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ORIGINAL ARTICLE

## Complications associated with hyperglycemia in liver transplant patients<sup>☆</sup>



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### KEYWORDS

Liver transplant;  
Graft rejection;  
Hyperglycemia

### Abstract

**Background:** Hyperglycemia is a frequent phenomenon in hospitalized patients that is associated with negative outcomes. It is common in liver transplant patients as a result of stress and is related to immunosuppressant drugs. Although studies are few, a history of diabetes and the presentation of hyperglycemia during liver transplantation have been associated with a higher risk for rejection.

**Aims:** To analyze whether hyperglycemia during the first 48 hours after liver transplantation was associated with a higher risk for infection, rejection, or longer hospital stay.

**Methods:** A retrospective cohort study was conducted on patients above the age of 15 years that received a liver transplant. Hyperglycemia was defined as a value above 140 mg/dl and it was measured in three different manners (as an isolated value, as a mean value, and as a weighted value over time). The relation of hyperglycemia to a risk for acute rejection, infection, or longer hospital stay was evaluated.

**Results:** Some form of hyperglycemia was present in 94% of the patients during the first 48 post-transplantation hours, regardless of its definition. There was no increased risk for rejection (OR: 1.49; 95% CI: 0.55-4.05), infection (OR: 0.62; 95% CI: 0.16-2.25), or longer hospital stay between the patients that presented with hyperglycemia and those that did not.

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*Conclusions:* Hyperglycemia during the first 48 hours after transplantation appeared to be an expected phenomenon in the majority of patients and was not associated with a greater risk for rejection or infection and it had no impact on the duration of hospital stay.

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## PALABRAS CLAVE

Trasplante hepático;  
Rechazo del injerto;  
Hiperglucemia

## Complicaciones asociadas a la hiperglucemia en pacientes trasplantados de hígado

### Resumen

*Antecedentes:* La hiperglucemia es un fenómeno frecuente en los pacientes hospitalizados asociado a desenlaces negativos, y es frecuente en los pacientes trasplantados de hígado como un fenómeno de estrés y asociada a medicamentos inmunosupresores. Aunque los estudios son escasos, el antecedente de diabetes, así como la hiperglucemia durante el trasplante hepático, se han asociado con mayor riesgo de rechazo.

*Objetivo:* Estudiar si la hiperglucemia durante las primeras 48 h después de un trasplante hepático se asocia a un mayor riesgo de infección, rechazo o estancia hospitalaria.

*Métodos:* Estudio de cohorte de tipo retrospectivo en pacientes mayores de 15 años que recibieron un trasplante hepático. Se definió la hiperglucemia como un valor superior a 140 mg/dl y se midió de 3 maneras diferentes (como un valor aislado, como la media de los valores y como un valor ponderado en el tiempo) y se analizó su relación con el riesgo de rechazo agudo, infección y tiempo de estancia hospitalaria.

*Resultados:* Un 94% de los pacientes presentó alguna forma de hiperglucemia durante las primeras 48 h postrasplante independientemente de cómo esta fue definida, y no hubo un mayor riesgo de rechazo (OR: 1.49; IC 95%: 0.55-4.05), infección (OR: 0.62; IC 95%: 0.16-2.25) o tiempo de estancia hospitalaria entre los pacientes que la presentaron y los que no.

*Conclusión:* La hiperglucemia durante las primeras 48 h después de un trasplante pareciera ser un fenómeno esperable en la mayoría de pacientes y no se asocia a un mayor riesgo de rechazo, infección y no impacta en el tiempo de estancia hospitalaria.

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## Introduction

Hyperglycemia is defined as any glucose value > 140 mg/dl.<sup>1</sup> It occurs in 32 to 38% of all hospitalized patients, 41% of all the critically ill, 44% of patients with heart failure, and up to 80% of patients after cardiac surgery; between 30 and 80% of those individuals have no history of diabetes.<sup>2</sup> Stress hyperglycemia is that which presents in patients with no history of diabetes and is usually transitory. It is caused by counterregulatory hormones (such as cortisol and adrenaline) and by the increase in insulin resistance,<sup>3,4</sup> but the most important factor appears to be hepatic gluconeogenesis.<sup>5</sup> Hyperglycemia in the hospitalized patient, especially those that have undergone transplantation, can also be the consequence of the use of different types of medication, such as glucocorticoids and other immunosuppressant drugs.<sup>6,7</sup>

The long-term deleterious effects of hyperglycemia are well-known, especially those related to micro and macrovascular damage.<sup>8,9</sup> In the context of the acute patient, hyperglycemia produces changes in the immune system<sup>10</sup> and coagulation.<sup>11</sup> In addition, fluctuations in glucose levels induce apoptosis in the endothelial cells, causing endothelial dysfunction.<sup>12</sup>

In the patient with no history of diabetes, hyperglycemia is a mortality marker, especially in those patients in intensive care units (ICUs). It is also associated with longer periods of hospital stay and a greater risk for postoperative infection.<sup>13-15</sup> Hyperglycemia has additionally been associated with adverse events in patients with acute myocardial infarction<sup>16-19</sup> and with cerebrovascular disease (CVD).<sup>20,21</sup>

On the other hand, diabetes is a frequent comorbidity in patients on the liver transplantation waiting list, presenting in 65% of them.<sup>22</sup> Despite this fact, there is scant evidence that hyperglycemia is a risk factor for negative outcomes in patients that have undergone transplantations, even though, in general, diabetes is associated with a worse outcome in liver transplantation patients. The prevalence of post-transplantation diabetes is as high as 31-38%,<sup>23</sup> and these patients are at a higher risk for cardiovascular complications, such as high blood pressure and coronary disease, as well as a higher mortality rate, compared with those patients that do not develop diabetes.<sup>24,25</sup> Likewise, patients that develop post-transplantation diabetes have a higher number of acute rejection episodes, and infectious and neurologic complications.<sup>26-28</sup>

Different mechanisms have been proposed by which hyperglycemia could produce graft damage and increase

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