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LEUKO-GLYCEMIC INDEX AS A PREDICTOR OF ACUTE INTRAHOSPITAL COMPLICATIONS IN ADULTS WITH ISCHEMIC STROKE IN THE SALVADOR BIENVENIDO GAUTIER HOSPITAL IN THE DOMINICAN REPUBLIC

Índice leucoglucémico como predictor de complicaciones intrahospitalarias agudas en adultos con enfermedad vasculocerebral isquémica en el Hospital Salvador Bienvenido Gautier de República Dominicana

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Abstract

Background: Ischemic stroke is an important cause of morbidity, mortality, and disability worldwide. Hyperglycemia and leukocytosis are considered markers of poor prognosis, the index resulting from the combination of these variables could represent a valuable tool in the prognosis.
Objective: To determine the leuko-glycemic index (LGI) as a predictor of complications in ischemic stroke for over 18-year-old patients in a hospital in the Dominican Republic.
Methods: Data were collected through a digital form of 12 questions implemented in the KoboToolbox software. The sample consisted of 161 patients selected by non-probability sampling for convenience. Through the Receiver Operating Characteristic (ROC) curve and a

Resumen

Antecedentes: La enfermedad vasculocerebral isquémica es una causa importante de morbimortalidad y discapacidad en todo el mundo. La hiperglucemia y la leucocitosis se consideran marcadores de mal pronóstico, el índice resultante de su combinación podría representar una herramienta valiosa en el pronóstico.
Objetivo: determinar el índice leucoglucémico (ILG) como predictor de complicaciones en ictus isquémico en pacientes mayores de 18 años en un hospital de la República Dominicana.
Métodos: La recolección de datos se obtuvo a través de un formulario digital de 12 preguntas implementado en el software KoboToolbox. La muestra estuvo constituida por 161 pacientes seleccionados por muestreo no probabilístico por conveniencia. A través de la curva Operativa

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Youden index of 0.35, an LGI cut-off point of 1,566 was obtained.
Results: Among the cases, 97 evolved without complications, and 64 presented complications, highlighting aspiration pneumonia. The complicated cases presented a high LGI with an arithmetic mean of 2,328.39. The predominant age group was 66 to 75 years and the sex was male. Additionally, there was a high prevalence of smoking, coffee, and herbal tea consumption among the study population. Furthermore, systemic arterial hypertension stood out as a comorbidity. Most presented a mild alteration of the level of consciousness based on the first neurological evaluation made using the Glasgow Coma Scale (GCS). Multifocal ischemic lesions preponderated. The majority were discharged alive.
Conclusion: The LGI stands as a valuable predictor, forecasting complications in individuals with ischemic stroke.

Keywords: Glycemic index, complications, stroke, hospital, Dominican Republic.

Característica del Receptor (ROC) y un índice de Youden de 0.35, se obtuvo un punto de corte ILG de 1,566.
Resultados: De los casos, 97 evolucionaron sin complicaciones, y 64 presentaron complicaciones, destacando la neumonía por aspiración. Los complicados presentaron un ILG elevado con una media aritmética de 2,328.39. El grupo de edad predominante fue 66 a 75 años y el sexo fue masculino. Adicionalmente, hubo una mayor presentación del consumo de tabaco, café y tisanas. Además, se destacó la hipertensión arterial sistémica como comorbilidad. La mayoría presentó una leve alteración del nivel de conciencia basado en la primera evaluación neurológica según la Escala de Coma de Glasgow. Predominaron las lesiones isquémicas multifocales. La mayoría fueron dados de alta vivos.
Conclusión: El ILG se establece como un valioso predictor, ya que pronostica las complicaciones en individuos con ictus isquémico.

Palabras clave: Índice glucémico, complicaciones, accidente cerebrovascular isquémico, hospital, República Dominicana.

Introduction

Projecting its impact on a global level, ischemic stroke assumes a crucial role in the incidence of morbidity, mortality, and widespread disability[1]. In an unexpected revelation from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019 Stroke Collaborators, an overwhelming 12.2 million incident cases, 101 million prevalent reports, 143 million disability-adjusted life-years (DALYs), and 6.55 million deaths were attributed to stroke[2]. Indeed, in 2022 nearly 7 million Americans older than 20-year-old reported having had one[3]. In the Caribbean region, the Dominican Republic is positioned as the third-ranking country in ischemic stroke mortality. The daily incidence is 59 cases per day, extrapolated to 583 weekly reports and 2,333 cases per month, with associated hospital care costs estimated at DOP 700,000.00 (USD 11,967.40)[4, 5].

