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**Risk factors associated with hospital-acquired pneumonia: a literature review**

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## From outbreak to strategy: the hospital epidemiologist as an agent of change in the prevention of healthcare-associated infections (HAIs)

by Rodolfo del Campo-Ortega\*

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Healthcare-associated infections (HAIs) represent one of the most persistent and complex challenges for hospital systems. Their emergence is not an isolated event, but rather the manifestation of accumulated failures in care processes, infrastructure, work organization, and institutional culture. In this scenario, the hospital epidemiologist occupies a key position: not as a data producer, but as a translator of operational reality, a facilitator of change, and a generator of decisions.

Epidemiological analysis acquires meaning when it allows us to interpret patterns, anticipate risks, and transform information into concrete actions. It is not enough to calculate rates or prepare monthly reports: the true impact occurs when data makes the invisible visible, provokes discomfort, sparks dialogue, and leads to decisions that improve patient safety. This is the difference between monitoring and transformation. Interpretation is not simply saying whether a rate is green, yellow, or red; it is understanding what has failed in the processes. For example, if the rate of ventilator-associated pneumonia is high, the analysis must go beyond the numbers: it's about evaluating whether the process of setting up, maintaining, and weaning from mechanical ventilation is being carried out properly. Do we have the correct fixation system? Are artificial noses available and changed as frequently as needed? Are the sensors installed, reused, or not even in place? Is the humidification and heating system working correctly? Is the patient properly positioned? Is oral hygiene being performed? Is weaning being assessed promptly by the medical team? Do we have closed suction circuits? Are suction traps being used? Is the staff trained to perform suctioning? Is antimicrobial treatment based on specific microbiological cultures? Etc. The rate tells us how quickly patients progress from a non-infected state to one with pneumonia, and as epidemiologists, our duty is to interpret,

communicate, and point out areas for improvement. The more specific the analysis, the more tools we generate for decision-making.

### **Hospitals as ecosystems: culture, microorganisms, and missing decisions**

Hospitals are living in complex environments where the tension between clinical, operational, and administrative aspects is constant. Recent evaluations in hospital units show recurring patterns: implemented but fragile surveillance structures, preventive programs without effective oversight, incomplete records, deteriorating infrastructure, and weak leadership.

In this context, microorganisms not only inhabit patients: they colonize devices, hands, sheets, radiant warmers, faucets, and surfaces. Over time, they become part of the landscape, part of the shared normality. In many hospitals, the microbiota is so commonplace that no one even notices it anymore. Infection prevention ceases to be a priority when risk becomes routine.

Safe healthcare requires much more than supplies: it requires conviction. But institutional conviction is lacking when decision-makers are unaware of the true scope of the problem. In many hospitals, epidemiological reports are not reviewed, indicators do not guide action, and the epidemiologist's role is reduced to an operational one. Nationally, the lack of updates to regulatory frameworks such as NOM-045 confirms the structural shortcomings in this area.

### **Prevention vs. Reaction: The Active Role of the Hospital Epidemiologist**

A healthcare-associated infection (HAI) is, fundamentally, a manifestation of a lack of control. Preventing it requires intervening in processes before harm occurs. This is only possible by strengthening active surveillance, risk monitoring, and the standardization of preventive actions at every stage of care.

Evidence shows that the critical points are constant: use and handling of invasive devices, environmental cleaning and disinfection, food preparation and storage, handling of hospital linens, medication administration, hand hygiene, hazardous waste disposal—in general, the substantive processes of healthcare. Each of these processes must be monitored, understood, and supported with useful, timely epidemiological information translated into operational language.

The epidemiologist's work is therefore twofold: interpreting the data and interpreting the context. It is not enough to detect that the surgical infection rate is high; one must go to the operating room, observe the flow of patients,

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inquire about patient flow, review supplies, and listen to the staff. Only from this intersection between the numerical and the real can a meaningful intervention be generated.

### **Leading without imposing change as a relational process**

The leadership required to transform the HAI prevention system is not hierarchical or punitive, but relational and sustained. The epidemiologist is called upon to exercise leadership that connects evidence with action, fosters difficult conversations without breaking cooperation, and builds trust through clarity.

Leading in this context means staying focused when reports aren't read, persisting when priorities shift, and communicating when the risk isn't perceived. It means maintaining the tension between diagnosis and improvement without becoming frustrated, because change isn't decreed: it's cultivated. And it's cultivated best when ideas aren't imposed but emerge from the operational staff themselves. Listening, observing, engaging, and building collectively are more effective than ordering.

The most difficult thing to transform in a hospital isn't the supplies or the physical structures, but the behaviors. Prevention requires a new culture, where quality and patient safety are not slogans, but convictions. This is only achieved when change is embraced as our own, when we understand that preventing an infection is not about avoiding statistics: it's about protecting a person, a mother, a child, a grandparent who could have been part of our own family.

Therefore, doing what we are called to do—with conviction, with clarity, with evidence, with active listening, and with genuine commitment—is also exercising ethical leadership. Leadership that transforms because it convinces, not because it subjugates. Because it builds community, not bureaucracy. Because it reminds us that, even in the most adverse environments, it is always possible to aspire to something better.

Nothing more, and nothing less.

# Impact of healthcare-associated infections on hospital costs, length of stay, and mortality

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## Abstract

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**Introduction:** Healthcare-associated infections are a public health problem, mainly related to invasive medical procedures, as well as the condition of patients, such as those requiring admission to intensive care, increasing morbidity and mortality rates, and consequently increasing hospital costs by delaying patient discharge.

**Objective:** To identify the impact of healthcare-associated infections (HAIs) on hospital costs, length of stay, and mortality.

**Materials and methods:** An observational, descriptive, cross-sectional prevalence study was conducted.

**Results:** A total of 1791 infection records and 24 analyses were performed, revealing a predominance in males (55.6%). The predominant age groups were those over 65 years and under 1 year old. A correlation was found between healthcare-associated infections (HAIs) and extended hospital stay (R 0.932), hospital costs (R 0.734), and mortality (R 0.049). The infection that generated the highest costs due to extended stay was ventilator-associated pneumonia (VAP) (\$229,883,992.00).

**Conclusions:** A relationship was found between costs and healthcare-associated infections (HAIs), as well as with the resulting overstay. No relationship was found between deaths caused by the increase in HAIs. Invasive procedures continue to be a key factor in the costs generated.

**Keywords:** HAIs, INOSO, costs, overstay, mortality.

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## INTRODUCTION

The World Health Organization (WHO) defines healthcare-associated infections (HAIs) as “infections that affect a patient during care in a hospital or other healthcare facility, which were not present or incubating at the time of admission. They also include infections acquired in the hospital, but which manifest after discharge.” HAIs, also known as nosocomial or hospital-

acquired infections, are the most frequent adverse event during the provision of medical care, and can affect both patients and healthcare personnel.<sup>1,2</sup>

The Mexican Official Standard NOM-045-SSA2-2005, for the epidemiological surveillance, prevention, and control of nosocomial infections, describes them as a major problem of clinical and epidemiological importance because these infections impact morbidity and mortality rates, as well as directly complicating patient care costs.<sup>4</sup>

WHO reports show that more than 1.4 million people worldwide contract hospital-acquired infections. In developed countries, the prevalence of patients who acquire at least one healthcare-associated infection (HAI) during their hospitalization ranges from 5% to 10%, while in developing countries it varies between 5.7% and 19.1%, reaching a proportion greater than 25% of affected patients in some countries.<sup>2</sup>

General estimates of the impact of HAIs contribute to understanding their magnitude and potential consequences. European estimates indicate that HAIs cause 16 million days of excess hospital stay and 37,000 attributable deaths annually.<sup>7</sup> In Mexico, HAI-related mortality in secondary and tertiary care institutions is 43.8%, while the WHO estimates that 450,000 healthcare-associated infections occur in Mexico, causing 32 deaths per 100,000 inhabitants per year.<sup>2</sup>

In Intensive Care Units (ICUs), the situation is even more complex due to the proportion of patients with invasive devices and their critical condition, which often requires the use of broad-spectrum antibiotics, antacids, parenteral nutrition, or other patient-specific factors such as pre-existing comorbidities that have been associated with a higher risk of HAIs.<sup>8,9</sup>

Regarding the risk that healthcare-associated infections (HAIs) contribute to prolonged hospital stays, in Mexico this risk ranges from 5.9 to 9.6 days and, moreover, increases the probability of death by up to 6.9%, which implies a considerable increase in hospital costs.<sup>2,17</sup>

HAIs also represent a significant economic impact on healthcare facilities and on the cost of healthcare at the national level. Members of the Infection Prevention and Control (IPC) team must understand the financial burden of HAIs and be able to assess the savings that a given preventive intervention would represent.<sup>8,10</sup> Measuring the financial impact of an HAIs on healthcare services can be difficult. However, hospital-acquired infections can have various economic consequences, from delaying patient discharge, which leads to higher occupancy of hospital beds, to increasing the cost of antimicrobial

treatment and other interventions that the patient may require. They require greater use of diagnostic aids, increase costs in terms of infection prevention and control, and are often subject to legal proceedings.<sup>11,12</sup>

At the Mexican Social Security Institute, HAIs have various systems that support the process of collecting and analyzing information for the notification of probable, confirmed, and discarded HAIs, which are the Hospital Epidemiological Surveillance Unit (UVEH); the online platform for nosocomial infections (INOSO); and the system for adverse events, near misses, and sentinel events related to the Infection Prevention and Control system (VENCER II). The process and outcome indicator control panel, as well as the hospital committees where the results and functionality reports of the Committee for the Detection and Control of Healthcare-Associated Infections (CODECIAAS) are evaluated.<sup>8</sup>

The Official Gazette of the Federation, according to its latest update for 2023, presents the unit costs per level of medical care for the IMSS (Mexican Social Security Institute), establishing the cost per patient day in hospitalization and incubator at \$11,919.00 each. The cost per patient day in intensive care is \$62,705.00, the cost of wound care is \$358.00, clinical laboratory tests are \$152.00, radiodiagnostic studies are \$517.00, surgical interventions are \$38,830.00, and patients on mechanical ventilation are \$44,953.00 per day.

The objective of the study was to understand the impact of HAIs on hospital costs, length of stay and mortality at Regional General Hospital No. 1 Ciudad Obregón, Sonora.

## **MATERIALS AND METHODS**

The study was conducted at the Mexican Social Security Institute (IMSS): Regional General Hospital No. 1, Ciudad Obregón, Sonora, using an observational, descriptive, cross-sectional (prevalence) design. The study period was from December 26, 2017, to December 25, 2019.

The dependent variables were hospital costs, length of stay, and mortality, while the independent variable was healthcare-associated infections (HAIs).

The monthly analyses of HAIs reported by the Epidemiological Surveillance Unit of Regional General Hospital No. 1, Ciudad Obregón, Mexican Social Security Institute, were studied for the period of December 26, 2017, to December 25, 2019, totaling 1,791 infections. The monthly analyses included records of the number and type of HAIs, number of patients with HAIs, length of stay due to HAIs, monthly expenditures related to length of stay, and HAI-related mortality.

This represents the total number of infection records from the 24 censuses during the established period (1,791).

Data was obtained through a review of monthly analyses and the INOSO platform at Regional General Hospital 1, during the study period, totaling 1,791 infections, supplemented with information obtained from the Official Gazette of the Federation (DOF).

Inclusion criteria were records of patients with hospital-acquired infections, registered monthly on the INOSO platform; records of patients of both sexes; records of patients regardless of age; monthly analyses with monthly expenditures for hospitalizations and therapies; records of length of stay due to healthcare-associated infections (HAIs); and records of mortality associated with HAIs.

Exclusion criteria were records of patients with hospital-acquired infections imported from other units; records of patients with infections ruled out as healthcare-associated; monthly analyses without calculated monthly expenditures; and monthly analyses without records of mortality associated with HAIs. Exclusion criteria included patient records with incomplete data in the INOSO platform registry and incomplete monthly analyses.

The data were analyzed by reviewing sex, age, type of infection, length of hospital stay with infection (excess stay), costs associated with excess stay, and deaths. Costs, excess stay, and mortality (death due to or with HAIs) were considered dependent variables, while healthcare-associated infections were considered independent variables.

All information for the study was collected and recorded in a database created using a Microsoft Excel spreadsheet, which included the study variables as well as any supplementary information of interest. Once the database was completed, the analysis was performed using SPSS (Statistical Package for the Social Sciences) version 25. The results are presented in tables and graphs, along with their simultaneous interpretation.

For descriptive statistics, qualitative variables were summarized using frequency and percentage measures, while quantitative variables were summarized using measures of central tendency (mean, minimum, and maximum values) and measures of dispersion (standard deviation).

For inferential statistics, normality tests were performed. The risk of mortality with healthcare-associated infections (HAIs), sex, and type of infection was

analyzed, as well as the risk of HAIs in relation to type of infection by sex and overstay in relation to the number of HAIs. Associations for qualitative variables were assessed using the Chi-square test ( $\chi^2$ ); for quantitative variables, Student's t-test or Mann-Whitney U test was used, as appropriate.

For the quantitative variables of hospital overstay, costs associated with healthcare-associated infections (HAIs), and deaths, linear correlation and coefficient of determination were calculated, as well as HAI overstay by area of presentation, HAI costs by area, costs of overstay by area, and costs by type of infection. A 95% confidence level and a statistical significance level of 5% ( $p < 0.05$ ) were considered.

This study was conducted in accordance with the ethical guidelines for health-related research involving human subjects developed by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization, published in 2017. The local research committee granted the following registration number: R-2023-2601-072.

## RESULTS

An observational, descriptive, analytical, retrospective, and cross-sectional study was conducted. Of a total of 1954 records, 1791 met the inclusion, exclusion, and elimination criteria. Additionally, 24 monthly analyses were performed to obtain supplementary data.

Table 1 presents the general characteristics of the population. Regarding the distribution of cases by sex, males predominated, representing 55.67% (997) of the observations, while females represented 44.33% (794) of the cases. Frequencies were obtained by age group, showing that the largest group was those 65 years and older, comprising 37.2% (666), followed by those under 1 year old, comprising 17.2% (308). The 25-44 age group represents 9.0% (161), followed by the 50-59 age group with 8.4% (150) and the 1-4 age group with 7.4% (132). Next are the 60-64 age group with 6.5% (116) and the 5-9 age group with 5% (89). Less frequently represented are the 10-14 age group with 3.2% (58), the 45-49 age group with 2.9% (52), the 20-24 age group with 2.0% (36), and the 15-19 age group with 1.3% (23). The frequency of healthcare-associated infections studied is also described, with the most frequent being "Other" at 54.7% (979 cases), followed by ventilator-associated pneumonia (VAP) at 15.0% (269 cases), urinary tract infection (CAUTI) at 12.6%, surgical site infection (SSI) at 9.5% (170 cases), and central venous catheter-related infection (CLABSI) at 8.1% (146 cases).

Regarding the age of the participants, Table 2 describes the age range, from 0 years to 102 years, with a mean of 43.40 years and a standard deviation of  $\pm 32.428$  (SD).

**Table 1. General Characteristics of the Population**

		Frequency	Percentage
Sex	Female	794	44.3 %
	Male	997	55.7 %
Age groups	Children under 1 year old	308	17.2 %
	Ages 1 to 4 years old	132	7.4 %
	Ages 5 to 9 years old	89	5.0 %
	Ages 10 to 14 years old	58	3.2 %
	Ages 15 to 19 years old	23	1.3 %
	Ages 20 to 24 years old	36	2.0 %
	Ages 25 to 44 years old	161	9.0 %
	Ages 45 to 49 years old	52	2.9 %
	Ages 50 to 59 years old	150	8.4 %
	Ages 60 to 64 years old	116	6.5 %
Type of infection	Ages 65 and over	666	37.2 %
	Surgical site infection	170	9.5 %
	Ventilator-associated pneumonia	269	15.0 %
	Central venous catheter-associated STI	146	8.2 %
	Urinary catheter-associated UTI	227	12.7 %
	Other	979	54.7 %

The nominal scale data is presented in frequencies and percentages. Research protocol conducted in 2023, Ciudad Obregón, Sonora.

**Table 2. Descriptive statistics of the population**

	N	Minimum	Maximum	Mean	Dev. Std.
Age	1791	0	102	43.40	32.428

Quantitative data are presented as mean and SD (standard deviation), minimum and maximum average of the records (1791). Source: Research protocol carried out in 2023, Cd Obregón, Sonora.

Table 3 describes the descriptive statistics analyzed monthly regarding hospital overstay, with a minimum of 456 and a maximum of 1150 days, and a mean of 808.08 days ( $\pm 187.763$  SD). Monthly costs for healthcare-associated infections (HAIs) ranged from a minimum of \$4,584,927 to a maximum of \$16,188,753, with a mean of \$10,004,920.92 ( $\pm 2964,466.384$  SD). HAI-related deaths ranged from a minimum of 0 to a maximum of 5, with a mean of 2.67 ( $\pm 1.435$  SD). Regarding the risks associated with the variables, these can be observed in Table 4. The risk of mortality from HAIs was found to be an OR of 0.46 ( $p < 0.000$ ). Mortality by sex showed an OR of 1.05 for females and an OR of 0.95 for males ( $p = 0.853$ , both sexes). Regarding mortality by type of HAIs and sex, the risk of developing a surgical site infection (SSI) was OR 2.36 in females and OR 0.42 in males ( $p = 0.17$  for both sexes). The risk of developing ventilator-associated pneumonia (VAP) was OR 0.46 in females and OR 0.70 in males ( $p = 0.89$ , both sexes). The risk of developing a cardiovascular infection (CVI) was OR 1.14 in females and OR 0.88 in males ( $p = 0.89$ , both sexes). Regarding the association between the development of CAUTI in females, an OR of 0.42 was found for females and an OR of 2.33 for males ( $p=0.24$ , both sexes). For the risk of developing another infection, an OR of 2.39 was found in females and an OR of 0.15 in males ( $p=0.09$ , both sexes). Similarly, Table 4 presents the risks with respect to the type of HAIs according to sex, where SSI showed an OR of 0.81 for females and an OR of 1.23 for males ( $p=0.12$ ); as for VAP, it presented an OR of 1.29 for females and an OR of 0.78 for males ( $p=0.12$ ). Regarding the risk of developing CLABSI, an OR of 0.93 was found for females and an OR of 1.07 for males ( $p=0.69$ ). For CAUTI, an OR of 1.27 was found for females and an OR of 0.79 for males ( $p=0.09$ ); for the variable "Other," an OR of 0.89 was found for females and an OR of 0.93 for males ( $p=0.48$ ). Regarding the relationship between the number of HAIs and overstay, an OR of 100.35 was found ( $p<0.0001$ ). Table 5 presents the hypothesis tests where the relationship between the number of HAIs and overstay costs was sought, yielding a t-value of 16.534 ( $p<0.0001$ ); regarding the number of HAIs and overstay, a t-value of 20.751 was found ( $p<0.0001$ ). The relationship between the number of HAIs and mortality yielded a t-value of 21.943 ( $p<0.000$ ). The age of presentation was associated with the number of HAIs, with a t-value of 51.774 ( $p<0.0001$ ), and the costs by type of infection showed a t-value of 25.114 ( $p<0.0001$ ). Likewise, an association was sought between mortality and number of HAIs, finding a  $\chi^2$  of 37.17 ( $p<0.000$ ), mortality and sex with a  $\chi^2$  of 0.0341 ( $p=0.850$ ), mortality by type of infection where SSI showed  $\chi^2$  of 0.50 ( $p=0.480$ ), VAP with  $\chi^2$  of 1.84 ( $p=0.170$ ), CLABSI with  $\chi^2$  of 0.02 ( $p=0.900$ ), CAUTI with  $\chi^2$  of 2.94

(p=0.240) and Other with  $\chi^2$  of 2.94 (p=0.090). Regarding the association between the type of infection and sex, the following was found: SSI  $\chi^2=2.44$  (p=0.122), NAVM  $\chi^2$  of 2.42 (p=0.120), CLABSI  $\chi^2=0.16$  (p=0.690), CAUTI  $\chi^2=2.86$  (p=0.090) and Other  $\chi^2=0.51$  (p=0.480).

**Table 3. Descriptive statistics of the analyzes**

	N	Minimum	Maximum	Mean	Dev. Std.
Overstay	24	456	1150	808.08	187.763
Costs	24	\$4,584,927	\$16,188,753	10,004,920.92	2,964,466.384
Mortality	24	0	5	2.67	1.435

Quantitative data are presented as mean and SD (standard deviation), minimum and maximum averages. Source: Research protocol conducted in 2023, Ciudad Obregón, Sonora.

