Direct healthcare costs for patients hospitalized with Crimean-Congo haemorrhagic fever can be predicted by a clinical illness severity scoring system

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Crimean–Congo hemorrhagic fever (CCHF) is endemic in Turkey, with peak incidence of hospital admissions in the summer months. The aim of this pilot study was to evaluate the role of the severity grading score (SGS) in predicting length of hospital stay, laboratory usage, need for blood products, and hence total costs of patients. Thirty-five patients admitted to one specialist center in Turkey in 2013 and 2014 with PCR-proven CCHF. The mean (SD) age was 55 (±14) and 63% of the patients were male, with 8 (22.9%) mortality. Patients were classified by SGS into three groups with mortality as follows: low risk (0/19); intermediate (6/14); and high (2/2). The direct hospital cost of these admissions was at least $41 740 with median (range) of $1210 ($97–$13 054) per patient. There was a significant difference between low-risk and combined (intermediate–high) risk groups as 635 (97–1500) and 2264.5 (154–13 054), respectively ($p = 0.012$). In conclusion, a clinical grading score can be used to predict illness severity and to predict associated health care costs.

Keywords: Crimean–Congo hemorrhagic fever, Direct cost, Scoring system

Introduction

Crimean–Congo hemorrhagic fever (CCHF) virus is a member of the Nairovirus genus of the Bunyaviridae family and is endemic in Africa, the Balkans, the Middle East, and Asian countries. After the first CCHF cases in Turkey were reported in Tokat province in 2002, sporadic cases and outbreaks have continued to occur, with ongoing endemicity in some areas of the country.[1–3] In the years 2002 to 2014 inclusive, 9069 confirmed cases of CCHF were reported to the Turkish Ministry of Health.[4] This places a significant burden on the health care system, the cost of which has been examined in only two studies a decade ago.[5,6] A clinical severity grading score (SGS) has been developed empirically and validated prospectively to predict clinical disease progression and case fatality.[7,8] A similar clinical severity scoring index with less variables has also been proposed but awaits full prospective evaluation.[9]

These clinical scoring systems were primarily designed to guide patient triage and clinical management. The aim of this study was to enumerate the use of inpatient bed days, laboratory tests, and blood products for patients recently managed for CCHF in one of the eight referral units in Turkey and to quantify the associated costs. In addition, we examined whether costs could be predicted from the SGS scores.

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Materials and Methods

This was a retrospective study of all adults admitted with laboratory-confirmed CCHF to Ondokuz Mayis University Hospital in Samsun, Turkey, in 2013 and 2014. The demographic, clinical, and laboratory features of the patients were obtained from hospital health records and billing systems and were stored under anonymized study number on a standard pro forma. The diagnosis of CCHF was confirmed by real time PCR (Qiagen, Germany) in Samsun Public Health Agency reference laboratory and patients with clinically suspected CCHF and/or with positive serological tests but negative PCR were excluded.[2] The hospital is a designated regional center for management of patients with CCHF, using a comprehensive protocol for clinical data capture and management. Patient admission and discharge data are stored electronically, including date and time stamping for all events. The Samsun Public Health Agency reference laboratory is also a designated

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Table 1 Components of SGS for CCHF[7]

Items	Classification	SGS points
Aspartate transaminase	<5×ULNV	0
	≥5×ULNV	1
Alanine transaminase	<ULNV	0
	≥ULNV	1
Lactate dehydrogenase	<3×ULNV	0
	≥3×ULNV	1
White blood cells	<10 000 cells/μL	0
	≥10 000 cells/μL	1
Hepatomegaly	No	0
	Yes	1
Organ failure	No	0
	Yes	1
Bleeding	No	0
	Yes	1
Age	<60 years	0
	≥60 years	1
Platelets	≥100 000 cells/μL	0
	≥50 000, <100 000 cells/μL	1
	<50 000 cells/μL	2
Prolongation of PT	<3 s	0
	≥3 s, <6 s	1
	≥6 s	2
aPTT	<70	0
	≥70	1
INR	<1.6	0
	≥1.6	1

ULNV: upper limit of normal value, PT: prothrombin time, aPTT: activated partial thromboplastin time, INR: international normalized ratio.

Table 2 Average costs for each component of care

Item	Cost per item ($)
Inpatient bed day (without drugs, imaging)	12
Biochemistry blood panel	12
Complete blood count	1.3
Clotting studies	7.8
Blood products/unit	
• Erythrocyte suspension	37.8
• Plasma per unit	18.1
• Platelet suspension pack	17.9
• Platelet apheresis	145.9

regional center of the national laboratory system, with rigorous quality assurance of all diagnostic methods for CCHF. Under a national protocol, samples from all patients with suspected CCHF must be sent to this laboratory for confirmation, accompanied by a detailed questionnaire which includes demographic, epidemiological, and clinical patient details.