Moreover, hyperglycemia and leukocytosis assessed individually are considered markers of poor prognosis in patients with ischemic stroke[6-8]. For this reason, the leuko-glycemic index (LGI) could represent a valuable predictor of complications since it prognosticates in-hospital aggravations and mortality of ischemic etiology combining the inflammatory and metabolic response[9-12].

Previously, Asmat-Vasquez and collaborators reported that 56% of the deceased occurrences due to complications exhibited an LGI exceeding 1,600, with aspiration pneumonia as the primary aggravation in 67% of the cases[12]. In addition, Gonzalez and colleagues established the LGI as a robust predictor of complications, identifying dysphagia and pneumonia as common ones[10]. However, despite the substantial predictive capacity of the LGI for aggravations, minimal emphasis has been placed on illustrating its efficacy in a Caribbean population. Due to this fact, applying the LGI as an instrument allows for identifying and stratifying high-risk populations for complications.

Methods

Study design

An observational, descriptive, cross-sectional, and retrospective study was conducted at the neurology department of Salvador Bienvenido Gautier Hospital. This community hospital is located in Santo Domingo, the capital of the Dominican Republic.

The primary objective of the investigation was to determine the LGI as a predictor of complications in ischemic stroke in over 18-year-old patients in a hospital in the Dominican Republic. Moreover, the secondary objectives were to establish the relationship of age and sex with the presentation of complications, to specify toxic habits and to list comorbidities of complicated cases, to record leukocyte count and blood glucose, to indicate the level of consciousness according to the Glasgow Coma Scale at the admission of complicated patients, to distinguish the location of the ischemic lesion, to identify the presence of complications and group them, and to classify patients according to their discharge condition.

The study was performed between December 7th, 2022, and June 5th, 2023. The Salvador Bienvenido Gautier Hospital Ethics Committee submitted and approved the research protocol. The data was collected by the authors and a contributor (the name was mentioned in the acknowledgment section), and was analyzed and interpreted by the authors.

Participants

The population was constituted of 412 patients who were admitted to the clinical room of the Salvador Bienvenido Gautier Hospital between July and December 2022. The sample consisted of 161 patients.

The inclusion criteria were all patients over 18 years old who were admitted to the clinical ward of the Salvador Bienvenido Gautier Hospital in the period from July to December 2022 with a confirmed diagnosis of ischemic stroke by neuroimaging, as well as with a leukogram and blood glucose reported within the first 72 hours of admission. Nevertheless, the exclusion criteria were pregnant or puerperal patients, those with a documented diagnosis of hemorrhagic stroke, a systemic infection in the 7 days before the stroke, a hematological disease, an autoimmune disease or immunodeficiencies, some type of cancer or in remission, and those who have consumed corticosteroid treatment in the previous 6 months.

Data collection

The data were obtained through the clinical records reviewed and those were registered using a digital form consisting of 5 sections constituted by 9 multiple-choice questions, and 3 open questions applying the KoboToolbox software, which addressed epidemiological factors such as age, sex, toxic habits, and comorbidities, room analysis and neuroimaging reports, staging, and evolution.

Variables

The dependent variable of the study was the leukoglycemic index. Whereas, the independent variables were age, sex, toxic habits, comorbidities, leukocyte count, glycemia, level of consciousness, location of the lesion, presence of complications, complications, and discharge condition.

Data processing and analysis

The processing of the information was systematic, using an HP® 15 laptop with Windows 11, the statistical package of Microsoft Excel 2019, and the KoboToolbox software. The tables were processed through Microsoft Word 2019 and graphs were generated using GraphPad Prism version 10.1.2.

