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To Validate REMS Score in Patients with Diabetes and Sepsis-A Study in Rural Tumkur

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Abstract

Introduction : Hyperglycaemia is a commonly encountered complication in critically ill patients in the intensive care setting. It is associated with increased mortality and poor outcome in hospitalized patients. It is an accepted opinion that diabetes worsens prognosis of infection, particularly sepsis. With diabetes assuming alarmingly epidemic proportions in India, a study to evaluate the predictive ability of REMS (Rapid Emergency Medicine Scoring) in patients with diabetes & sepsis is attempted to gauge the impact on mortality and morbidity (length of hospital stay) so as to evolve a consensus on early and aggressive glycaemic control & treatment.

Aim & Objectives : To assess the predictive ability of REMS score for hospital mortality and length of stay in patients with type 2 diabetes mellitus and sepsis.

Materials & Methods : This was a prospective, observational study involving a total of 114 patients of both sexes, all cases of Sepsis with type 2 Diabetes Mellitus admitted in the emergency wards and the Intensive care units. To estimate the severity of sepsis, REMS (rapid emergency medicine score) scoring on the day of admission was tabulated and subsequently, the hospital mortality & length of stay (LOS), the outcome measures were calculated.

Results

- 114 patients were recruited for this study. The maximum number of patients was observed in age group between 61 to 70 years (24.6%). The mean age was 58.56 years (SD 14.51).
- Out of the total 114 patients, 74 were male patients (64.9%) & 40 were female patients (35.1%).
- Hyperglycemia with reference to elevated Random Blood Sugar according to the 2010 ADA criteria was seen in 80(70.2%) of the patients that were recruited for the study out of which 25 were females (62.5%) and 55 were males (74.3%).
- 35% of the total cases had severe uncontrolled Diabetes mellitus.
- Oral drugs are reported to be the preferred mode of treatment with 93 out of the 114 patients reporting use of the same.
- Death was observed in 9 patients in which 6 were female and 3 were male.
- Maximum number of deaths were seen in the group having HBA1c >11 & range of 8.1 - 9.4, where 3 deaths were recorded.

- Those with HbA1c 8.1-9.4% and >11% demonstrated higher mortality rate than those with HbA1c 6.5-8% and 9.5-11%.
- The Mean ± S.D values of length of hospital stay(LOS) was approximately 13.53 ± 10.39 days in survived diabetic patients which was statistically higher than those who died (P < 0.002).
- Patients who survived had significantly lower admission REM scores (5.94) than those who died (P < 0.001).
- REM scores were shown to be independent predictor of mortality in the same analysis.
- A multivariate analysis for hospital LOS has shown that HbA1c, REM score & age were not independently associated with longer hospitalization.

Conclusion: REM scores were shown to be independent predictor of mortality in the same analysis while HbA1c, REM score & age were not independently associated with longer hospitalization (Length of Stay).

Keywords: Sepsis, HbA1c, Mortality, Morbidity, REM score, Type 2 Diabetes Mellitus.

Introduction

Diabetes is increasingly becoming a public health challenge. As prevalence of type 2 Diabetes mellitus continues to increase worldwide, diabetes related complications leading to increased mortality & morbidity occurs as well, with substantial consequences for the individual as well as sizeable economic consequences for society and the health sector in particular. A large body of evidence has defined poor glycaemic control as a negative prognostic factor in critical illness. [1, 2] Hyperglycaemia has been defined as random glucose concentration greater than 200 mg/dl. The worldwide mortality rate of severe sepsis ranges from 28.6% to 49.6%. [3] The main reason for which diabetes predisposes to infection appears to be abnormalities of the host response, particularly in neutrophil chemotaxis, adhesion and intracellular killing. There is also evidence for defects in humoral immunity that also plays a substantial role in the pathogenesis. [4] Decreased functional capacity of organ systems as a whole in diabetic patients is also another important factor in pathogenesis. The prevalence of diabetes increases to approximately 15-30% among critically ill patients. When it comes to India, the concerns are alarming, ICMR-INDIAB 2011 data shows that India accounted for 62.4 million diabetics & interestingly, an EPIC II (Extended study of Prevalence of Infections in ICU, 2007) in India showed that 40% of admissions in ICU's were due to infections. Most of the diabetics in our country remain unrecognized as a result of inadequate access to healthcare and screening programs.

