year), and 65 years or older (0.7 per million per year); female sex (0.6 per million per year); and non-Hispanic African American race (0.7 per million per year). Standardized incidence ratios remained unchanged ($P = 0.05$) between 2001–2002 and 2009–2010 in the overall population and in each subgroup studied (Table 1 and Figure 1).

In 1995 and 1996, 254 patients began RRT because of ESRD from HUS, a rate of 0.5 cases per million per year (Table 1); similar or higher rates were seen with age 40–64 years (0.5 per million per year) and 65 years or older (0.9 per million per year), female sex (0.6 per million per year), white race (0.5 per million per year), and African American race (0.6 per

million per year). Standardized incidence ratios remained unchanged ($P = 0.05$) between 1995–1996 and 2009–2010 in the overall population (Table 1) and in each subgroup studied except female sex, for whom ratios fell to 0.74 by the 2009–2010 biennium.

In comparison to patients with ESRD from other causes, patients with ESRD from HUS were more likely to be characterized by (Table 2) age younger than 5 years (7.5% vs. 0.2% of patients with ESRD from other causes) and 5–19 years (10.2% vs. 1%), female sex (64.3% vs. 45.1%), white race (78.5% vs. 65.2%), and catheter use for hemodialysis (95.9% vs. 82.6%). After adjustment for age, sex, race, and ethnicity, associations of ESRD from HUS at baseline included RRT initiation in 1995–2000, younger age, female sex, white race, non-Hispanic ethnicity, hemodialysis as initial mode of RRT, venous catheters for hemodialysis vascular access, shorter predialysis nephrology care, lower body mass index, lower serum albumin, lower serum hemoglobin, and absence of vascular disease. Ranked by magnitude, adjusted odds ratios (AORs) for HUS were 2.0 or higher for age younger than 5 years (AOR 12.85 vs. 20–39 years) and 5–19 years (AOR 3.45 vs. 20–39 years), female sex (AOR 2.45), venous catheter for hemodialysis vascular access (AOR 4.3 vs. fistula), and prior nephrology care for 12 months or less (AOR 3.56). AORs were 0.5 or less for age 40–64 years (AOR 0.32 vs. 20–39 years) and 65 years or older (AOR 0.11 vs. 20–39 years), African American race (AOR 0.35 vs. white race), other race (AOR 0.35), Hispanic ethnicity (AOR 0.27), ischemic heart disease (AOR 0.34), peripheral vascular disease (AOR 0.25), diabetes (AOR 0.11), and body mass index 30 kg/m² or higher (AOR 0.47).

Over a mean observation period of 5.4 years, 44.8% of patients with ESRD from HUS died, compared with 51.3 % of matched patients without HUS over 4.95 years. Figure 2 shows mortality rates for ESRD patients with HUS and a matched cohort of ESRD patients without HUS. Overall mortality rates were lower in HUS patients than in controls (8.3 vs. 10.4 per 100 person-years, $P < 0.001$). Among demographic subgroups examined, mortality rates were comparable to rates for controls in many subgroups. However rates were lower for patients with ESRD from HUS who initiated RRT in 1995–2000 (7.5 vs. 10.1 per 100-person years, $P < 0.001$), and for those characterized by age younger than 5 years (1.2 vs. 3.2 per 100-person years, $P = 0.003$), 20–39 years (3.9 vs. 5.4 per 100-person years, $P = 0.005$), 40–64 years (10.7 vs. 12.7 per 100-person years, $P = 0.008$), and 65 years or older (27.1 vs. 37.4 per 100-person years, $P < 0.001$); female sex (8.1 vs. 11.2 per 100-person years, $P < 0.001$); and non-Hispanic white race/ethnicity (8.9 vs. 11.3 per 100-person years, $P < 0.001$). When the comparison was isolated to the first year after RRT initiation, mortality rates were higher in HUS patients than in controls overall (21.1 vs. 17.9 per 100 person-years, $P = 0.02$), and in patients characterized by RRT initiation between 2001–2005 (21.4 vs. 16.2 per 100-person years, $P = 0.03$), age 40–64 years (25 vs. 17.6 per 100-person years, $P = 0.002$), and female sex (22.2 vs. 18.1 per 100-person years, $P = 0.02$). By year 2 after RRT initiation, mortality rates in HUS patients were comparable overall to controls, and by year 3 were lower (Supplementary Table S1).

