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STUDY OF THE CLINICAL PROFILE AND IN-HOSPITAL OUTCOME PREDICTORS IN CRITICALLY ILL PATIENTS WITH TYPE II DIABETES MELLITUS ADMITTED IN MEDICAL INTENSIVE CARE UNIT

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ABSTRACT: The aim was to study the clinical profile and predictors of in-hospital outcome in critically ill patients with T2DM admitted in MICU. It also aimed to study the predictive value of different critical care scoring systems in T2DM patients. A prospective, cross sectional and observational study was conducted in General Medicine Department, "Dr. D. Y. Patil Medical College and Research Centre, Pimpri, Pune, India," between September 2020 to October 2022 with a sample size of 80 T2DM cases and 80 non-T2DM controls. Overall maximum number of study participants belong to the age group of 50-69 years, Patients with T2DM had higher chances of a prolonged ICU stay and a higher mortality rate due to their critical illness compared to the non-diabetic patients. However, their mortality rate was not associated with prolonged duration of ICU stay.All the major vital parameters and biochemical parameters including RFT, Serum electrolytes, Serum Lactate and Serum Pro-calcitonin were significantly worse in diabetic patients compared to non-diabetic patients at the time of admission to the MICU.APACHE IV, SAPS3 and SOFA scores were worse on the day of admission in the T2DM patients compared to the non-diabetic patients. Except MODS all scores on day 1 and on the day of outcome were worse in diabetic patients who died in the ICU. In conclusion APACHE IV has a good predictability over SAPS III, SOFA and MODS in critically ill T2DM patients.

Keywords: Clinical profile, critically ill patients, Type2 diabetic mellitus.

INTRODUCTION

Serious illnesses required admission of the patients to the Medical Intensive Care Units (MICU) are also very prevalent among T2DM patients as it is considered to be an immunocompromised state making them susceptible to serious complications and infections.Acute complications of diabetes, such as sepsis, strokes, acute coronary syndrome, hypoglycaemia, diabetic ketoacidosis (DKA) and hyper-osmolar hyperglycaemic states (HHS) need admission to intensive care units (ICU).

Infections have a significant influence in the morbidity and mortality of type 2 DM patients.[1] Several bacterial, fungal, viral and atypical micro-organisms can cause infections in T2DM patients.[2]Thus, diabetes mellitus may be a major or secondary contributor to the disease burden in the critically ill. Therefore, it is imperative to determine the clinical and biochemical variables that contribute to the adverse outcomes in the seriously ill T2DM patients in MICU.

Predictive scoring systems are measurements of illness severity used to forecast the outcomes, often death, of intensive care unit (ICU) patients. These scores are helpful to maintain uniformity of determining the treatment options, quality of care and predict in-hospital outcomes in critically ill.[3]The Acute Physiologic and Chronic Health Evaluation (APACHE) scoring system, the Simplified Acute Physiology Score (SAPS), Sequential Organ Failure Assessment (SOFA), and Multiple Organ Dysfunction Score (MODS) are the key scoring systems used to predict mortality in the ICU patients.

There are conflicting reports about the effect of hyperglycaemia on the mortality rate in critically ill patients. Few studies show that there was no effect of high blood sugar levels on the mortality in T2DM critically ill patients.[4] Few other studies showed that patients who are hyperglycaemic and critically ill have a higher mortality rate than patients who are normoglycemic.[5]

MATERIAL AND METHODS

A prospective, cross sectional and observational study conducted in General Medicine Department, "Dr. D. Y. Patil Medical College and Research Centre, Pimpri, Pune, India," between September 2020 to October 2022 with a sample size of 80 T2DM cases and 80 non-T2DM controls.

Inclusion Criteria for cases:

1. Age more than 18 years
2. Patient admitted in the medical intensive care unit and who was a diagnosed case of T2DMor who has

i) Fasting Blood sugar level ≥126 mg/dl,
ii) Random Blood Sugar ≥ 200 mg/dl,
iii) HbA1c ≥ 6.5 On admission to MICU.

