Investigation of glucose, serum insulin levels, and insulin resistance in patients with major burn: a retrospective cross-sectional study

- Yavuz Yakut, Pt, PhD.,¹

ABSTRACT

BACKGROUND: Many studies have reported that insulin resistance (IR) is present and persistent in patients with major burns; however, the evidence remains insufficient. This study was planned to investigate insulin levels and IR in the early post-traumatic period in patients with major burns and to determine the prevalence of IR after burn injury.

METHODS: This study included 68 patients. These patients were followed up once a week for 4 weeks after hospitalization. In the follow-up examinations, demographic and burn injury characteristics; HbA1c, procalcitonin serum glucose, and insulin levels; and IR were evaluated.

RESULTS: IR was seen in some weeks only in 25 of the 68 patients included in the study. Among all patients, IR was determined in only 11 (16.17%) patients from the 1st day of hospitalization until discharge. Patients with and without IR were evaluated as 2 groups, and their biochemical parameters were compared, and no significant difference was found between glucose and procalcitonin levels (P>0.05). Glucose levels were >100 mg/dL in the first few weeks in all patients who were followed up; however, they returned to the normal range in the following weeks.

CONCLUSION: In patients with IR, there was insufficient evidence to conclude that the condition persists. We believe that the HOMA-IR value is not directly related to burn injuries and that other additional pathologies may cause it during treatment.

Keywords: Burns; Glucose metabolism; hyperglycemia; hypermetabolic state; insulin resistance.

INTRODUCTION

After a major burn, pathophysiological responses, such as inflammation, muscle loss, disruption of the glucose system, and hypermetabolism, that affect all organs occur, and these changes may last for 2–3 years.^[1,2] Hypermetabolism after burns is a major clinical issue. In patients with a burn area of ≥20%, all systems of the body create a metabolic response to this injury. This hypermetabolic response consists of two phases. The "ebb" phase is observed during the first 1–3 days after the burn. Similar to a short-term "fight or flight" re-

sponse, there is a decrease in tissue perfusion and a temporary drop in metabolic rate. This decrease can also be seen in organ function and blood flow rate. This is followed by the "flow phase," which is characterized by increased superficial tissue perfusion, adrenergic stress, glucocorticoid levels, and inflammatory cytokine levels. In response to severe burn injuries, changes in hormone and cytokine levels activate many energy-dependent biochemical processes.^[2]

Hypermetabolism causes a high demand for energy at the cellular level. To meet this intense energy need, glycolysis, gly-

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cogenolysis, gluconeogenesis, lipolysis, and proteolysis may increase after burn injuries. There are studies in the literature that report persistent hyperglycemia in both pediatric and adult burn patients after discharge from the intensive care unit.[3] Insulin resistance (IR) and hyperglycemia cause delayed wound healing and muscle catabolism. High cortisol and catecholamine levels inhibit insulin's anabolic functions by increasing glucose delivery to vital organs. Catecholamines inhibit both insulin secretion and glucose uptake, impairing glucose excretion and causing peripheral IR. In addition, proinflammatory cytokines such as glucagon and interleukin-6 play a role in modulating glycogenolysis, gluconeogenesis, and insulin signal transduction, which increase hyperglycemia and IR.[3] Studies and reviews in the literature indicate that the hypermetabolic response that occurs after burns leads to the deterioration of glucose metabolism mentioned above and persistent IR.[4-7] Most studies in the literature have focused on pediatric patients. [4-7] Therefore, the present study aimed to investigate serum insulin levels and IR in adult patients with severe burns as well as determine whether insulin levels are influenced by other additional pathologies or factors. Another aim of this study was to provide a different perspective on the changes in insulin levels after a burn injury, determine the prevalence of IR after a burn injury, and contribute to the literature on this subject.

MATERIALS AND METHODS

Patients aged 18 years and older who were considered to have major burns according to the American Burn Association classification and who were not unconscious were included in the study. [8] Patients with other conditions besides burn injury (e.g., inhalation injury, sepsis), which could affect the evaluation processes of the study, were excluded from the study.

The patients were tested for Glycosylated hemoglobin A1c (HbA1c) on the 1st day, as it may affect their insulin levels and IR. Patients with HbA1c values above normal limits were not included in the study.