Table 3 shows AHRs for death in patients with ESRD from HUS. Regarding absolute size, mortality hazards ratios were 1.5 or greater for age 40–64 years (AHR 2.61 vs. 20–39 years) and age 65 years or older (AHR 5.58 vs. 20–39 years), and 0.67 or less for age younger than

5 years (AHR 0.37 vs. 20–39 years) and 5–19 years (0.39 vs. 20–39 years), peritoneal dialysis (AHR 0.65 vs. hemodialysis), pre-emptive transplant (AHR 0.12 vs. hemodialysis).

Figure 2 shows rates of listing for transplant in patients with ESRD from HUS and in matched controls. Overall listing rates were lower for HUS patients than for controls (7.6 vs. 8.6 per 100 person-years, $P = 0.04$); however, rates were comparable for all subgroups examined except age 5–19 years (10.6 vs. 14.9 per 100-person years, $P = 0.01$) and 20–39 years (8.9 vs. 11.6 per 100-person years, $P = 0.01$). Table 3 shows AHRs for listing for patients with ESRD from HUS. Regarding absolute size, AHRs were 0.67 or less for age 65 years or older (AHR 0.14 vs. < 20–39 years) and diabetes (AHR 0.62).

Overall transplant rates were lower in HUS patients than in controls (6.9 vs. 9 per 100 person-years, $P < 0.001$, Figure 2). Differences in rates were seen for all subgroups except patients characterized by RRT initiation in 2006–2010 (7.7 vs. 9.3 per 100-person years, $P = 0.17$), age 40–64 years (4.9 vs. 5.4 per 100-person years, $P = 0.39$), age 65 years or older (0.9 vs. 1.0 per 100-person years, $P = 0.82$), Hispanic ethnicity (6.5 vs. 9.4 per 100-person years, $P = 0.12$), and other race (8.4 vs. 6.7 per 100-person years, $P = 0.60$). A similar pattern was observed for the first year after dialysis initiation; however, by year 2, transplant rates for HUS patients were comparable to rates for matched controls overall and in all subgroups studied (Supplementary Table S1). Table 3 shows AHRs for transplant for patients with ESRD from HUS. Regarding absolute size, AHRs were 1.5 or greater for age younger than 5 years (AHR 2.55 vs. 20–39 yrs) and age 5–19 years (AHR 1.59 vs. 20–39 years), and 0.67 or less for age 40–64 years (AHR 0.63 vs. 20–39 years), age 65 years or older (AHR 0.11 vs. 20–39 years), and African American race (AHR 0.51).

Discussion

We found that the incidence of ESRD from HUS remained largely unchanged over the past decade and indeed over the past 15 years of observation. While it is tempting to hypothesize that the discouraging trends in HUS-related RRT may reflect lack of effective treatments for HUS over the study period, the non-experimental design of our study precludes a definitive answer. There are many other plausible explanations for the smooth incidence of ESRD from HUS, such as a stable incidence of HUS in the population, a lack of change in progression to ESRD among patients with HUS, an increase in HUS balanced by a slower rate of progression to ESRD, or a decline in HUS in association with a quicker rate of progression to ESRD. Our study cannot determine this because of lack of information on true incident cases in the general population. The implication of the isolated apparent decline in ESRD incidence in females by the 2009–2010 biennium standardized against rates in 1995–1996 is unclear, with lack of a synchronous decline over the past decade. Multiple plausible explanations include improved diagnostic and disease labeling practices over the time frame, a treatment effect despite the lack of specific therapies, or a chance observation.

Novel mechanistic-based therapies for HUS are now emerging. In 2011, the US Food and Drug Administration granted accelerated approval for the use of Eculizumab in the treatment of aHUS based on promising non-randomized evidence and despite high

cost.^{12, 15–19} Therefore, our study is perhaps timely, since it defines outcomes such as survival on RRT for patients with ESRD from HUS, which is surprisingly good, before widespread use of Eculizumab.