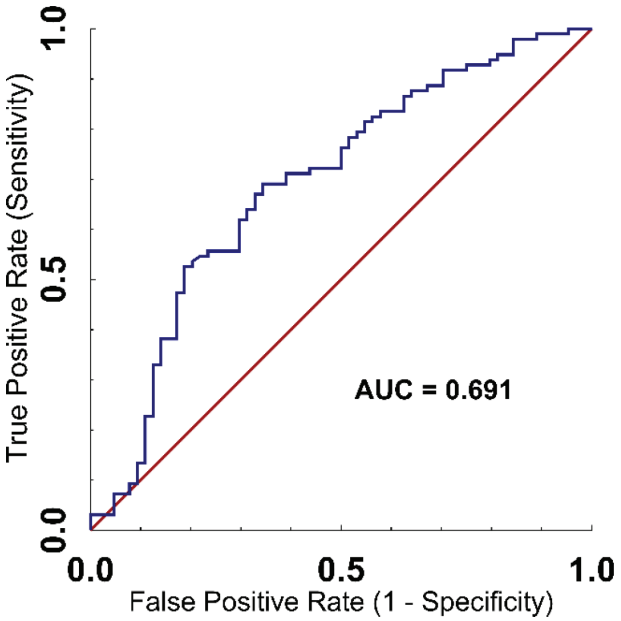
Subsequently, we derived the Leuko-Glycemic Index (LGI) for each case within our sample using the following formula[13].

LGI = (glycemia [mg/dL] · leukocyte count [10^6/L]) / 1,000

To determine the cut-off value of the LGI of the sample, the Receiver Operating Characteristic (ROC) curve was used, evaluating the Area Under the Curve (AUC) of the sample, which yielded a sensitivity of 66%, a specificity of 69% and an AUC of 0.691 with a standard error of 0.043, and a 95% confidence interval of 0.606 to 0.777 (Figure 1).

From then on, the dichotomy of complicated and uncomplicated cases resulted in a very close sensitivity and specificity, to discern the cut-off point the Youden index was used, following the formula (sensitivity + specificity - 1)[14], extrapolated to:

Figure 1. The Receiver Operating Characteristic (ROC) curve illustrates an Area Under the Curve (AUC) of 0.691. The red diagonal reference line is depicted, and each cut-off point deviating from the reference diagonal is presented in blue



Youden index = (0.66 + 0.69) – 1 = 0.35

Thence, this allowed us to determine by way of the EPITOOLS software, that the cut-off value of the leuko-glycemic index for the sample was 1,566.

Limitations of the study

The restraints of this investigation were 187 incomplete clinical records that were found by the researchers confining the sample selection. Moreover, and related to the used methodology, non-probability sampling for convenience was used, which could potentially introduce bias and restrict the applicability of the findings. Also, the study period, which was from July to December 2022, might not have captured seasonal variations or long-term trends in ischemic stroke complications.

Results

The study findings indicate that 44.72% (n=72) of cases surpassed the predetermined LGI threshold of 1,566. Notably, among 39.75% (n=64) patients who experienced complications, a substantial 65.62% (n=42) exhibited a heightened LGI, having a linked arithmetic mean of 2,328.39 and an associated standard deviation of 1,530.85. In contrast, in non-complicated patients, 60.24% (n=97) demonstrated a significantly lower LGI, evidenced by an arithmetic mean of 1,475.67 with a corresponding standard deviation of 945.23 (Table 1) (Figure 2).

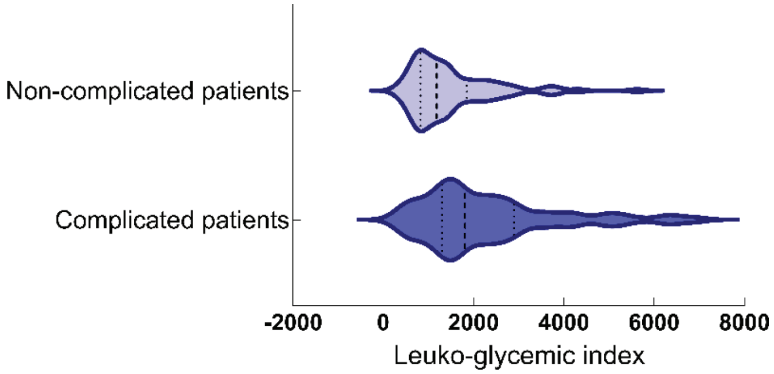
Furthermore, in the cohort of individuals who experienced complications, a noteworthy 32.81% (n=21) belonged to the age group of 66 to 75 years old, 39.06% (n=25) were female while 60.94% (n=39) were male. Among complicated patients, 39.06% (n=25) presented toxic habits, with smoking, coffee, and tisanes being predominant in 72% (n=18), followed by alcoholism in 40% (n=10). On the other hand, comorbidities were prevalent