The nutritional types and diets of all patients were similar in all groups. All patients received similar medical care and surgical interventions from their first admission to the hospital until discharge. Data for this retrospective cross-sectional study were obtained from the electronic health records of the 25 Aralik State Hospital Burn Center (intensive care unit and service ward).

This study included 92 patients with major burns. The data of 24 patients with HbA1c values above normal limits were excluded from the study. Data from 68 patients were evaluated in the study. All patients in this study were assessed from their first admission to the hospital until discharge. (Since all patients were discharged at 4 week, the 1st day and 4-week values were recorded. Patients who had to stay in the hospital longer than 4 weeks were not included in the study be-

cause it could affect the homogeneity of the study).

Glycosylated hemoglobin AIc (HbAIc) levels, serum glucose levels, insulin levels, IR, and procalcitonin biochemical values of patients in all groups were recorded weekly from the 1st day of hospitalization. The HOMA-IR parameter, which is widely used in the clinic and has high reliability, was used for the IR of the patients included in the study.^[9]

Biochemical parameters were measured in the 25 Aralık State Hospital Laboratories. Both the initial and weekly values of the measured parameters were recorded.

Statistical Analysis

SPSS 24.0 for Windows was used for the data analysis of this descriptive cross-sectional study. A value of P < 0.05 was considered statistically significant. In descriptive analyses, variables determined by numerical measurements were expressed as arithmetic averages and standard deviations (mean \pm SD). The Kolmogorov-Smirnov test was used to investigate the normal distribution of biochemical parameters. The Student's t-test was used because the data had a normal distribution. The Spearman correlation test was used to investigate the correlation between the data. Binary logistic regression was performed to determine why IR continues in patients.

Ethical Approval and Consent to Participate

Ethics approval for this study was obtained from the Hasan Kalyoncu University Health Sciences Non-Interventional Research Ethics Committee (approval was obtained on December 18, 2018, with the decision number 2018–48). All patients included in the study were informed about the study, and they signed a consent form.

RESULTS

The study included 68 patients (20 females and 48 males). Patients ranged in age from 18 to 65 years. When the burn injuries of the patients were evaluated, it was found that 51 (75%) had flame burns and 12 (17.6%) had electrical burns. Furthermore, all groups had burn injury percentages ranging from 20% to 85% (Table 1).

While IR was seen in some weeks only in 25 of the 68 patients included in the study (Fig. I), the incidence of IR by week is also shown in Figure 2. Among all patients, IR was determined only in 11 (16.17%) patients from the 1st day of hospitalization until discharge (Fig. 3).

Patients with and without IR were evaluated as two groups, and their biochemical parameters were compared (Table 2). While insulin levels were higher in patients with IR (P<0.05), no significant difference was found between glucose and procalcitonin levels (P>0.05) (Table 2). While glucose levels decreased in both groups, no significant difference was found between the groups (Table 3) (P>0.05). It was determined that insulin levels decreased in the group with IR (Table 3).

Glucose levels were >100 mg/dL in the first few weeks in all

Table I.	Characteristics	of potionts	with hum	iniumiaa
Table I.	Characteristics	of patients	with burn	iniuries

	All patients n=68	Patients with IRa n=43	Patients without II n=25
Age (years) (X±SDb)	34.5±15.6	32.16±18.07	34.3±13.6
(Min–Max)	18–65	18–65	18–61
Gender n (%)			
Female	20 (29.41)	10 (23.25)	10 (40)
Male	48 (70.59)	33 (76.25)	15 (60)
Burn type n (%)			
Flame	51 (75)	30 (69.7)	21 (84)
Electric	12 (17.6)	9 (20.9)	3 (12)
Scalding	4 (5.8)	3 (6.9)	I (4)
Chemical	l (l.6)	I (2.5)	0
Burn Percentage			
(X±SD)	32.8±11.8	35.11±12.6	31.8±11.7
(Min–Max)	20–85	20–85	20–55

patients who were followed up; however, they returned to the normal range in the following weeks (Fig. 4).

There was a weak correlation between IR, the percentage of burns, and procalcitonin levels (Table 4). On the other hand,

in the binary logistic regression analysis performed to determine why IR persisted in 11 patients, no significant relationship was found (Table 5).