Inclusion Criteria for controls:

i) All admissions to the MICU who are above the age of 18years
ii) Not a known case of Type 2 diabetes

Exclusion Criteria for study subjects:

i) Age < 18 years

ii) Pregnancy

iii)HIV positive patients

iv)Known case of Diabetes Mellitus Type-1

Statistical Analysis:

The collected data were entered into Microsoft Excel. SPSS version 23(Statistical Package for Social Sciences) was used to analyse the data. Frequency and percentages were used to express the Categorical variables and Mean and Standard Deviation were used for expressing the continuous variables. Association between categorical variables was calculated using chi square or Fischer exact test. Association between continuous variables was calculated using student T test. Various predictive scores (APACHE IV, SOFA, SPAS, and MODS) were compared for their predictability and superiority in T2DM patients using (Receiver operator characteristic) ROC analysis and Area under curve (AUC) values. All the applied tests were two tailed with a P value of less than 0.05 considered as statistically significant.

OBSERVATIONS AND RESULTS

There were total 160 study subjects out of which 80 were having T2DM and 80 were without T2DM. Mean age of the T2DM patients was 60.06 ± 9.03 and that of the control group was 47.93 ± 18.05 years. Maximum number of study subjects with T2DM were in the age group of 50 to 59 years (40%). Whereas in the nondiabetic group, maximum number of study subjects were in the age group of 19 to 29 years (21.3%). Overall maximum number of study participants belong to the age group of 50-69 years.

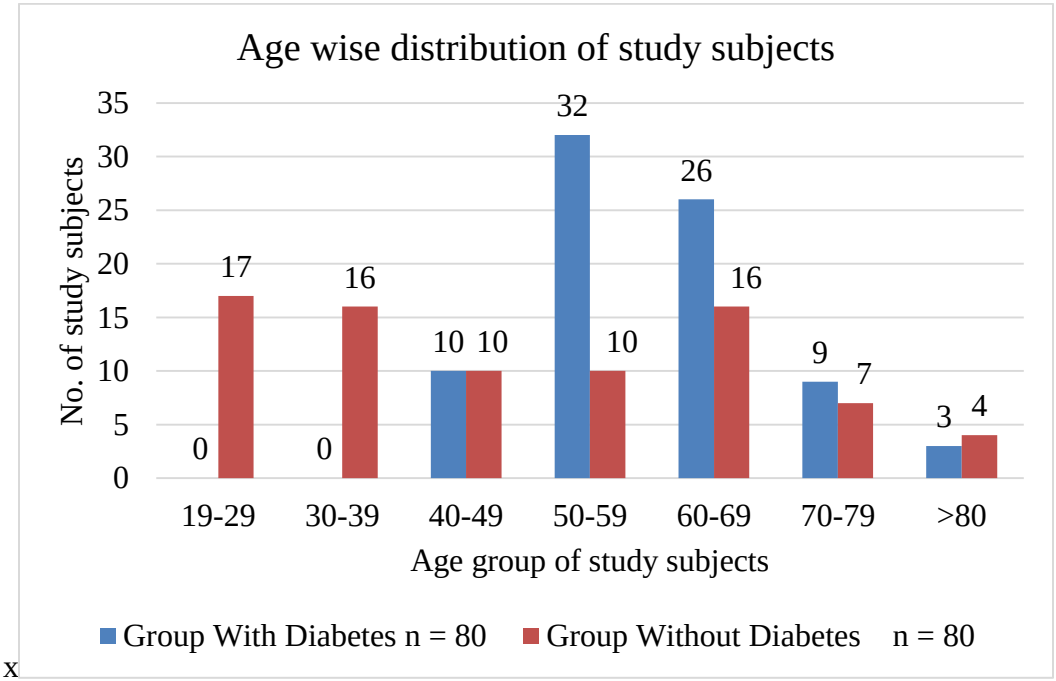

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Figure 1: Age wise distribution of study subjects.

Table 1: Gender wise distribution of study subjects.

Gender	Diabetics n = 80 (%)	Non-Diabetics n = 80 (%)	Total
Female	35 (43.8%)	41(51.3%)	76 (47.5%)
Male	45 (56.2%)	39 (48.7%)	84 (52.5%)

M:F ratio was 1.3:1 for diabetic group and it was 0.9:1 in non-diabetic group. On applying chi square test there was no statistically significant difference in gender distribution among study groups (p value = 0.429, not significant).

Majority of patients with T2DM were having the disease for less than 10 years (85%). Only 15% study subjects had T2DM for more than 10 years.

Maximum (68.8%) subjects were on oral hypoglycaemic drugs and 31.3% were on insulin only or insulin + OHA therapy.

