

Glycosylated hemoglobin level in patients with and without surgical site infection after hysterectomy

Concentración de hemoglobina glucosilada en pacientes no diabéticas con y sin infección de sitio quirúrgico posterior a la histerectomía

Sebastián Carranza-Lira*, Francisco D. Serrano-Estrada, Eunice López-Muñoz, Luz María Hernández-Jiménez, and María Eugenia Chavarría-Olarte

High Specialty Medical Unit, Hospital de Gineco-Obstetricia "Luis Castelazo Ayala", Instituto Mexicano del Seguro Social, Mexico City, Mexico

Abstract

Background: Surgical site infection (SSI) occurs in 11-12% of surgeries. The glycosylated hemoglobin (HbA1c) has been found to be significantly elevated in those who presented infection. **Objective:** The objective of this study was to compare the concentration of HbA1c between patients with and without SSI after hysterectomy. **Methods:** In healthy, post-operative women with total abdominal (open) hysterectomy, the HbA1c serum concentration was measured (normal < 5.7%) and the difference between those who presented SSI and other risk factors for SSI were compared with Mann-Whitney U-test was used. The HbA1c values were stratified as normal or abnormal and were contrasted with the presence or absence of SSI by means of X². **Results:** Twenty-seven women without SSI and 20 with SSI were studied. The pre-operative glucose was and 88 (70-99) mg/dl and 86 (70-99) mg/dl for the groups with and without SSI, respectively. The HbA1c was significantly higher in the group with ISQ 5.6% (5-8) versus 6.5% (5.2-8.2). The sensitivity of HbA1c with cut point < 5.7 was 80% and the specificity was 51.9%. **Conclusion:** HbA1c can serve as a prognostic criterion of ISQ.

Keywords: Infection. Surgical site. Glycosylated hemoglobin. Hysterectomy.

Resumen

Antecedentes: La infección del sitio quirúrgico (ISQ) se presenta en el 11-12% de las cirugías. La hemoglobina glucosilada (HbA1c) se ha encontrado significativamente elevada en los pacientes que presentan infección. **Objetivo:** Comparar la concentración de HbA1c entre pacientes con y sin ISQ posterior a una histerectomía. **Método:** En mujeres sanas posoperadas de histerectomía total abdominal (abierto) se midió la concentración sérica de HbA1c (normal < 5.7%) y se comparó la diferencia entre las que presentaron ISQ y las que no. Se investigaron también otros factores de riesgo para ISQ. Se utilizó la prueba U de Mann Whitney. Los valores de HbA1c se estratificaron como normales o anormales, y se contrastaron con la presencia o no de ISQ por medio de la prueba ji al cuadrado. **Resultados:** Se estudiaron 27 mujeres sin ISQ y 20 con ISQ. La glucosa preoperatoria fue de 88 (70-99) y 86 (70-99) mg/dl para los grupos con y sin ISQ, respectivamente. La HbA1c fue significativamente mayor en el grupo con ISQ (5.6%; 5-8) que en el grupo sin ISQ (6.5%; 5.2-8.2). La sensibilidad de la HbA1c con un punto de corte < 5.7 fue del 80% y la especificidad fue del 51.9%. **Conclusión:** La HbA1c puede servir como criterio pronóstico de ISQ.

Palabras clave: Infección. Sitio quirúrgico. Hemoglobina glucosilada. Histerectomía.

Correspondence:

*Sebastián Carranza-Lira

Puente de Piedra, 150-422, Torre 1

Col. Toriello Guerra

C.P. 14050, Tlalpan, Ciudad de México, México

E-mail: drsebastiancarraznala@gmail.com

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Introduction

Surgical site infection (SSI) occurs in 11-12% of surgical procedures, while for hysterectomies, this frequency is 1.7%^{1,2}; however, this figure may be underestimated, given that many times infection becomes evident once the patient has been discharged³.

SSI can be superficial, deep, compromise an organ, or be located in intraperitoneal or retroperitoneal spaces. Superficial SSI is that which occurs within the first 30 days after surgery and is limited to the skin and subcutaneous tissue, plus any of the following criteria: purulent discharge, surgical site secretion positive culture, or when the clinician opens an incision that is painful, soft, swollen, erythematous, or warm. Deep infection is that which occurs within 30 days after surgery and involves deep soft tissues, such as fascia and muscle. Those that occur in organs or in spaces also do it within 30 days after surgery, excluding superficial and deep planes^{2,4,5}. In two-thirds of cases, infections are superficial, and in gynecology, the most common is cellulitis at the incision site and on the vaginal dome⁶. It should be noted that hysterectomy is considered a contaminated clean surgery. At "Luis Castelazo Ayala" Obstetrics-Gynecology Hospital High Specialty Medical Unit, in 2017, according to the gynecology department records, 1,067 total abdominal hysterectomies were performed, out of which 72 had superficial wound infection, nine had deep infection, and 20 had organ and space infection.