Table 2. Comparison between HOMA-IR with patients and without HOMA-IR with patients n=68

	Patients without HOMA-IRa n=25 X±SDb	Patients with HOMA-IR n=43 X±SD	t	P-value	
Weight	72.20±5.95	73.37±8.91	-0,500	0.619	
Glucose-0	108.12±2.60	II6.26±33.32	-1.063	0.292	
Glucose I	98.48±12.26	101.58±21.28	-0.666	0.508	
Glucose2	97.24±14.52	99.47±8.68	-0.793	0.431	
Glucose3	94.04±18.02	98.74±11.21	-1.329	0.188	
Glucose4	100.08±14.90	98.27±10.05	0.489	0.627	
Procc-0	1.25±1.95	2.13±7.36	-0.568	0.572	
ProcI	1.98±4.32	2.36±5.69	-0.281	0.780	
Proc2	3.11±7.30	3.89±10.08	-0.332	0.741	
Proc3	1.99±5.29	2.13±3.91	-0.120	0.905	
Proc4	0.58±0.76	1.28±3.46	-0.930	0.356	
Insulin-0	6.82±4.60	11.10±8.58	-2.303	0.024*	
Insulin I	7.05±3.18	9.49±6.51	-1.715	0.091	
Insulin2	6.83±3.72	9.70±4.90	-2.317	0.024*	
Insulin3	6.79±2.98	II.20±6.42	-2.769	0.008*	
Insulin4	7.31±3.62	10.03±4.99	-1.894	0.065	

*P<0.05. aHOMA-IR, Homeostasis model assessment-estimated insulin resistance; bSD, Standard deviation; cproc, Procalcitonin. 0: 1st day; 1: 1st week; 2: 2nd week; 3: 3rd week; 4: 4th week.

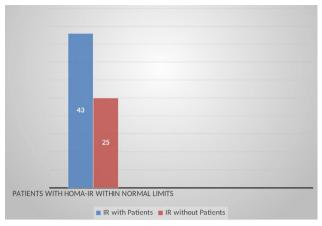


Figure 1. Prevalence of insulin resistance

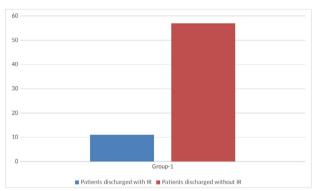


Figure 2. Prevalence of insulin resistance by week

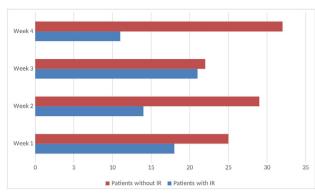


Figure 3. Number of patients discharged with insulin resistance

DISCUSSION

In this retrospective cross-sectional study of serum insulin levels and IR in patients with major burns, only a few patients had IR. There was insufficient evidence that this condition was persistent in patients with IR.

The first studies on how burn injury affects glucose metabolism in patients were published in the 1960s. [10] Allison et al. examined six patients using the glucose intolerance test. They suggested that the patients had IR, but the results were inconclusive. [10] Wilmore et al. reported in 1976 that fasting blood glucose increased in the acute period due to hypermetabolism in burn patients but then returned to normal. [11]

The sample size and homogeneity of the groups were ex-

Table 3.	Delta values of all parameters and comparison between groups n=68	
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	Patients without HOMA-IRan=25 X±SD ^b	Patients with HOMA-IR n=43 X±SD	t	P-value	
Glucose-delta	-14.15±31.49	-18.76±34.58	0.422	0.675	
Procc-delta	-0.30±1.44	-0.84±8.17	0.595	0.555	
Insulin-delta	0.66±4.02	-1.12±11.24	0.305	0.762	

*P<0.05. aHOMA-IR: Homeostasis model assessment-estimated insulin resistance; bSD: Standard deviation; cproc: Procalcitonin; delta, first and last measurement change.