Table :2 Distribution of the study subjects according to the Co-morbidities present.

Comorbidities	Group	
	Diabeticsn = 80 (%)	Non-Diabeticn = 80 (%)
Hypertension	22 (27.5%)	20 (25%)
Ischemic Heart Disease	6 (7.6%)	4 (5%)
Thyroid disorder	5(6.3%)	5(6.3%)
Chronic Obstructive Pulmonary Diseases (COPD)	2(2.6%)	3 (3.9%)

Among both study groups most common observed co-morbidity was hypertension (27.5% vs 25%). Ischemic heart disease, COPD and Bronchial Asthma were the other comorbidities found in the participants.

Total 77.5% patients in the study stayed for less than 7 days in the ICU. Among the T2DM group patients more than 7 days of ICU stay was seen in 22.5% cases whereas only 5% of non-diabetic patients stayed for more than 7 days in the ICU. T2DM patients had a significantly higher chance of staying for more than a week in the ICU compared to the controls (Fischer exact test $P < 0.05$).

Total mortality rate was 15%. Mortality in DM group was 21.3% and in non-DM group it was 8.2%. The death rate in DM group was statistically significantly higher than non-DM group. (chi square test p = 0.046, significant).

Table 3: Correlation of duration of ICU Stay and immediate in-hospital outcome in DM group.

ICU Stay	In-Hospital outcome in Diabetes group	
	Death	**Survival**
<7 days	10 (16.40%)	51 (83.60%)
>7 days	07 (36.85%)	12 (63.15%)
Total	19 (23.75%)	61 (76.25%)

Total 61 patients stayed for less than 7 days in the ICU. Out of the 61 patients, 10 (16.40%) patients died and 51 patients (83.60%) survived. Total 19 patients stayed in the ICU for more than 7 days, out of which 7 (36.85%) patients died and 12 (63.15%) patients survived. Overall mortality in diabetic was 23.75%. There was no correlation between the duration of the ICU stay and in-hospital mortality in the DM group. On applying Fischer exact test there was no statistically significant difference in duration of stay and mortality (death) among diabetics (p value > 0.05).

Table 4: Vital parameters among the study groups on the day of admission to the ICU.

Parameters	Diabetics	Non-Diabetics	P value
Body Temperature	37.9+1.42	37.17+0.92	0.001
Pulse Rate	106.3+18.11	112.05+14.5	0.028
Systolic Blood Pressure	90.03+29.15	100.13+10.64	0.001
Diastolic Blood Pressure	58.25+15.21	69.63+8.08	0.001
Mean Arterial Pressure	64.6+19.26	73.61+8.48	0.001
Respiratory Rate	24.49+5.55	22.73+3.12	0.047
Glasgow Coma Scale (Median Value)	15 (12-15)	15 (10-15)	0.442

All the vital parameters (Temperature, Pulse, Respiratory rate, Blood pressure and Mean arterial pressure) were statistically significantly different between the patients with and without T2DM. (Student T test p value < 0.05) except the Glasgow Coma Scale which was comparable between the two groups. (p value >0.05).

Table 5 : Comparison of mean values of different scores in T2DM subjects who died vs those who survived (Based on their in-hospital outcomes).

Scoring system	Death	Survived	P Value
APACHE score Day1	61.24+8.18	40.67+15.2	0.0001
APACHE score on the day of outcome	79.41+17.45	20.59+9.87	0.001
SAPS3 score Day1	64.11+8.2	56.88+9.9	0.0001
SAPS3 on the day of outcome	72.88+9.9	47.42+9.3	0.001
SOFA Day1	5.78+3.2	3.9+3.3	0.001
SOFA Day3	6.8+3.7	4.65+2.78	0.001
SOFA on the day of outcome	9.53+4.86	2.79+2.21	0.014

MODS Day1	5+3.2	5.32+3.5	0.735
MODS Day 3	7.63+4.3	3.68+2.4	0.001
MODS on the day of outcome	10.76+5.2	2.3+1.64	0.001

Survived – day of outcome is the day when the patient was shifted out of the ICU
Death – day of outcome is the day of death

Table above shows comparison of mean values of different scores in T2DM patients based on their immediate in-hospital outcome (death vs survival groups). Except MODS on Day 1 all the other scores were worse (statistically significantly different) in the T2DM patients who died vs those who survived (Student's T test $p < 0.05$).