There are multiple factors involved in the genesis of infection, such as age, obesity⁷, diabetes, smoking, infections elsewhere in the body, colonization by other types of microorganisms, altered immune response, surgery duration, surgical brushing duration, abdominal wall skin antisepsis (chlorhexidine vs. povidone-iodine)⁸, pre-operative vaginal cleansing⁹, pre-operative shaving or non-shaving, antimicrobial prophylaxis⁷, operating room ventilation, instrument sterilization, foreign bodies in the surgical wound, drainages, hemostasis, failure to obliterate dead space (closure or not of subcutaneous cellular tissue)¹⁰, subcutaneous cellular tissue thickness > 3 cm¹¹, and tissue trauma¹².

Infections are more common in diabetic patients¹³ (21% of patients with sepsis are diabetic¹⁴). Hyperglycemia within the first 48 h after surgery has been associated with increased risk of infection¹⁵; a glucose level > 12 mmol/L on the 1st day of the post-operative period has been reported to increase

6 times the risk of nosocomial infection¹⁶. The mechanisms to explain this increase in the risk of infection include, among others, a decrease in polymorphonuclear cells chemotaxis¹⁷, lower production of superoxide in relation to increased glucose concentrations¹⁸, phagocytosis alterations¹⁹, opsonization defects^{13,20}, monocyte chemotaxis defects²¹, and CD152 increased expression by T lymphocytes, which is known to down-regulate the immune response²².

Glycosylated hemoglobin (HbA1c) is an indicator of metabolic control of the previous 3 months^{23,24}. Recent studies have analyzed the usefulness of measuring HbA1c before surgery to detect untreated or poorly controlled diabetic patients and have found that it is significantly elevated in those who develop infections²⁵. Furthermore, in foot and ankle surgery, HbA1c was directly related to the risk of infection, which was 15% higher in this group²⁶. However, there is no record in the hospital on how many patients who undergo hysterectomy and develop SSI have HgbA1c alterations, given that HgbA1c is not part of systematic pre-operative evaluation.

For all of the above, the purpose of this study was to compare HbA1c concentration between patients with and without SSI after hysterectomy.

Methods

This study prospective, cross-sectional, and comparative study in non-diabetic women without cervical-vaginal infection after total abdominal (open) hysterectomy surgery. Once informed consent was signed, all patients were taken a 5-mL sample of peripheral blood in a tube with EDTA to measure HbA1c concentration, which was performed by immune agglutination inhibition in latex using commercial kits (Hemoglobin A1c, Reagent Kit, Ref. 10698915. Siemens DCA Systems). HbA1c value was considered normal when it was < 5.7% and abnormal when it was ≥ 5.7%. In addition, the following data were investigated: age, comorbidity (such as hypertension), smoking, excessive alcohol consumption, previous surgeries, body mass index (BMI, weight in kg/height in m²), panniculus adiposus thickness, transoperative bleeding, and surgical time. All patients received antibiotic prophylaxis with cefuroxime (750-mg single-dose), as well as one dose of vaginal metronidazole the night before surgery; the antiseptic used for abdominal wall and vaginal pre-operative cleansing was povidone-iodine. After surgery, the patient clinical evolution was monitored, and the presence or not of

SSI was determined during hospitalization and within 30 days after the intervention. In those with SSI, the type of infection was specified.

Pre-operative levels of hemoglobin (g/dL), leucocytes ($10^3 \mu\text{L}$), platelets ($10^3 \mu\text{L}$), neutrophils ($10^3 \mu\text{L}$), lymphocytes ($10^3 \mu\text{L}$), monocytes ($10^3 \mu\text{L}$), eosinophils ($10^3 \mu\text{L}$), basophils ($10^3 \mu\text{L}$), and glucose concentrations were analyzed; the latter had to be $\leq 100 \text{ mg/dL}$ for patients to be included in the study.

The sample size was calculated considering an alpha-type error of 0.05 and a power of 80%, with a difference between means of 0.83 and a standard deviation of 0.95 for Group I and 0.76 for Group II, with 23 patients finally being included in Group I and 17 in Group II (Medcalc V 18.5).

Between-group comparison was carried out with Mann–Whitney’s U-test. Subsequently, HbA1c values were stratified as normal or abnormal, and contrasted with the presence or not of SSI by means of the Chi-square test. Sensitivity and specificity were calculated using ROC curves. Variables that were significantly associated with the status of infection were introduced in a logistic regression model.

The protocol was approved by the Local Health Research Committee and the Research Ethics Committee with approval number R-2018-3606-017, and patients signed the informed consent document.