Table 1. Leuko-glycemic index in ischemic stroke as a predictor of complications for over 18-year-old patients in the Salvador Bienvenido Gautier Hospital in the Dominican Republic

Variable	Arithmetic Mean	s†	CoV‡	W stadistic§	P-value‖	Lower to Upper CI (95%)¶
Complicated patients	2,328.39	1,530.85	0.657	0.883	<0.0001	1,946-2,711
Non-complicated patients	1,475.67	945.23	0.640	0.840	<0.0001	1,285-1,666

† Standard deviation. ‡ Covariance. § Kendall's Coefficient of Concordance. ‖ Significance level. ¶ Confidence interval.
Source: own elaboration.

Figure 2. The density distribution of cases among complicated and non-complicated patients. The initial vertical line signifies the first quartile (Q_1), the second denotes the mean (Q_2), and the final line represents the third quartile (Q_3)



in 98.43% (n=63), with systemic arterial hypertension having the greatest impact in 88.89% (n=56), pursued by diabetes mellitus in 61.90% (n=39) (Table 2).

From the observation of the sociodemographic variables, we were able to reveal that 65.63% (n=42) of the complicated patients had a high LGI; of whom 54.76% (n=23) were male, 64.29% (n=27) presented toxic habits, 97.62% (n=41) suffered from comorbidities, standing out in 76.19% (n=32) of them diabetes mellitus. Regarding the age group, 4.76% (n=2) were 36-45 years old, 7.14% (n=3) were 46-55 years old, 28.57% (n=12) were 56-65 years old, 28.57% (n=12) were 66-75 years old, 19.05% (n=8) were 76-85 years old, and 11.9% (n=5) were over 85 years old. With this, we demonstrate that elevated LGIs occur in a greater proportion of male patients, diabetics, and consumers of toxic habits, observing a decrease in LGI levels at both ends of these age groups.

Regarding leukocyte count, complicated patients exhibited an arithmetic mean of 10.80×10^6/L, while glycemia resulted in a mean of 210.25 mg/dL. In contrast, non-complicated patients had an arithmetic mean leukocyte count of 8.32×10^6/L, and a mean of 176.1 mg/dL in their glycemia (Table 3).

In assessing the level of consciousness upon admission using the Glasgow Coma Scale (GCS) among patients who developed complications, 51.56% (n=33) showed a mild alteration, 28.12% (n=18) a moderate alteration, and 20.31% (n=13) a severe alteration. Regarding lesion location, a total of

Table 2. Sociodemographic characteristics in patients over 18 years old with a complicated ischemic stroke in the Salvador Bienvenido Gautier Hospital in the Dominican Republic

Variable	n=64 (39.75%)
Age	
36-45 years	n=4 (6.25%)
46-55 years	n=3 (4.68%)
56-65 years	n=16 (25%)
66-75 years	n=21 (32.81%)
76-85 years	n=13 (20.31%)
Over 85 years	n=7 (10.93%)
Sex	
Male	n=39 (60.94%)
Female	n=25 (39.06%)
Toxic habits	
Smoking	n=18 (72%)
Alcoholism	n=10 (40%)
Coffee	n=18 (72%)
Tisanes	n=18 (72%)
Illicit drugs	n=1 (4%)
Denied	n=20 (31.25%)
Comorbidities	
HBP ‡	n=56 (88.89%)
Previous stroke	n=32 (50.79%)
DM §	n=39 (61.90%)
Dyslipidemias	n=9 (14.28%)
Obesity	n=8 (12.69%)
IHD ‖	n=8 (12.69%)
CKD ¶	n=5 (7.93%)
Others **	n=2 (3.17%)
Denied	n=1 (1.56%)

‡ High blood pressure. § Diabetes mellitus. ‖ Ischemic heart disease. ¶ Chronic kidney disease. ** Such as atrial fibrillation, congestive heart failure, peripheral venous insufficiency, and chronic obstructive pulmonary disease (COPD).
Source: own elaboration.

23.60% (n=38) exposed multifocal lesions. Notably, the frontal lobe was identified as the most affected for 11.18% (n=18) of cases (Table 4).