Apprehension regarding recurrent aHUS after renal transplant may partially explain why rates of listing and transplant were lower in patients with ESRD from HUS than in matched controls.^{2, 20–22} The likelihood of transplant was lower in African American patients over the study period; while the design of the our study precludes a definitive explanation, the racial disparity in transplant rates in the United States has been observed for most other causes of ESRD.^{23,24}

The retrospective registry-based design and lack of information about treatments given prior to the onset of ESRD are potential limitations to our study. In addition, we were unable to discern case-specific causes of HUS such as Shiga-toxin-associated-HUS and atypical forms, or identify which particular genetic complement defect was responsible. In interpreting our findings, it is important to note that a diagnosis of HUS may encompass cases associated with underlying systemic infections, autoimmune diseases, and certain medications among other causes.^{1–8} It is also therefore possible that changing trends in the incidence of individual specific causes of HUS may not have been appreciated where present.

However, despite its limitations, we believe that our study provides some useful information. The incidence of ESRD from HUS remained unchanged over the past decade. Although mortality of patients with ESRD from HUS in year 1 following RRT initiation exceeded mortality of patients with ESRD from other causes, overall and in certain subgroups, and despite a lower likelihood of renal transplant, long-term survival was superior for patients with HUS. Given the cost of novel therapies, cognizance of the incidence and prognosis of ESRD from HUS may aid in nephrology care planning, particularly where resource are finite.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Trends in the burden of end-stage renal disease from hemolytic uremic syndrome in the US, with incidence ratios standardized against both the 1995–1996 and the 2001–2002 biennia separately. Standardization factors against 1995–1996 were age, sex and race, while those against 2001–2002 were age, sex and race/ethnicity. Error bars show 95% confidence intervals. RRT, renal replacement therapy; SIR, standardized incidence ratio.

Figure 2.

Outcome rates of patients with ESRD from HUS ($n = 2202$ [98.3%]) and a control group without HUS, matched according to year of RRT initiation (in 1-year intervals), age (in 1-year intervals), sex, race, and ethnicity at RRT initiation. Parameters shown are rates per 100 person-years, with error bars showing 95% confidence intervals. A formal tabulation of numerical estimates is available in Supplementary Table S1. AA, African American; ESRD, end-stage renal disease; HUS, hemolytic uremic syndrome; RRT renal replacement therapy.

Standardized incidence ratios of end-stage renal disease from hemolytic uremic syndrome requiring renal replacement therapy, 1995–2010 and 2001–2010

Table 1

Subgroup	Standardized Incidence Ratio, vs. 1995–1996									
	Rate	1995–1996	1997–1998	1999–2000	2001–2002	2003–2004	2005–2006	2007–2008	2009–2010	
Biennium										
Cases/million population		254/268	294/274	301/281	287/286	297/291	284/297	277/303	247/308	
All	0.5 (0)	1.12 (0.07)	1.12 (0.06)	1.04 (0.06)	1.04 (0.06)	0.97 (0.06)	0.92 (0.06)	0.8 (0.05)		
Age, years										
< 5	0.4 (0.1)	1.52 (0.35)	1.6 (0.35)	1.51 (0.34)	1.27 (0.31)	1.46 (0.33)	1.78 (0.36)	1.71 (0.35)		
5–19	0.3 (0)	1.05 (0.16)	1.19 (0.17)	1.16 (0.16)	0.91 (0.15)	1.21 (0.17)	1.27 (0.17)	1.05 (0.15)		
20–40	0.3 (0)	1.12 (0.14)	1.29 (0.15)	1.24 (0.15)	1.25 (0.15)	1.23 (0.15)	1.14 (0.15)	1.06 (0.14)		
40–64	0.5 (0.1)	1.19 (0.11)	0.91 (0.09)	1.02 (0.1)	1.15 (0.1)	0.96 (0.09)	0.82 (0.08)	0.75 (0.08)		
65	0.9 (0.1)	1.15 (0.12)	1.26 (0.13)	0.86 (0.1)	0.91 (0.11)	0.78 (0.1)	0.83 (0.1)	0.69 (0.08)		
Sex										
Male	0.3 (0)	1.11 (0.11)	1.15 (0.11)	1.05 (0.11)	1.17 (0.11)	1.1 (0.11)	1.02 (0.1)	0.91 (0.1)		
Female	0.6 (0)	1.13 (0.08)	1.1 (0.08)	1.03 (0.08)	0.98 (0.07)	0.91 (0.07)	0.87 (0.07)	0.74 (0.06) ^a		
Race/ethnicity										
White	0.5 (0)	1.08 (0.07)	1.06 (0.07)	0.99 (0.07)	0.98 (0.07)	0.91 (0.06)	0.9 (0.06)	0.83 (0.06)		
African American	0.6 (0.1)	1.39 (0.19)	1.27 (0.17)	1.16 (0.16)	1.29 (0.17)	1.23 (0.16)	0.95 (0.14)	0.62 (0.11)		
Other	0.2 (0.1)	0.89 (0.47)	2.05 (0.61)	1.85 (0.55)	1.31 (0.45)	1.21 (0.42)	1.34 (0.42)	1.05 (0.36)		
Biennium										
Cases/million population		287/286	297/291	284/297	277/303	247/308				
All		0.5 (0)	1.02 (0.06)	0.96 (0.06)	0.92 (0.06)	0.8 (0.05)				
Age, years										
< 5	0.5 (0.1)	0.86 (0.21)	1.01 (0.23)	1.25 (0.25)	1.21 (0.25)	0.93 (0.14)				
5–19	0.3 (0)	1.01 (0.12)	1.01 (0.12)	0.95 (0.12)	0.88 (0.12)	0.75 (0.08)				
20–40	0.6 (0.1)	1.13 (0.1)	0.95 (0.09)	0.81 (0.08)	0.75 (0.08)					

