

**CONTRIBUTION OF EARLY HYPERGLYCEMIA AND HYPOALBUMINEMIA TO MULTIPLE ORGAN DYSFUNCTION SYNDROMES (MODS) IN MULTITRAUMA PATIENTS**

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**Background:** Recent randomized prospective data suggest that early hypoglycemia and hypoalbuminemia are associated with MODS in multitrauma patients. **Objective:** this study was to determine the contribution of early blood glucose elevation and decrease serum albumin in Trauma Emergency Department or ICU patients. **Methods:** We prospectively collected multitrauma patients with Injury Severity Score (ISS)  $\geq 18$ , blood glucose, serum albumin, between 14 – 81 years old, admitted to level I Trauma Centre at Kandou General Hospital Manado for eleven months periods from September 2015 until July 2016. Sequential Organ Failure Assessment (SOFA) Score was used to determine MODS during hospitalization. **Results:** A total of 51 multitrauma patients were included in this study. The mean age was 31.73 years old, male 41(80.4%) and female 10(19.6%). Serum glucose level  $> 126$  mg/dl occurred in 34 (66.7%) patients and  $\leq 126$  mg/dl occurred in 17 (33.3%) patients. Serum albumin level  $< 3,5$  gr/dl occurred in 31 (60.8%) patients and  $\geq 3,5$  gr/dl occurred in 20 (39.2%) patients. **Conclusion:** Early hyperglycemia as defined by glucose  $>126$ mg/dl and hypoalbuminemia as defined by albumin  $<3,5$ gr/dl are associated with significantly higher MODS rates in multitrauma patients independent of injury characteristics. The present of early hyperglycemia and hypoalbuminemia may allow early identification of trauma patients who are at risk for MODS.

**Keywords:** Multitrauma, Hyperglycemia and Hypoalbuminemia, MOD

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**INTRODUCTION**

Recent randomized prospective data suggest that early hypoglycemia and hypoalbuminemia are associated with MODS in multitrauma patients. The Objective of this study was to determine the contribution of early blood glucose elevation and decrease serum albumin in Trauma Emergency Department or ICU patients. The aim of this study is to construct an instrument to predict the development of MODS in Multitrauma patients using clinical and laboratory data available in the first day at emergency department (Hospital) setting.

Hyperglycemia and hypoalbuminemia occurs commonly in critically ill patients and

associated with significant morbidity and mortality in them. The relationship between hyperglycemia, hypoalbuminemia and poor outcome is even more pronounced after traumatic injury compared with critically ill patients admitted for other reasons. The stress response after acute injury promotes insulin resistance and an overall hyperglycemic state, secondary to the acute effects of corticosteroid, growth hormone, glucagon, and catecholamine release. The level of hyperglycemia soon after trauma event is thought to correlate with the severity of injury a patient sustains.<sup>1,2,3</sup> In the other hand, trauma can lead to a cytokine response, which increases vascular permeability, dilutes serum albumin from infusions and accelerates the removal of albumin from the circulation.<sup>4,5</sup> Hyperglycemia and hypoalbuminemia in trauma patients have long been reported to be an independent predictor of increased morbidity and mortality.<sup>4,5,6,7</sup>

**METHODS**

We prospectively collected multitrauma patients with Injury Severity Score (ISS)  $\geq 18$ , blood glucose, serum albumin, between 14 – 81 years old, admitted to level I Trauma Centre at Kandou General Hospital Manado for eleven months periods from September 2015 until July 2016. Admission serum glucose and serum albumin values were obtained on each patient. Patients were than stratified by serum glucose level  $\leq 126$  mg/dl vs.  $> 126$  mg/dl and serum albumin level  $\geq 3,5$  gr/dl vs.  $< 3,5$  gr/dl. Patients with preinjury diagnosis of diabetes mellitus were excluded from the analysis of this study to minimize the overlap and confusion between acute stress hyperglycemia and diabetic hyperglycemia. Because we did not measure hemoglobulin A1c level in our patients, it is possible that we may have included those patients with previously undiagnosed diabetes mellitus. Medical history was obtained directly from the patient or from the family if the patient was unable to be interviewed. Patients had chronic illness as comorbidities, previous mayor trauma with or without surgery were excluded. The study had ethical clearance approved by education and ethics review board.

Sequential Organ Failure Assessment (SOFA) Score was used to determine MODS during hospitalization. The diagnosis of MODS was made based on the SOFA score criteria. SOFA identifies organ dysfunction and failure across six organ system. SOFA consists of measures of PaO<sub>2</sub>/FIO<sub>2</sub> ratio (respiration system), platelet count

(hematology system), GCS (central nervous system), mean arterial pressure and inotropic (cardiovascular system), urine output and creatinine level (renal system) and total bilirubin (liver-digestive system). The occurrence of MODS is defined as a SOFA score of 1 or 2 points and MOF as a SOFA score  $\geq 3$  in at least 2 organ systems.<sup>10</sup> We used X<sup>2</sup> or fisher exact test model to determine level of significance and odd ratio in determine of risk estimate.