Olsson, Terent and Lind evaluated the predictive accuracy of the scoring system Rapid Acute Physiology score (RAPS) in nonsurgical patients attending the emergency department (ED) regarding in-hospital mortality and length of stay in hospital (LOS), and investigated whether the predictive ability of RAPS could be improved by elaborating the system. For all patients seeking assistance in the emergency department, RAPS (including blood pressure, respiratory rate, pulse rate and Glasgow coma scale) was calculated. The RAPS system was extended by including the peripheral oxygen saturation and patient age (Rapid Emergency Medicine score, REMS) and this new score was calculated for each patient. A sample REMS scoring chart is given below:-

	Score				
Variable	0	+1	+2	+3	+4
Age (years)	<45		45–54	55–64	
MAP (mm Hg)	70–109		110–129 50–69	130–159	>159 ≤49
Heart rate (bpm)	70–109		110–139 55–69	140–179 40–54	>179 ≤39
RR (breaths/min)	12–24	25–34 10–11	6–9	35–49	>49 ≤5
O_2 saturation (%)	>89	86–89		75–85	<75
GCS	14 or 15	11–13	8–10	5–7	3 or 4

The statistical associations between the two scoring systems and in-hospital mortality as well as LOS in hospital were examined. They concluded that the REMS was superior to RAPS in predicting in-hospital mortality. Similar results were obtained in the major patient groups (chest pain, stroke, coma, dyspnoea and diabetes), in all age groups and in both sexes. The association between REMS and LOS was modest (r = 0.47, P = 0.0001).

Other studies also demonstrated the efficacy of the REM score which is basically an attenuated version of the APACHE scoring criteria. Ha et al. showed that among a number of scoring models for predicting mortality in patients developed, only the Rapid Emergency Medicine Score (REMS) and Worthing Physiological System (WPS) were validated in developing countries. [5] In another study, the validity of the Emergency Trauma Score (EMTRAS) and Rapid Emergency Medicine Score (REMS) for predicting in-hospital mortality in patients with trauma was evaluated. Furthermore, REMS and the EMTRAS with 2 other scoring systems were compared: the Revised Trauma Score (RTS) and Injury Severity score (ISS). It was postulated that the ability to predict in-hospital mortality quickly and accurately could lead to improved patient outcomes. [6]

To improve the Rapid Acute Physiology Score (RAPS) as a predictor of in-hospital mortality in the nonsurgical emergency department (ED) by including age and oxygen saturation, and to compare this new system, Rapid Emergency Medicine Score (REMS) was compared with the Acute Physiology and Chronic Health Examination (APACHE II) with regards to predictive accuracy. This new scoring system, REMS, had the same predictive accuracy as the well-established, but more complicated, APACHE II.[7] .Zoubi et al. aimed to assess the fitness of four scoring systems for hospitalized septic patients. The Modified Early Warning Score (MEWS), Simple Clinical Score (SCS), Mortality in Emergency Department Sepsis (MEDS) score and Rapid Emergency Medicine Score (REMS) & concluded that The SCS and REMS are the best scoring criteria currently to predict the mortality of patients with sepsis.

Materials & Methods

The study was conducted at Sri Siddhartha Medical College Hospital & Research Centre, a private medical college in rural Tumakuru, from November 2016 to April 2018. A total of 114 patients of both sexes, all cases of Sepsis with type 2 Diabetes Mellitus admitted in the emergency wards and the ICU's participated in the study. Written Informed consent was taken for the study from the participants after explaining the nature of the study.