65	0.7 (0.1)	1.08 (0.12)	0.94 (0.12)	1.01 (0.12)	0.84 (0.1)
Sex					
Male	0.3 (0)	1.11 (0.11)	1.05 (0.1)	0.98 (0.1)	0.88 (0.09)
Female	0.6 (0)	0.97 (0.07)	0.91 (0.07)	0.89 (0.07)	0.76 (0.06)
Race/ethnicity					
Non-Hispanic white	0.5 (0)	0.97 (0.07)	0.93 (0.07)	0.93 (0.07)	0.88 (0.06)
Non-Hispanic African American	0.7 (0.1)	1.11 (0.15)	1.1 (0.15)	0.83 (0.12)	0.56 (0.1)
Hispanic	0.2 (0.1)	1.49 (0.3)	0.95 (0.23)	0.96 (0.23)	0.67 (0.18)
Other	0.3 (0.1)	0.62 (0.29)	0.88 (0.32)	1.1 (0.34)	0.78 (0.28)

Note: Parameter estimates are rates per million per year or standardized incidence ratios (standardized to 2001–2002) with standard deviation in parentheses. With PE denoting Point Estimate, CL Confidence Limit, Obs Observed Incidence Rate, Exp Expected Incidence Rate from rates seen in 2001–2002, standardized incidence ratios were estimated and reported as [PEObs/PEExp] ([5% CLObs/PEExp]–[95% CLObs/PEExp]). *P* values refer to comparisons of observed rates and rates expected when those seen in 2001–2002 were applied to the years under consideration. *P* = 0.05 (vs. 2001–2002) for all comparisons unless otherwise stated.

^a_{0.01} *P* value < 0.05.

Since Hispanic ethnicity has been routinely tabulated in US census documents only from 2000 onward, we performed a separate analysis from 2001 to consider Hispanic ethnicity, using the 2001–2002 biennium for standardization. Four race/ethnicity categories were used for this analysis, non-Hispanic white, non-Hispanic African American, Hispanic, and other race/ethnicity. For standardized incidence ratios standardized against the 1995–1996 biennium, we used three race categories: white, African American, and other.

Table 2Baseline characteristics at initiation of renal replacement therapy ($n = 1,557,117$)

