

## Measures of Risk for Sepsis and Mortality in Severe Burned Patients with Stress Induced Hyperglycemia

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### Abstract

**Background:** Hyperglycemia as a medical condition due to diabetes or other underlying conditions like Stress-Induced Hyperglycemia and sepsis as a life-threatening medical condition are two of the challenges faced during burn treatment.

**The purpose** of this study was to evaluate the risk for sepsis and mortality for the patients with critical hyperglycemic values during the disease.

**Material and Methods:** This is an observational retrospective cohort study conducted in the Service of Burns of the University Hospital Centre "Mother Teresa" in Tirana (UHCT), Albania from 1st January 2010 to 31st December 2014. Patients were categorized as having euglycemia (mean BG values ranging from 80-120 mg/dl), moderate hyper Sepsis was defined according to the ABA Consensus Panel Publication for Infection and Sepsis glycemia (mean BG values <180 mg/dl) or critical hyperglycemia (mean BG values ≥180 mg/dl). to evaluate the impact of the presence of critical hyperglycemia during the disease in sepsis and mortality, we performed Relative risk, Odds ratio

**Results:** Those who had overall hyperglycemia (Moderate and Critical) had 2.6 times the risk for sepsis compared to those who were in the euglycemia group. Analyzing the risk of mortality in patients with overall hyperglycemia during the disease, we observed that the chance of a bad outcome was 2.7 times more likely to occur if the patient had hyperglycemia (RR=2.7).

**Conclusions:** Glucose values on admission, as one of the derangement features of burn shock, are prognostic factors in critical hyperglycemia during burn disease and have a close relationship with other outcomes (sepsis and mortality).

**Keywords:** Burns, Hyperglycemia, Sepsis, mortality.

### Introduction

The stress response relating to critical illness refers to the systemic response to severe injury or infection. Severe burns covering more than 40% of Total Body Surface Area (TBSA) are typically followed by a period of stress, inflammation and hypermetabolism. During this period, we can observe a hyperdynamic circulatory response with in-

creased body temperature, glycolysis proteolysis and futile substrate cycling. The hyperglycemic condition from dys-regulated glucose homeostasis has been defined stress hyperglycemia. Patients with severe burns experiencing a kind of trauma undergo, among others, disturbances in glucose homeostasis, possibly leading to Stress Induced Hyperglycemia (SIH) [1]. Hyperglycemia as a medical condition due to diabetes or other underlying conditions like SIH and sepsis as a life-threatening medical condition are two of the challenges faced during burn treatment.

The purpose of this study was to evaluate the risk for sepsis and mortality for the patients with critical hyperglycemic values during the disease.

### Material and Methods

This was an observational retrospective cohort study conducted in the Service of Burns of the University Hospital

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Centre “Mother Teresa” in Tirana (UHCT), Albania. UHCT is a tertiary level hospital in Albania. The study was approved by the Institutional Board of the Ministry of Health and Social Support.

We observed adult burn patients ( $\geq 20$  years old) admitted to the ICU of the Burn Service in the UHCT from 1st January 2010 to 31st December 2014. Children and non-burn related admissions (Stevens-Johnson/toxic epidermal necrolysis, necrotizing fasciitis and chronic wounds) were excluded from the study.

Patients were categorized as having euglycemia (mean BG values ranging from 80-120 mg/dl), moderate hyperglycemia (mean BG values  $<180$  mg/dl) or critical hyperglycemia (mean BG values  $\geq 180$  mg/dl) [2]. Patients with critical hyperglycemia during burn disease were treated according to the insulin regimen: basal-bolus therapy with a correctional insulin scale, with a total daily dose of 0.3-0.5 unit/kg/day.

Sepsis was defined according to the ABA Consensus Panel Publication for Infection and Sepsis [3].

### Statistical Analysis

The normally distributed continuous data are reported as the mean + standard deviation and analyzed using One-way ANOVA. The categorical data are expressed as frequency distributions and the z-score was used to determine whether differences existed between two population proportions. Outcome Cross tabulations are done for Sepsis and Glucose Values. In order to answer our clinical question: to evaluate the impact of presence of critical hyperglycemia during the disease in sepsis and mortality, we performed Relative risk, Odds ratio. SPSS 23 was used for statistical analysis. Values were considered significant with  $p < 0.05$ .