Inclusion Criteria

1. Adult patients aged >18 years.
2. Patients with established diagnosis of type 2 diabetes mellitus (either HbA1c levels/plasma glucose cutoffs as per ADA norms) .
3. Sepsis defined according to SIRS criteria.

Exclusion Criteria

1. End stage malignant disease and patients on long term steroids/immunosuppressive therapy

2. Patients who have undergone any blood transfusion before admission (less than 4 months before the date of admission).

The sample size for the study was estimated to be a minimum of 114. Data was collected from patients by detailed clinical history followed by a clinical examination and relevant investigations in a specially detailed proforma. The purpose of the study was explained to the patients in their native tongue and informed consent obtained. Only those patients that satisfied the inclusion criteria were enrolled in the study.

To estimate the severity of sepsis, REMS (rapid emergency medicine score) scoring was calculated on day of admission. The patient were followed up on days 1, 3, 5 & 7 where his/her vitals were checked and severity gauged. (improvement/deterioration) and survival rates calculated. Hospital mortality and length of stay (LOS), the outcome measures were calculated.

Analysis

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data is made, **Assumptions: 1.**Dependent variables should be normally distributed, 2.Samples drawn from the population should be random, Cases of the samples should be independent

Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test were used to find the significance of study parameters on categorical scale between two or more groups, Non-parametric setting for Qualitative data analysis. Fisher Exact test used when cell samples are very small.

Multivariate analysis was performed to analyse the length of stay and hospital mortality which are the outcome measures. Hospital mortality and hospital length of stay [LOS] were calculated using logistic regression and multiple regression respectively.

Significant figures

* Moderately significant (P value:0.01<P ≤ 0.05)** Strongly significant (P value: P≤0.01)

The Statistical software namely SPSS 18.0, and R environment ver.3.2.2 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

Results

One hundred and fourteen patients with diagnosis of type 2 diabetes mellitus & sepsis requiring admission to ICU & the emergency wards of Sri Siddhartha Medical College Hospital, from 1st November 2016 to 30th April 2018 were recruited.

Table 1: Age distribution of patients studied

Age in years	No. of patients	%
20-30	3	2.6
31-40	11	9.6
41-50	24	21.1
51-60	27	23.7
61-70	28	24.6
71-80	14	12.3
>80	7	6.1
Total	114	100.0

Mean ± SD: 58.56±14.51

The above table documents the age distribution amongst the 114 patients recruited for the study. The mean age was 58.56 years (SD 14.51). The maximum number of patients

was observed in age group between 61 to 70 years (24.6%). The least number of patients was in the age group of between 20 to 30 years (2.6%).

Table 2: Gender distribution of patients studied

Gender	No. of patients	%
Female	40	35.1
Male	74	64.9
Total	114	100.0

The above table shows the gender distribution among the study population. Out of the total 114 patients, 74 were male patients (64.9%) & 40 were female patients (35.1%)

Table 3: Etiology-wise diagnosis distribution of patients studied

Medical/surgical diagnosis	Gender		Total
	Female	Male	
Medical case	25(62.5%)	32(43.2%)	57(50%)
Surgical case	15(37.5%)	42(56.8%)	57(50%)
Total	40(100%)	74(100%)	114(100%)

P=0.050+, Significant, Chi-Square Test

The above table shows the etiology of the cases admitted in the ICU and emergency wards. In both medical & surgical cases, the incidence was more in males than females which is statistically significant. Total number of medical cases and surgical cases are 57 each. Males make about 43.2% of the medical cases (32) whereas they make about 56.8% of the surgical cases (42).