The demographic and laboratory parameters required to generate the SGS on admission of patients were obtained from the records, as summarized in Table 1. According to this scoring system: if the SGS score is ≤4, the disease severity is low: SGS score of 5–8 is intermediate; and SGS ≥ 9 is categorized as high-risk group.[9] The hospital outcome (mortality), length of hospitalization (initially in hours, converted to days), number and types of blood tests performed, the number of blood products transfused, and total hospital costs were recorded for each patient. Expenditure on drugs and other clinical consumables including imaging is factored into the daily cost of an occupied hospital bed for these patients. However, expenditure on CCHF-related infection control precautions could not be quantified in this retrospective study and was not included. Averaged costs for each component were obtained from the hospital authorities and are summarized in Table 2 (expressed in US$ equivalents).

The Statistical Package for the Social Sciences (SPSS) version 15.0 for Windows (SPSS Inc., Chicago Illinois, USA) was used for the statistical analysis. Nonparametric data were expressed as median (min–max). The intermediate and high SGS groups were analyzed as one group and compared to the low-risk group. Quantitative parameters (average age of the patients, the mean follow-up period in the hospital, and mean numbers of laboratory investigations) were compared using Student's *t*-test. The comparison of hospital costs in different SGS groups was performed using the Mann–Whitney *U*-test because of differences in the distributions. Proportions for categorical variables were compared using the *Chi-square* test. A p-value < 0.05 was considered significant in all analysis. Patients were not approached for consent as this was not deemed necessary for an anonymized study of health care usage.

Table 3 Comparison of applied procedures and direct hospital costs in different SGS risk groups

		Severity grading score group		
Parameter	Total (*n* = 35)	Low risk (*n* = 19)	Intermediate and high risk (*n* = 16)	*p*-value
Age (Mean ± SD)	55 (±14)	52.5 (±15.7)	58.8 (±11.9)	0.194
Period of hospitalization (Mean ± SD) days	5.9 (±2.8)	6.01 (±2.41)	5.70 (±3.34)	0.754
Number of tests Mean ± SD				
CBC	7 (3.7)	7.2 (±3.4)	6.8 (±4)	0.754
INR	6 (±3)	6.3 (±2.5)	5.8 (±3.5)	0.661
Biochemical panel	6.7 (±3.3)	6.8 (±2.8)	6.4 (±3.9)	0.726
FFP (number of patients who received)	57	0	7	0.002
Mean (SD) packs		0	1.6 (±4.2)	0.021
Platelet suspension	125			
Number of patients who received		8	13	0.036
Mean (SD) packs		1.14 (1.96)	6.2 (±6.3)	0.02
Erythrocyte suspension (number of patients who received)	12	0	3	0.086
Mean (SD) packs		0	0.8 (±1.8)	0.336
Death	8	0	8	0.001
Number of patients				
Hospital bill (USD) Median (min–max)	41740	635 (97–1500)	2264.5 (154–13054)	0.012

CBC: complete blood count, INR: international normalized ratio, FFP: fresh frozen plasma.

Results

Data were obtained for all 15 eligible patients in 2013 and all 20 eligible patients in 2014. Thirty-eight other patients admitted with possible or probable CCHF in these two years were omitted from the study as they did not meet the full case definition. Patients had a mean (SD) age of 55 (±14) years and 22 (63%) were male. According to the SGS scoring system, 19 (54%) patients were classified as low risk, 14 (40%) were intermediate, and 2 (6%) were in the high-risk group. Eight (22.9%) patients died, of whom six were categorized in the intermediate SGS group, and two were in the high-risk group. The total hospitalization period of the patients was 4931 h with a mean (SD) 141(±68) hours. The total laboratory tests requested included 246 CBC – mean (SD) 7 (±3.7) per patient; 233 biochemical tests – mean (SD) 6.7 (±3.3), and 212 INR tests – mean (SD) 6 (±3).

One hundred and ninety-four blood products given to 22 (63%) patients including 125 platelet suspensions, 57 fresh frozen plasma units, and 12 erythrocyte suspensions. The minimum total direct cost of all patient admissions was $41 740, with a median (range) cost of $1210 ($97–13 054). There was no difference in laboratory costs between the low and combined higher risk SGS groups, but the use of blood products and total costs were significantly higher in the higher risk group (Table 3). The additional cost of the personnel protective equipment which includes gloves, gown, and masks was $82/patient and has not been added to the total direct cost of the patients.