Moreover, in the 42 complicated patients that elevated the LGI, 59.52% (n=25) of them presented a mild level, 21.43% (n=9) a moderate level, and 19.05% (n=8) a severe level; accompanied by a multifocal location and a greater involvement in the frontal lobe territory. However, of the 22 patients who succumbed to complications, 45.45% (n=10) of them were admitted with a severe level of consciousness according to the GCS, 36.36% (n=8) with a moderate level and 18.18% (n=4) with a mild level. Therefore, we denote that the location of the lesion influences the level of consciousness according to the GCS if it is combined with comorbidities, toxic habits, and middle and later adulthood, leading to the appearance of fatal complications for patients.

Likewise, 39.75% (n=64) manifested complications while 60.25% (n=97) did not. Among the reported aggravations, 39.06% (n=25) developed aspiration pneumonia, followed by structural epilepsy in 23.43% (n=15) and urinary tract infection in 18.75% (n=12). Additionally, 62.50% (n=40) of patients presented other diverse complications such as cerebral edema, electrolyte imbalance, acid-base disorders, acute kidney disease, and others (Table 5) (Figure 3). Furthermore, in terms of the patients' outcomes, 86.33% (n=139) were discharged alive, while 13.66% (n=22) succumbed due to complications (Table 5).

Discussion

The examination of the LGI in our study has revealed compelling insights into its potential as a predictive biomarker for complications in the studied population. A determined LGI cut-off point of 1,566, surpassed by a substantial portion of

Table 3. Blood glucose and leukogram in patients over 18 years old with ischemic stroke in the Salvador Bienvenido Gautier Hospital in the Dominican Republic

Variable	Arithmetic Mean	s†	CoV‡	Lower to Upper CI (95%)§
Complicated patients				
Blood glucose¶ Leukogram**	210.25 10.80	99.97 4.15	0.475 0.384	185.3- 235.2 9.77- 11.84
Non-complicated patients				
Blood glucose¶ Leukogram**	176.1 8.32	92.19 3.05	0.523 0.366	157.5-194.7 7.70-8.93

† Standard deviation. ‡ Covariance. § Confidence interval. ¶ Expressed in mg/dL. ** Expressed in × 10^6 cells/L.
Source: own elaboration.

Table 4. Localization of the ischemic lesion in cases with ischemic stroke using computed tomography

Variable	n=161 (100%)
Localization of the lesion	
Frontal lobe	n=18 (11.18%)
Parietal lobe	n=3 (1.86%)
Temporal lobe	n=4 (2.48%)
Occipital lobe	n=5 (3.10%)
Brainstem	n=4 (2.48%)
Multifocal	n=38 (23.60%)
Others	n=32 (19.87%)
Not specified	n=65 (40.37%)

Source: own elaboration.

Table 5. Evolution in over 18-year-old patients with ischemic stroke

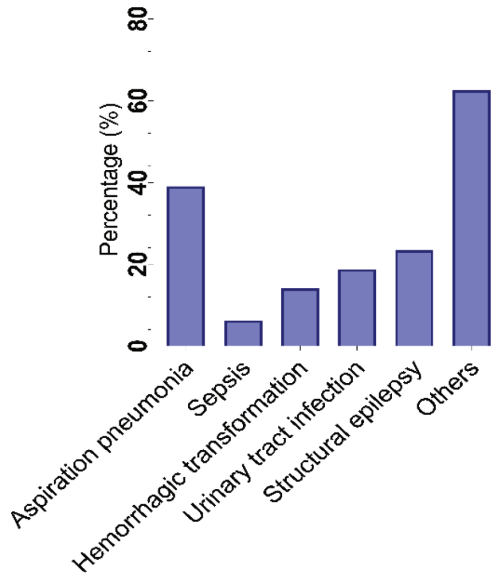
Variable	n=161 (100%)
Presence of complications	
Yes	n=64 (39.75%)
No	n=97 (60.25%)
Complications	
ASP ‡	n=25 (39.06%)
Sepsis	n=4 (6.25%)
HT §	n=9 (14.06%)
UTI ‖	n=12 (18.75%)
SE ¶	n=15 (23.43%)
Others	n=40 (62.50%)
Discharge condition	
Alive	n=139 (86.33%)
Deceased	n=22 (13.66%)

‡ Aspiration pneumonia. § Hemorrhagic transformation. ‖ Urinary tract infection. ¶ Structural epilepsy.
Source: own elaboration.

complicated cases, highlights its discriminative capability. Similarly, Gonzalez and colleagues found that complications increased with higher LGI values, especially beyond the 1,021 cut-off point[10].