**Table 4. Risk relationship statistics according to study variables**

	Variable	Risk		95% CI		P value	
Mortality related to HAIs, by sex and type of infection presentation	HAIs	0.46		0.36 - 0.59		.000*	
	Sex	F	1.05		0.63 - 1.74		0.853
		M	0.95		0.57 - 1.58		0.853
	Type of HAIs	SSI	F	M	F	M	
			2.36	0.42	0.20 - 27.39	0.04 - 4.93	
		NAP	F	M	F	M	
			0.46	0.70	0.15 - 1.43	0.70 - 6.81	
		CLABSI	F	M	F	M	
1.14			0.88	0.15 - 8.70	0.12 - 6.63		
CAUTI	F	M	F	M			
Other*	F	M	F	M			
		0.42	2.33	0.10 - 1.83	0.55 - 9.99		
		2.39	0.15	0.87 - 6.57	0.15 - 1.14		
HAIs regarding sex and type	Type of HAIs	F	M	F	M		
		SSI	0.81	1.23	0.62 - 1.06	0.95 - 1.60	
	NAP	F	M	F	M		
		1.29	0.78	0.94 - 1.76	0.57 - 1.07		
	CLABSI	F	M	F	M		
		0.93	1.07	0.66 - 1.31	0.76 - 1.51		
CAUTI	F	M	F	M			
Other*	F	M	F	M			
		1.27	0.79	0.96 - 1.68	0.59 - 1.04		
		0.89	0.93	0.89 - 1.29	0.77 - 1.13		
Overstay in relation to HAIs	Overstay	100.35		69.47 - 144.95		.000*	

Quantitative data are presented as odds ratios (OR), confidence intervals (CI), and p-values. Source: Research protocol conducted in 2023, Ciudad Obregón, Sonora. \* Includes: Primary bacteremia (not demonstrated); bronchitis, acheobronchitis, tracheitis without evidence of pneumonia; conjunctivitis, empyema secondary to procedures, endocarditis, endometritis, necrotizing fasciitis, phlebitis, nosocomial gastroenteritis, skin and soft tissue infections in burn patients, skin and soft tissue infection, catheter insertion site infections, laboratory-confirmed sexually transmitted infections (STIs), urinary tract infections (UTIs) not associated with urinary catheters, meningitis or ventriculitis, clinical pneumonia not associated with a ventilator, acute otitis media, peritonitis, rhinopharyngitis and pharyngotonsillitis, and acute sinusitis.

**Table 5. Hypothesis test statistics for related variables**

Variables		Statistic	P value	
T Student	Number of HAIs - Costs per Extended Stay	16.534	.000*	
	Number of HAIs - Total Extended Stay	20.751	.000*	
	Number of HAIs - Deaths	21.943	.000*	
	Age – HAIs	51.774	.000*	
	Total Costs - Type of Infection	25.114	.000*	
Chi-squared	Mortality - HAIs	37.17	.000*	
	Mortality - Sex	0.0341	0.85	
	Mortality - Type of HAI	ISQ	0.50	0.48
		NAVM	1.84	0.17
		STI-CVC	0.02	0.9
		UTI-CU	1.36	0.24
		Other*	2.94	0.09
	Type of HAIs - Sex	ISQ	2.44	0.12
		NAVM	2.42	0.12
		STI-CVC	0.16	0.69
		UTI-CU	2.86	0.09
Other*		0.51	0.48	

Quantitative data from Student's t-tests, qualitative data from chi-square tests and p-values are presented. Source: Research protocol conducted in 2023, Cd Obregón, Sonora. \*Includes: Primary bacteremia, not demonstrated; bronchitis, tracheobronchitis, tracheitis without evidence of pneumonia; conjunctivitis, empyema secondary to procedures, endocarditis, endometritis, necrotizing fasciitis, phlebitis, nosocomial gastroenteritis, skin and soft tissue infections in burn patients, skin and soft tissue infection, catheter insertion site infections, laboratory-confirmed STIs, UTIs not associated with urinary catheters, meningitis or ventriculitis, clinical pneumonia not associated with a ventilator, acute otitis media, peritonitis, rhinopharyngitis and pharyngotonsillitis, acute sinusitis.

**Table 6. Correlation and variability statistics**

Variables		R	R square
HAIs	Overstay	0.923	0.853
	Costs of overstay	0.734	0.538
	Deaths	0.049	0.002
Regarding stay – HAIs	Hospital overstay	0.927	0.859
	ICU overstay	0.902	0.813
Costs – HAIs	HAIs in hospitalization	0.927	0.859
	HAIs in ICU	0.902	0.813
Costs - regarding stay	General overstay	0.855	0.731
	Hospital overstay	1.000*	1.000*
	ICU overstay	1.000*	1.000*
Costs - type of infection	Type of infection	0.436	0.19

Quantitative data are presented as Pearson's R and R-squared. Source: Research protocol conducted in 2023, Cd Obregón, Sonora.

The correlation and variability are determined in Table 6, where the variables number of HAIs and overstay have a Pearson R of 0.923 and  $R^2$  of 0.853; the number of HAIs and costs due to overstay R 0.734 and  $R^2$  0.538; the number of HAIs and deaths R 0.049 and  $R^2$  0.002; overstay due to HAI in hospitalization R 0.927 and  $R^2$  0.859 and in overstay in ICU with R 0.902 and  $R^2$  0.813. Regarding the costs due to HAIs according to the area, for hospitalization an R 0.927 and for ICU an R 0.902 and  $R^2$  0.813. Regarding the relationship between costs and the excess stay generated, an R of 1.000 and an  $R^2$  of 1.000 were found for hospitalization, an R of 1.000 and an  $R^2$  of 1.000 for ICU, while for general excess stay an R of 0.855 and an  $R^2$  of 0.731. Finally, the relationship between costs and types of infection presented an R of 0.436 and an  $R^2$  of 0.190.

## DISCUSSION.

As Scott, Culler, and Rask (2019) state, healthcare-associated infections (HAIs) lead to increased costs due to prolonged hospital stays, the need for diagnostic tests, and hospital bed occupancy, among other factors. However, although this topic has been previously studied, it remains an area of opportunity for comprehensive care and addressing the changes it can generate in a hospital.<sup>11</sup> According to our study, regarding age groups, the predominant group is those over 65 years old (37.2%), followed by those under 1 year old (17.2%). This indicates that the highest incidence of HAIs is found at the extremes of life, which could be associated with complications such as chronic diseases or prematurity in the case of newborns. According to the types of infection, based on the established variables, the predominance is found in Other with 54.7%, followed by VAP with 15% and UTI with 12.7%. However, considering that the study included in the variable “Other” all HAIs that did not have a history of an invasive procedure, it could be considered that the value is biased by the number of HAIs included in a single variable, so in reality VAP occupies first place, followed by CAUTI, determining that the greater presence of infections is associated with a previous invasive procedure, as mentioned by Perozo, Castellano González and Gómez Gamboa (2020), according to their study.<sup>6</sup>

In the development of the hypothesis tests, a student's t-test was performed where statistical significance was found in related variables. On the other hand, a statistically significant chi-square test ( $\chi^2$ ) was found for mortality and HAIs (0.000\*), which contrasts with the calculated odds ratio (OR = 0.46), which is also statistically significant, indicating no association between

mortality and HAIs. The remaining associated variables did not show statistical significance in this study.

The relationship between HAIs variables and hospital costs, length of stay, and mortality was analyzed using linear correlation and the coefficient of determination to assess variability. The association between HAIs variables and hospital costs showed a strong, positive linear correlation (Pearson's R 0.734), indicating that costs increase proportionally with HAIs incidence. Similarly, 53.8% of the cost variability can be explained by the occurrence of HAIs. The relationship between HAIs variables and length of stay also showed an extremely strong, positive linear correlation (Pearson's R 0.923), indicating that length of stay increases proportionally with HAIs incidence. Furthermore, 85.3% of the variability in length of stay can be explained by the number of HAIs. In contrast, the relationship between HAIs and mortality showed a very weak correlation (Pearson's R 0.049), considering that  $R=0$  means that there is no linear correlation, and the variability was 2%, which means that the model does not explain any variability; this contrasts with what was described by Barrasa Villar, Aibar Remón et al. (2017), where they established a significant relationship in the three variables studied.<sup>17</sup> Ortiz Mayorga, Pineda Rodríguez, Dennis and Porras (2018), describe in their study the relationship between the cost of HAIs management and prolonged stay prior to its appearance, as described in this study where a strong linear correlation (Pearson's R 0.855) was found between general overstay and the costs for it, explaining that as overstay increases, hospital costs also increase, with a variability of 73.1%. Likewise, a comparison was made between hospitalization and ICU areas, where the relationship of both with overstay showed a perfect linear correlation with 100% variability, explaining that increased overstay increases hospital costs. Furthermore, the relationships between overstay and total HAIs, and HAIs costs by area, showed an extremely strong linear correlation (Pearson's R 0.927) for hospitalization with 85.9% variability for both relationships, and a strong linear correlation (Pearson's R 0.902) for ICUs with 81.3% variability for both relationships, indicating that as HAIs increase, overstay increases, and increased HAIs increase costs.

Regarding the relationship between costs and the type of infection, a moderate linear correlation was found (Pearson's R 0.436) with a variability of 19%, indicating that costs cannot be explained by the type of infection. The main objective of this research was to determine the impact of healthcare-associated infections (HAIs) on hospital costs, length of stay, and mortality at Regional General Hospital No. 1 in Ciudad Obregón, Sonora. The study period prior to

the COVID-19 pandemic (2020 to 2023) was chosen to minimize bias. The analysis revealed that HAIs were more prevalent in males (55.6%) than in females, with ventilator-associated pneumonia (VAP) being the most common infection (15.08%), followed by urinary tract infections (CAUTI) (12.62%). The results obtained demonstrate that the increase in HAIs significantly impacts costs and length of stay, regardless of the area of presentation, as there is a positive correlation between the two. However, although mortality is related to HAIs, it was not demonstrated that the increase in HAIs impacts mortality itself.

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## Effectiveness of alcohol solutions at different concentrations as a disinfectant for hand hygiene

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### Abstract

**Introduction:** Healthcare-associated infections are the leading cause of prolonged hospital stays, as well as leading cause of long-term disability, increased deaths, and increased costs. Hand hygiene has been a highly effective intervention in reducing healthcare-associated infections; however, the alcohol concentration range is very wide (60% to 95%), in line with WHO recommendations.

**Objective:** To evaluate the effectiveness of alcohol-based solutions at different concentrations as hand hygiene disinfectants for healthcare personnel and family members of patients at Regional General Hospital 1, Ciudad Obregón, Sonora.

**Materials and methods:** A quasi-experimental study was carried out which included health personnel working at the Regional General Hospital 1 and relatives of hospitalized patients in the different services (the caregiver), the hand hygiene technique was performed in vivo and in vitro to assess susceptibility according to the 5 most frequent microorganisms in Infections associated with health care and with a pattern of antimicrobial multi-resistance from March 1 to July 31, 2015.

**Results:** The reduction obtained with 90% alcohol solution was 97.79% at 10 seconds and 98.67% at 30 seconds, with 60% a reduction of 76.68% and 82.42% respectively; a greater reduction was observed with 90% alcohol solution and hand hygiene technique: 98.06% at 10 seconds and 99.20% at 30 seconds.

**Conclusions:** The 90% alcohol solution was the factor that showed statistical significance for both Gram positive and Gram-negative bacteria.

**Keywords:** Effectiveness, alcohol solutions, Healthcare-associated infections.

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## INTRODUCTION

A healthcare-associated infection (HAI) is a localized or systemic condition, resulting from an infectious agent or its toxins, contracted by a patient during treatment in a hospital or other healthcare facility and which was neither present nor in the incubation phase at the time of admission.<sup>1</sup>

Worldwide, it is estimated that more than 1.4 million people contract hospital-acquired infections; between 5% and 10% of patients admitted to hospitals in developed countries will contract one or more infections. In the United States of America (USA), one in every 136 hospitalized patients becomes seriously ill from a hospital-acquired infection, equivalent to 2 million cases and approximately 80,000 deaths annually.<sup>2</sup>

This generates an average cost ranging from \$382.00 to \$1,833.00 US per case; In Canada, the annual cost of nosocomial infections is \$0.3 to \$1 billion; in Germany, the annual cost is estimated at \$0.3 to \$0.6 billion.

HAIs are the leading cause of prolonged hospital stays, as well as long-term disability, increased deaths, and increased costs.<sup>4</sup>

Several studies have shown that poor hand hygiene is the most common cause of HAIs.<sup>5, 6</sup> Similarly, it has been observed that handwashing with alcohol-based solutions prevents the transmission of nosocomial pathogens by healthcare workers, as alcohols possess antimicrobial activity attributed to their ability to denature proteins.<sup>7, 8</sup>

Alcohol-based solutions, at concentrations of 60% to 95%, are more effective, while higher concentrations are less potent, as proteins do not denature easily in the absence of water. They also reduce hand hygiene time. They have been shown to have excellent in vitro germicidal activity against gram-positive and gram-negative bacteria, including multidrug-resistant pathogens, *Mycobacterium tuberculosis*, and several fungi. Some enveloped viruses, such as the Human Immunodeficiency Virus, Herpesvirus, Influenza, and Respiratory Syncytial Virus, are sensitive to alcohol.<sup>7, 8</sup>

It is therefore important to practice proper hand hygiene to reduce healthcare-associated infections. Various guidelines recommend that handwashing be performed with alcohol-based solutions at a concentration of 60% for a period of 30 seconds to be effective. The World Health Organization even establishes guidelines for preparing alcohol-based solutions, thus ensuring greater effectiveness.<sup>9, 10, 11</sup>

It is worth noting the rise in the use of alcohol-based solutions in recent years, as mentioned by Angeles et al. (2005) in their clinical trial conducted at the IMSS La Raza Medical Center (CMN la Raza), where they compared the effectiveness of using alcohol gel and the traditional hand disinfection technique in reducing CFUs on the hands of doctors and nurses, obtaining a CFU-Log10 reduction of 0.7 versus 1.53 ( $p \leq 0.01$ ); observing that the nurses group had a greater reduction in CFUs-Log10 than the doctors ( $p < 0.05$ ).

In 2004, at the Department of Medicine of the State University of Maringá, Brazil, Hernandez et al. compared the effectiveness of alcohol-based hand gel with traditional handwashing for the elimination of agents such as *Acinetobacter baumannii*, methylcylin-resistant *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis*, *Pseudomonas aeruginosa*, and *Candida albicans*. They concluded that handwashing with liquid soap reduced the number of microorganisms by 93.83%, 100% povidone-iodine, and 99% alcohol-based hand gel. They also demonstrated that 4 of 6 microorganisms analyzed with the different disinfectants were removed.<sup>13</sup>

On the other hand, Alvarado et al. (2008) studied the antiseptic capacity of two different brands of alcohol-based hand gel, without specifying the final alcohol concentration, and compared its effectiveness with a 70% liquid alcohol solution. They found that the greatest antimicrobial effects for both gels were obtained after 30 s and for liquid alcohol after 1 minute. An ANOVA distribution was used for statistical analysis and it was concluded that the alcohol presentation does not interfere with the percentages of bacterial reduction and the time for maximum bacterial inhibition is 30 s. 14 Kampf and Hollingsworth (2008) evaluated the bactericidal activity of an ethanol-based hand gel in 15 s and its efficacy against 11 gram-positive bacteria, 16 gram-negative bacteria, and 11 emerging bacterial pathogens. Each strain was evaluated in quadruplicate; They found that hand gel (85% ethanol) reduced 11 gram-positive and 16 gram-negative bacteria by more than 5 logs in 15 seconds and that it has a broad bactericidal spectrum. 15 Herruzo-Cabrera et al. (2001) studied the effects of various alcohol solutions on the resident and acquired microbiota, comparing them with conventional handwashing in vivo and in vitro. Significant differences were found in both designs. Handwashing barely modified the native or acquired microbiota (only 0.1 to  $< 2$  logs) and did not eliminate *Staphylococcus aureus* and gram-negative bacteria (34–23%;  $P > 0.05$ ). However, N-duopropenide reduced the acquired microbiota by 5 logs and the native microbiota by more than 2 logs, as well as *S. aureus* and gram-negative bacteria (33–1.3%;  $P < 0.01$ ).

## MATERIALS AND METHODS

The study was conducted at Regional General Hospital No. 1, located in Ciudad Obregón, Sonora. The study period ran from March 1 to July 31, 2015. A quasi-experimental, double-blind study was conducted with healthcare personnel and family members of patients who met the inclusion criteria.

The sample size was calculated and yielded 52 participants. The study included healthcare personnel (physicians, nurses, and residents) working at the Northwest National Medical Center in Ciudad Obregón, Sonora, as well as family members of hospitalized patients (only the caregiver) from departments with the highest incidence of healthcare-associated infections (internal medicine, gynecology and obstetrics, surgery, traumatology, orthopedics, pediatrics, and emergency departments). Individuals with product allergies, dermatitis, prior hand hygiene, family members other than the patient's caregivers, or visibly dirty hands were excluded, and samples contaminated during transport or planting were eliminated.

The dependent variable was hand disinfection effectiveness, and the independent variables were the use of alcohol-based hand sanitizers at different concentrations, sex, adverse reactions, hand hygiene technique recommended by the WHO, hand rubbing time, assigned service, type of worker, and pathogen isolated.

The study protocol was submitted to the local research committee, and written consent was obtained from study participants.

The alcohol-based hand sanitizer was prepared at different concentrations (60% and 90%) according to the WHO-recommended guidelines for the preparation of hand sanitizer formulations. This was carried out as follows: 96% ethanol (8333 ml) was poured into a 10-liter plastic bottle fitted with a screw-top cap, 3% hydrogen peroxide (417 ml) was added, and 98% glycerol (145 ml) was added using a measuring cylinder. The bottle was then filled to the 10-liter mark with sterile distilled water. Once the preparation was completed, it was immediately capped to prevent evaporation. The solution was mixed by gentle shaking, and the solution was distributed into 100-ml plastic containers. The bottles were quarantined for 72 hours to eliminate any spores present in the alcohol or bottles. Quality control was monitored using an alcohol breathalyzer.

Initially, a hand sample was taken with a swab moistened with 0.45% saline solution, rubbing it over the entire surface. The swab was then placed in Brain-

Heart Infusion (BHI) broth. Subsequently, 2 ml of alcohol-based solution at 60% and 90% concentrations was applied to the hands, and hands were washed. Most healthcare personnel performed this procedure using the WHO-recommended technique, while patient family members did not. Samples were taken again 10 and 30 seconds after application. The collected samples were taken to the laboratory, incubated for 4 hours, and cultured using the mass plating technique with a 0.1 ml calibrated loop in base agar for CFU counting. For microorganism identification, samples were plated on blood agar, MacConkey agar, and mannitol salt agar. They were kept in incubation for 24 hours, at the end the colonies were isolated for identification by direct observation on a plate, as well as observation with a microscope and if necessary they were introduced to the VITEK 2. As a complement to the study, in vitro susceptibility tests were performed with a suspension of bacteria in a test tube with 0.45% saline solution as a diluent, it was verified that it had an optical density of 0.5 McFarland and dilutions 1:2, 1:4, 1:8, 1:16 and 1:32 were made with the different concentrations of alcohol solution (2 ml), the sample was homogenized by vortexing and the inhibition of strains was evaluated at 10s and 30s, a sample was taken with the calibrated loop extended on the plate, it was left to incubate for 24 hours and the CFU count was performed, the microorganisms were selected according to their development in cultures of hospitalized patients, the five most common or outbreak-causing pathogens (*Acinetobacter baumannii* complex, *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Stenotrophomonas maltophilia*) were identified, and the pattern of antimicrobial multidrug resistance was established.

A form was created in Epi Info 7® for all participants, including healthcare personnel and family members of hospitalized patients. A univariate analysis was then performed, applying frequency and central tendency measures depending on the type of variable, as well as proportions for qualitative variables.

Quantitative variables were evaluated using ANOVA statistics. A bivariate analysis was also performed using the Mann-Whitney U test. For qualitative variables, the chi-square test was used. Risk assessment was performed using Hazard Ratio. Multivariate analysis was performed using Cox proportional hazards. The software used was STATA® and Epi Info 7®.

## RESULTS

Data was collected from a total of 132 participants of both sexes over a five-month period. The study participants were 31.06% male and 68.93% female. The categories included were attending physicians (13.63%), resident physicians (23.48%), nurses (40.15%), and patient family members (caregivers) (22.72%). The alcohol-based hand sanitizer was applied in equal proportions to each study subject. Of the total participants, 71.96% performed hand hygiene using the WHO-recommended technique, and 28.03% did not (Table 1). According to microorganism development, 18 Gram-positive strains (64.28%) and 10 Gram-negative strains (35.71%) were isolated, totaling 171 bacteria. Among these strains, coagulase-negative Staphylococcus (20.46%) were isolated in order of frequency, followed by Acinetobacter baumannii complex (18.12%), Staphylococcus haemolyticus (8.77%), Staphylococcus hominis (8.77%), and Staphylococcus warneri (7.60%) (Table 1).