### Results

A total of 785 patients including children were admitted to our facility over the period of study. Three hundred and forty-six (44%) were adults. Fifty of these 346 patients died. Overall mortality was 14.5%. Mean length of stay (LOS) in hospital was  $14.1 \pm 17.1$  days. Mean age was  $48.6 \pm 16.9$  years old. Categorization according to BMI revealed a normal distribution, peaking in the overweight group (BMI range 25-29.9 kg/m<sup>2</sup>) with 154 patients (44.5%) (Table 1).

On admission there were 144 patients or 41.6% with euglycemia, 148 patients or 42.8% with moderate hyperglycemia and 54 patients or 15.6% with critical hyperglycemia. During the disease from the total number 204 were with euglycemia, 118 with moderate hyperglycemia and only 24 or 7% were with critical hyperglycemia. The last group of patients was treated with insulin according the service protocols. Observing the 24 patients who presented critical hyperglycemia during burn disease, 2 (8.3%) of them had normal glucose values on admission; 6 (25%) had moderate hyperglycemia on admission, while only 16 (66.7%) of them had critical values on admission. On the other hand, observing the 54 patients with critical hyperglycemia on admission, 16 (29.6%) had critical BG values during disease, 26 (48.1%) had moderate BG values during disease and only 12 (22.3) had normal BG values during disease.

Patients belonging to the critical hyperglycemia group had a mean BSA of  $39.3 \pm 23.05\%$ . There was a predominance of full-thickness burns in 19 patients (79.2%). Sepsis occurred in 90 patients, and prevalence of sepsis in adult burn patients in our center was 26%. Of the 90 patients with sepsis, 32 (36% of 90) had normal BG values during burn disease, constituting 15.7% of the euglycemic group ( $n=204$ ), 44 patients or almost 50% had moderate values

Table 1 - Demographic data for adult and elderly patients with severe burns

Variables	All patients (n=346)	Euglycemia (n=204)	Moderate Hyperglycemia (n=118)	Critical Hyperglycemia (n=24)	P-value
Age, years, mean (SD)	48.6 (16.9)	46.2(17)	51.5 (16.2)	55.8 (15.9)	0.002
Glucose values on admission, mg/dl, mean (SD)	149 (57.9)	129.4 (39.1)	162.7 (48.4)	248.4 (100.4)	<0.001
Glucose values on admission % (n)					
Euglycemia	41.6(144)	58.8 (120)	18.6(22)	8.3(2)	<0.001
Moderate Hyperglycemia	42.8(148)	35.3(72)	59.3(70)	25(6)	
Critical Hyperglycemia	15.6 (54)	5.9 (12)	22 (26)	66.7(16)	
BSA%, mean (SD)	31.8(23)	26.3 (18.4)	39.8 (27.2)	39.3 (23.05)	<0.001
Predomination of full-thickness (yes)	78.6(272)	73.5 (150)	87.3 (103)	79.2(19)	0.015
Presence of sepsis (yes) % (n)	26 (90)	15.7(32)	37.3(44)	58.3(14)	<0.001
LOS, days, mean (SD)	14.1 (17.1)	11.2(13)	16.2 (16.9)	28.9 (33.5)	<0.001
Mortality, deaths % (n)	14.5 (50)	8.3 (17)	24.6(29)	16.7(4)	<0.001

Table 2 - Relative risk for sepsis and mortality according glucose values categorization (during the disease)

Sepsis (n = 90)					
Glucose values categorization	No	Yes	Relative Risk	Odds Ratio (95% CI)	p value
Euglycemia (n=204)	172	32	1.0 (reference)		
Moderate Hyperglycemia (n=118)	74	44	2.3	1.6 to 3.5	<0.0001
Critical Hyperglycemia (n=24)	10	14	3.7	2.3 to 5.9	<0.0001
Overall hyperglycemia	84	58	2.6	1.7 to 3.7	<0.0001
Mortality (Deaths) (n=50)					
Glucose values categorization	No	Yes	Relative Risk	Odds Ratio (95% CI)	p value
Euglycemia (n=204)	187	17	1.0 (reference)		
Moderate Hyperglycemia (n=118)	89	29	2.9	1.6 to 5.1	0.0002
Critical Hyperglycemia (n=24)	20	4	2	0.7 to 5.4	0.1759
Overall hyperglycemia	109	33	2.7	1.6 to 4.8	0.0002

during burn disease constituting 37.3% of the moderate group (n=118) and 14 patients or 15% had critical values during burn disease constituting 58.3% of the critical group.

Analyzing outcomes (sepsis and mortality) in patients with overall hyperglycemia during the disease (84 patients), we calculated Relative Risk and Odds Ratio (Table 2).