Table 4. Correlation table of weekly insulin resistance values and burn percentage and procalcitonin values

	Burn pei	rcentage	Proc. I	st week	Proc. 2	nd week	Proc.3i	rd week	Proc.4t	h week	Proc.51	th week
	r	Р	r	P	r	Р	r	P	r	P	r	Р
IR-I	-0.041	0.796	0.051	0.747								
IR-2	-0.062	0.700			0.430	0.005						
IR-3	-0.398	0.009					-0.201	0.202				
IR-4	0.003	0.983							-0.068	0.667		
IR-5	0.055	0.774									-0.156	0.412

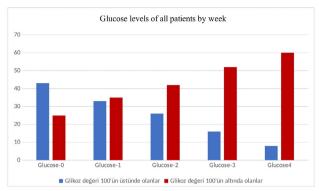


Figure 4. Glucose levels of all patients by week

tremely low in both of these studies. In addition, no information was provided on the patients' previous blood sugar levels in the studies. In this study, all of the patients included in the study were adult patient groups, and the sample size was larger than the studies in the literature. In addition, the HbAIc levels of all patients included in the study were checked on the Ist day, and the data of the patients above the reference values were excluded from the study in order not to affect the results of the study. We think that this aspect of our study gives more objective results, and patients hospitalized with burn injuries should have their HbAIc levels checked.

In four different studies conducted in 2009, 2010, and 2011, it was reported that IR might be persistent and long-term in pediatric patients with burn injuries. [12-15] In all studies, the patient population consisted of pediatric patients. Therefore, the persistent nature of IR in these studies could be attributed to the patients' young age.

(a) Dependent variable: IR-1st week n=11								
Model	uc		sc	t	Sig.			
	В	Standard error	Beta					
I (Constant)	4.695	1.528		3.073	0.022			
sex	-0.133	0.585	-0.059	-0.227	0.828			
BP	-0.066	0.032	-0.524	-2.032	0.088			
procl	-2.285	1.173	-0.507	-1.949	0.099			
(a) Dependent varial	ole: IR-2nd week n=1	1						
I (Constant)	-2.937	3.438		-0.854	0.421			
sex	1.6	1.266	0.389	1.264	0.247			
BP	0.127	0.082	0.555	1.55	0.165			
Proc2	-4.166	2.949	-0.503	-1.412	0.20			
(a) Dependent varial	ole: IR-3rd week n=1 I							
I (Constant)	0.039	2.295		0.017	0.987			
sex	1.704	0.998	0.567	1.708	0.131			
BP	0.02	0.059	0.121	0.347	0.739			
Proc3	-0.534	0.85	-0.26	-0.628	0.55			
(a) Dependent varial	ole: IR-4th week n=1 I							
I (Constant)	-0.4	3.155		-0.127	0.903			
sex	0.963	1.225	0.303	0.786	0.457			
BP	0.066	0.067	0.369	0.983	0.359			
Proc4	-0.159	0.78	-0.083	-0.204	0.844			
(a) Dependent varial	ole: IR-5th week n=1 I							
I (Constant)	3.014	1.703		1.77	0.12			
sex	-0.889	0.616	-0.334	-1.443	0.192			
BP	0.066	0.034	0.444	1.915	0.097			
Proc5	1.417	0.674	0.471	2.103	0.074			

There are studies in the literature that show that antibiotic use causes mitochondrial dysfunction and adversely affects the intestinal flora.^[16-20]

Therefore, antibiotics may be the cause of IR in pediatric patients. The patients in the present study ranged in age from 18 to 65 years. Antibiotics were not used as part of the patients' routine treatment plans in the present study. In our study, the reason why IR and hyperglycemia were seen as transient and not persistent may be the absence of an antibiotic in the routine treatment program of the patients.

In a study conducted in 2017 with adult burn patients, Rehou et al. stated that changes in glucose tolerance in adult burn patients may be similar to changes in pediatric burn patients. ^[21] However, in that study, the glucose and insulin levels of the patients were assessed using samples taken at 30, 60, 90, and 120 min.

In this study, the values of all patients included in the study were recorded on the 1st day and at the 1st, 2nd, 3rd, and 4th weeks. It was observed that glucose levels, which were high in the 1st week, returned to normal levels in the following weeks (Figures 2 and 3). In addition, among all patients in the study, only 11 had permanent IR (Fig. 3). Rehou et al. in their study, insulin values only covered the 1st day.^[21] We think that only the measurements taken on the 1st day may be misleading; a weekly evaluation of the parameters may give more reliable results.

The procalcitonin marker is a highly reliable marker that provides information about the diagnosis of sepsis and the severity of the burn in burn patients. [22,23] Although it was observed that the procalcitonin marker was at higher levels in patients with IR, no statistical difference was found (P>0.05, (Table 2)). We think that the weak correlation between the incidence of IR and the elevation of procalcitonin in burn patients is due to the small number of participants (Table 4).