**Table 1. General characteristics of health personnel and patient caregiver and most frequent microorganisms**

Variable	Number	Percentage
<b>Gender</b>		
Male	41	31.06%
Female	91	68.93%
<b>Category</b>		
Primary care physicians	18	13.63%
Resident physicians	31	23.48%
Nurse	53	40.15%
Patient caregiver	30	22.72%
<b>Hand hygiene</b>		
with technique	95	71.96%
without technique	37	28.03%
<b>Gram positive microorganisms</b>	18	64.28%
<b>Gram negative microorganisms</b>	10	35.71%
<b>Most common microorganisms</b>		
Staphylococcus coagulasa negativo	35	20.46%
Acinetobacter baumannii complex	31	18.12%
Staphylococcus haemolyticus	15	8.77%
Staphylococcus hominis	15	8.77%
Staphylococcus warneri	13	7.60%

**Source:** Analysis of information obtained at the Regional General Hospital 1, Obregon, Sonora.

The reduction obtained with the 90% alcohol solution was 97.79% at 10 s and 98.67% at 30 s. The reduction obtained with the 60% solution was 76.68% and 82.42%, respectively. A greater reduction was observed with 90% alcohol solution using hand hygiene: 98.06% at 10 s and 99.20% at 30 s (Table 2).

**Table 2. CFU inhibition at 10s and 30s**

Variable	CFU Previous/Mean	CFU 10s	CFU 30s
90% alcohol solution	226.61	97.79%	98.67%
60% alcohol solution	238.09	61.75%	82.42%
Hand hygiene with technique	202.49	76.68%	85.96%
Hand hygiene without technique	307.4	83.26%	97.48%
90% alcohol solutions with hand hygiene technique	200.44	98.06%	99.20%
90% alcohol solutions without hand hygiene technique	294.94	97.16%	97.45%
60% alcohol solutions with hand hygiene technique	204.58	54.81%	73.28%
60% alcohol solutions without hand hygiene technique	319.21	72.51%	97.51%

Proportions at 10s and 30s. CFU: Colony Forming Units, s: seconds.

**Source:** Analysis of information obtained at the Regional General Hospital 1, Obregon, Sonora.

Colony-forming unit inhibition was evaluated using analysis of variance (ANOVA), which compared the inhibition with 90% alcohol solution, obtaining a  $p < 0.001$ , with a mean of 226.61 CFU in the pre-culture, with development of 5 CFU at 10 s and 3.01 CFU at 30 s after application of the alcohol solution. When applied with 60% alcohol solution, a  $p = 0.03$  was obtained, with a mean of 238.09 CFU in the pre-culture, 91.6 CFU at 10 s, and 41.85 CFU at 30 s (Table 3).

**Table 3. Inhibition of CFU dependent on alcohol solution and hand hygiene technique**

Variable	CFU Previous/Mean	CFU 10s/Mean	CFU 30s/Mean	p value
90% alcohol solution	226.61	5	3.01	<0.001
60% alcohol solution	238.09	91.06	41.85	0.003
Hand hygiene with technique	202.49	47.21	28.42	0.001
Hand hygiene without technique	307.4	51.45	7.74	0.001
90% alcohol solutions with hand hygiene technique	200.44	3.87	1.59	0.001
90% alcohol solutions without hand hygiene technique	294.94	8.37	7.5	0.001
60% alcohol solutions with hand hygiene technique	204.58	92.43	54.66	0.077
60% alcohol solutions without hand hygiene technique	319.21	87.73	7.94	0.032

P values calculated using ANOVA; CFU at 10 and 30 seconds were compared with the previous CFU. CFU: Colony Forming Units, s:seconds

**Source:** Analysis of information obtained at the Regional General Hospital 1, Obregon, Sonora.

Regarding hand hygiene with the technique, a  $p < 0.001$  was observed, with a mean of 202.49 CFU before, 47.21 CFU after 10 seconds, and 28.42 CFU after 30 seconds. When hand hygiene was performed without the technique, a  $p < 0.001$  was observed, with a mean of 307.40 CFU before, 51.45 CFU after 10 seconds, and 7.74 CFU after 30 seconds (Table 3). Regarding the use of 90% alcohol solution with hand hygiene technique, a  $p < 0.001$  was found with a mean of 200.44 in the previous, 3.87 at 10s and 1.59 at 30s, the same solution, but without technique presented a  $p < 0.001$ , with 294.94 CFU in the previous, 8.37 at 10s and 7.5 at 30s; A difference was noted with the 60% alcohol solution with the technique, as it presented a  $p=0.07$ , not being statistically significant with a mean reduction of 92.43 CFU at 10 s and 54.66 CFU at 30 s. However, without the technique, a  $p=0.03$  was obtained, with a

mean reduction of 87.73 at 10 s and 7.94 CFU at 30 s from a previous development of 319.21 CFU .

**Table 4. Reduction of microorganisms at 10s and 30s**

Variable	HR* 10s	95% CI	p value	HR* 30s	95% CI	p value
90% alcohol solution	0.62	0.47-0.82	0.004	0.57	0.39-0.84	0.002
Hand hygiene technique	1.02	0.76-1.37	0.87	0.86	0.60-1.24	0.447
Category						
Nurse	1.01	0.78-1.30	0.927	0.86	0.60-1.23	0.417
Resident physician	1.02	0.77-1.36	0.868	0.85	0.55-1.31	0.442
Gram negative	1.19	0.93-1.52	0.189	1.31	0.93-1.83	0.135

95% CI: 95% Confidence Interval/Statistically significant p-value <0.05. Risk was assessed using HR: Hazard Ratio, s=seconds.

Source: Analysis of information obtained at the Regional General Hospital 1, Obregon, Sonora.

The risk was evaluated through Hazard Ratio (HR), observing that the application of 90% alcohol solution represents a protective factor for the development of microorganisms at 10s (HR 0.62; 95% CI, 0.47-0.82; p<0.001), with no difference with the hand hygiene technique. (HR 1.02; 95% CI, 0.76-1.37; p=0.87) a comparison was made between nurses and resident physicians, without showing differences between them (HR 1.01; 95% CI, 0.78-1.30; p=0.92) and (HR 1.02; 95% CI, 0.77-1.36; p=0.86), finally Gram-negative microorganisms were evaluated (HR 1.19; 95% CI, 0.93-1.52; p=0.18) (Table 4). The same was done at 30s, and again, the protective factor was found to be 90% alcohol solution (HR 0.57; 95% CI, 0.39-0.84; p < 0.001), hand hygiene technique (HR 0.86; 95% CI, 0.60-1.24; p = 0.44), category (nurses and medical residents) (HR 0.86; 95% CI, 0.60-1.23; p = 0.41) and (HR 0.85; 95% CI, 0.55-1.31; p = 0.44). There was no difference in Gram-negative bacteria (HR 1.31; 95% CI, 0.93-1.83; p = 0.13) (Table 4). In the analysis by microorganisms a difference was observed with alcoholic solution and hand hygiene technique mainly, as in the case of *Acinetobacter baumannii* complex with 90% and 60% alcoholic solution (previous CFU/mean 272.91; CFU 10s/mean 6.33; CFU 30s/mean 4.5; p<0.001), (previous CFU/mean 236.93; CFU 10s/mean 50.06 CFU 30s/mean 7.85; p=0.01) with and without hand hygiene technique (previous CFU/mean 258.90; CFU 10s/mean 19.8; CFU 30s/mean 5.42; p<0.001), (previous CFU/mean 418.8; CFU 10s/mean 51.5 CFU 30s/mean 25; p=0.03), having a similar behavior in the case of Gram positives (Tables 5-9).

**Table 5. Coagulase-negative Staphylococcus isolated from the hands of healthcare personnel and patient caregivers**

Variable	CFU	CFU	CFU	p value
	Previous/Mean	10"/Mean	30"/Mean	
90% alcohol solution	209.77	5.27	2	0.007
60% alcohol solution	253.07	36.61	10	0.015
Hand hygiene with technique	214.26	12.57	6.15	<0.001
Hand hygiene without technique	259.33	29.44	0.28	0.05
90% alcohol solutions with hand hygiene technique	215.93	7	2.5	0.001
90% alcohol solutions without hand hygiene technique	193.33	0.66	0.4	0.037
60% alcohol solutions with hand hygiene technique	211.6	21.5	12	0.025
60% alcohol solutions without hand hygiene technique	391.33	87	0	0.536

P values calculated using ANOVA; CFU at 10 and 30 seconds were compared with the previous CFU. Most common microorganism. CFU: Colony Forming Units, s = seconds

Source: Analysis of information obtained at the Regional General Hospital 1, Obregon, Sonora.

**Tabla 6. Acinetobacter baumannii complex aislado en manos de personal de salud y cuidadores de pacientes**

Variable	CFU	CFU	CFU	p value
	Preview/Mean	10"/Mean	30"/Mean	
90% alcohol solution	272.91	6.33	4.5	0.002
60% alcohol solution	236.93	50.06	7.85	0.01
Hand hygiene with technique	258.9	19.8	5.42	<0.001
Hand hygiene without technique	418.8	51.5	25	0.038
90% alcohol solutions with hand hygiene technique	325.7	7.6	5.4	0.001
90% alcohol solutions without hand hygiene technique	466.4	0.25	0	0.15
60% alcohol solutions with hand hygiene technique	198.18	30.9	5.45	0.019
60% alcohol solutions without hand hygiene technique	343.5	102.75	16.66	0.406

Valores de p calculados mediante ANOVA; se comparo UFC a los 10s y 30s con UFC previo. UFC: Unidades Formadoras de Colonias, s=segundos.

Source: Analysis of information obtained at the Regional General Hospital 1, Obregon, Sonora.

**Tabla 7. Staphylococcus haemolyticus isolated from the hands of healthcare personnel and patient caregivers.**

Variable	CFU	CFU	CFU	p value
	Preview/Mean	10"/Mean	30"/Mean	
90% alcohol solution	170.66	4.66	0	0.09
60% alcohol solution	317.33	27.33	10.83	0.093
Hand hygiene with technique	150.1	7.5	0.4	0.035
Hand hygiene without technique	387.8	26.2	12.2	0.128
90% alcohol solutions with hand hygiene technique	116.5	2	0	0.298
90% alcohol solutions without hand hygiene technique	279	10	0	0.39
60% alcohol solutions with hand hygiene technique	200.5	15.75	1	0.143
60% alcohol solutions without hand hygiene technique	551	50.5	30.5	0.507

P values calculated using ANOVA; CFU at 10 and 30 seconds were compared with the previous CFU. CFU: Colony Forming Units, s = seconds.

Source: Analysis of information obtained at the Regional General Hospital 1, Obregon, Sonora.

**Tabla 8. Staphylococcus hominis isolated from the hands of healthcare personnel and patient caregivers**

Variable	CFU	CFU	CFU	p value
	Preview/Mean	10"/Mean	30"/Mean	
90% alcohol solution	516.85	3.14	2.33	0.147
60% alcohol solution	294.5	18.83	5.16	0.077
Hand hygiene with technique	466.44	14.5	5.14	0.082
Hand hygiene without technique	247.4	3.8	1.8	0.233
90% alcohol solutions with hand hygiene technique	688	4.4	3.5	0.176
90% alcohol solutions without hand hygiene technique	89	0	0	0.445
60% alcohol solutions with hand hygiene technique	189.5	31.33	7.33	0.281
60% alcohol solutions without hand hygiene technique	353	6.33	3	0.375

P values calculated using ANOVA; CFU at 10 and 30 seconds were compared with the previous CFU. CFU: Colony Forming Units, s = seconds..

Source: Analysis of information obtained at the Regional General Hospital 1, Obregon, Sonora.

**Tabla 9. Staphylococcus warneri aislado en manos de personal de salud y cuidadores de pacientes**

Variable	CFU	CFU	CFU	p value
	Preview/Mean	10"/Mean	30"/Mean	
90% alcohol solution	58.33	4	0	0.01
60% alcohol solution	51.28	21.14	6.14	0.277
Hand hygiene with technique	77.37	19.87	5	0.016
Hand hygiene without technique	18	2.6	0.6	0.271
90% alcohol solutions with hand hygiene technique	55.6	4.8	0	0.051
90% alcohol solutions without hand hygiene technique	113.66	45	13.33	0.225
60% alcohol solutions with hand hygiene technique	....	...	....	....
60% alcohol solutions without hand hygiene technique	4.5	3.25	0.75	0.241

Valores de p calculados mediante ANOVA; se comparo UFC a los 10s y 30s con UFC previo. UFC: Unidades Formadoras de Colonias, s=segundos.

Source: Analysis of information obtained at the Regional General Hospital 1, Obregon, Sonora.

A difference was observed in the Mann-Whitney U test regarding the use of alcohol-based hand rub ( $p < 0.001$  at 10 s;  $p < 0.001$  at 30 s) and the combination of alcohol-based hand rub with and without hand hygiene ( $p = 0.003$ ;  $p = 0.039$ , respectively). This was not the case for the hand hygiene technique, where no difference was observed ( $p = 0.356$ ) (Table 10).

**Table 10. Reduction of CFU at 10s and 30s with alcohol solution and hand hygiene technique.**

Variable	CFU		p value	CFU	
	Preview/Median	10s/Median		30s/Median	p value
90% alcohol solution	63.22	50.77	<0.001	51.03	0.001
60% alcohol solution	67.78	79.01		69.35	
Hand hygiene with technique	65.36	64.65	0.852	59.05	0.356
Hand hygiene without technique	65.85	65.94		64.66	
90% alcohol solutions with hand hygiene technique	41.47	36.17	0.001	37.88	0.003
90% alcohol solutions without hand hygiene technique	47.53	52.83		51.13	
60% alcohol solutions with hand hygiene technique	13.65	11.27	0.02	11.69	0.039
60% alcohol solutions without hand hygiene technique	16.91	18.74		18.41	

p values calculated using Mann-Whitney U; CFU: Colony Forming Units, s: seconds. Sol: solution.

**Source:** Analysis of information obtained at the Regional General Hospital 1, Obregon, Sonora.

A chi-square test was performed to determine differences in the microbiota developed by healthcare personnel and patient caregivers. No differences in the development of microorganisms were observed with this method ( $p=0.10$ ).

In the multivariate analysis performed using Cox proportional hazards, it was observed that the 90% alcohol solution reduced the bacterial load up to twofold more when rubbed for 30 s (HR of 2.13; 95% CI, 1.19-3.81;  $p = 0.01$ ), while the hand hygiene technique had no association (HR 1.08; 95% CI, 0.55-2.12;  $p = 0.81$ ) and Gram-negative bacteria were also not statistically significant (HR 0.67; 95% CI, 0.34-1.32;  $p = 0.25$ ) (Table 11). When analyzing the CFU reduction at 30 s, a difference was only observed with the alcohol solution, with a HR of 2.42; 95% CI, 1.50-3.89;  $p < 0.001$ . This difference was corroborated in the multivariate analysis. No differences were observed for the remaining variables (Table 12).

**Table 11. Multivariate analysis of the reduction of microorganisms at 30s**

Variable	HR*	95%CI	p value
<b>90% alcohol solution</b>	2.13	1.19-3.81	0.011
<b>Hand hygiene technique</b>	1.08	0.55-2.12	0.81
<b>Gram negative</b>	0.67	0.34-1.32	0.259

Cox proportional hazards. 95% CI: 95% confidence interval. Statistically significant p-value <0.05. s: seconds.

**Source:** Analysis of information obtained at the Regional General Hospital 1, Obregon, Sonora.

**Table 12. Multivariate analysis of the reduction of Colony Forming Units at 30s**

Variable	HR*	95%CI	p value
<b>90% alcohol solution</b>	2.42	1.50-3.89	<0.001
<b>Hand hygiene technique</b>	1.14	0.66-1.96	0.636
<b>Gram negative</b>	0.86	0.52-1.44	0.586

Cox proportional hazards. 95% CI: 95% confidence interval. Statistically significant p-value <0.05. HR: Hazard ratio, s:seconds.

**Source:** Analysis of information obtained at the Regional General Hospital 1, Obregon, Sonora.

It is worth mentioning that contaminated samples were excluded from the analysis. In vitro tests performed with the five main microorganisms that developed at Regional General Hospital 1 with a pattern of antimicrobial multidrug resistance, a significant reduction in CFU was observed with the 90% alcohol solution, which was greater at 30 s in most dilutions. This was the case with the 60% alcohol solution, where a smaller reduction was observed, especially in microorganisms such as *Klebsiella pneumoniae* and *Acinetobacter baumannii* complex (Table 13).

## DISCUSSION.

The presence of HAIs represents a serious problem for patient safety, and their prevention should be a priority in healthcare institutions.<sup>3</sup>

The main objective of this study was to evaluate the effectiveness of alcohol-based solutions at different concentrations as a disinfectant for hand hygiene among healthcare personnel and patients' families. This was achieved by observing a reduction in CFUs with the use of 60% and 90% alcohol-based solutions. The latter was more effective, achieving a greater reduction within 30 seconds. This is in agreement with Kampf G and Ostermeyer C., who demonstrated the efficacy of alcohol-based solutions at concentrations between 60% and 95%, conferring efficacy against Gram-positive and Gram-negative bacteria.<sup>7</sup>

Similarly, a considerable reduction in CFU was observed when performing hand hygiene in 10 s, which is slightly lower than the WHO recommendation and the time observed in the Kampf and Hollingsworth study, which evaluated the bactericidal activity of an ethanol-based hand gel in 15 s, finding efficacy against 11 gram-positive bacteria, 16 gram-negative bacteria, and 11 emerging bacterial pathogens.<sup>15</sup> Therefore, hand hygiene is the main measure whose effectiveness in preventing HAIs has been demonstrated. Such is the case of Angeles et al. in their clinical trial, which demonstrated the effectiveness of using alcohol gel for hand disinfection by reducing CFUs in the hands of doctors and nurses, obtaining a Log<sub>10</sub> CFU reduction of 1.53 ( $p < 0.01$ ). They observed that the nurses had a greater Log<sub>10</sub> CFU reduction than the doctors ( $p \leq 0.05$ ), which is consistent with the results of this study regarding CFU reduction. However, there is a discrepancy regarding the reduction in the categories since no difference was observed between them.<sup>12</sup>

In the bivariate analysis, a difference was observed with the alcohol-based hand sanitizer, but this was not the case for the hand hygiene technique.

In the multivariate analysis, a difference was observed only with the alcohol-based hand sanitizer, both for the reduction of microorganisms (HR: 2.13; 95% CI, 1.19–3.81) and for Colony-Forming Units (HR: 2.42; 95% CI, 1.50–3.89).

In this study, a 97.79% reduction was observed at 10 seconds, with a greater reduction achieved at 30 seconds, reaching 98.67% with the 90% alcohol-based hand sanitizer. This correlates with the results of Hernandez in Brazil, who compared the effectiveness of alcohol-based hand sanitizer with traditional handwashing. They concluded that the alcohol-based hand sanitizer reduced the risk of up to 99% and significantly removed Gram-negative bacteria. There are studies such as that of Alvarado et al., which investigated the antiseptic properties of alcohol gel without specifying the concentration and 70% liquid alcohol. They found a greater effect with alcohol gel after 30 seconds and with liquid alcohol up to one minute after application. This aspect is not consistent with this study, since a significant reduction was observed after 10 seconds; however, this could have been due to the lower ethanol concentration than the one used in this study.<sup>14</sup>

In vitro tests, a greater reduction in CFU was observed with the 90% alcohol solution than with the 60% solution, which is consistent with what Herruzo-Cabrera demonstrated in the comparative study of conventional handwashing and alcohol-based solutions in vivo and in vitro, where a greater reduction in CFU was found with the latter, including Gram-negative microorganisms. The use of alcohol gel offers several benefits, including faster hand hygiene, fewer adverse reactions (which occurred in only 2% of participants in this study), immediate availability at the patient's bedside, and lower cost.

This work provides a basis for future research to evaluate antimicrobial resistance and sensitivity *in vivo* hand hygiene studies, as well as serving as a basis for reconsidering proper hand hygiene.

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# Main risk factors associated with surgical site infection in adult patients treated in a general surgery service

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## Abstract

**Introduction:** Surgical site infections (SSIs) account for 20% of all healthcare-associated infections (HAIs). After a surgical procedure, one-third of patients will contract one. Consequently, this results in a 7- to 11-day increase in hospital stay and a 2- to 11-fold increased risk of death compared to operated patients who did not contract one. This triggers a significant increase in morbidity, hospital stay, and costs.

**Objective:** To identify the main risk factors associated with the presentation of a surgical site infection (SSI) in adult patients undergoing surgery in the general surgery service.

**Materials and methods:** This is an observational, analytical, retrospective, and cross-sectional case-control study nested within a cohort. A review of medical records and databases will be conducted. A non-probability sample of consecutive cases will be used to determine if there is a correlation between them, using contingency tables to obtain odds ratios.

**Results:** The odds ratios (OR) with statistical significance for BMI were normal 0.365 (95% CI 0.130 - 1.027, p 0.050), overweight 0.273 (95% CI 0.126 - 0.592, p<0.001), and grade I obesity 4.571 (95% CI 2.032 - 10.284, p 0.001). A previous healthcare-associated infection (HAI) was found in 28.3% of cases and in 5% of controls, with an OR of 7.512 (95% CI 2.068 - 27.278, p 0.001).