**RESULTS**

A total of 51 multitrauma patients were included in this study. The mean age was 31.73 years old, male 41 (80.4%) and female 10 (19.6%). The majority 48 (94%) patients of admission due to traffic accident the remainder 2 (4%) patients were due to fall from height and 1 (2%) patient was due to penetrating injury (criminal Violence) (see table 1).

**Table 1.** Demographic and characteristics of the study sample

Characteristics	f	%
<b>Sex</b>		
Male	41	80.4%
Female	10	19.6%
<b>Cause</b>		
Traffic accident	48	94%
Criminal violence	1	2%
Fall from heights	2	4%
<b>Total</b>	51	100%

**Table 2** Glucose \* MODS cross tabulation

Glucose	MODS		Total	X <sup>2</sup> Test
	Positive	Negative		
$> 126$ mg/dl	30 (78.9%)	4 (30.8%)	34(66.7%)	X <sup>2</sup> = 10.117 (P<0,001)
$\leq 126$ g/dl	8 (21.1%)	9(69.2%)	17 (33.3%)	
<b>Total</b>	38 (100.0%)	13 (100.0%)	51(100.0%)	

**Table 3** Albumin \* MODS cross tabulation

Albumin	MODS		Total	X <sup>2</sup> Test
	Positive	Negative		
$< 3,5$ gr/dl	30 (78.9%)	1 (7.7%)	31 (60.8%)	X <sup>2</sup> = 20.632 (P<0,001)
$\geq 3,5$ gr/dl	8 (21.1%)	12 (92.3%)	20 (39.2%)	
<b>Total</b>	38 (100.0%)	13 (100.0%)	51(100.0%)	

From all multitrauma samples, Serum glucose level > 126 mg/dl occurred in 34 (66.7%) patients and ≤ 126 mg/dl occurred in 17 (33.3%) patients. Serum albumin level < 3,5 gr/dl occurred in 31 (60.8%) patients and ≥ 3,5 gr/dl occurred in 20 (39.2%) patients. Serum glucose level > 126 mg/dl developed MODS occurred in 30 (78.9%) patients and ≤ 126 mg/dl occurred in 8 (21.1%) patients and remainder had no MODS. Serum albumin level < 3,5 gr/dl developed MODS occurred in 30 (78.9%) patients and ≥ 3,5 gr/dl 8 (21.1%) patients and remainder had no MODS (see table 2).

Patient's glucose in the > 126 mg/dl had a significantly higher rate of MODS than patient's glucose in the ≤ 126 mg/dl. MODS had significantly higher glucose level at admission and during the 24 hour of admission ( $p < 0,001$ ) statistically significant. Risk estimate odds ratio [OR]=8.438 (95% confidence interval [CI]:2.05-34.6). Patients albumin in the < 3,5 gr/dl had a significantly higher rate of MODS than patients albumin in the ≥ 3,5 gr/dl. MODS had significantly lower albumin level at admission and during 72 hour of admission ( $p < 0,001$ ) statistically significant. Risk estimate odds ratio [OR] = 45.000 (95% confidence interval [CI]:5.06-399.68).

## DISCUSSION

The present of early hyperglycemia and hypoalbuminemia may allow early identification of trauma patients who are at risk for MODS and result in more aggressive targeted resuscitation and better referral allocation based on regional trauma system. Early hyperglycemia as defined by glucose > 126 mg/dl and hypoalbuminemia as defined by albumin < 3,5 gr/dl are associated with significantly higher MODS rate in multitrauma patients independent of injury characteristic.

However, these results suggest that early hyperglycemia is a marker of severe physiologic derangement post injury, with a higher mortality risk attributable to MODS.

These results are in contrast to previous studies, where early hyperglycemia has been shown to be associated with a higher mortality in patients after injury. Sung et al. showed in a prospective analysis on 1.003 consecutive trauma patients a three fold higher risk of overall infectious complications in patients with early hyperglycemia. Similarly, Yendamuri et al. found that early hyperglycemia was independently associated with a threefold higher risk of pneumonia and urinary tract infection (UTI).<sup>8,9</sup>

Albumin is an abundant plasma protein that is thought to have a stabilizing effect on the endothelium and help maintain capillary permeability to micro molecules. Serum albumin

level however can also change in altered conditions such as dehydration, sepsis, trauma and liver disease irrespective of nutritional status. The stress associated with surgery or trauma increase protein and energy requirements by creating a hyper metabolic, catabolic state. This can thus lead to the onset of protein calorie malnutrition within a few days.<sup>4,5</sup>

Hypoalbuminemia in the medical population also had a greater risk of infective complications and poor functional outcome during hospitalization than those with normal or higher serum albumin concentrations. In a small retrospective matched pair study, involving 51 hospital emergency department admission hypoalbuminemia in blunt trauma patients was shown to be an independent predictor of delayed mortality: patients with albumin levels < 3,4 gr/dl were 2,5 times more likely to die compared to patients with normal albumin levels.<sup>6,7</sup>

## CONCLUSION

Hyperglycemia and hypoalbuminemia are associated with significantly higher MODS rates in multitrauma patients. The present of early hyperglycemia and hypoalbuminemia may allow early identification of trauma patients who are at risk for MODS and result in more aggressive targeted resuscitation and better referral allocation based on regional trauma system. Further studies are needed to determine whether an anti-inflammation used shall prevent hypoalbuminemia.

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