Results

Twenty-seven women without SSI and 20 with SSI were evaluated; among the latter, in 18, there was skin and subcutaneous cell tissue infection, and in the other two, there was also aponeurosis involvement. No difference was found between groups in terms of age, weight, height, and BMI (Table 1). With regard to history of hypertension, smoking, and alcohol consumption, there were no differences between both groups. Women with SSI more often had a history of the previous surgery (75 vs. 25%; $p < 0.016$). Transoperative bleeding in both groups was 250 mL (100–400). Panniculus adiposus thickness, transoperative bleeding, and surgical time showed no differences between groups. Hemoglobin, leucocytes, differential count, and platelets were no different between groups (Table 2). Pre-operative glucose concentration was 88 (70–99) mg/dL in the group with SSI and 86 (70–99) mg/dL in the group without SSI, with no significant difference between both. HbA1c was significantly higher in the group with SSI, 6.5% (5.2–8.2), in comparison

Table 1. General data of women without and with surgical site infection

	No surgical site infection	Surgical site infection	p
Age, years	46 (31–54)	47 (40–74)	0.141
Weight (Kg)	73.0 (58–84)	72.0 (58–82)	0.597
Height (m)	1.53 (1.43–1.64)	1.52 (1.43–1.64)	0.762
Body mass index	29.5 (24.0–38.3)	30.9 (21.6–34.7)	0.974

Table 2. Blood count and glucose analysis results in women without and with surgical site infection

	No surgical site infection	Surgical site infection	p
Hemoglobin (g/dL)	13.5 (11–16)	13.5 (11–16)	0.613
Leucocytes ($10^3 \mu\text{L}$)	7.8 (5.4–13.0)	8.5 (5.4–13.0)	0.483
Platelets ($10^3 \mu\text{L}$)	250.0 (150–507)	214.0 (162–507)	0.262
Neutrophils ($10^3 \mu\text{L}$)	60.0 (50.0–87.0)	64.0 (50.0–87.0)	0.309
Lymphocytes ($10^3 \mu\text{L}$)	16.0 (6.0–70.0)	16.0 (6.0–70.0)	0.713
Monocytes ($10^3 \mu\text{L}$)	7.0 (4.0–19.0)	6.5 (4.0–19.0)	0.974
Eosinophils ($10^3 \mu\text{L}$)	1.0 (0.1–5.0)	1.0 (0.1–5.0)	0.303
Basophils ($10^3 \mu\text{L}$)	0.900 (0.3–5.0)	0.800 (0.3–5.0)	0.559
Glucose (mg/dL)	86.0 (70–99)	90.0 (70–99)	0.093

with 5.5% (5–8) in the group without SSI ($p < 0.002$). HbA1c was 18% higher in the group with SSI.

The proportion of women with BMI > 27 and elevated HbA1c was higher in the group with SSI (63.2 vs. 55.63%; $p = 0.476$), without the difference being statistically significant. The proportion of women with SSI was higher in those with elevated HbA1c than in those with normal HbA1c (80 vs. 20%; $p < 0.036$). There was no difference in the proportion of women without and with SSI and BMI > 27 (81.5 vs. 80%; $p = 0.593$).

HbA1c sensitivity with a cutoff point < 5.7 was 80%, and specificity was 51.8%; positive predictive value (PPV) was 55.2%, and negative predictive value (NPV) was 77.8%. With a cutoff point < 6.15 ,

sensitivity was 70% and specificity was 77.8%; PPV was 70% and NPV was 77.8%. Considering a cutoff point < 6.15 , sensitivity was 70% and specificity 78%; PPV was 70% and NPV was 77.8%. In the logistic regression analysis, statistical significance was preserved for a previous history of surgery (7.7; 95% confidence interval [CI]: 1.50-39.3; $p < 0.014$) and $HbA1c \geq 5.7$ (5.1; 95% CI: 1.1-22.9; $p < 0.033$) as infection predictors.

Discussion

HbA1c concentrations were evaluated in hysterectomized women with and without SSI in this study. This evaluation was carried out in the post-operative period assuming that the obtained value reflected the metabolic status.

Different factors are involved in the genesis of SSI, including metabolic control^{15,16}. In women without diabetes, HbA1c elevation may reveal slight alterations in glucose concentration, which are unknown to patients, who are unaware of the presence of carbohydrate metabolism alterations, but that nonetheless increase the risk of infection by modifying the immune response and leucocyte functionality^{17,22}.

In this study, when factors such as age, BMI, panniculus adiposus thickness, surgical time, trans-surgical bleeding, use of antibiotic prophylaxis, pre-operative antisepsis, and absence of cervical-vaginal infection were analyzed, no difference was found between groups, which allowed HbA1c to be considered as an auxiliary that should be considered when assessing SSI risk.

In this study, HbA1c was 18% higher in the group with SSI, similar to what was reported in another study, where patients with infection had 15% higher levels²⁶.

HbA1c sensitivity with a cutoff point < 5.7 was 80%, and specificity was 51.8%, with a PPV of 55.2% and a NPV of 77.8%, which is adequate, since when wanting to predict the risk of SSI, sensitivity is the most appropriate parameter.

One of the strengths of this study had is that both groups were homogeneous, except for previous history of surgery, but it allowed for HbA1c to be given a specific weight. One of its weaknesses is that the sample size is small, which is why a larger number of patients should be recruited and validate these results before including HbA1c determination as part of pre-operative evaluation.

All the above allows concluding that HgA1c can be helpful for predicting the risk of SSI in patients, in whom total abdominal hysterectomy is to be practiced.

Conflicts of interests

The authors declare that there is no conflicts of interests.

Ethical disclosures

Protection of people and animals. The authors declare that no experiments have been performed on humans or animals for this research.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained informed consent from the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

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