**Conclusions:** Although there are situations both before and during the surgical procedure that can be difficult to control, this study demonstrates that those that are controllable and applicable by health personnel can become more relevant.

**Keywords:** Infections, surgical site, surgeries, risk factors

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## INTRODUCTION

The World Health Organization (WHO) defines Healthcare-Associated Infections (HAIs) as infections that affect a patient during care in a hospital or

healthcare facility, which were not present or incubating at the time of admission and which may even manifest after the patient's discharge.

They are considered one of the major global health problems, compromising patient safety and directly impacting the quality of care in healthcare facilities.

Surgical Site Infections (SSIs) account for 20% of all HAIs. It is estimated that after a surgical procedure, approximately one-third of patients will contract one. This can lead to an increase of 7 to 11 days in hospital stay and a 2 to 11-fold increased risk of death compared to surgical patients who did not contract an infection. This results in a significant increase in morbidity, hospital stay, and costs.

Surgical site infections (SSIs) account for 20% of all healthcare-associated infections (HAIs) in a hospital unit. It is expected that after a surgical procedure, one-third of patients will develop an SSI, resulting in a 7- to 11-day increase in postoperative hospital stay and a 2- to 11-fold increased risk of death compared to surgical patients who did not develop an SSI.<sup>1</sup>

While the causes of SSI development are multifactorial, they are a strong indicator of the quality, safety, and efficiency of healthcare services. Timely identification of predisposing risk factors and appropriate application of preventive measures leads to a decrease in morbidity and mortality, and consequently, in the costs associated with prolonged hospital stays, additional surgical procedures, and antimicrobial use.<sup>2</sup>

The Ministry of Health, through the Hospital Network for Epidemiological Surveillance (RHOVE), has published definitions of healthcare-associated infections (HAIs) in the "Manual of Standardized Procedures for Hospital Epidemiological Surveillance, RHOVE," with the aim of standardizing clinical and laboratory criteria, and thus ensuring proper surveillance, prevention, and control of these infections.<sup>5</sup> The Mexican Social Security Institute (IMSS) also maintains the Healthcare-Associated Infection Registry System (INOSO), where HAIs detected through active and passive surveillance by Hospital Epidemiological Surveillance Units (UVEH) are recorded.

In both platforms, consistent with global statistics, surgical site infections (SSIs) constitute 20 to 30% of all healthcare-associated infections (HAIs) reported annually. They were among the top ten reported infections, out of the twenty-five defined, during 2022, and the leading cause of infection in the General Surgery department.<sup>6</sup>

Surgical site infections (SSIs) are defined as infections that occur at the site of an incision, which may involve skin, subcutaneous tissue, fascia, muscle, organs, spaces, or implants. They can occur within the first 30 days or up to a year after surgery, depending on the type of infection and the surgery performed.<sup>7</sup> SSIs are classified as follows: superficial incision, deep incision, and organ/space incision.<sup>7</sup>

Not all surgeries will have the same degree of contamination at the time of the procedure; therefore, it is useful to categorize them to facilitate comparisons and adjust SSI rates.<sup>7</sup> These classifications are clean, clean with implant, clean-contaminated, contaminated, and dirty or infected.<sup>7</sup>

Several pathophysiological factors are known to contribute to surgical site infections (SSIs), which can be divided into factors related to the surgical procedure, microbial factors, factors related to adherence to preventive practices, and patient-related factors.<sup>8</sup>

In Mexico, the Hospital Epidemiological Surveillance Network issued an Epidemiological Overview in August 2022 regarding healthcare-associated infections (HAIs) reported in the country. From January 1 to August 31, 2022, a total of 36,425 HAIs were reported. For the General Surgery service alone, 5,959 SSIs were registered across all classifications.<sup>6</sup>

The Ministry of Health and the Mexican Social Security Institute (IMSS) consider SSIs to be among the priority pathologies to be identified promptly, in order to act as quickly as possible and thus reduce the risks identified in critical procedures. Establishing continuous improvement processes that contribute to the prevention of risks, adverse events, and sentinel events arising from healthcare processes.

The objective of this study was to identify the main risk factors associated with the development of surgical site infections in adult patients undergoing surgery in the general surgery department.

## **MATERIALS AND METHODS**

The study took place at General Hospital No. 14, located in Hermosillo, Sonora. It is a Level II Care Unit with 326 available beds; of which 200 are authorized (census beds) and 126 are unauthorized (non-census beds). It also has 36 consulting rooms, 1 emergency room, 3 information modules, 5 inpatient services, 8 operating rooms, 1 administrative area, and a physical medicine and rehabilitation service.

A case-control study was conducted, where the cases were patients who underwent surgery and developed a surgical site infection (SSI) during the study period, and the controls were the same number of patients who underwent surgery during the same period but did not develop an SSI. Patients over 18 years of age, of both sexes, who underwent surgery between January 1 and December 31, 2022, were included. Patients under 18 years of age, patients who underwent surgery in a year other than 2022, patients treated in the gynecology and obstetrics service, patients treated in the orthopedics and traumatology service, patients who underwent surgery in another unit, and patients with surgical site infections not recorded on the INOSO platform were excluded. Patients with incomplete information in their electronic medical records, study population, and sample size were also excluded.

The independent variables included in the study were: age, pre- and postoperative hospital stay, systemic hypertension, type 2 diabetes mellitus, obesity, chronic kidney disease, cancer, rheumatoid arthritis, chronic infections, other comorbidities, surgical time, operating room, surgical specialty, surgical shift, preoperative diagnostic classification by organ systems, smoking, safe intervention packages for surgical site infection (SSI) prevention (defined as a series of interventions to be performed before, during, and after surgery, antibiotic prophylaxis, open or closed surgical approach, degree of surgical wound contamination, use of invasive methods (central venous catheter, mechanical ventilation, Foley catheter), and having a previous healthcare-associated infection (HAI) within the last 30 days. The dependent variable was surgical site infection, according to current regulations.

Data collection was retrospective and cross-sectional to obtain an overview of the unit's health status at a specific point in time. Data analysis was performed using SPSS v.24 statistical software. Quantitative variables for demographic characteristics were obtained using descriptive statistics such as means, modes, and proportions. Contingency tables were used to determine the correlation between independent and dependent variables, obtaining odds ratios with a 95% confidence interval. The chi-square test was then applied to verify statistical significance.

Based on the regulations of the General Health Law regarding health research, this research is without risk, as only patient data were collected and no invasive protocols that could harm the study subjects were performed. This study was conducted respecting the ethical codes established in the Declaration of Helsinki 1964, in its 2013 version, as well as those established in the Mexican Standards of the Official Gazette of the SSA of 1962.

## RESULTS

One hundred surgical site infections were recorded during the study period. Based on the formula for two proportions, it was determined that the study population should consist of 25 cases. However, it was decided to use 100% of the cases registered on the INOSO platform. After applying the inclusion, exclusion, and elimination criteria, a total of 60 records were selected for the cases and 60 records for the controls.

The sociodemographic characteristics were as follows: 55% were women (n=33), and 45% were men (n=27). Regarding age, the mean age was 54.2 years. The patients' ages were classified into ranges, with the highest frequency in the 60-69 age range (21.7%) (Table 1).

**Table 1. Sociodemographic characteristics**

Variables	Case		Control	
	N	%	N	%
Man	27	45%	27	45%
Woman	33	55%	33	55%
<b>Age range</b>				
20 - 29 years	6	10%	6	10%
30 - 39 years	8	13.30%	8	13.30%
40 - 49 years	11	18.30%	11	18.30%
50 - 59 years	10	16.70%	10	16.70%
60 - 69 years	13	21.70%	13	21.70%
People over 70 years old	12	20%	12	20%
<b>Schooling</b>				
Has not completed any formal education	1	1.70%	0	0%
Incomplete primary education	13	21.70%	7	11.70%
Completed primary education	10	16.70%	8	13.30%
Secondary education	18	30.00%	14	23.30%
Vocational training	10	16.70%	24	40.00%
University education	8	13.30%	7	11.70%
<b>Smoking</b>				
Active	13	21.70%	10	16.70%
Suspended	7	11.70%	6	10.00%
Passive	2	3.30%	0	0.00%
Void	38	63.30%	44	73.30%

Source: Data collection sheet obtained from the survey and instruments, analyzed with SPSS program

In the cases, the predominant educational level was secondary education (30%), while in the controls, it was middle school education (40%). An odds ratio (OR) was calculated for each educational level, finding that secondary education was a protective factor (OR 0.3, 95% CI 0.128–0.704, p-value 0.005) (Table 2).

The OR for active smoking was 1.383 (95% CI 0.732–3.461), with a p-value of 0.487, indicating no statistical significance (Table 2).

**Tabla 2. Análisis bivariado de las características sociodemográficas como factor de riesgo**

	Case		Control		OR	CI 95%	p value
	N	%	N	%			
<b>Age range</b>							
20 - 29 years	6	10%	6	10%	1	0.303 - 3.296	1
30 - 39 years	8	13.30%	8	13.30%	1	0.349 - 2.865	1
40 - 49 years	11	18.30%	11	18.30%	1	0.394 - 2.521	1
50 - 59 years	10	16.70%	10	16.70%	1	0.383 - 2.612	1
60 - 69 years	13	21.70%	13	21.70%	1	0.420 - 2.384	1
People over 70 years old	12	20%	12	20%	1	0.409 - 2.446	1
<b>Schooling</b>							
Has not completed any formal education	1	1.70%	0	0%	2.017	1.658 - 2.418	0.315
Incomplete primary education	13	21.70%	7	11.70%	2.094	0.771 - 5.688	0.142
Completed primary education	10	16.70%	8	13.30%	1.3	0.475 - 3.560	0.609
Secondary education	18	30.00%	14	23.30%	1.408	0.624 - 3.178	0.409
Vocational training	10	16.70%	24	40.00%	0.3	0.128 - 0.704	0.005
University education	8	13.30%	7	11.70%	1.165	0.394 - 3.44	0.783
<b>Smoking</b>							
Active	13	21.70%	10	16.70%	1.383	0.554 - 3.455	0.487
Suspended	7	11.70%	6	10.00%	1.189	0.375 - 3.771	0.769
Passive	2	3.30%	0	0.00%	2.034	1.693 - 2.444	0.154
Void	38	63.30%	44	73.30%	0.628	0.289 - 1.366	0.239

Source: Data collection sheet obtained from the survey and instruments, analyzed with SPSS program

Analyzing comorbidities, the presence of comorbidity resulted in an OR of 1.737 (95% CI 0.792–3.81, p-value 0.166), also without statistical significance. Regarding BMI, grade I obesity predominated in the cases (53.3%), while overweight was the most common finding in the controls (55%). The statistically significant odds ratios (ORs) for BMI were normal 0.365 (95% CI 0.130–1.027,  $p < 0.050$ ), overweight 0.273 (95% CI 0.126–0.592,  $p < 0.001$ ), and grade I obesity 4.571 (95% CI 2.032–10.284,  $p < 0.001$ ) (Table 3).

In addition, Diabetes Mellitus (DM) (OR 0.843, 95% CI 0.375–1.896,  $p = 0.680$ ), Systemic Arterial Hypertension (SAH) (OR 0.762, 95% CI 0.369–1.571,  $p = 0.461$ ), and chronic kidney disease (CKD) (OR 0.237, 95% CI

0.026–2.188,  $p = 0.171$ ) were considered, which is not statistically significant. The frequency of cancer was 18.3% in both cases and controls (OR 1.000, 95% CI 0.397–2.521,  $p = 1.000$ ). A prior healthcare-associated infection (HAI) was found in 28.3% of cases and 5% of controls, with an odds ratio (OR) of 7.512 (95% CI 2.068–27.278,  $p < 0.001$ ), which was statistically significant. (Table 3)

**Table 3. Bivariate analysis of comorbidities as a risk factor**

	Case		Control		OR	CI 95%	p value
	N	%	N	%			
<b>Comorbidity</b>							
Present	45	75.00%	38	63.30%	1.737	0.792 - 3.81	0.166
Absent	15	25.00%	22	36.70%			
<b>Body Mass Index</b>							
Normal	6	10.00%	14	23.30%			
Overweight	15	25.00%	33	55.00%	0.273	0.126 - 0.592	0.001
Grade I Obesity	32	53.30%	12	20.00%	4.571	2.032 - 10.284	0.001
Grade II Obesity	6	10.00%	1	1.70%	6.556	0.756 - 56.219	0.051
Grade III Obesity	1	1.70%	0	0.00%	2.017	1.658 - 2.418	0.315
<b>Diabetes Mellitus</b>							
Controlled	15	25.00%	17	28.30%	0.843	0.375 - 1.896	0.68
Uncontrolled	12	20.00%	8	13.30%	1.625	0.612 - 4.316	0.327
Absent	33	55.00%	35	58.30%			
<b>Systemic Hypertension</b>							
Controlled	24	40.00%	28	46.70%	0.762	0.369 - 1.571	0.461
Uncontrolled	3	5.00%	2	3.30%	1.526	0.246 - 9.478	0.648
Absent	33	55.00%	30	50.00%			
<b>Acute Renal Failure</b>							
Absent	54	90.00%	55	91.70%			
Mild G1-G2	1	1.70%	4	6.70%	0.237	0.026 - 2.188	0.171
Moderate G3a-G3bG	4	6.70%	1	1.70%	4.214	0.457 - 38.865	0.171
Severe G4-G5	1	1.70%	0	0.00%	2.017	1.658 - 2.418	0.315
<b>Cancer</b>							
Absent	49	81.70%	49	81.70%	1	0.397 - 2.521	1
Present	11	18.30%	11	18.30%			
<b>Previous Healthcare-Associated Infection (HAI)</b>							
Present	17	28.30%	3	5.00%	7.512	2.068 - 27.278	0.001
Absent	43	71.70%	57	95.00%			

Source: Data collection sheet obtained from the survey and instruments, analyzed with SPSS program

Regarding the surgical event, in both cases and controls, the type of intervention was 56.7% scheduled and 43.3% urgent; the surgical approach was 90% open and 10% closed; and the classification of the degree of surgical wound contamination was 35% clean, 48.3% clean-contaminated, and 16.7%

contaminated. The most frequent specialty was general surgery (88.3%), and the digestive system was the most affected (65%). The most frequent shift for cases was the morning shift at 36.7% (OR 2.316, 95% CI 1.018–5.269, p 0.043), and for controls, the afternoon shift at 53.3% (OR 0.375, 95% CI 0.183–0.771, p 0.007). Operating room Q1, with a frequency of 25% in cases and 10% in controls, yielded an OR of 3.000 (95% CI 1.075–8.370, p 0.031), which was statistically significant (Table 4).

**Table 4. Bivariate analysis of the characteristics of the surgical procedure**

	Case		Control		OR	CI 95%	p value
	N	%	N	%			
<b>Type of surgical intervention</b>							
Urgent	26	43.30%	26	43.30%	1	0.486 – 2.059	1
Scheduled	34	56.70%	34	56.70%			
<b>Surgical time</b>							
Greater than 120 minutes	38	63.30%	23	38.30%	2.779	1.327 - 5.820	0.006
Less than 120 minutes	22	36.70%	37	61.70%			
<b>Shift that performed the surgery</b>							
Morning	22	36.70%	12	20.00%	2.316	1.018 – 5.269	0.043
Afternoon	21	35.00%	32	53.30%	0.375	0.183 – 0.771	0.007
Night shift a	6	10.00%	0	0.00%	2.111	1.740 – 2.562	0.012
Night shift b	4	6.70%	5	8.30%	0.786	0.200 – 3.081	0.729
Accumulated hours	7	11.70%	11	18.30%	0.588	0.211 – 1.638	0.306
<b>Operating room</b>							
Q1	15	25%	6	10%	3	1.075 – 8.370	0.031
Q2	16	27%	14	23%	1.195	0.522 – 2.734	0.673
Q3	9	15%	12	20%	0.706	0.273 – 1.825	0.471
Q4	2	3%	6	10%	0.31	0.060 – 1.604	0.143
Q5	11	18%	15	25%	0.637	0.280 – 1.619	0.375
Q6	0	0%	1	2%	1.017	0.984 – 1.051	0.315
Q8	3	5%	1	2%	3.105	0.314 – 30.734	0.309
U1	4	7%	5	8%	0.786	0.200 – 3.081	0.729
<b>Specialty that performed the surgery</b>							
General surgery	53	88.30%	53	88.30%	1	0.328 -3.049	1
Oncologic surgery	6	10.00%	6	10.00%	1	0.303 – 3.296	1
Plastic and reconstructive surgery	1	1.70%	1	1.70%	1	0.061 – 16.366	1
<b>Classification by systems</b>							
Cardiorespiratory	2	3.30%	2	3.30%	1	0.136 – 7.341	1
Digestive	39	65.00%	39	65.00%	1	0.472 – 2.117	1
Musculoskeletal	17	28.30%	17	28.30%	1	0.452 – 2.212	1
Integumentary	2	3.30%	2	3.30%	1	0.136 – 7.341	1
<b>Surgical wound classification</b>							
Clean	21	35.00%	21	35.00%	1	0.472 – 2.117	1
Clean-contaminated	29	48.30%	29	48.30%	1	0.489 – 2.046	1
Contaminated	10	16.70%	10	16.70%	1	0.383 – 2.612	1
<b>Pre-surgical hospital stay</b>							
Greater than 24 hours	39	65.00%	26	43.30%	2.429	1.163 - 5.071	0.017
Less than 24 hours	21	35.00%	34	56.70%			
<b>Post-surgical hospital stay</b>							
Greater than 24 hours	41	68.30%	25	41.70%	3.021	1.430 - 6.382	0.003
Less than 24 hours	19	31.70%	35	58.30%			
<b>Use of invasive methods</b>							
Not used	35	58%	58	96.70%			
Venous catheter Central venous catheter	14	23%	0	0.00%	2.304	1.854 - 2.864	0.001
Mechanical ventilation	12	20%	0	0.00%	2.25	1.822 - 2.778	0.001
Foley catheter	19	32%	2	33.30%	13.44	2.966 - 60.890	0.001

Source: Data collection sheet obtained from the survey and instruments, analyzed with SPSS program

Surgical time exceeding 120 minutes yielded an OR of 2.779 (95% CI 1.327–5.820,  $p$  0.006), which was also statistically significant. The pre-surgical stay yielded an OR of 2.429 (95% CI 1.163 - 5.071,  $p$  0.017) and the post-surgical stay an OR of 3.021 (95% CI 1.430 - 6.382,  $p$  0.003), both with statistical significance. (Table 4)

The use of invasive methods was found to have the following odds ratios: central venous catheter use (OR) 2.304 (95% CI 1.854–2.864,  $p$  < 0.001), mechanical ventilation (OR) 2.250 (95% CI 1.822–2.778,  $p$  < 0.001), and Foley catheter use (OR) 13.439 (95% CI 2.966–60.890,  $p$  < 0.001), all of which were statistically significant. (Table 4)

The frequencies of surgical site infections were classified as follows: 38.3% superficial, 43.3% deep, and 18.3% organ/space (Table 5).

**Table 5. Types of Surgical Site Infection**

Type of infection	Case	%	Control	%
Superficial	23	38.30%	0	0
Deep	26	43.30%	0	0
Organ and space infection	11	18.30%	0	0

Source: Data collection sheet obtained from the survey and instruments, analyzed with SPSS program

Omission of the prevention package represents an OR 3.281 (95% CI 1.358 - 7.925,  $p$  0.007), with statistical significance. Failure to maintain glucose levels within the suggested ranges (OR 4.349, 95% CI 1.486 - 12.726,  $p$  0.005) and failure to maintain preoperative temperature within the suggested ranges (OR 2.570, 95% CI 1.011 - 6.529,  $p$  0.043) were also statistically significant. (Table 6).

## DISCUSSION.

According to the data obtained in this study, a 5% difference was found between sexes, with a frequency of 45% for males and 55% for females.

Analyzing the sociodemographic characteristics, for the age variable, the mean was 54.2 years and the median was 52.5 years, consistent with Peñuela in Colombia (201), who found a significant difference in patients over 54 years of age (OR 5.37;  $p$  0.014)<sup>16</sup>. Fernández et al. in Cuba (2016) also corroborated that adulthood is a decisive non-modifiable factor in postoperative infections<sup>17</sup>.

For the education variable, having a high school diploma was found to be a protective factor against the development of a surgical site infection (SSI).