Variable	Hemolytic Uremic Syndrome		
	Yes, %	No, %	AOR (95%CI)
<i>n</i>	2241	1,554,876	
Year			
1995–2000	37.9	31.3	1.12 (1.01–1.23)
2001–2005	32.4	32.6	1 (Reference)
2006–2010	29.8	36.1	0.85 (0.76–0.94)
Age, years			
< 5	7.5	0.2	12.85 (10.72–15.39)
5–19	10.2	1	3.45 (2.95–4.04)
20–39	22.9	8.6	1 (Reference)
40–64	39	41.3	0.32 (0.29–0.35)
65	20.4	48.9	0.11 (0.1–0.13)
Sex			
Male	35.7	54.9	1 (Reference)
Female	64.3	45.1	2.45 (2.25–2.67)
Race			
White	78.5	65.2	1 (Reference)
African American	18	28.7	0.35 (0.31–0.39)
Other	3.5	6.1	0.35 (0.28–0.43)
Hispanic ethnicity			
Non-Hispanic	93.6	87.1	1 (Reference)
Hispanic	6.4	12.9	0.27 (0.23–0.32)
Ischemic heart disease			
No	93.4	75.9	1 (Reference)
Yes	6.6	24.1	0.34 (0.29–0.41)
Diabetes			
No	91.9	50.2	1 (Reference)
Yes	8.1	49.8	0.11 (0.1–0.13)
Alcohol abuse			
No	98.7	98.5 ^a	1 (Reference) ^a
Yes	1.3	1.5	1.08 (0.75–1.57)
Drug abuse			
No	98.9	98.9 ^a	1 (Reference) ^a
Yes	1.1	1.1	0.95 (0.64–1.41)
Mode of RRT			
Hemodialysis	84.3	90.5	1 (Reference)
Peritoneal dialysis	12.4	7.8	0.61 (0.53–0.7)
Preemptive transplant	3.3	1.7	0.52 (0.41–0.66)

Hemolytic Uremic Syndrome			
Variable	Yes, %	No, %	AOR (95%CI)
Initial hemodialysis access			
Fistula	3.3	13.8	1 (Reference)
Graft	0.8	3.6	0.94 (0.35–2.49)
Catheter	95.9	82.6	4.3 (2.78–6.65)
Prior nephrology care, months			
> 12	9.4	24.2	1 (Reference)
12	90.6	75.8	3.56 (2.79–4.55)
eGFR, mL/min/1.73 m ²			
15	85.7	89.7	1 (Reference) ^a
> 15	14.3	10.3	0.93 (0.81–1.06)
Body mass index, kg/m ²			
< 30	82.4	69.6	1 (Reference)
30	17.6	30.4	0.47 (0.42–0.53)
Albumin, g/dL			
3.5	28.6	35.2	1 (Reference)
< 3.5	71.4	64.8	1.55 (1.4–1.72)
Hemoglobin, g/dL			
< 9	40.9	28.8	1 (Reference)
9	59.1	71.2	0.63 (0.58–0.69)
Cerebrovascular disease			
No	96.3	90.6	1 (Reference) ^c
Yes	3.7	9.4	0.57 (0.39–0.83)
Peripheral vascular disease			
No	97.3	86	1 (Reference)
Yes	2.7	14	0.25 (0.2–0.33)
Smoking			
No	93.1	93.8 ^a	1 (Reference) ^a
Yes	6.9	6.2	1.07 (0.81–1.42)

Note: Parameter estimates are presented as column percentages or odds ratios, with 95% confidence intervals in parentheses. As data fields for predialysis vascular access for hemodialysis and nephrology care before RRT were not available before the 2005 version of the Medical Evidence Report, the denominators for these variables consisted of 36.7% of the study population for whom the 2005 version of the form was completed.

Missing data: initial hemodialysis access (63.3 %); prior nephrology care, months (59.4 %); eGFR, mL/min/1.73 m² (1.5 %); body mass index, kg/m² (4.7 %); albumin, g/dL (25.2 %); hemoglobin, g/dL (11.1 %).

AOR, adjusted (by logistics regression, with age, sex, race, ethnicity as adjusters) odds ratio; CI, confidence interval; eGFR, estimated glomerular filtration rate; RRT, renal replacement therapy.

^a*P* value 0.05.

^b_{0.01} *P* value < 0.05.

^c_{0.001} = *P* value < 0.01.