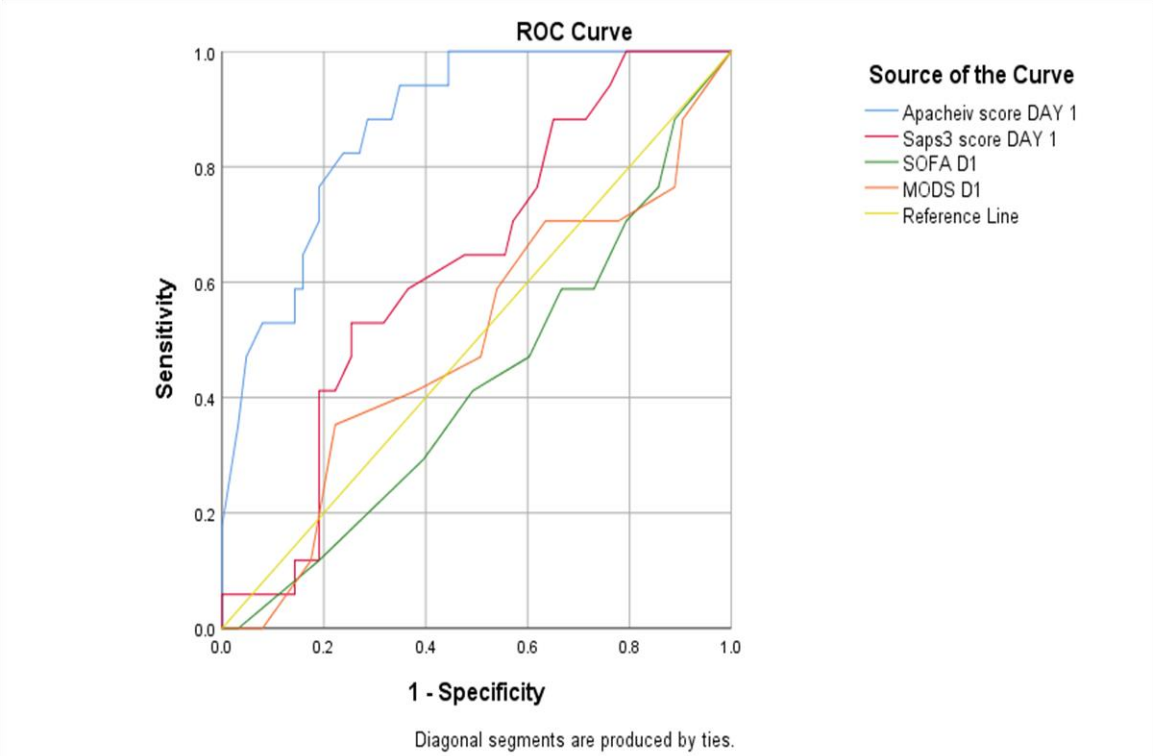

Figure 2: Area under curve (AUC) of different scoring systems on the day of admission among diabetic subjects

The above figure shows values of Area under curve (AUC) of different scores on the day of admission among diabetic subjects. On applying ROC Curve analysis to predict the mortality of different scoring systems in T2DM subjects it was found that the APACHE IV score Day 1 (AUC of 0.873) was the strongest predictor of mortality ($p < 0.05$). Other scoring systems (SAPS3, SOFA and MODS) were not significantly associated with T2DM patients.($p > 0.05$).

DISCUSSION

In our study, majority of critically ill T2DM patients were above the age of 50 years. Several studies have been done till date to understand the impact of ageing on T2DM and its complications.[6-8]

There was a slight male preponderance in the prevalence of critically ill T2DM patients compared to females (M:F -1.3:1) which was not seen in the control group (M:F – 0.9:1). Several old and recent studies have shown male gender predominance in the occurrence of Diabetes.[9,10] T2DM is a lifestyle disorder often associated with obesity and hypertension. Obesity is often associated with female gender. Also, data from developing countries like Pakistan and Iran suggest rising prevalence of lifestyle disorders including T2DM in females. [11,12]However, our data differed from these findings. Thus, further studies with larger sample sizes and investigations into role of female hormones and T2DM occurrence are warranted to know the true impact of gender on T2DM.