Table 4: Treatment regularity distribution of patients studied

Treatment regularity	Gender		Total
	Female	Male	
Regular	17(42.5%)	41(55.4%)	58(50.9%)
Irregular	23(57.5%)	33(44.6%)	56(49.1%)
Total	40(100%)	74(100%)	114(100%)

P=0.188, Not Significant, Chi-Square Test

The above table demonstrates the adherence to treatment, out of the 114 patients studied 58(50.9%) patients reported regularity in the taking treatment. Males constitute 55.4% (41 patients) of this group while females constitute about 42.5% (17 patients)

Table 5: Clinical symptoms distribution of patients studied

Clinical symptoms	Gender		Total (n=114)
	Female (n=40)	Male (n=74)	
Fever	30(75%)	55(74.3%)	85(74.6%)
Ulcer	17(42.5%)	37(50%)	54(47.4%)
Respiratory system symptoms	17(42.5%)	23(31.1%)	40(35.1%)
Cardiovascular symptoms	8(20%)	7(9.5%)	15(13.2%)
Abdominal symptoms	12(30%)	17(23%)	29(25.4%)
Central nervous system symptoms	7(17.5%)	7(9.5%)	14(12.3%)
Other constitutional symptoms	7(17.5%)	17(23%)	24(21.1%)

The above table shows the clinical distribution of symptoms amongst all the patients that were recruited for the study. Fever (74.6%) dominated all the symptoms with 85 of all the 114 patients. Ulcers & swelling (47.4%) rang in 2nd with 54 of the 114 patients reporting the same. Respiratory symptoms like cough/ breathlessness were 3rd with 40 of the 114 patients presenting to the hospital with those complaints (35.1%). Cardiovascular complaints were reported by 15 of the 114 patients (13.2%). Abdominal complaints were seen in 29 patients while central nervous system involvement was seen in 14 of the 114 patients. Other atypical constitutional symptoms were reported by 24 of the 114 patients.

Table 6: Mortality distribution of patients studied

Mortality	Gender		Total
	Female	Male	
SURVIVORS	34(85%)	71(95.9%)	105(92.1%)
NON SURVIVORS	6(15%)	3(4.1%)	9(7.9%)
Total	40(100%)	74(100%)	114(100%)

P=0.064,Non-Significant, Fisher Exact Test

The above table shows the mortality distribution of the patients studied. Out of the 114 patients studied, death was observed in 9 patients in which 6 were female and 3 were male. There is no statistical difference found in the mortality distribution based on gender.

Table 7: REM distribution in relation to mortality of patients studied

REM	Mortality		Total
	Survivors	Non-Survivors	
0	4(3.8%)	0(0%)	4(3.5%)
1-10	93(88.6%)	5(55.6%)	98(86%)
11-20	8(7.6%)	4(44.4%)	12(10.5%)
Total	105(100%)	9(100%)	114(100%)
Mean ± SD	5.94±3.15	11.11±4.51	6.35±3.54

P<0.001**, Significant, Student t test

The above table records the REM score and its correlation to mortality. REM score between 1 &10 had 93 survivors and 5 deaths whereas the REM score between 11 & 20 had 8 survivors and 4 deaths. REM score at admission were shown to be association with hospital mortality among the study population. Patients who survived had significantly lower admission REM scores (5.94) than those who died (P < 0.001).

Table 8: Logistic Regression for the risk of mortality in patients with diabetes

Model	Odds Ratio	95% C.I	P-Value
AGE	1.028	.967 – 1.094	0.377
REM	1.425	1.126 – 1.804	0.003
HBA1C	0.966	.667 – 1.399	0.855

In multivariate analysis by logistic regression, Age & HbA1c were not deemed to be an independent predictive factor of hospital mortality. REM scores were shown to be independent predictor of mortality in the same analysis.