Those who had overall hyperglycemia (Moderate and Critical) had 2.6 times the risk for sepsis compared to those who were in euglycemia group. The risk for sepsis of patients with critical hyperglycemia among those with overall hyperglycemia was 3.7 times as high as the risk of sepsis among those who did not have critical hyperglycemia.

The risk for mortality for patients with overall hyperglycemia was 2.7 times the risk for mortality to the patients with euglycemia during the disease. It was the same as for patients with moderate hyperglycemia and with critical hyperglycemia (No statistical significance).

## Discussion

Homeostasis is the maintenance of a stable internal environment in an organism through careful regulation of many parameters, including maintaining blood glucose levels within the narrow range of 60–120 mg/dl. Patients with severe burns experience one of the most severe disruptions of homeostasis. Clinical situations associated with glucose homeostasis disorders are previous diagnosis of diabetes, SIH and relative deficiency of insulin in the preoperative period. Based on many studies, hyperglycemia might have different biological or clinical implications and has been associated with an increased risk of adverse outcomes [4, 5, 6].

A significant proportion of mortality and morbidity in severely burned patients with SIH is attributable to hypermetabolic response [7, 8]. Results of various studies researching altered metabolism and the role of insulin in the treatment of burn patients indicate that improvement in BG

levels results in lower rates of hospital complications and mortality [9, 10, 11, 12, 13, 14].

In this clinical and epidemiological study, we have tried to assess the effect of critical hyperglycemia on admission as a real forerunner on outcome (sepsis and mortality) in adult patients with severe burns.

Analyzing sepsis and its distribution in the three groups of patients, we noticed that sepsis (n=90) was present in 32 patients (35.6%) in the euglycemic group, in 44 patients (48.8%) in the moderate hyperglycemic group and in 14 (15.6%) in the critical hyperglycemic group. We noticed that the majority of patients with sepsis (58 out of 90 patients or 64.4%) had hyperglycemia during disease. While analyzing sepsis within each group, we noticed differences. In the euglycemic group composed of 204 patients, there were 32 (15.6%) patients diagnosed with sepsis; in the moderate hyperglycemic group of 118 patients, 44 (37.2%) had sepsis; and in the critical hyperglycemic group of 24, 14 (58.2%) had sepsis. We noticed that sepsis was present in the majority of patients with critical hyperglycemia, which is consistent with recent studies [7].

Analyzing sepsis and the risk of developing it in patients with critical hyperglycemia during the disease, we observed a relative risk of 3.7, meaning that the chance of sepsis is 270% higher if the patient presents with critical hyperglycemia during the disease. An OR of 1.7 indicates that the odds for sepsis are higher in the group with overall hyperglycemia (Moderate and critical) (Odds Ratio >1). In absolute values that would mean that the incidence of sepsis is 30% smaller in the group without hyperglycemia during the disease.

Analyzing mortality, we noticed that out of 50 deaths in total, 17 (34%) were patients with euglycemia, 29 (58%) were patients with moderate hyperglycemia and only 4 (8%) were in the critical hyperglycemic group. If we look at mor-

tality as the proportion of deaths within groups, we notice that the highest mortality 24.6% (29 deaths) was in the moderate hyperglycemic group, followed by 16.7% (4 deaths) in the critical hyperglycemic group and the lowest values, 8.3% (17 deaths), in the euglycemic group.

Analyzing the risk of mortality in patients with overall hyperglycemia during the disease, we observed that the chance of a bad outcome was 2.7 times more likely to occur if the patient had hyperglycemia (RR=2.7). With an OR of 2.0 for patients with critical hyperglycemia and 2.9 for patients with moderate hyperglycemia, we concluded that the odds for a bad outcome were higher but similar within groups (OR>1). On the other side we have noticed that there was no statistical significance for patients in critical hyperglycemia group because these patients were treated with insulin which can serve as a therapeutic agent in patients with burns and plays an important role in prognosis of severe burn patients

## Conclusions

Glucose values on admission, as one of the derangement features of burn shock, are prognostic factors in critical hyperglycemia during burn disease, and have a close relationship with other outcomes (sepsis and mortality). Testing for critical hyperglycemia in the first 24 hours of admission should be done with caution to predict a probable critical hyperglycemic event during the course of burn disease.

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## Conflict of Interest Statement

There is no conflict of interest

## Authorship Contribution

The first author has done the conception or design of the work and data collection and analysis.

The second author has done the data analysis and interpretation as well as drafting the article and critical revision of the article.

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