In addition, we think that the reason for the lack of significance in the regression analysis between IR and procalcitonin in II patients with IR in all weeks is due to the small number of participants (Table 5). Correlation studies are needed between the incidence of IR in burn patients and the elevation of procalcitonin markers.

CONCLUSION

In the present study, IR was observed in patients at different weeks during hospitalization, but the number of patients discharged with IR was very small, implying that IR is not persistent. We believe that HOMA-IR is not directly related to burn injuries and that other additional parameters, such as using antibiotic may cause it during treatment. However, there is a need for further studies, particularly on sepsis and the use of antibiotics.

The burn center where the study was conducted is a center where Syrian refugees also apply, as well as Turkish citizens.

The number of Syrian patients in the study was around 40%. Since professional translators assisted in communicating with these patients, there were no problems. However, due to the fact that these patients were transferred to other centers from time to time, the follow-up periods in our study and the number of patients included in the study were adversely affected.

Ethics Committee Approval: This study was approved by the University of Health Sciences Hasan Kalyoncu University Research Ethics Committee (Date: 18.12.2018, Decision No: 2018-48).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: M.A.Ç., A.E.; Design: M.A.Ç., A.E., K.B., A.G., Y.Y.; Supervision: M.A.Ç., A.E., A.G.; Materials: A.E., A.G.; Data collection and/or processing: M.A.Ç., K.B., Y.Y.; Analysis and/or interpretation: M.A.Ç., K.B., Y.Y.; Literature search: M.A.Ç., A.E.; Writing: M.A.Ç., Critical review: M.A.Ç., A.E.

Conflict of Interest: None declared.

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ORİJİNAL ÇALIŞMA - ÖZ

Majör yanıklı hastalarda glikoz, serum insülin düzeyleri ve insülin direncinin araştırılması: Retrospektif kesitsel bir çalışma

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AMAÇ: Literatürde majör yanıklı hastalarda insülin rezistansının görüldüğü ve bunun persistan olduğunu belirten yayınlar olsa da yeterli düzeyde değildir. Bu çalışma, majör yanıklı hastalarda travma sonrası erken dönemde insülin seviyeleri ile insülin rezistansını araştırmak ve insülin rezistansının görülme sıklığını belirlemek amacıyla planlandı.

GEREÇ VE YÖNTEM: Çalışmaya toplam 68 hasta alındı. Çalışmaya dahil edilen tüm hastaların hastaneye yatışlarından itibaren 4 hafta boyunca haftalık olarak değerlendirmeleri yapıldı. Değerlendirmede demografik bilgiler, yanık hasarının özellikleri, HbA1c, açlık serum glukoz düzeyleri, procalcitonin, insülin seviyeleri ile insülin direnci (IR) gibi parametrelere bakıldı.

BULGULAR: Hastaların yanık yaralanmaları değerlendirildiğinde; 69 (%75) hastada alev yanığı, 15 (%16.3) hastada elektrik yanığı saptandı. Çalışmaya alınan 68 hastanın sadece 25'inde bazı haftalarda IR görüldü. Sadece 11 (%16.17) hastada, hastaneye kabul edildikleri birinci günden taburcu olana kadar IR belirlendi. IR olan ve olmayan hastalar 2 grup olarak değerlendirildi, biyokimyasal parametreleri karşılaştırıldı ve glukoz ve prokalsitonin düzeyleri arasında anlamlı fark bulunamadı (p>0.05). Takip edilen tüm hastalarda ilk hafta glukoz düzeyi >100 mg/dl olarak belirlendi ancak sonraki haftalarda bu değerler normal referans aralığındaydı.

SONUÇ: Majör yanıklı hastalarda serum insülin düzeylerinin ve insülin rezistansının araştırıldığı bu retrospektif kesitsel çalışmada hastaların sadece bir kısmında insülin direncine rastlandı. İnsülin direncinin görüldüğü hastalarda ise bu durum persistant olduğuna dair yeterli kanıtlara ulaşılamadı. Sonuç olarak, Homa-IR'nin direkt yanık travmasıyla ilgisi olmadığı ve tedavinin seyri sırasında başka ek patolojilerin buna sebep olabileceği görüşündeyiz.

Anahtar sözcükler: Glikoz metabolizması; hiperglisemi; hipermetabolik durum; insülin direnci; yanıklar.

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