Discussion

The largest study to show an adverse effect of diabetes on mortality in sepsis was conducted in a large group of Danish patients with community-acquired pneumonia and that particular study found that patients with diabetes had a higher risk of mortality (OR 1.2).[9] Patients with diabetes may also have various co-morbidities that may worsen outcomes: it is debatable whether these conditions should be adjusted for, since many are caused by diabetes. It is postulated that deranged neuroendocrine homeostasis increased levels of cortisol, glucagon, and epinephrine & that is responsible for the elevated blood sugars. [9]With regards to systems most involved in patients with diabetes and sepsis, one study by Kefteridis et al. showed urinary tract infections to be more common among adults with diabetes and more severe cases lead to pyelonephritis and bacteremia. The researchers involved in this study found that subjects with diabetes had longer hospitalization (10 days versus 7 days; p < 0.001), and greater mortality rates (12.5% versus 2.5%;p <0.01) than those without diabetes.[10] Other studies also seemed to support this observation.[11] Our study, showed that Respiratory system was primarily involved in most patients landing up in our hospital with 35.1% {only medical diagnosis}. This finding aligned with the findings reached by Barati et al. [12]In this study, the age distribution amongst the 114 patients recruited for the study was documented. The mean age was 58.56 years (SD 14.51). Barati et al. in their study reported that out of 300 septic patients, 158 (52.7%) had diabetes mellitus with the mean age (± SD) of 52.7±28.4 years. They also reported that Mortality rate increased with aging.[12] Our study did not show any association between increasing age & mortality.Out of the total 114 patients recruited in our study, 74 were male patients (64.9%) & 40 were female patients (35.1%). Other studies have also had higher proportion of patients being male. [12, 13] Chang et al. reported that the risk for mortality was statistically significantly increased in male

patients (OR 1.3). [13] No such association was reported in our study.Ghanem-Zoubi et al, in their study have validated the use of REM scoring criteria as a means of predicting mortality patterns of patients with sepsis in general medicine departments. [102]In our study, REM scores were shown to be independent predictor of mortality in the analysis. REM score has an odds ratio (OR) of 1.425 with a “p” value of a 0.003 which showed strong correlation.Other findings in our study included Hyperglycemia with reference to elevated Random Blood Sugar according to the 2010 ADA criteria was seen in 80(70.2%) of the patients that were recruited for the study. Fasting Blood Sugar > 126 mg/dl as per the 2010 ADA criteria for the diagnosis of Diabetes Mellitus were seen in 91 patients (79.8%). Post prandial blood sugar > 200 mg/dl was seen in 101 of the 114 patients (88.6%). HbA1c >11 synonymous with poorly controlled diabetes was found in 41 out of the 114 patients (36%).Out of the 114 patients studied, death was observed in 9 patients in which 6 were female and 3 were male. Etiology-wise total number of medical cases and surgical cases are 57 each. Males make about 43.2% of the medical cases (32) whereas they make about 56.8% of the surgical cases (42). The mean duration of Diabetes Mellitus in the patients admitted in the ICU’s is 96.89±89.84 months. Amongst clinical symptoms, Fever (74.6%) dominated all the symptoms with 85 of all the 114 patients reporting the same. Hba1c was classified as having moderately controlled (6.5-8%), poorly controlled (8.1-11%) and uncontrolled diabetes (>11%) and survivors and non survivors were grouped accordingly. Maximum number of deaths were seen in patients having HBA1c >11 where 3 deaths were recorded and the HBA1c in the range of 8.1 - 9.4 which also had 3 deaths in the group. Though statistical significance was not present, clinical significance was present as financial status played a significant role. Attenders of patients with high HbA1c values decided to take the patient home against medical advice when explained the poor prognosis. Mortality rates recorded In-hospital would have been higher if patients stayed back & continued undergoing treatment. Maximum number of patients though were present in the HbA1c range of >11 with 41 patients out of the 114 patients. The Mean ± S.D values of LOS was approximately 13.53 ± 10.39 days in survived diabetic patients which was statistically higher than those who died ($P < 0.002$). REM score at admission were shown to be association with hospital mortality among the study population. Patients who survived had significantly lower admission REM scores (5.94) than those who died ($P < 0.001$). Maximum deaths were recorded in the age group of 71-80 years (4 deaths). Mean age in survivors was 57.54 years (SD 14.18). Mean age in non survivors is 70.44 years (SD 13.58).

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