**Table 6. Bivariate analysis of the application of the Safe Action Prevention Package**

Variable	Case		Control		OR	CI 95%	p value
	N	%	N	%			
<b>Safe Actions Prevention Package</b>							
No evidence of application of the 5 safe actions	22	36.66%	9	15.00%	3.281	1.358 - 7.925	0.007
Evidence of application of the 5 safe actions	38	63.34%	51	85.00%			
<b>Hair removal</b>							
Hair removal that does not meet the suggested	8	13.33%	3	5.00%	2.923	0.736 - 11.609	0.114
Hair removal, 20 to 30 minutes before surgery, with electric clippers or scissors	52	86.67%	57	95.00%			
<b>Antibiotic prophylaxis</b>							
Omission of pre-surgical antimicrobial prophylaxis	18	30.00%	11	18.30%	1.909	0.811 - 4.493	0.136
Timely and appropriate application of pre-surgical antimicrobial prophylaxis	42	70.00%	49	81.70%			
<b>Glucose levels</b>							
Glucose levels outside the suggested range	17	28.33%	8	13.33%	4.349	1.486 - 12.726	0.005
Blood glucose levels between 110 and 180 mg/dL before, during, and in the first 24 hours post-surgery	43	71.67%	52	86.67%			
<b>Pre-surgical body temperature</b>							
Temperature outside the suggested range before surgery	17	70.00%	8	85.00%	2.57	1.011 - 6.529	0.043
Temperature between 35.5 and 37.9°C before surgery	43	26.70%	52	13.30%			
<b>Post-surgical body temperature</b>							
Temperature outside the suggested range after surgery	6	90.00%	59	96.70%	6.556	0.764 - 56.219	0.051
Temperature 35.5 and 37.9°C after surgery	54	8.30%	1	1.70%			
<b>Surgical wound classification</b>							
No evidence of surgical wound classification in medical record	4	6.67%	3	5%	1.357	0.290 - 6.341	0.697
Evidence of surgical wound classification in medical record	56	93.33%	57	95%			

Source: Data collection sheet obtained from the survey and instruments, analyzed with SPSS software

For BMI, grade I obesity was the most frequent category for cases, and overweight for controls. The odds ratio (OR) suggests obesity as a risk factor and overweight as a protective factor. This agrees with the findings of Hidalgo-Costilla et al. in Mexico in 2015, who established an OR of 2.234 (95% CI 1.563–3.194)<sup>18</sup>, and with those of Figuerola in Spain

in 2016, who reported an association between surgical site infection (SSI) and obesity (OR 1.2; CI 1.0–1.4;  $p < 0.05$ ).<sup>22</sup>

Although the results show that diabetes mellitus and systemic hypertension did not show statistical significance as a predisposition to developing a surgical site infection, there is evidence demonstrating this association, as in the case of García Díaz with 190 patients (OR 3.43;  $p < 0.01$ ).<sup>19</sup> Another study by Ramos et al. indicates a significant association between diabetes and surgical site infection (OR 8.67; 95% CI 1.53–49.30;  $p < 0.015$ ).<sup>20</sup>

Chronic Kidney Disease, by itself, does not appear to represent a risk factor as such, but it could be associated with multiple complications that may precede a surgical site infection.<sup>3,5,8</sup>

Although in this study cancer was not investigated as a risk factor per se, but rather as a characteristic also present in the controls, Velasco et al. established this parameter as a predictive risk factor for SSI among patients with cancer (OR 3.76, 95% CI 1.76–8.03).<sup>21</sup>

A healthcare-associated infection in a previous area represents a significant risk for developing a surgical site infection, as the presence of a distant infection has been shown to increase the SSI rate by 2.7 times.<sup>24</sup>

Although the following characteristics were intentionally sought to be present in the same proportion in both cases and controls, there is evidence that there is a greater risk of developing a surgical site infection in urgent surgery than in elective surgery (Peru 2019, OR 1.26; CI 1.89–3.45;  $p < 0.021$ )<sup>25</sup>, in an open approach than in a closed one (Colombia 2017, OR 3.62; CI 1.56–8.39;  $p < 0.00$ , Spain 2018 RR 0.10; CI 0.01–0.79,  $p < 0.05$ , United States 2010 OR 0.28; CI 0.25–0.31)<sup>26,27,28</sup>, if the wound classification is clean-contaminated (Brazil 2017 OR 2.7; CI 2.1–3.5;  $p < 0.001$ )<sup>29</sup>. Consequently, it is not difficult to believe that the service that presents the highest frequency of this condition is general surgery, as well as that the system with the highest frequency after an intervention resulting in an SSI is the digestive system, related to the fact that most of its procedures have these characteristics.

A surgical time exceeding 120 minutes was associated with a risk factor for surgical site infection (SSI), a finding confirmed in other studies. In 2017, Cheng et al., through a systematic review of several studies, found a statistically significant association, establishing that there is almost twice the likelihood of developing this type of infection.<sup>32</sup>

Regarding the surgical shift, the morning shift was the most frequent, establishing it as a risk factor, along with the night shift. On the other hand,

for the control group, the afternoon shift was the most frequent, and it was found to be a protective factor. Operating room Q1 was identified as a risk factor for the development of an SSI.

Hospital stays exceeding 24 hours, both before and after surgical procedures, significantly increase the risk of surgical site infection (SSI). This finding was confirmed by Rodrigues (Brazil, 2017), who established a statistical relationship between a preoperative stay longer than 24 hours and SSI (OR 2.3; CI 2.0–2.8;  $p < 0.001$ ).<sup>29</sup>

The use of invasive procedures has been shown to be a risk factor that can significantly increase the likelihood of developing a surgical site infection. This may be due to the invasive procedure itself creating an entry point for microorganisms, thus promoting infection, or to the susceptibility and comorbidities of patients requiring this type of management. However, there is no precedent confirming or ruling out the influence of invasive procedures on the development of SSIs, leaving an opportunity for further investigation.

Safe practice bundles for the prevention of surgical site infections (SSIs) comprise a series of tasks to be implemented by healthcare personnel. A substantial body of scientific evidence supports the significant reduction in the risk of developing SSIs.<sup>1,2,3,4,5,6,7,2</sup> This study was no exception, as the characteristics attributed to healthcare showed statistical significance, including the analysis of the use of safe practice bundles.

Antibiotic prophylaxis did not demonstrate statistical significance; however, evidence from Gallagher et al. in a 2018 systematic review indicates that antibiotic prophylaxis likely reduces the incidence of SSIs (RR 0.67, CI 0.53–0.85).<sup>30</sup> Despite this, other research studies disagree, such as that of Del Moral, who concludes that adequate antibiotic prophylaxis did not influence surgical site infection (RR 1.15; CI 0.31–2.99;  $p > 0.05$ )<sup>31</sup>.

Monitoring glucose levels between 110 and 180 mg/dL is the first safe step in the surgical site infection (SSI) prevention package. High stress levels, such as those experienced during surgery, combined with glucose levels below 110 mg/dL or above 180 mg/dL, cause abnormalities in monocyte and polymorphonuclear neutrophil function, decreased intracellular bactericidal activity, and glycosylation of immunoglobulins,<sup>33</sup> which favor the development of infection. The results obtained are consistent with this, as in the HGZ 14 CUQ hospital, uncontrolled blood glucose was associated with a 4.3 times greater risk of developing an SSI.

Monitoring body temperature is part of the safe measures for preventing infections<sup>7,23</sup>, so it is expected that a temperature outside the suggested range (35.5 to 37.9°C) increases the risk of developing a surgical site infection (SSI) by 2.5 times.

While surgical wound classification is a parameter that helps determine the most appropriate therapeutic approach for the patient, as it can indicate the likelihood of complications, the lack of classification evidence in the medical record does not represent a statistically significant risk.

The microorganisms most frequently found in the cultures were primarily *Escherichia coli*, followed by *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Enterococcus faecalis*. This coincides with the findings reported nationally by the DGE on the RHOVE6 platform. When studying the characteristics of patients with confirmed surgical site infections (SSIs), a majority had a secondary education or lower, and a significant number had a history of smoking.

Continuing with the analysis of past medical history, a significant portion of the sample presented comorbidities, such as obesity, diabetes mellitus, and systemic hypertension, and the poor control of these conditions was noteworthy.

Regarding the characteristics of the surgical procedure itself, elective surgeries were more frequent, as were open surgeries, with the majority of surgical wounds classified as clean-contaminated. However, the most relevant finding in this study was the application and adherence to safety protocols, which depend on the competence of the healthcare personnel. Therefore, there is an opportunity to implement these measures, which greatly contribute to the positive outcomes for patients. Although there are situations both before and during the surgical procedure that can be difficult to control, this study demonstrates that those controllable and applicable by healthcare personnel can be of greater importance. Therefore, it is crucial to continue training all medical staff on the importance of implementing these measures, showing them the impact on patient outcomes, the use of supplies, and hospital space, both when using them and when not.

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# Presentation of COVID-19 on staff working in a General Hospital

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## Abstract

**Introduction:** The COVID-19 pandemic directly affected morbidity and mortality rates among healthcare workers, which had an impact on medical care.

**Objective:** To determine the incidence of COVID-19 in staff working at the General Hospital of the Zone.

**Materials and methods:** An observational, descriptive, retrospective, and cross-sectional study was conducted. Participants included staff members of General Hospital Zone 14 who contracted COVID-19. Surveys were carried out to staff to verify data and investigate other factors of interest that could provide new segmentation for the analysis. Absolute frequencies were described. A chi-square test was performed. The study was conducted in strict adherence to ethical standards and the principles stipulated in the Federal Regulations Code of the United Mexican States and the Regulations of the General Health Law Regarding Research.

**Results:** Of the affected staff, 61.2% were female and 38.8% were male; nursing staff were the most affected at 26.5%. A frequency of 6.4 per 10 workers was calculated, and the case fatality rate was 0.26% for the period studied.

**Conclusions:** Being a healthcare worker increased the risk of COVID-19 infection, and among the staff, the most affected department was nursing.

**Keywords:** COVID-19, SARS-CoV-2, health personnel.

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## INTRODUCTION

On March 11, 2020, the World Health Organization (WHO) declared the most recent pandemic, which began with the novel coronavirus, named SARS-CoV-2.

The origin of this pandemic is described as in Asia, in the Chinese province of Hubei, in the city of Wuhan. The combination of various factors that had been developing for some time, such as climate change resulting in ecosystem

modification and loss of biodiversity, and globalization, which brings with it travel and international trade, may have influenced the emergence of this pandemic, allowing the virus to jump from the bat reservoir to the human species.

Coronaviruses, composed of RNA, have a high capacity to mutate and recombine, which facilitates their ability to change from their reservoir to another type of host. Based on these characteristics of the virus, theories have emerged that the COVID-19 epidemic could also have occurred from human to human without the intervention of another species. The SARS-CoV-2 virus has characteristics like bat coronaviruses, beginning with the way it initiates an infection (using the angiotensin-converting enzyme of the cell receptor).<sup>10</sup>

By March 11, 2021, one year after the start of the declared COVID-19 pandemic, there were a total of 117,983,661 cases and 2,620,207 deaths globally, affecting a total of 236 countries by that date<sup>11</sup>. The situation as of March 11, 2022, was a total of 56 countries, territories, or areas affected, with a total of 148,781,050 confirmed cases and 2,660,300 deaths. By then, with vaccination campaigns already in place, the following data was collected on doses administered: 1,713,622,142<sup>12</sup>. After March 13, 2020, infections began to be reported among medical personnel. By then, confirmed local cases had increased, surpassing imported cases.<sup>13</sup>

From the beginning of the pandemic, uncertainty gripped people worldwide, especially those directly dealing with the disease, such as healthcare workers. In fulfilling their duty to provide medical care to COVID-19 patients, they had no option to stay home and quarantine. This led to fear among healthcare workers of becoming infected by themselves or their families. Coupled with a lack of supplies and hospital beds, this had repercussions on both the physical and mental health of active healthcare personnel, as well as a steadily increasing number of infections.<sup>14</sup> By May 8, 2020, 152,888 healthcare workers worldwide had been reported to have contracted COVID-19, with a total of 1,413 deaths reported by that date. Women were the most affected, accounting for 71.6% of infections, while most deaths were among men, at 70.8%. Among healthcare workers, nurses were the most frequently infected (38.6%), and physicians accounted for the highest percentage of deaths (51.4%).<sup>15,16</sup>

A study of healthcare workers in the United Kingdom found that the main risk factor for COVID-19 infection was treating patients without adequate personal protective equipment, whether suspected or confirmed cases. To a

lesser extent, comorbidities and the specific roles of physicians were also contributing factors.<sup>17</sup>

By August 23, 2020, 97,632 cases of COVID-19 had been reported among healthcare workers in Mexico, with nurses accounting for 42% and physicians for 27%. These figures increased as the pandemic progressed.<sup>19,20,21</sup>

The COVID-19 pandemic in Mexico brought about changes in the actions of healthcare personnel and the healthcare systems needed to confront this new emerging situation. Therefore, it is crucial to understand that one of the pillars of healthcare most affected during the pandemic was healthcare personnel, who were directly impacted by the type of activities they performed and their direct contact with people suspected of or already infected with COVID-19. They also witnessed firsthand the devastation that arose during the pandemic, from morbidity and mortality to shortages of supplies and long working hours.<sup>22</sup> Due to the way SARS-CoV-2 is transmitted, healthcare personnel were directly exposed through their daily duties, with serious consequences. From January 2020 to May 2021, it was estimated that between 80,000 and 180,000 healthcare personnel died worldwide.<sup>25</sup> In Mexico, 542,986 confirmed cases of COVID-19 were registered among healthcare personnel. Cases as of December 31, 2022 26. The figures in the state of Sonora of confirmed COVID-19 cases in healthcare personnel as of January 31, 2022 totaled 12,648 cases, increasing to 15,946 by December 2022<sup>27</sup>.

Therefore, the objective of the study was to determine the incidence of COVID-19 in personnel working in a General Hospital.

## **MATERIALS AND METHODS**

The study was conducted at General Hospital No. 14 with a Burn Unit, a secondary care facility of the Mexican Social Security Institute (IMSS), located in Hermosillo, Sonora. This medical unit has 326 beds available; 200 are registered beds and 126 are unregistered beds, in addition to 41 consultation rooms, 2 emergency rooms, 3 information desks, 5 inpatient wards, 1 administrative area, and 1 physical medicine and rehabilitation service. The staff is classified into 5 areas: (1) administrative, with a total of 223 employees; (2) Delegation, with 11 employees; (3) finance and systems, with 9 employees; (4) medical, with 1,505 employees; and (5) economic and social benefits, with 3 employees.

An observational, descriptive, retrospective, and cross-sectional study was conducted among healthcare personnel of various categories. From March 23, 2020, to January 31, 2022.

Information was collected from the various databases available at the unit for the study of cases of viral respiratory diseases (SINOLAVE), as well as the SPPSTIMSS database (Workers' Health Prevention and Promotion Services of the Mexican Social Security Institute).

The collected information was integrated into an Excel database of healthcare personnel infected during the COVID-19 pandemic in the previously determined period. The dependent variable was COVID-19 infection, and the independent variables were age, sex, blood type, comorbidity, systemic hypertension, diabetes, chronic inflammatory lung disease, obesity, smoking, job category, work shift, and exposure in other workplaces. The sample size was calculated to estimate a proportion with a 95% confidence level, resulting in a sample size of 826. Participants included IMSS (Mexican Social Security Institute) personnel assigned to General Zone Hospital No. 14 with a Burn Unit, regardless of sex or age. Participants had to have a positive rapid antigen test and/or RT-PCR test for SARS-CoV-2 and be registered on the SINOLAVE platform as a confirmed case.

Those who did not work at General Zone Hospital No. 14 with a Burn Unit during the period from March 23, 2020, to January 31, 2022, were excluded.

Healthcare personnel who refused to participate in the survey, either in writing or by telephone, or who could not be located, were also excluded.

Measures of disease frequency, specifically rates (prevalence and case fatality rate), were calculated. Measures of central tendency were also calculated for the quantitative variables. Nominal qualitative variables were measured using proportions to determine the percentage of SARS-CoV-2 infections across different hospital categories and work shifts, as well as the percentage of healthcare workers according to sex, blood type, and comorbidities. Prevalence odds ratios were calculated to estimate risk. The chi-square test was used for independent variables. Data analysis was performed using SPSS Statistics 29.

To comply with the principles that ensure moral, ethical, and legal requirements for health research, we adhered to the Declaration of Helsinki, the Nuremberg Code, the General Health Law, the Regulations of the General Health Law Regarding Health Research, the Belmont Report, the Federal Regulations Code of the United Mexican States, and any other applicable regulations.

## RESULTS

A total of 1,149 workers were identified as having contracted COVID-19, out of 1,785 registered on the payroll and 1,617 on disability leave issued by the occupational health physician at SPPSTIMSS. This information was cross-referenced with the SINOLAVE database to define the study group. The incidence rate was 6.4 per 10 workers during the study period. Three staff deaths occurred, representing a case fatality rate of 0.26% among those diagnosed with COVID-19.

The study population included healthcare personnel from all categories, departments, and shifts who were on duty during the study period. An analysis was conducted to identify the relationship between the staff's work characteristics and their susceptibility to COVID-19 infection. The results indicate that the nursing department was the most affected, with 26.5% of cases, followed by physicians at 5.9%, social work at 3.5%, and conservation at 3.4%. Regarding the risk assessment of working overtime for nurses, it can be observed that the greatest risk was found when working a normal shift. Regarding the variable "works in other workplaces (medical unit, hospital, clinic, etc.)," 25.5% responded yes, with an odds ratio (OR) of 0.3, indicating a higher risk without traveling to other workplaces. When analyzing overtime hours worked in the physician category, 27.3% reported working overtime, while 14.7% did not. Working overtime was found to be riskier, with an OR of 2. When analyzing work in other workplaces within the same category, 52.9% reported doing so, and 7.4% reported not. With an OR of 6.0, traveling to other workplaces was interpreted as a higher risk. The use of personal protective equipment (PPE) was also reviewed in this category, where 15.9% of the total participants reported using it, with an OR of 1.0, indicating that it neither poses a risk nor protects against illness. In the Cleaning category... Regarding hygiene, only 9.1% of respondents reported working overtime. The risk estimate for the overtime cohort is interpreted as a higher risk with an odds ratio (OR) of 1.5. For those working at other workplaces, with an OR of 0.3, we interpret commuting to other workplaces as a protective factor, perhaps due to the different activities performed at their other jobs. Analyzing the use of personal protective equipment (PPE), 6.3% reported using it. Although no one reported not using PPE, the OR of 1.0 can be interpreted as a duality between the protection and the risk associated with its use.

The analysis showed that the highest percentage of infections was in the female group at 61.2%, compared to 38.8% for males. Furthermore, the measures of central tendency for the age variable yielded an average of 37.2 years, with 50% of infected workers being 37 years old and the most frequent age being 35 years.

Regarding the blood type findings, it was found that infected participants with blood type O were the most affected at 56.6%, followed by those with blood type A at 32%. An interesting finding from the analysis related to comorbidities in the workers is that only 18.5% reported having any type of comorbidity or chronic illness. And only 14.2% reported smokers during the study period.

Regarding the course of the illness, 272 workers (96.8%) experienced outpatient treatment, and only 9 workers (3.2%) were hospitalized. Additionally, only 5.3% reported requiring oxygen.

Within the study group, the morning shift (45.2%) had the highest rate of infection, followed by the afternoon shift (28.1%). Regarding overtime, although there was a staff shortage due to infections and an increased workload resulting from the pandemic-related surge in cases, very few (7.8%) were working overtime.

Regarding the use of personal protective equipment (PPE), 3.6% of staff responded that they did not use it while caring for COVID-19 patients. When asked about having had an infected family member before developing symptoms, 22.8% reported having had such a family member, and 10% of those family members were healthcare workers. Regarding the workers who mentioned working at other workplaces (medical unit, hospital, clinic, etc.), only 18.1% responded affirmatively. Finally, 87.5% reported having contracted COVID-19 at least once or twice, and 35 participants, or 12.5%, reported having been infected three or four times.

## **DISCUSSION.**

The findings from this study, resulting from cross-referencing information between databases and surveys, revealed a total of 1,149 workers infected with COVID-19. As mentioned by Gómez-Ochoa SA. et al. (2021), healthcare workers, being the first responders for COVID-19 patients, are more exposed to contracting the disease and, in turn, to infecting other patients or individuals.

Analyzing the study results, specifically regarding the variable of sex, it was observed that the highest percentage of infections was among women (61.2%), representing a total of 172 women. In contrast, the total number of male workers who contracted COVID-19 was 109, representing 38.8% of the participants. The average age at presentation for both sexes was 37.2. It is important to mention that at the beginning of the pandemic, healthcare personnel with certain risk factors, in this case advanced age, were allowed to

stay home to protect themselves from infection. This aligns with Padrón HS, 2022, who described an average age of 37 years due to allowing workers over 60 to retire.

The results of this study also found that the nursing department had the highest number of infected workers. This could be due to the specific nature of their work, as mentioned by Gómez-Ochoa SA. et al, 2021<sup>18</sup>, when alluding in their study to a greater contagion of SARS-CoV-2 by the nursing team, this is explained by the greater amount of time that said personnel spends in close contact with the patient, for their part Bandyopadhyay S. et al, 2020<sup>16</sup> mentions that the category with the highest rate of contagion was nursing at 38%, it is also mentioned that the risk of doctors of certain specialties is greater when they are specialties that are in more direct contact with nasal secretions, but that the risk of the rest of the specialties should not be minimized.