ADDICTIONS AMONG THE STUDY SUBJECTS

In this study, prevalence of addictions among study subjects. Alcohol (58.8% vs 67.5%) and smoking/tobacco chewer (60% vs 72.5%) were the addictions found among study groups. Proportion of smokers/tobacco chewers and alcoholics were more in non-diabetic group compared to the diabetic group. Both the addictions were present in total 43 subjects (24 diabetics and 19 non-diabetics).

Cigarette smoking/Tobacco chewing and Alcohol consumption are independent and modifiable risk factors of diabetes. They are risk factors for many diseases like Chronic Obstructive Pulmonary disease, Stroke, Ischaemic Heart disease, Malignancy, etc which may cause critical illness requiring intensive care.[13,14]

DURATION OF DIABETES IN THE STUDY SUBJECTS

In this study, majority of the critically ill patients with T2DM were having the disease for less than 10 years (85%). T2DM is a multisystem illness that, as it progresses, is linked with the development of microvascular and macrovascular complications that impair the quality of life of patients and increase diabetes-related morbidity and death.[15]

The influence of pre-existing DM on ICU patient outcomes is mediated by intricate pathophysiological pathways. Long-term diabetes mellitus would result in microvascular alterations and impairment, which would lead to reduced oxygen supply and organ failure.[16] On the other hand, the microvascular dysfunction associated with diabetes generates chronic hypoxia that results in tissue preconditioning, which may contribute to increased resistance to acute ischemia episodes.[17]

Conversely, the microvascular dysfunction associated with diabetes produces chronic hypoxia that leads in tissue preconditioning, which may contribute to enhanced resistance to acute ischemia events.[18,19] A study done by Dart AB et al., showed that young age was not at all protective against the multisystem effects and complications of T2DM, and the time to develop these complications was same as that in the elderly.[20]

OTHER CO-MORBIDITIES

In our study, the most common observed co-morbidity was hypertension (27.5% and 25% respectively) in both the study groups. Other co-morbidities were ischemic heart disease (7.6%) followed by thyroid diseases (6.3%) and chronic obstructive pulmonary diseases (COPD) (2.6%). In a study done by Iglay K et al., in the United States on 1,389,016 patients with T2DM,

the most common co-morbidities included obesity (78.2%), hypertension (82.1%) and hyperlipidaemia (77.2%). Chronic kidney disease (24.1%), and cardiovascular disease (21.6%) were few other co-morbid conditions.[21]Chronic diseases, such as COPD, T2Dm, Hypertension, malignancies etc. have long term and persistent effects often leading to frequent hospitalisations due to complications. Presence of co-morbid conditions in a critically ill patient may be the cause of prolonged ICU stay and adds to the health care burden.[22]

The prime example of this fact has recently been corroborated during the Covid-19 pandemic where several studies have indicated that the presence of T2DM and other chronic conditions like hypertension, chronic respiratory, cardiac and renal diseases, and cancer had a significantly higher mortality compared to those without these co-morbidities.[23,24]

DURATION OF ICU STAY

Among the T2DM group, 18 of 80 patients stayed for more than 7 days in the ICU (22.5%) whereas only 5% of non-diabetic patients stayed for more than 7 days in the ICU which was significantly different. Thus, the presence of a chronic disorder like T2DM prolonged the hospital stay which may in turn adversely affect the outcome of the patients due to increased risk of nosocomial infections.

Chronic hyperglycemia is known to be connected with higher mortality and morbidity in diabetic individuals.[25] The effect of hyperglycemia on the mortality rate of hospitalised critically sick patients is becoming more recognised.

However, the findings of the current study showed that the death rate was significantly higher (21.3% vs 8.2%) in diabetic than non-diabetic group critically ill patients (p=0.046). This was similar to a study conducted in the United States on 2030 severely sick individuals.[26]

In current study the overall mortality rate was 15% among all the study subjects (n = 160). However, the mortality rate did not depend on the length of the ICU stay in diabetic patients (Fischer exact test $P > 0.05$). In a US study on critically ill patients in the medical ICU, T2DM patients who had a tight glucose control (Glucose < 180 mg/dL) had lower mortality rate. Also the Suboptimal glycaemic control during the ICU stay significantly increased the odds of prolonged hospital stay.[27]