Discussion

This is the first study to demonstrate an association between severity of CCHF illness according to a standardized severity of illness scoring system and direct hospital costs of looking after such patients. The SGS scoring system is designed primarily for the triage of patients at their first clinical evaluation. This study suggests that it can also be used to predict the need for blood products and potential cost of admitting patients with CCHF.

The direct cost of treatment increases significantly with the severity of the disease. There is a considerable cost difference between low SGS score and intermediate–high-grade patients ($p = 0.012$). There have been two published cost analyses regarding management of CCHF from Turkey. Bakir *et al.*[5] compared survival and mortality in patients with CCHF and identified the mean hospital bills for each group, amounting to $1199 and $2142, respectively, in 2005, with no statistically significant difference. Ozkurt *et al.*[6] compared the hospital costs of patients treated with ribavirin to a control CCHF patient group in 2006, and again, there was no difference between respective average costs of $941 and $1012. The estimated current average cost of admission of a patient is $1210 in this study. Applying these costs to the 9069 cases notified in Turkey between 2002 and 2014, the total cost is equivalent to at least 9069 × $1200, or $10 882 800. These studies demonstrate the minimum economic burden of CCHF hospitalization in Turkey. Overall costs will be substantially higher if they include patients with probable or suspected CCHF who are managed using the same protocols.

There are other implications of this small retrospective study. The mean hospitalization period of patients was 6 days and the mean number of CBC, biochemical tests, and INR tests performed were 7, 6.7, and 6, respectively, meaning that blood examinations were performed at least once a day for each patient. These are all part of routine management of patients with CCHF in our hospital, and samples are sent to at least three different branches of the laboratory. The frequency of blood sampling and testing poses potential threats to health care staff on the ward and possibly to laboratory personnel. Health care workers are at occupational risk for CCHF infection via needle stick injuries, skin or mucosal contact with contaminated blood and handling specimens.[10,11] Nosocomial acquisition of CCHF is related to high mortality rates among health care staff.[12] Prediction of the need for laboratory tests and cross-matching for blood products using the SGS scoring system can be used to underscore the total risk that individual patients may pose to health care staff regarding needle stick and other potential virus exposures. This risk can be minimized by careful management of the patients as well as implementation of infection control precautions.

The average cost of personnel protective equipment was $82 for each patient in the optimal follow-up period. However, the need for these equipment increases particularly in severe patients due to frequent sampling and close follows, so hospital costs of the patients are closely related to risk category.

The demographic and clinical profile of the patients included in this study is similar to those managed in centers across Turkey,[1,4–9] although the average age was a little higher (55 years vs. 47 years in many series) and intermediate risk patients with a higher mortality are overrepresented in our patient cohort compared to general local experience.[13] This is expected, as the center is a tertiary referral center accepting higher risk patients. There is a high index of suspicion for CCHF in all patients presenting with fever, history of tick bite, and/or thrombocytopenia and we believe that all such patients were screened for CCHF using PCR according to the national protocol, although we have no data to confirm this. The proportion of patients initially suspected as having CCHF but excluded from the study (38 excluded, 35 included) is similar to general experience in our institution and in other centers.[14] Although the study was based on retrospective data, all patients were managed using detailed protocols for data capture and no patients were excluded because of lack of available records. We believe the results are generalizable to all patients treated in Turkish hospitals for CCHF. However, this study underestimates direct hospital costs as hidden costs such as the provision of adequate infection control materials and full labor and investigational costs have not been included. Nor does it include any opportunity costs for the patient and family such as travel costs to hospital for relatives visiting, time lost from work, etc. The costs associated with each component of hospital stay might be considerably larger in another national health care setting but these could be substituted in our simple model to estimate direct costs in other countries.

In summary, the SGS for severity of illness categorized patients with CCHF into appropriate risk groups regarding hospital outcome (mortality), length of hospital stay, and the need for blood products. The results reaffirm the potential for the SGS to be used to identify those patients at first diagnosis, who should be prioritized for referral to a specialist treatment center, and to predict demand (and associated hazards to staff) for blood products and complex supportive care. It is the first study to show a difference in the costs of looking after severely ill patients with CCHF, compared to low-risk patients. Severity of illness scoring systems has been used in other settings to predict hospital outcomes and the cost of hospital admission with other communicable and noncommunicable diseases.[15–17] We suggest that this approach should be validated prospectively in a larger cohort of CCHF patients in several centers and that the two currently proposed scoring systems be directly compared.

Conflict of Interest

The authors declared that there are no conflicts of interest. NJB is partially funded by the National Institute for Health Research Health Protection Research Unit (NIHR HPRU) in Emerging and Zoonotic Infections, a partnership between the University of Liverpool, Liverpool School of Tropical Medicine and Public Health England (PHE). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, the Department of Health, or PHE.

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