Moreover, our examination of demographic factors showcased a notable portion of complicated cases' age distribution in the 66 to 75-year-old. Additionally, gender composition revealed a higher occurrence of aggravations in males compared to females. These align with the findings of Hernandez-Sanchez and collaborators, who reported a mean age of 71.4 years old, predominantly men; and with Goldstein, who estimated a 9% 30-day stroke mortality rate due to complications for 65-74 years old[15, 16].

Figure 3. The proportion of complications in ischemic stroke in the Salvador Bienvenido Gautier Hospital expressed as a percentage



The inspection of toxic habits and comorbidities among complicated patients further enhances our understanding of the multifactorial nature of complications. Smoking emerged as a predominant toxic habit while co-occurring diseases such as systemic arterial hypertension, diabetes mellitus, and previous stroke had a substantial impact. This correlates with the study conducted by Asmat-Vasquez, which noted that the most prevalent associated conditions were systemic arterial hypertension and diabetes mellitus[12].

The investigation into leukocyte count and glycemia provided significant differences in these parameters reinforcing their conjugated potential as objective indicators of condition severity. Nevertheless, as reported by Gonzalez et al., the mean leukocyte count and glycemia were 9.36 × 10^6/L and 123.50 mg/dL, respectively[10].

Likewise, complicated patients showed mild alteration in the level of consciousness and multifocal lesions with a predominance in the frontal lobe, contributing to the complexity of the clinical presentation. However, Asmat-Vasquez and collaborators, reported 61% presenting a moderate level of consciousness upon admission[12]. This observed phenomenon may be attributed to the time gap between the identification of the condition by family members and the subsequent admission to the hospital[16]. Correspondingly, Ropper and associates, underline the frontal lobe as most affected in convoluted scenarios[17].

Finally, outcomes analysis revealed that most patients were discharged alive, suggesting a favorable prognosis for the majority. However, a portion of patients experienced complications, particularly aspiration pneumonia. In contrast, Zarranz and colleagues reported complication rates ranging from 60% to 95%[18], this could be associated with the growing aging trend of the population[19]. According to Chamorro, early post-stroke infections often result from induced immunosuppression due to brain parenchyma damage[20], and Asmat-Vasquez et al. identified pneumonia as the primary complication in about 67% of cases, and 93.59% of cases being discharged alive[12].

Conclusions

This research aimed to prove that LGI can effectively predict complications in ischemic stroke. Despite facing difficulties in gathering information from 187 incomplete clinical records, acknowledging the predictive potential of LGI enables healthcare providers to conduct timely risk assessments and interventions, empowering them to proactively manage stroke aggravations and improve patient outcomes.

Based on these outcomes, practitioners should emphasize the necessity of smoking cessation, adopting a Mediterranean diet, promoting physical exercise, and ensuring stringent medical control of

comorbidities. Identifying predominant complications, like aspiration pneumonia, underscores the need for early identification, close monitoring, and preventive measures, including an upright posture during meals and sleep, a full liquid diet, speech therapy, avoiding solid oral medication, and caregiver education. To better understand the implications of these results, future studies could delve into widening the sample size, orchestrating multicenter investigations concentrated on high-risk populations, and integrating the National Institute of Health Stroke Scale (NIHSS) as a compass to navigate the intricate landscape of stroke impact, facilitating strategic post-acute care.

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Authors' contribution

The authors confirm their contribution to the paper as follows: conception and design of the study: Alarice Francisco, Mabel Alcantara y Misael Rijo; Data Collection: Alarice Francisco, Mabel Alcantara y Misael Rijo, analysis and interpretation of results: Alarice Francisco, Mabel Alcantara y Misael Rijo; preliminary manuscript preparation: Alarice Francisco. All authors reviewed the results and approved the final version of the manuscript.

Ethical considerations

The ethics committee of the study hospital approved the investigation. In the same way, the present project was governed under the principles of privacy and confidentiality promulgated in the Declaration of Helsinki of 1964 and its revision of 1975. Likewise, it was based on the bioethical principles of non-maleficence, beneficence, and justice. No conflicts of interest were declared by the authors.

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