An interesting finding is that it was previously believed that workers at higher risk were those with comorbidities, as Camacho-Servín BA. et al. (2021) noted in their study, which concluded that a higher risk of death and severe illness were associated with being a healthcare worker who contracted COVID-19 and having comorbidities as a risk factor. In contrast to this study, the number of infected workers (participants) with comorbidities was low (18.5%), compared to 81.5% who denied having comorbidities or chronic diseases. Among the comorbidities reported by participants in this study, the main ones were "other" comorbidities (42%), systemic hypertension (23%), and diabetes (17%).

The incidence of smoking among infected staff was low, with only 14.2% reporting smokers during their COVID-19 infection within the study period. This, combined with the low incidence of comorbidities and the low smoking rate among affected staff, may have contributed to the 96.8% outpatient course observed in the workers in this study. This aligns with the findings of Garrote A and Bonet R. (2022), who reported direct damage from tobacco to the respiratory system. This would explain why many participants in this study did not require oxygen (only 5.3%), and why the outpatient course is associated with a mild case of the disease.

It is important to note that, given that most workers had an outpatient course, 69.4% of them implemented the following combinations of techniques to prevent infection in the hospital: handwashing, sanitizing with gel, use of PPE, and physical distancing. It is important to mention that due to the number of patients during the peak of the pandemic, maintaining social distancing and avoiding crowds became a difficult task to accomplish.

In addition to identifying workers who had to travel to other work centers as a potential source of infection, the study also investigated whether any family members had contracted COVID-19 before the onset of their symptoms. This was considered because quarantine guidelines were still in place during the study period, making it common for family members to infect each other, especially if they lived in the same household. The results showed that the risk of infection from family members was greater than 20%, meaning that 1 in 5 workers infected at least one family member (or other individuals) outside of their workplace.

During the study period, 87.5% of workers reported having been infected 1 to 2 times, and 12.5% reported 3 to 4 times. This explains why the number of work absences exceeds the total number of workers infected with COVID-19, as previously mentioned. Furthermore, the multiple infections are reasonable considering the variants that the SARS-CoV-2 virus presented during the pandemic.

Analyzing the above in general, we found that the nursing department was the most affected, with 26.5% of infections. Breaking down the job categories, the highest percentage was for general nurses at 12.5%, followed by non-family physicians at 8.4%, general nursing assistants at 6.5%, specialist nurses at 3.8%, and nursing assistants at 3.8%. Cleaning and hygiene (2.1%) showed the highest rate of infection, as previously mentioned, among job categories with the most direct contact with patients and/or in patient areas, such as cleaning and hygiene staff.

The job characteristics that increase the risk of COVID-19 infection are those involving direct contact with patients. This means that departments with the most patient contact are at the highest risk. On the other hand, it's important to remember that contrary to initial beliefs, having comorbidities or being a smoker is not a risk factor that should prevent someone from continuing their work duties. The fact that many workers recovered on an outpatient basis and did not require oxygen is correlated with the low mortality rate, indicating adaptation to the virus.

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# Risk factors for latent tuberculosis in contacts of patients with active pulmonary tuberculosis

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## Abstract

**Introduction:** Latent tuberculosis is the condition in which a person is infected with *Mycobacterium tuberculosis* without showing any clinical or radiological signs of active disease. It is estimated that more than a third of the world's population has this infection and that between 5% and 10% will develop the active form, thus contributing to the global burden of the disease.

**Objective:** To determine the risk factors associated with latent tuberculosis infection (LTBI) in contacts of patients with active pulmonary tuberculosis.

**Materials and methods:** An observational, cross-sectional, and analytical study was conducted between June and December 2024, using the tuberculin skin test (PPD) application census carried out at Family Medicine Unit No. 47. Eighty-two contacts of patients with active pulmonary tuberculosis were included. Data were analyzed using SPSS v26 with descriptive statistics, bivariate analysis, and binary logistic regression.

**Results:** The prevalence of LTBI was 37.8%, similar to that reported previously. A significant association was observed between having a partner and PPD positivity ( $p=0.019$ ;  $OR=1491.78$ ), while male sex showed an inverse association ( $p=0.011$ ;  $OR=0.11$ ). Urban origin was associated with a higher probability of infection ( $p=0.002$ ;  $OR=8.75$ ).

**Conclusions:** TB-related illness continues to be a public health problem, highlighting the need to strengthen detection and prevention strategies among contacts of patients with active tuberculosis.

**Keywords:** Latent tuberculosis; Contacts; Risk factors; contact tracing; public health.

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## INTRODUCTION

Latent tuberculosis is the condition of a person already infected with *Mycobacterium tuberculosis* (MTb), demonstrated by a positive purified

protein derivative for tuberculosis (PPD) test, but without evidence of clinical signs or radiological findings compatible with active disease. It is estimated that more than a third of the population has latent tuberculosis infection (LTBI), and 5% to 10% (Gong, 2021) of the population with latent tuberculosis will develop the disease in its active form. Therefore, reactivation of tuberculosis has represented a serious public health problem in terms of tuberculosis eradication.

Recent data indicate that China has the highest burden of LTBI worldwide, with approximately 350 million people latently infected (Gong, 2021). These figures suggest that a significant percentage of the population with LTBI and the lack of differential diagnosis, along with active tuberculosis (TBa), may be potential reasons for the high morbidity and mortality from tuberculosis in countries with a high burden of this disease. Tuberculosis (TB) is an infectious disease that has caused morbidity and mortality and has affected humanity for over 20,000 years, making it one of the leading causes of death worldwide (Gong, 2021). The disease is caused by a group of bacteria from the order Actinomycetales, family Mycobacteriaceae, specifically the *M. tuberculosis* (MTb) complex. The bacilli are spread in the environment when an infected person expels them into the air by coughing or speaking. It primarily affects the lungs, but can affect other organs.

Factors such as malnutrition, alcoholism, addictions, impaired immune response, and even poor housing conditions are known to influence the development of the disease.

The objective of this study was to evaluate the risk factors associated with latent TB infection in contacts of patients with active pulmonary tuberculosis.

## **MATERIALS AND METHODS**

The study was conducted at Family Medicine Unit No. 47, IMSS Tabasco, as an analytical cross-sectional observational study from June 1 to December 31, 2024. The study population consisted of 164 contacts of patients with active pulmonary tuberculosis, registered at UMF No. 47. The sample size was calculated in EpiDat using the formula for estimating a proportion in a finite population, considering a 95% confidence level, a 5% margin of error, and an expected proportion based on previous studies (47%), resulting in an estimated total of 115 participants. Contacts of patients with active pulmonary tuberculosis were included, regardless of age or sex, provided they underwent PPD testing. Individuals without contact with patients with active pulmonary tuberculosis and those who did not undergo PPD testing were excluded.

A cross-sectional analytical observational study was conducted using data obtained from a survey administered to residents of Family Medicine Unit No. 47 of the Mexican Social Security Institute (IMSS) in Villahermosa, Tabasco. Data from the PPD vaccination census conducted by the epidemiology department of UMF No. 47 were also reviewed, as well as contact tracing data from the National Epidemiological Surveillance System (SINAVE) platform for identifying risk factors.

From the data obtained, records that did not meet the pre-established inclusion and exclusion criteria due to incomplete information or data inconsistencies were excluded. Following this process, the final sample consisted of 82 individuals who met all the defined methodological criteria and were included in the statistical analysis.

Using the obtained sample, a database was created and analyzed using SPSS version 26, where measures such as prevalence, prevalence ratio, and relative risk were calculated. Additionally, a multivariate binary linear regression analysis was performed to correlate the independent variables with the dependent variable.

## RESULTS

A total of 82 contacts were analyzed. Of these, 26.8% were men and 73.2% were women (Table 1).

The highest level of education was high school for both sexes, while the lowest level of education was for contacts with no schooling.

Regarding the initial diagnosis of the sputum smear-positive patients, 100% had pulmonary involvement. Of the analyzed sample, the variable of the type of contact the participants had with their sputum smear-positive patient showed that intimate contact represented the highest percentage at 62.2%, followed by frequent contact at 36.6%, and lastly, sporadic contact at 1.2%.

According to the length of time the contacts lived with patients with active pulmonary tuberculosis, only 20.7% lived with the patient for less than a year, compared to 79.3% who lived with them for more than a year.

Of the comorbidities identified in the contacts, 39% presented some degree of obesity, followed by 24.4% who were overweight. Among chronic degenerative diseases, the most frequent was diabetes mellitus (DM) at 12.2%, while other comorbidities, such as arthritis or kidney disease, represented 6.1%. Systemic arterial hypertension (SAH) and the coexistence of DM and

SAH were also observed in 6.1% of cases. Regarding a history of substance abuse, only one contact (1.2%) reported alcohol consumption (Table 1).

**Table 1. Characteristics of the study group**

Variable		N
<b>Sex</b>	Male	25
	Female	60
<b>Age Groups</b>	1 to 4	2
	5 to 9	7
	10 to 14	9
	15 to 19	6
	20 to 24	3
	25 to 44	29
	45 to 49	7
	50 to 59	11
	60 to 64	3
<b>Socioeconomic Level</b>	65 and over	5
	Low	0
	Lower Middle	68
	Upper Middle	13
<b>Education Level</b>	High	1
	Primary	21
	Secondary	18
	High School	29
	Bachelor's Degree	11
<b>Origin</b>	No Schooling	3
	Urban	33
	Semi-urban	44
<b>Employed</b>	Rural	4
	Yes	33
<b>BMI</b>	No	49
	Underweight	0
	Normal	30
	Overweight	20
<b>Initial TB Diagnosis</b>	Obesity	32
	Pulmonary	82
<b>Type of Contact</b>	Intimate	51
	Frequent	30
	Sporadic	1
<b>Relationship</b>	Parents	4
	Partner	10
	Children	22
	Siblings	4
	Other	42
<b>Length of Cohabitation</b>	Less than one year	17
	More than one year	65
<b>Comorbidities</b>	Diabetes mellitus (DM)	10
	Hypertension (Hyperter)	5
	Alcoholism	1
	DM/Hypertension	5
	Other	5
<b>BCG Vaccination</b>	Yes	81
	No	1
<b>PPD Test</b>	PPD Test	82
	Positive	31
<b>Result</b>	Negative	51
	Acid-Fast Bacilli	2

Note: PPD Census Database of UMF No. 47

98.9% of the contacts had a history of BCG vaccination. Of the contacts who underwent tuberculin skin testing, 62.2% had a negative result, while 37.8% were positive (Table 2).

**Table 2. Frequency and prevalence of PPD results in participants.**

Variable	N	%
With Latent TB	31	37.8
Without Latent TB	51	62.2

Note: PPD Census Database of UMF No. 47

In the bivariate analysis comparing sex and PPD result, a higher proportion of latent tuberculosis infection (LTBI) was observed in women (83.9%) compared to men (16.1%). The chi-square test showed no difference when comparing these two variables ( $\chi^2 = 2.907$ ;  $p = 0.888$ ), indicating that latent tuberculosis infection does not show a sex predilection (Table 3).

**Table 3. Chi-square according to sex and latent tuberculosis infection.**

Sex	ILTB* presented		Total	$\chi^2$	p-value
	Yes	No			
Female	26	34	60	2.907	0.088
Male	5	17	22		

\*ILTB: Latent Tuberculosis Infection

Note: PPD Census Database of UMF No. 47

A comparison of latent tuberculosis diagnosis and place of origin revealed a statistically significant difference ( $\chi^2 = 9.441$ ;  $p = 0.01$ ). These results suggest that geographic origin significantly influences the occurrence of the event (Table 4). In the group with the kinship variable, the comparison between kinship and the diagnosis of latent tuberculosis infection (LTBI) was statistically significant ( $\chi^2=8.624$ ;  $p=0.031$ ). This indicates that having any type of kinship with a patient with active tuberculosis is a factor for having latent tuberculosis infection (Table 5).

The odds ratio is a measure of association that compares the probability of an event in two different groups, calculated as the ratio of the chances of an event between individuals exposed to a risk factor and those who are not.

The calculation is based on a 2x2 table that classifies individuals as sick/healthy and exposed/not exposed.

For the sex variable, the relative risk estimate was 0.385 (95% CI: 0.125-1.179), meaning that men have a lower risk of LTBI compared to the female population.

**Table 4. Chi-square according to origin and latent tuberculosis infection.**

Origin	ILTB* presented		Total	x <sup>2</sup>	p-value
	Yes	No			
Urban	19	14	33	9.441	0.01
Semi-urban	11	34	45		
Rural	1	3	4		

\*ILTB: Latent Tuberculosis Infection

Note: PPD Census Database of UMF No. 47

**Table 5. Chi-square according to kinship and latent tuberculosis infection.**

Relationship	ILTB* presented		Total	x <sup>2</sup>	p-value
	Yes	No			
Parents	1	3	4	10.259	0.031
Partner	8	2	10		
Children	5	17	22		
Siblings	1	3	4		
Others	16	26	42		

\*ILTB: Latent Tuberculosis Infection

Note: PPD Census Database of UMF No. 47

Regarding the origin of the contacts, the risk was 4.185 (95% CI: 1.620-10.809), meaning that those living in urban areas have a four times greater risk of latent tuberculosis infection compared to those living in semi-urban and rural areas.

For the risk assessment related to education level, contacts with only a primary school education had a risk estimate of 1.732 (95% CI: 0.633-4.736), meaning that, compared to other education levels, this population has twice the risk of latent tuberculosis infection.

As for socioeconomic level, those with a middle-to-upper-class level had a risk of 1.509 (95% CI: 0.456-4.988), and compared to other income levels, they had a 1.5 times greater risk of latent tuberculosis infection.

Regarding the type of contact with sputum smear-positive patients, those with frequent contact had a risk of 1.444 (95% CI: 0.575-3.627), which, compared to the other types of contact (intimate and sporadic), presented a 1.4 times greater risk of experiencing the studied event.

Of the variable that includes the relationship of contacts to the sputum smear-positive patient, those who are partners of these patients had a risk of 8.522 (95% CI: 1.675–43.353), which showed a significant difference compared to the other types of relationship. This result suggests that the partners of patients with active pulmonary tuberculosis have an 8 times greater risk of developing latent tuberculosis.

Among comorbidities, contacts who were overweight had a risk of 2.567 (95% CI: 0.917–7.185), meaning that those with this comorbidity have twice the risk of having latent tuberculosis infection (LTBI).

For diabetes mellitus, the risk was 1.769 (95% CI: 0.468–6.687), which means that those with diabetes mellitus have a 1.7 times greater risk of having LTBI. Contacts with obesity had a risk of 1.510 (95% CI: 0.607–3.755), meaning they have a 1.5 times greater risk of having LTBI. (Table 6)

**Table 6. Association between risk factors for latent tuberculosis infection**

Variables	OR	CI 95%
Male	0.385	0.125-1.179
Urban origin	4.185	1.620-10.809
Primary education	1.732	0.633-4.736
Middle-to-upper socioeconomic level	1.509	0.456-4.988
Frequent contact	1.444	0.575-3.627
Partner	8.522	1.675-43.353
Overweight	2.567	0.917- 7.185
Diabetes mellitus	1.769	0.468-6.687
Obesity	1.51	0.607-3.755

Note: PPD Census Database of UMF No. 47

The prevalence ratio compares the prevalence of a disease in an exposed group versus an unexposed group and is calculated by dividing the prevalence in the exposed group by the prevalence in the unexposed group.

For this analysis, the prevalence ratio between sex and the diagnosis of latent tuberculosis infection (LTBI) was 1.258 (95% CI: 0.982–1.612), suggesting that female participants had a higher prevalence of latent tuberculosis compared to male participants; however, this difference did not reach statistical significance.

According to the origin of the contacts, the prevalence ratio between contacts from urban areas and latent tuberculosis infection was 2.233 (95% CI: 1.319–3.780), and for semi-urban areas it was 0.548 (95% CI: 0.327–0.919),

indicating that contacts from urban areas have a higher prevalence of latent tuberculosis compared to those who do not live in such areas. For urban areas, this difference did not reach statistical significance, while for semi-urban areas it did.

Regarding the educational level variable, among contacts with primary education, the prevalence ratio between this group and the PPD result was 1.496 (95% CI: 0.720-3.106); those with secondary education had a prevalence ratio of 1.047 (95% CI: 0.454-2.415); those who completed high school had a prevalence ratio of 0.866 (95% CI: 0.465-1.613); and those with a bachelor's degree had a prevalence ratio of 0.940 (95% CI: 0.299-2.953). Based on these results, the prevalence of TB infection was 1.4 times higher among contacts with only primary education. However, the confidence interval was not statistically significant.

In the group of salaried contacts, the risk was 0.715 (95% CI: 0.395–1.295), while in the group of unsalaried contacts, the risk was 1.234 (95% CI: 0.872–1.1747). Based on these data, the prevalence of LTBI is 1.2 times higher in the unemployed group compared to those with some form of employment, but according to our confidence interval, the data did not reach statistical significance.

The risk was also analyzed according to the socioeconomic level of the contacts. Those in the lower-middle income category had an risk of 0.897 (95% CI: 0.721–1.117), while those in the upper-middle income category had an risk of 1.410 (95% CI: 0.521–3.814). Based on the values obtained, it is interpreted that among contacts with a medium-high socioeconomic level, the prevalence of latent tuberculosis is 1.4 times higher than among those with a medium-low income. However, the confidence interval did not reach statistical significance.

One of the main factors that can contribute to the occurrence of this event is the type of contact with the sputum smear-positive patient. From this analysis, the risk for contacts in the close contact category was 0.897 (95% CI: 0.625-1.288); for those with frequent contact with the patient with active tuberculosis, the risk was 1.258 (95% CI: 0.713-2.219). With this analysis, the prevalence of developing latent tuberculosis infection (LTBI) is 1.2 times higher in those with frequent contact with sputum smear-positive patients than in those with close contact; however, the confidence interval values exceed one, so the data are not statistically significant.

In the kinship category, those who are parents of patients with active tuberculosis had a risk of 0.548 (95% CI: 0.060-5.043); those who are

partners, the risk obtained was 6.581 (95% CI: 1.492-29.019); those who are children of sputum-positive patients, the PR was 0.484 (95% CI: 0.198-1.180); as for siblings, the risk was 0.548 (95% CI: 0.060-5.043); and those who fall into the "Other" category, the risk was 1.012 (95% CI: 0.656-1.563). According to our results, it is interpreted that the partners of patients with active tuberculosis have a higher prevalence of latent tuberculosis infection, 2.4 times higher compared to other family members.

Regarding the length of time contacts have lived with sputum smear-positive patients, the prevalence ratio for those who lived with active patients for less than one year was 0.897 (95% CI: 0.369-2.183), while for those who lived with them for more than one year, the prevalence ratio was 1.028 (95% CI: 0.821-1.287). This means that the prevalence of a positive PPD test is 1.028 times higher in the population that has lived with a tuberculosis patient for more than one year than in those who have lived with them for less time. Despite the risk, the confidence interval exceeds one, so it is not statistically significant.

In the section on comorbidities, contacts diagnosed with DM had a prevalence ratio (PR) of 1.645 (95% CI: 0.518-5.229); with HHS it was 1.097 (95% CI: 0.194-6.203); the PR of overweight contacts was 2.011 (95% CI: 0.941-4.297); for obese contacts, the prevalence ratio was 1.280 (95% CI: 0.748-2.190); in contacts with both DM and HHS, a PR of 1.097 (95% CI: 0.194-6.203) was obtained; these data show that those contacts with any comorbidity have a higher prevalence of LTBI than those without. (Table 7)

A binary logistic regression analysis was performed to determine the factors associated with the diagnosis of latent tuberculosis infection.

Relevant sociodemographic and clinical variables were included in the model: Male sex showed an inverse association with the occurrence of the event ( $p = 0.011$ ; OR = 0.11; 95% CI: 0.02–0.61), indicating a lower probability of presentation compared to female sex.

Contacts of urban origin maintained a significant association with a positive result ( $p = 0.002$ ; OR = 8.753; 95% CI: 2.206–34.732), indicating that people living in urban areas have a significantly higher probability of presenting with latent tuberculosis infection compared to those living in semi-urban and rural areas.

Among those with kinship ties to patients with active tuberculosis, a significant association was observed between those who were partners of these patients ( $p = 0.004$ ; OR = 63.774; 95% CI: 3.728–1090.950). This suggests

that partners of sputum smear-positive patients have a lower risk of developing latent tuberculosis infection (LTBI).