BLOOD PARAMETERS AMONGST STUDY SUBJECTS

On comparison of mean values of biochemical parameters in the two groups on the day of admission to the ICU, following were the findings: The haemoglobin and Liver function tests (LFT) were comparable between the groups (p value >0.05). Total leukocyte counts (TLC) were significantly higher, renal function tests (RFT) were worse; Serum Albumin, PT-INR, serum Sodium and Potassium were significantly lower in T2DM group compared to the controls. Serum Lactate levels and Serum procalcitonin were statistically significantly higher in diabetics (p value <0.05). All the parameters of Arterial Blood gas analysis (ABGA) and the Glasgow Coma Scale (GCS) on day one of ICU admission were comparable between the two groups ($p > 0.05$). However, the vital parameters (Temperature, Pulse, Respiratory rate, Blood pressure and Mean arterial pressure) were statistically significantly different between the patients with and without T2DM (Student T test p value < 0.05).

T2DM is an immunocompromised state thus, increasing the incidence of infections. Hyperglycaemia promotes immunological dysfunction, resulting in damage to the humoral and cell-mediated immunity and predisposes the patients to various skin and soft tissue infections, Urinary tract infections, pneumonias etc. Thus, the TLC, serum lactate and serum pro-calcitonin which are markers of infection may have been higher in the diabetic group in our study compared to non-diabetic patients.

According to epidemiological research, poorly managed diabetes is a risk factor for a variety of infectious illnesses. Among the co-morbidities linked with greater morbidity and death in COVID-19 infections, diabetes stands out. Several variables, including co-morbidities (hypertension, obesity, and cardiovascular illnesses), altered ACE2 receptor expression, immunological dysregulation, alveolar and endothelial dysfunction, and enhanced systemic coagulation, may be to blame.[28]

ABGA, which measures the blood pH, partial pressure of CO_2 and O_2, and bicarbonate levels, is an essential diagnostic test in all critically ill patients and especially in diabetics who often have acid-base imbalance due to uncontrolled hyperglycaemia.[29] In a 2016 research conducted in Turkey on diabetic patients having cardiac surgery, it was shown that intra-operative glucose management did not have an effect on arterial blood gas parameters, serum electrolytes, or haemoglobin when compared to traditional glucose control.[30] In our study, the ABGA and Haemoglobin values were not significantly different between T2DM and non-diabetic groups however, the serum electrolytes were significantly different between the groups.

SCORING SYSTEMS TO PREDICT MORTALITY

With so many scoring systems to determine the prognosis of critically ill patients, it is imperative to know which scoring system is better in T2DM patients. In our study we tried to compare the predictability of mortality among T2DM and non-T2DM patients admitted to ICU using APACHE IV, SAPS3, SOFA and MODS scores and through AUC under the ROC curves.

When the mean values of different scores on the day of admission were compared between the cases and the controls, except SAPS3 (Student T test $p > 0.05$) all the other scores (APACHE IV, SAPS3 and SOFA) were significantly worse in T2DM patients compared to those without T2DM (Student T test p value <0.05).

Also, all the scores except MODS done on day 1 were significantly higher in the T2DM patients who eventually died compared to the patients who survived. All the scores in T2DM patients were significantly worse on the day of outcome in patients who died compared to those who survived ($p < 0.05$).

APACHE IV score on day 1 had the highest predictability for mortality in critically ill T2DM patients (AUC of 0.873, at 95% confidence interval; 0.792-0.955, $p<0.05$). Rest of the scores (SAPS3, SOFA and MODS) had low predictability for mortality ($p>0.05$).All the above mentioned scores have been used to predict mortality in critically ill but to our knowledge, no studies have been done till date to test predictability exclusively in critically ill diabetes patients. In our study, among various scoring systems, the APACHE IV score was superior to other scores in predicting in-hospital mortality in critically ill in diabetic subjects.[31]

CONCLUSION

In conclusion clinical severity scoring systems are widely used in intensive care, and when applied to the populations for whom they were designed and validated, they may influence mortality prediction, risk stratification, resource usage, and optimization of patient outcomes.

In our study also we tried to find out predictability of mortality during hospital stay among diabetic critically ill patients using different scoring system.

Study concludes that APACHE IV has a good predictability over SAPS III, SOFA and MODS in critically ill T2DM patients. There is need to conduct multicentric large cohort study for generalisation of our study findings.

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