Table 3Adjusted hazards ratios for outcomes on dialysis therapy, patients with HUS ($n = 2241$)

Variable	Reference	Outcomes		
		AHR Death	AHR Listing	AHR Transplant
Group	%/yrs. follow-up	44.8/5.4	28.9/3.7	24.8/3.8
Initial RRT 1995–2000	2001–2005	1.02 (0.88–1.18) ^a	0.99 (0.82–1.19) ^a	1.21 (1–1.46) ^a
Initial RRT 2006–2010	2001–2005	0.84 (0.7–1.01) ^a	1.07 (0.86–1.32) ^a	0.9 (0.71–1.15) ^a
Age < 5 yrs	Age 20–39 yrs.	0.37 (0.22–0.61)	1.53 (1.19–1.98)	2.55 (1.99–3.26)
Age 5–19 yrs	Age 20–39 yrs.	0.39 (0.26–0.59)	1.17 (0.91–1.5) ^a	1.59 (1.24–2.03)
Age 40–64 yrs.	Age 20–39 yrs.	2.61 (2.15–3.16)	0.78 (0.64–0.95) ^b	0.63 (0.51–0.79)
Age 65 yrs.	Age 20–39 yrs.	5.58 (4.56–6.83)	0.14 (0.09–0.23)	0.11 (0.06–0.2)
Female sex	Male	0.85 (0.74–0.96) ^b	0.99 (0.83–1.17) ^a	0.88 (0.74–1.04) ^a
African American race	White	1.01 (0.85–1.19) ^a	0.87 (0.71–1.08) ^a	0.51 (0.4–0.65)
Other race	White	0.77 (0.49–1.22) ^a	0.98 (0.66–1.46) ^a	0.73 (0.48–1.11) ^a
Hispanic ethnicity	Non-Hispanic	0.85 (0.63–1.13) ^a	0.94 (0.7–1.27) ^a	0.73 (0.53–1.01) ^a
Ischemic heart disease	Absent	1.42 (1.16–1.74)	0.64 (0.35–1.18) ^a	0.7 (0.36–1.38) ^a
Diabetes	Absent	1.18 (0.96–1.44) ^a	0.62 (0.4–0.97) ^b	1.25 (0.83–1.9) ^a
Alcohol abuse	Absent	1.07 (0.66–1.71) ^a	0.72 (0.3–1.76) ^a	0.68 (0.22–2.12) ^a
Drug abuse	Absent	0.93 (0.5–1.75) ^a	0.41 (0.15–1.09) ^a	0.27 (0.07–1.1) ^a
Peritoneal dialysis	Hemodialysis	0.65 (0.46–0.93) ^b	1.21 (0.92–1.6) ^a	1.11 (0.85–1.45) ^a
Preemptive transplant	Hemodialysis	0.12 (0.04–0.38)	.	.
Vascular access ^d				
Graft	Fistula	4.44 (0.89–22.2) ^a	0 (0–.) ^a	1.2 (0.14–10) ^a
Catheter	Fistula	2.22 (0.7–6.97) ^a	1.35 (0.33–5.5) ^a	0.51 (0.23–1.11) ^a
Nephrology care 12 mth.	12	1.47 (0.79–2.71) ^a	1.3 (0.77–2.18) ^a	0.73 (0.45–1.18) ^a
eGFR > 15 mL/min/1.73 m ²	15	1.04 (0.82–1.31) ^a	0.78 (0.6–1.01) ^a	0.81 (0.63–1.05) ^a
Body mass index 30 kg/m ²	< 30	0.82 (0.69–0.98) ^b	0.93 (0.74–1.18) ^a	0.8 (0.61–1.04) ^a
Albumin < 3.5 g/dL	3.5	1.27 (1.07–1.5) ^c	1.02 (0.84–1.23) ^a	0.93 (0.76–1.14) ^a
Hemoglobin 9 g/dL	< 9.0	0.91 (0.79–1.04) ^a	0.93 (0.78–1.1) ^a	0.96 (0.8–1.15) ^a
Cerebrovascular disease	Absent	0.49 (0.22–1.11) ^a	0.71 (0.29–1.74) ^a	0.43 (0.11–1.78) ^a
Peripheral vascular disease	Absent	1.26 (0.92–1.71) ^a	1.29 (0.69–2.42) ^a	1.25 (0.62–2.52) ^a
Smoking	Absent	0.79 (0.45–1.39) ^a	1.01 (0.57–1.76) ^a	0.95 (0.46–2) ^a

Hazards ratios are adjusted for age, sex, race, and ethnicity and are presented with 95% confidence intervals in parentheses. $P < 0.001$ unless otherwise indicated.

AHR, adjusted hazards ratio; eGFR, estimated glomerular filtration rate; RRT, renal replacement therapy.

^a P value 0.05.

^b $0.01 = P$ value < 0.05.

^c 0.001 = *P* value < 0.01

^d For hemodialysis.

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