**Tabla 7. Factores asociados a infección latente por tuberculosis según la razón de momios ajustada**

Variables	OR	IC 95%
Femenino	1.258	0.982-1.612
Procedencia urbana	2.233	1.319-3.780
Procedencia semiurbana	0.548	0.327-0.919
Primaria	1.496	0.720-3.106
Secundaria	1.047	0.454-2.415
Bachillerato	0.866	0.465-1.613
Licenciatura	0.94	0.299-2.953
Asalariados	0.715	0.395-1.295
No asalariados	1.234	0.872-1.1747
Nivel socioeconómico medio- bajo	0.897	0.721-1.117
Nivel socioeconómico medio-alto	1.41	0.521-3.814
Contacto íntimo	0.897	0.625-1.288
Contacto frecuente	1.258	0.713-2.219
Padres	0.548	0.060-5.043
Pareja	6.581	1.492-29.019
Hijos	0.484	0.198-1.180
Hermanos	0.548	0.060-5.043
Otro parentesco	1.012	0.656-1.563
Convivencia menor a un año	0.897	0.369-2.183
Convivencia mayor a un año	1.028	0.821-1.287
Diabetes mellitus	1.645	0.518-5.229
Hipertensión arterial	1.097	0.194-6.203
Sobrepeso	2.011	0.941-4.297
Obesidad	1.28	0.748-2.190
DM/HAS	1.097	0.194-6.203

Note: PPD Census Database of UMF No. 47

**Tabla 8. Factors associated with latent tuberculosis in the multivariate logistic regression model.**

Variable	B	Standard error	Wald	df	Sig.	OR	CI 95%	
							Lower	Upper
Urbana	2.169	0.703	9.517	1	0.002	8.753	2.206	34.732
Pareja	4.155	1.449	8.227	1	0.004	63.774	3.728	1090.95
Sexo	-2.168	0.851	6.488	1	0.011	0.114	0.022	0.607
Asalariado	-0.818	0.665	1.513	1	0.219	0.441	0.12	1.625
Nivel socioeconómico medio-alto	-1.779	1.126	2.498	1	0.114	0.169	0.019	1.533
Contacto íntimo	-1.7	0.73	5.426	1	0.02	0.183	0.044	0.764
Tiempo de convivencia	0.441	0.827	0.284	1	0.594	1.555	0.307	7.87
Diabetes	0.809	0.836	0.935	1	0.334	2.245	0.436	11.564
Hipertensión arterial	-3.539	1.804	3.85	1	0.05	0.029	0.001	0.996
Sobrepeso	0.821	0.723	1.29	1	0.256	2.274	0.551	9.382
Constante	3.257	4.698	0.48	1	0.488	25.96		

Specified variables: Urban, Partner, Sex, Salaried, Middle-high socioeconomic level, Intimate contact, Time of cohabitation, Diabetes mellitus, High blood pressure, Overweight.

Note: PPD Census Database of UMF No. 47

Intimate contact was negatively associated with the occurrence of the event ( $p = 0.020$ ;  $OR = 0.18$ ;  $95\% CI: 0.04-0.76$ ). This finding suggests that maintaining intimate contact significantly decreases the probability of the event occurring. Similarly, systemic arterial hypertension (SAH) was found to

be less likely to be associated with the event ( $p = 0.050$ ;  $OR = 0.029$ ; 95% CI: 0.001–0.996), decreasing the probability of latent tuberculosis infection.

The variables salaried employment, socioeconomic level, cohabitation time, diabetes mellitus, and overweight did not show statistical significance in this model.

## DISCUSSION.

In this study, the prevalence of PPD positivity was 37.8% (95% CI: 27.3–48.3), indicating that more than one-third of the participants showed immunological evidence of *Mycobacterium tuberculosis* infection. This prevalence is consistent with values reported in intermediate-risk populations by various authors. For example, Martínez et al. (2020), in a study of healthcare workers at a public hospital, observed a prevalence of 35.2%, while Hernández et al. (2019) documented 41% in household contacts of patients with TB. Similarly, Gómez et al. (2021) reported prevalences between 30% and 45% in communities with a history of sustained exposure. These figures, together with the present result, reinforce the evidence that latent infection remains a significant problem in exposed populations or those with social conditions that favor transmission.

However, the prevalence found was higher than that observed in studies of the general population, such as the one by Sánchez et al. (2018), who reported 18% in individuals with no history of contact. This difference could be explained by the characteristics of the studied population, where factors such as prolonged cohabitation, high housing density, and close contact predominate—elements that increase the probability of exposure to the tuberculosis bacillus. Furthermore, methodological differences—such as the PPD cutoff point, the application technique, or the inclusion of individuals vaccinated with BCG—may also influence the variability between studies.

Regarding associated factors, the results showed that having a partner was significantly associated with a higher probability of PPD positivity ( $p = 0.019$ ;  $OR = 1491.78$ ; 95% CI: 3.29–674, 638.93). This finding could be related to a greater degree of close contact and prolonged cohabitation, as suggested by Flores et al. (2020), who found that intimate contact and cohabitation were determining factors for the transmission of the infection. Similarly, Castro et al. (2017) identified that the number of cohabitants and the duration of exposure are relevant factors for contagion, especially in family or partner contexts. In contrast, male sex and the presence of hypertension behaved as inversely associated factors, although the latter could be influenced by age or

a confounding effect, as also discussed by Mendoza et al. (2020) in studies of comorbidities and immunological susceptibility.

Regarding sex, several authors have reported differences in the immunological response to the PPD test, observing greater reactivity in women, possibly due to a hormonal effect or greater access to health services, which increases detection. This pattern agrees with the present study, where male sex was associated with a lower probability of positivity, a result that coincides with that described by Ramos et al. (2022) and Hernández et al. (2019). On the other hand, although the multivariate model included variables such as educational level, occupation, and nutritional status, none showed a significant association. This behavior has also been reported in similar studies, where structural determinants (such as socioeconomic level) influence PPD positivity indirectly, through housing conditions and access to health services, rather than through a direct effect.

Taken together, the findings confirm that LTBI remains a relevant health problem, even in populations without active disease, and that interpersonal exposure factors play a key role in its persistence. The differences found with other studies can be attributed to sample composition, population size, heterogeneity in diagnostic criteria, and local sociodemographic characteristics.

Finally, it is important to acknowledge that the limited sample size ( $n=82$ ) and the presence of wide confidence intervals for some variables may have affected the precision of the estimates, which constitutes a methodological limitation. However, the overall consistency with previous studies supports the validity of the results and underscores the need to strengthen detection and prevention strategies for latent tuberculosis infection in community and family settings.

This research allowed us to determine the prevalence of latent tuberculosis infection (LTBI) using the PPD test and to analyze associated factors in a specific population. The results obtained reflect that LTBI continues to be a current public health problem, especially in groups with prolonged exposure or in contexts where living conditions facilitate the transmission of *Mycobacterium tuberculosis*. The PPD positivity rate was 37.8% (95% CI: 27.3%–48.3%), meaning that more than one-third of the individuals tested had latent tuberculosis infection. This value is higher than that reported in general population studies, but similar to that found in research conducted in intermediate-risk populations or those with a history of contact with active tuberculosis cases. This suggests that continuous exposure, close cohabitation,

and socio-environmental conditions can significantly influence the probability of infection, even in the absence of active disease.

In the multivariate analysis, three factors of interest were identified: having a partner, male sex, and the presence of hypertension. The variable "having a partner" showed a positive and significant association with PPD positivity, which could be explained by a higher frequency of close contact, prolonged cohabitation, or indirect exposure to risk environments through the partner or family. This result reinforces the importance of the home environment as a transmission site and the need to strengthen screening and follow-up of intrafamilial contacts. On the other hand, male sex and hypertension behaved as inversely associated factors. Although the relationship between sex and susceptibility to tuberculosis infection is not entirely consistent across studies, some authors have suggested that immunological and hormonal differences may influence the response to the PPD test, in addition to possible biases in exposure or detection. In the case of hypertension, its apparent protective effect could be explained by lower exposure or by confounding factors related to age or more frequent medical care; therefore, this result should be interpreted with caution and explored in subsequent studies. In contrast, variables such as educational level, occupation, body mass index, diabetes mellitus, and alcohol consumption did not show a significant association with the PPD result. However, it is possible that these factors act indirectly, through structural conditions or social determinants that were not fully captured in this analysis. The study had limitations inherent to the sample size ( $n = 82$ ), which may have affected the stability of some estimates and increased the width of the confidence intervals. Nevertheless, the model showed an adequate fit and allowed for the identification of epidemiologically relevant associations. Furthermore, the cross-sectional nature of the study prevents the establishment of causal relationships; therefore, longitudinal research is recommended to confirm the direction of the associations found. Despite these limitations, the results contribute to understanding the magnitude and determinants of latent tuberculosis infection in local populations. The findings highlight the need to strengthen early detection, surveillance, and prevention strategies, especially in groups with risk factors for continuous exposure or close contact. They also underscore the importance of incorporating latent tuberculosis infection screening into tuberculosis control programs, not only for index cases but also for their contacts and the community at large. Finally, this study reaffirms the relevance of addressing tuberculosis from a comprehensive perspective, considering the social and familial determinants that influence the transmission and persistence of the infection. The implementation of preventive actions, health education, and sustained

epidemiological surveillance are key elements for reducing the burden of latent infection and preventing progression to active forms of the disease, thus contributing to the achievement of national and international tuberculosis control goals.

Based on the results obtained in this research on latent tuberculosis infection (LTBI) and their comparison with available scientific evidence, the following recommendations are made to strengthen tuberculosis prevention, detection, and control measures at the local and community levels. These suggestions aim to translate the study's findings into practical strategies that contribute to reducing the transmission of *Mycobacterium tuberculosis* and the progression of latent infection to active disease:

1. Strengthen screening strategies for LTBI. It is necessary to implement ongoing LTBI detection campaigns using the PPD test in high-risk groups, especially household members and partners of patients with active tuberculosis. This would allow for the timely identification of infected individuals and reduce progression to active disease.
2. Promote medical follow-up and epidemiological surveillance of contacts. The study results show that close cohabitation is a determining factor for PPD positivity. Therefore, it is recommended to establish protocols for tracing and monitoring household contacts, prioritizing those with frequent or prolonged exposure.
3. Strengthen health education and health communication. It is essential to develop educational interventions aimed at the general population and at-risk groups that promote understanding of the transmission, prevention, and treatment of latent tuberculosis infection. Health education can help reduce stigma and increase adherence to screening and control programs.
4. Train health personnel in the identification and management of latent tuberculosis infection (LTBI). It is recommended to strengthen the ongoing training of medical and nursing staff in the reading, interpretation, and follow-up of the PPD test, as well as in the appropriate management of positive cases and their timely referral to specialized care units.
5. Incorporate LTBI detection into institutional and community programs. Given that latent infection represents a significant reservoir of transmission, its inclusion in tuberculosis control programs is a priority. Integrating screening into community campaigns or occupational health assessments could expand coverage and reduce the risk of outbreaks.

6. Promote local investigation and continuous surveillance. Studies with larger samples and longitudinal designs are recommended to establish causal relationships and evaluate the impact of identified associated factors. Active surveillance is also necessary to understand local trends in the prevalence and resistance of *Mycobacterium tuberculosis*.

7. Consider the social determinants of health in control strategies. Given that transmission is related to housing conditions, overcrowding, and access to health services, it is suggested that an intersectoral approach be incorporated that includes improving social and environmental conditions as an integral part of the fight against tuberculosis.

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# Covid-19 as a risk factor for the development of stroke

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## Abstract

**Introduction:** The post-acute phase of SARS-CoV-2 infection (long Covid, >90 days) has been associated with vascular sequelae; however, local evidence is required on whether the severity of the acute condition, approximated by hospitalization, increases the subsequent risk of cerebrovascular disease (CVD).

**Objective:** To determine the association between hospitalization for acute Covid-19 and the subsequent development of stroke.

**Materials and methods:** A retrospective, analytical, 1:1 matched case-control observational study was conducted in Villahermosa, Tabasco (March 15, 2020–December 31, 2024). Cases were patients with an incident diagnosis of stroke, and controls were patients without stroke, selected from the same population group. Matching was performed by age and sex (caliper  $\pm 5$  years). Data sources included institutional reporting databases (SINOLAVE) and medical records. Paired odds ratios (ORs) and adjusted ORs were estimated using conditional logistic regression.

**Results:** One hundred and sixty pairs ( $n=320$ ) were analyzed. A history of hospitalization for COVID-19 was associated with a higher probability of stroke in the adjusted model (aOR=4.45; 95% CI: 2.40–8.25;  $p<.001$ ). Hypertension showed the strongest association (aOR=6.26; 95% CI: 3.16–12.40;  $p<.001$ ). The main association was consistent in sensitivity analyses for the functional specification of age (OR 4.45–5.24) and stable in LOPO (range 4.25–4.95).

**Conclusions:** Hospitalization for Covid-19 during the acute phase was independently associated with a higher risk of stroke in the period consistent with prolonged Covid, supporting the need for focused clinical surveillance in patients with severe acute illness.

**Keywords:** COVID-19, Long COVID, Cerebrovascular Disease, Risk Factors, Case-Control Studies

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## INTRODUCTION

The SARS-CoV-2 pandemic constituted a global health event of great magnitude, with hundreds of millions of accumulated cases and millions of deaths reported worldwide (WHO, 2023). In Mexico, as of June 25, 2023, 7,633,335 confirmed cases of SARS-CoV-2 infection and 334,336 attributable deaths had been reported, according to national epidemiological surveillance systems. The distribution of the healthcare burden showed a clear predominance of outpatient management (90.43%), while 9.57% of cases required hospitalization, reflecting the proportion of patients who presented severity criteria during the acute phase. In the state of Tabasco, 222,063 confirmed cases and 6,189 deaths were documented, with a hospitalization rate of 6.93%. This epidemiological behavior was observed in a context marked by a high population prevalence of Cardiometabolic comorbidities constitute a set of predisposing factors that increase the risk of clinical complications and worse outcomes associated with SARS-CoV-2 infection (CONAHCYT, CentroGeo, GeoInt, & DataLab, 2023).

At the Mexican Social Security Institute (IMSS), the cumulative care provided during the health emergency reached almost 11 million people, reflecting the healthcare burden and institutional relevance of the problem (IMSS, 2023).

At the same time, cerebrovascular disease (CVD) maintains a substantial burden in terms of mortality and disability. Globally, it is recognized as one of the leading causes of death and disability, with a considerable economic impact (Feigin et al., 2022). In Mexico, cerebrovascular diseases were among the leading causes of death; in 2022, CVD was the seventh leading cause of death nationally, with 35,977 deaths registered (INEGI, 2023). In this scenario, the relevant question is not limited to the acute effects of the infection but extends to its potential persistent vascular consequences in the post-acute phase.

Long COVID (also referred to as post-acute sequelae of SARS-CoV-2 infection) is conceptualized as a chronic systemic state following primary infection, lasting at least three months and with a continuous or fluctuating course (Fineberg et al., 2024). Its clinical importance lies in its heterogeneity, its disabling potential, and its involvement of multiple systems, notably neurological and vascular manifestations (Ong et al., 2023; Rushikesh Ramrao Timewar et al., 2023). The pathophysiological plausibility of cerebrovascular outcomes in the post-acute period is supported by mechanisms of endothelial dysfunction, hemostatic activation, and a prothrombotic/microangiopathic

state, with persistent thromboinflammatory phenomena following virological resolution (Ahamed & Laurence, 2022; Giustino et al., 2020; Martins-Gonçalves et al., 2023). Furthermore, it has been proposed that cerebral microvascular alterations and changes in cerebrovascular reactivity could contribute to neurovascular vulnerability in long COVID, with implications for outcomes such as stroke (Fekete et al., 2025; Pommy et al., 2023; Koutsiaris & Karakousis, 2025). Additionally, clinical reviews have highlighted the relationship between COVID-19 and ischemic stroke within the neurological spectrum of the disease (Sagris et al., 2021).

From an epidemiological perspective, there is evidence of an increased risk of stroke following SARS-CoV-2 infection, with findings suggesting gradients according to the severity of the acute illness. In a Danish national cohort, an increased risk of stroke was observed in the acute phase, and this excess risk persisted in the post-infection period among those Cases requiring hospitalization were among those that did not show a long-term increase in stroke rates, while those managed in the community did not (Skov et al., 2024). Nationally, local research on post-COVID stroke has also been documented, although with methodological limitations that do not necessarily resolve the role of the severity of the acute episode (Moreno et al., 2022). Taken together, this background supports the need to specifically estimate whether a history of hospitalization for COVID-19 during the acute phase is associated with a higher occurrence of stroke in the post-acute context, particularly in populations with high exposure and cardiometabolic comorbidities (CONAHCYT, CentroGeo, GeoInt, & DataLab, 2023).

Within this framework, the objective of this study was to determine the association between a history of hospitalization for SARS-CoV-2 infection during the acute phase and the development of cerebrovascular disease in the context of prolonged COVID-19 in patients enrolled at Family Medicine Unit No. 47.

The objective was to determine the association between a history of hospitalization for Covid-19 during the acute phase of the infection and a greater development of stroke, compared to having Covid-19 on an outpatient basis in beneficiaries assigned to UMF No. 47 in the context of prolonged Covid (>90 days).

## **MATERIALS AND METHODS**

The study was conducted in Villahermosa, Tabasco, using data from patients registered at Family Medicine Unit (UMF) No. 47. The design was observational, analytical, matched 1:1 case-control, retrospective, from March

15, 2020, to December 31, 2024. The study population consisted of patients registered at UMF 47 with a history of COVID-19 infection during the period of March 15, 2020, to December 31, 2024. Cases were patients registered at UMF 47 with an incident diagnosis of stroke during the study period. Controls were patients registered at UMF 47 without stroke during the same period, selected from the same population group. A consecutive non-probability sampling was performed using the databases of patients reported in the Online Notification System for Epidemiological Surveillance (SINOLAVE). A minimum sample size was calculated, considering a 1:1 matched study type. A McNemar approach was used, which utilizes an expected proportion of discordant pairs. With these values, the minimum theoretical number of pairs required to detect a difference between discordances was estimated to be estimated with  $\alpha=0.05$  (two-tailed), a power of 80, and assuming an expected OR of 2.05 and a total pair discordance of 0.50. The sample size was calculated using the formula for matched case-control studies with a discordant pairs approach. The matched odds ratio and pair discordance were also calculated. It was established that the minimum size required to guarantee the statistical validity of the study was 133 pairs (266 participants). However, to reduce the impact of potential losses, an additional 10% was added. This adjustment was made to ensure the robustness of the analysis and the representativeness of the sample, increasing the total number of pairs to the required 147 (294 subjects). Inclusion criteria for cases were over 18 years, a history of SARS-CoV-2 infection confirmed by laboratory testing (PCR or rapid test), a first-time diagnosis of stroke, ICD-10 codes (I63, I64, I67, I69), and a diagnosis following a history of SARS-CoV-2 infection with radiological confirmation.

Patients with a history of stroke prior to SARS-CoV-2 infection, stroke diagnosed less than 90 days after SARS-CoV-2 infection, insufficient or incomplete information for follow-up, or referred to another hospital were excluded. This study was conducted at General Hospital No. 46 of the Mexican Social Security Institute in Villahermosa, Tabasco. Information was obtained through the digital health ecosystem from emergency and inpatient medical records. The online notification system for epidemiological surveillance was also consulted to identify all patients registered at the Family Medicine Unit. No. 47 patients who had been notified of COVID-19 (SINOLAVE) at General Hospital No. 46 were included in the study. To identify potential cases, a specific search was conducted for hospital discharged patients with diagnoses compatible with cerebrovascular disease, using ICD-10 coding (Cerebral infarction, acute cerebrovascular accident, and other defined cerebrovascular pathologies). Selected cases were confirmed by

reviewing clinical notes and, when available in the medical record, corroborated with imaging studies and/or a clinical description consistent with the diagnosis. To evaluate the development of stroke as a complication following the acute phase of COVID-19, hospitalization during the acute phase was considered the primary exposure. Furthermore, to focus the analysis on the post-acute period compatible with prolonged COVID, the cerebrovascular event was defined as occurring at least 90 days after the COVID-19 episode, as determined by the documented date of diagnosis and/or hospital admission as recorded in the medical record. To ensure temporal comparability and minimize bias arising from differences in observation time, an index date was established for each case-control pair. In cases, this date corresponded to the first confirmed diagnosis of stroke; in controls, the same index date as the matched case was assigned, verifying through documentation that the control remained stroke-free up to that point and had clinical follow-up in the unit. Figure 3 illustrates the case and control selection scheme. Using the obtained sample, a database was created. Subsequently, statistical analysis was performed using R software version 4.5.2. The analysis was conducted in three stages. The first stage involved a systematic evaluation of the database quality, examining the completeness of the information and compliance with the 1:1 matched case-control design. The second stage focused on descriptive and inferential statistics, including confidence intervals and p-values. The bivariate analysis included McNemar's exact test and paired odds ratios (ORs). For the multivariate analysis, conditional logistic regression was used to calculate the adjusted ORs for each variable. The third stage involved complementary evaluation tests to document internal consistency. Standardized differences, sensitivity analysis based on the age variable using 3 models (Linear age, Categorical age, age with natural splines with  $df=3$ ), the stability of the estimator was also evaluated against possible influential pairs with a LOPO (Leave-one-pair-out) model.

## RESULTS

A systematic evaluation of the database quality was conducted to verify internal consistency, completeness of information, and adherence to the 1:1 matched case-control design. All variables included in the analysis had zero missing values. Dichotomous variables were correctly coded in binary format (0 = No, 1 = Yes). The age variable showed plausible value for the analyzed population, maintaining a range consistent with the clinical context and without extreme values suggestive of data entry or measurement errors.

Furthermore, it was confirmed that each pair contained a single case with a confirmed diagnosis of cerebrovascular disease (CVD = 1) and a single control without such a diagnosis (CVD = 0). This preliminary review ensured compliance with the matched design and allowed for bivariate and multivariate analyses conditioned on the matching. Initially, 167 pairs (334 participants) were identified; however, 7 pairs were excluded after applying the exclusion criteria and confirming that they had the necessary information, resulting in a final sample of 160 pairs (320 participants). The characteristics of the study population are described below. The 320 participants comprised 160 pairs with a 1:1 matching ratio, with 160 patients who had experienced a stroke and 160 who had not. The average age was similar in both groups, with a mean of 62.9 years and a standard deviation of  $\pm 14.6$  years, confirming adequate age balance resulting from the matching. Regarding sex, the distribution was equitable between cases and controls, with 51.9% women and 48.1% men in both groups, indicating complete control of this variable in the study design. The age distribution showed a similar composition in cases and controls, with a predominance of participants  $\geq 65$  years old (cases: 44.4%; controls: 45.6%). The median age was comparable (cases: 62.5; controls: 63.0), and the interquartile range was close (cases: 17; controls: 19), reinforcing the age comparability achieved through matching. Regarding the exposures and comorbidities analyzed, a history of hospitalization for COVID-19 during the acute phase was considerably more frequent in the case group (51.2%) compared to the control group (19.4%). Similarly, the prevalence of hypertension (69.4% in cases vs. 29.4% in controls) and diabetes mellitus (44.4% in cases vs. 23.8% in controls) was higher in the case group. In contrast, the proportions of obesity (30.0% vs. 29.4%) were higher in the control group. The prevalence of diabetes (29.4%) and dyslipidemia (28.8% vs. 25.0%) was similar between both groups. Finally, smoking was more frequent in controls (49.4%) than in the cases (37.5%). Table 1.

**Table 1. Baseline characteristics of the pairs.**

Variable	Cases n(%)	Controls n(%)
Female	83(51.9)	83(51.9)
Male	77 (48.1)	77 (48.1)
Hospitalization for COVID-19	82 (51.2)	31 (19.4)
Hypertension	111 (69.4)	47 (29.4)
Diabetes	71 (44.4)	38 (23.8)
Obesity	48 (30.0)	47 (29.4)
Dyslipidemia	46 (28.8)	40 (25.0)
Smoking	60 (37.5)	79 (49.4)

Note: Percentages were calculated within each group (cases and controls).

N=160

The comparison of the history of hospitalization for Covid-19 and the development of stroke was analyzed using McNemar's test. Bivariate analysis was performed respecting the paired structure for the study type. For age, the paired Wilcoxon test was applied, yielding results without evidence of a statistically significant difference between cases and controls ( $p = .264$ ). For dichotomous variables, the exact McNemar test was used, and the paired odds ratio (OR) was estimated based on discordant pairs. A positive association was observed between hospitalization for Covid-19 and stroke (OR = 3.12, 95% CI [1.97, 4.95],  $p < .001$ ), with 99 discordant pairs, providing a large sample size for this estimation. Similarly, hypertension was the variable with the strongest association with the development of stroke, with an odds ratio (OR) of 5.00 (95% CI: 2.92–8.55;  $p < .001$ ), supported by 96 discordant pairs, along with diabetes mellitus, which also showed a statistically significant association, with an OR of 2.50 (95% CI: 1.52–4.10;  $p < .001$ ), based on 77 discordant pairs. In contrast, obesity (OR = 1.03, 95% CI [0.64, 1.66],  $p = 1.000$ ; 67 discordant pairs) and dyslipidemia (OR = 1.22, 95% CI [0.73, 2.03],  $p = .519$ ; 60 discordant pairs) did not show a statistically significant association. On the other hand, smoking showed an inverse association (OR = 0.55, 95% CI [0.33, 0.91],  $p = .025$ ; 65 discordant pairs). Furthermore, the effective information for each exposure was corroborated using the number of discordant pairs, as described by their "information ratio" (discordant/pairs). This ratio varied by exposure, being highest for a history of hospitalization (0.62) and hypertension (0.60), thus contextualizing the relative precision of the estimates for each variable. Table 2.

Variable	OR	95%CI	<i>p</i>
Hospitalization for COVID-19 (acute phase)	3.12	[1.97, 4.95]	< .001
Hypertension	5	[2.92, 8.55]	< .001
Diabetes mellitus	2.5	[1.52, 4.10]	< .001
Obesity	1.03	[0.64, 1.66]	1
Dyslipidemia	1.22	[0.73, 2.03]	0.519
Smoking	0.55	[0.33, 0.91]	0.025

Note. For dichotomous variables, McNemar exact and paired OR were used.

A conditional logistic regression was used, adjusting for major comorbidities, and a history of hospitalization for COVID-19 was found to be associated as an independent risk factor for the development of stroke with an odds ratio (OR) of 4.45 (95% CI: 2.40–8.25;  $p < 0.001$ ). This result indicates that after controlling confounding variables and covariates, patients with a history of

hospitalization for COVID-19 were more than four times more likely to develop stroke. Regarding comorbidities, the most relevant for this study were hypertension, which also demonstrated an independent association with the development of stroke, with an OR of 6.26 (95% CI: 3.16–12.40;  $p < 0.001$ ), positioning it as one of the most significant risk factors within the analytical model. Diabetes mellitus also showed a moderate positive trend with an OR of 2.06, which, although it did not reach statistical significance (95% CI: 0.92–4.65;  $p = 0.080$ ), suggests a possible effect that could be confirmed by increasing the sample size. Meanwhile, obesity, with an OR of 0.62; (95% CI: 0.25–1.54,  $p = 0.3$ ) and dyslipidemia with OR 1.81 (95% CI: 0.72–4.59;  $p = 0.304$ ) did not show statistically significant associations with the development of stroke in the adjusted model. Relevantly, smoking was associated with a lower risk of stroke (OR 0.41; 95% CI: 0.20–0.85;  $p = 0.018$ ), a finding that likely reflects residual confounding, selection bias, or survivor bias, rather than a true protective effect. Following the descriptive and inferential analysis, complementary evaluations were conducted to document the model's internal consistency and the robustness of the results. This evaluation was incorporated to demonstrate that the estimated association between a history of hospitalization during the acute phase of a COVID-19 infection and the development of stroke was not due to specific specification assumptions or driven by influential pairs, and that the matching scheme achieved the expected balance in the priori defined variables. Initially, the performance of the matching was evaluated using a descriptive balance diagnosis based on standardized differences (SDN). The results of the post-1:1 matching evaluation showed that the variables used as matching criteria exhibited almost perfect balance. For example, age had an SDN of 0.01 and male sex 0.00, confirming adequate comparability between cases and controls considering these characteristics. In parallel, the behavior of other clinical covariates not used in the matching was described. These showed relevant differences between groups, such as a history of hospitalization for COVID-19 (SMD = 0.67) and hypertension (SMD = 0.80), which is consistent with their differential distribution in a case-control design and corroborates the need to consider these adjustment variables within the multivariate model. Table 3.

In the main model, the OR for hospitalization was 4.45; when categorized by age, the OR was 5.24; and when modeled with splines, the OR was 4.47. Statistical significance was maintained in all three approaches ( $p < .001$ ), with consistent confidence intervals, which supports the finding that it does not depend on a specific way of incorporating age into the model.

**Table 3. Conditional logistic regression model stratified by PAR**

Variable	adjusted OR	95% CI	<i>p</i>
Hospitalization for COVID-19 (acute phase)	4.45	[2.40, 8.25]	< .001
Hypertension	6.26	[3.16, 12.40]	< .001
Diabetes mellitus	2.06	[0.92, 4.65]	0.08
Obesity	0.62	[0.25, 1.54]	0.304
Dyslipidemia	1.81	[0.72, 4.59]	0.209
Smoking	0.41	[0.20, 0.85]	0.017

Note. Pairwise stratified model (strata [PAR]). OR = odds ratio; CI = confidence interval.

Furthermore, to assess the stability of the estimator against potentially influential pairs, a leave-one-pair-out (LOPO) approach was chosen. This procedure involved re-estimating the conditional model in 160 iterations, excluding a different pair in each iteration, to identify whether the effect size depended disproportionately on specific observations. Importantly, in no iteration did the estimator fall below 1, nor was statistical significance lost (0 iterations with  $p > .05$ ), confirming the robustness of the estimated effect and ruling out its being conditioned by a limited number of highly influential pairs.

## DISCUSSION.

The results of this research provide local evidence on the long-term cerebrovascular impact of prolonged COVID-19. The main finding of this study is that a history of hospitalization for COVID-19 acts as a severity marker, quadrupling the probability of developing a stroke (aOR 4.45), independent of age and other classic risk factors for the disease. These data are consistent with the "severity gradient" hypothesis proposed by Skov et al. (2024) and Taquet et al. (2021), who observed that thrombotic risk remains significantly elevated in patients who required hospitalization or intensive care, compared to those managed on an outpatient basis.

When comparing our results with the regional study by Moreno et al. (2022) in Veracruz, our study demonstrated a clear statistical association ( $p < 0.001$ ). This favorable difference for our research is likely due to the rigor of the matched design and multivariate adjustment, tools that allowed us to eliminate the effect of confounding variables that could have diluted the association in previous, less controlled studies.

A relevant finding is that hypertension (aOR 6.26) was the strongest predictor in our population. This suggests a "double hit" pathophysiological mechanism: an endothelium chronically damaged by hypertension that suffers

acute and sustained damage from the systemic inflammation of COVID-19, described by Ahamed and Laurence (2022) as persistent endotheliopathy. In this context, hospitalization for COVID-19 is not only a contributing factor but also an indicator of an inflammatory burden that destabilizes an already vulnerable vascular system.

An important point to highlight is the history of smoking, as it showed an apparent protective effect (aOR 0.41). This finding should not be interpreted as a genuine biological effect, but rather as a manifestation of methodological bias, specifically survival bias. It is plausible that smokers with severe SARS-CoV-2 infection experienced higher mortality during the acute phase, which led to their exclusion from the follow-up cohort for cerebrovascular risk assessment. Consequently, the analyzed population would be predominantly composed of subjects with a lower cumulative smoking burden or with physiological characteristics that confer greater resilience, generating a systematic distortion in the estimate and underscoring the need to interpret this result within a framework of bias control and sensitivity analysis.

Finally, the lack of a significant association with obesity (aOR 0.62) and dyslipidemia (aOR 1.81) in the adjusted model contrasts with classic literature. This could reflect that, in the studied population, there is a limitation derived from the inadequate recording of these conditions in electronic records, propose that the metabolic risk is mainly absorbed by hypertension and diabetes, or that the thrombotic mechanism induced by the virus follows pathways independent of traditional lipid atherosclerosis.

The findings of this study provide evidence that the history of hospitalization for COVID-19 is independently associated with the subsequent development of stroke in the studied population, in the context of prolonged COVID-19, with a more than fourfold increased probability of the event compared to patients who required outpatient management.

A significant interaction with pre-existing comorbidities was established, primarily hypertension, which remains the most relevant baseline risk factor, exacerbating vascular damage in post-COVID patients.

Furthermore, the severity of acute COVID-19 (inferred from the need for hospitalization) has clinical repercussions that extend beyond the acute phase of the disease, corroborating the need to consider stroke as a relevant late complication. For the interpretation of the results, limitations inherent to the retrospective design and the quality of the data sources should be considered. The existence of a potential information bias associated with underreporting in institutional databases is acknowledged, which could lead to an

underestimation of comorbidities such as obesity and dyslipidemia. Furthermore, the absence of formal diagnosis or coding during medical care is identified as generating a risk of misclassification, potentially distorting estimates and explaining the lack of statistical significance observed in the multivariate model. Additionally, a relevant limitation was identified in the measurement of the exposure factor: although hospitalization was used as an operational marker of severity, the heterogeneity in the quality of clinical records made it impossible to accurately stratify the level of in-hospital severity, including critical variables such as the need for mechanical ventilation or admission to the ICU. This limitation restricts the possibility of performing a dose-response analysis regarding the impact of clinical severity on vascular risk. Finally, the study is susceptible to survival bias, as its focus was on events occurring in the post-acute stage (>90 days), excluding patients who died during the critical phase of the infection. This is particularly relevant given that it has been established that patients with active COVID-19 generally present with the most severe symptoms and the highest thrombotic risk. Despite the limitations, this study demonstrates methodological rigor that supports the validity of its findings. Key strengths include the matched design and rigorous control of confounding variables. The application of 1:1 matching by sex and age, using caliper matching of  $\pm 5$  years, ensured optimal comparability between groups, reducing the confounding impact of age, already considered the main risk factor for stroke. Additionally, the analytical rigor distinguishes this study from traditional descriptive approaches. The use of a conditional logistic regression model allowed for the independent estimation of the association between hospitalization for COVID-19 and the development of stroke, while simultaneously adjusting for the effect of clinically relevant covariates such as hypertension and diabetes mellitus. Finally, the rigorous case definition strengthens the study's internal validity. The exclusive inclusion of patients with laboratory-confirmed COVID-19 (PCR or rapid test) and cerebrovascular events verified by imaging and ICD-10 coding minimizes the risk of misclassification, helping to ensure that the results accurately represent the phenomenon analyzed. Given the findings of this study, such as the history of hospitalization as a clinical marker for the development of stroke, the following should be considered: The need for post-acute follow-up in patients with a history of complications during the acute phase of SARS-CoV-2 infection, especially if they have a history of intensive care unit admission. Patient education strategies should be developed for individuals with a history of COVID-19 complications, focusing on the identification of focal neurological symptoms, especially those with comorbidities such as hypertension and diabetes mellitus. It is recommended

to strengthen the quality of clinical records to accurately assess risk gradients and thereby improve the precision of future local research.

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# Risk factors associated with hospital-acquired pneumonia: a literature review

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## Abstract

**Introduction:** Hospital-acquired pneumonia (HAP) is one of the main healthcare-associated infections (HAIs), significantly impacting morbidity, mortality, and operating costs of the healthcare system.

**Objective:** Identify and synthesize the determining risk factors for the development of HAP and ventilator-associated pneumonia (VAP) according to the scientific evidence published between 2021 and 2026.

**Materials and methods:** A systematic literature review was conducted in PubMed and SciELO using DeCS/MeSH descriptors and Boolean operators. Original studies and meta-analyses in adult populations were selected.

**Results:** Three risk dimensions were identified: intrinsic host factors (age >65 years, chronic comorbidities), diagnostic-therapeutic interventions (mechanical ventilation, reintubation, previous use of antibiotics) and hospital environment factors (prolonged stay in ICU).

**Conclusions:** Invasive mechanical ventilation and the frailty of critically ill patients constitute the core risk factors. Early stratification of these factors is imperative for the implementation of prevention bundles.

**Keywords:** Hospital-acquired pneumonia; Nosocomial pneumonia; Risk factors; Mechanical ventilation; Hospital-acquired infection.

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## INTRODUCTION

Hospital-acquired pneumonia (HAP), also known as nosocomial pneumonia, is an infection of the lung parenchyma that develops 48 hours or more after hospital admission, without evidence of infection at the time of admission. This condition is one of the most frequent healthcare-associated infections and is associated with increased morbidity and mortality, prolonged hospital stays, and greater healthcare resource utilization.

Within this group, ventilator-associated pneumonia (VAP) is the most severe and frequent form in intensive care units (ICUs). Several recent studies have

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demonstrated that multiple factors related to the patient, medical interventions, and the hospital environment influence its development.

Objective: To conduct a literature review of recent scientific literature (2021–2026) available in PubMed and SciELO, to identify the main risk factors associated with the development of hospital-acquired pneumonia in hospitalized patients, particularly in intensive care units.

## MATERIALS AND METHODS

An electronic search was conducted in the PubMed and SciELO databases using the following keywords: “hospital-acquired pneumonia,” “nosocomial pneumonia,” “ventilator-associated pneumonia,” “risk factors,” “hospital-acquired pneumonia,” and “risk factors.” These keywords were combined using Boolean operators AND/OR. For example: (“hospital-acquired pneumonia” OR “nosocomial pneumonia”) AND (“risk factors”) AND (2021:2026).

The selection criteria were as follows:

Inclusion criteria:

- Articles published between 2021 and 2026.
- Original studies, systematic reviews, or meta-analyses.
- Studies in hospitalized adults.
- Studies analyzing risk factors for hospital-acquired or ventilator-associated pneumonia.

Exclusion criteria:

- Studies published before 2021.
- Pediatric articles.
- Case reports or small series.
- Studies without risk factor analysis. The titles and abstracts of the identified articles were reviewed. Subsequently, those that met the established criteria were selected, and the full text was analyzed to extract relevant data.

The selected articles were evaluated considering the type of study design, sample size, statistical analysis, and control for confounding variables. The included studies primarily consisted of prospective cohorts, retrospective studies, systematic reviews, and meta-analyses.

The results of the articles were compared considering the consistency of the identified risk factors, the magnitude of association (Odds Ratio or Risk Ratio), and the heterogeneity among hospital populations.

## RESULTS AND DISCUSSION

### Intrinsic Host Factors (Biological Determinants)

Current evidence confirms that immunosenescence in patients over 65 years of age is an independent predictor of NIH (Lee et al., 2021). The loss of protective airway reflexes and altered oropharyngeal colonization facilitate microaspiration. Likewise, the presence of comorbidities such as diabetes mellitus, chronic kidney disease (CKD), and COPD creates a pro-inflammatory pulmonary microenvironment and a deficient immune response, increasing susceptibility to opportunistic pathogens (Alfares et al., 2023).

### Factors Related to Medical Interventions

Invasive mechanical ventilation (IMV) remains the most critical modifiable risk factor. The presence of the endotracheal tube eliminates the natural barrier of the glottis, facilitates the formation of bacterial biofilm, and serves as a conduit for the aspiration of contaminated secretions.

- Reintubation and Prolonged Mechanical Ventilation: Recent studies (Li et al., 2024) suggest that the risk increases exponentially after the seventh day of ventilation.
- Selective Antibiotic Pressure: Indiscriminate antibiotic use prior to NIH is associated with a significantly higher risk of carbapenem-resistant *Pseudomonas aeruginosa* and *Acinetobacter baumannii* infections (Russo et al., 2025).

### Environmental Factors and Clinical Management

Prolonged stays in critical care areas (ICUs) increase exposure to highly virulent nosocomial flora. Other devices, such as nasogastric tubes, alter gastric pH and promote gastroesophageal reflux, favoring retrograde bacterial migration into the bronchial tree.

## CONCLUSION

Hospital-acquired pneumonia remains one of the healthcare-associated infections with the greatest impact on hospital morbidity and mortality.

Main conclusions of the selected articles		
Author / Year	Identified risk factors	Main findings
Lee H. et al., 2021	Advanced age, prolonged hospital stay, mechanical ventilation, comorbidities.	The combination of age over 65 years and mechanical ventilation significantly increases the risk of hospital-acquired pneumonia.
Yang H. et al., 2022	Prolonged intubation, ICU stay, prior antibiotic use.	Mechanical ventilation and the use of broad-spectrum antibiotics were independent risk factors.
Alfares A. et al., 2023	Advanced age, COPD, mechanical ventilation, central venous catheter	Cardiopulmonary comorbidities increase the risk of nosocomial pneumonia.
Martin-Loeches I. et al., 2022	Mechanical ventilation, aspiration, bacterial colonization	VAP remains the most common form of hospital-acquired pneumonia.
Papazian L. et al., 2023	Intubation, endotracheal tube biofilm, duration of ventilation	Duration of mechanical ventilation is one of the most important determinants.
Yao W. et al., 2024	Advanced age, immobility, chronic lung disease	Frailty and prolonged immobilization increase the risk of hospital-acquired
Li X. et al., 2024	Mechanical ventilation >7 days, reintubation, aspiration	Prolonged ventilation and reintubation significantly increase the risk.
Russo A. et al., 2025	Prior bacterial colonization, prolonged ICU stay	Colonization with multidrug-resistant bacteria is an important predictor.
Torres A. et al., 2022	Mechanical ventilation, deep sedation, aspiration	Preventive packages are recommended to reduce VAP.
Kollef M. et al., 2022	Invasive devices, prolonged ventilation, prior antibiotic use	Prevention should focus on reducing invasive devices.

Recent scientific evidence shows that its development is influenced by multiple risk factors, including prolonged mechanical ventilation, endotracheal intubation, advanced age, comorbidities (diabetes, COPD, chronic kidney disease), prolonged hospital stay, prior antibiotic use, and the presence of invasive devices, among others.

Early identification of patients with these risk factors is essential for implementing prevention strategies, such as infection control programs, safe mechanical ventilation protocols, and hospital epidemiological surveillance.

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