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EDITORIAL

Common mistakes in reporting the material and methods section of an article

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For scientific discoveries to be considered valid, whether theoretical or empirical, a phenomenon must be described precisely. Scientists must employ appropriate counterfactuals, eliminate competing explanations, and use well-designed methods to ensure that claims are accurate and reproducible. Valid empirical findings must also be reliable, enabling other researchers to reproduce the results or replicate the effects using data collected in similar contexts. Only discoveries meeting these rigorous standards can contribute meaningful scientific insights, form the basis of theoretical frameworks, or inform policy decisions.

However, over several decades, a vast body of literature has documented the persistent failure of published articles to provide sufficient information. Among these issues, the shortcomings in the Materials and Methods section are particularly noteworthy. For instance, in an analysis of 80 articles selected from the *Evidence-Based Medicine* journal between 2005 and 2006, omissions of crucial aspects of study methods, such as inclusion and exclusion criteria and precise details of interventions, were identified in more than 50% of the articles[1]. The methods section of a study answers two broad questions: (1) how and why the data were obtained and (2) how the data were analyzed. However, without a clear description of how a study was conducted, other researchers and readers cannot judge whether the findings are reliable. Moreover, an inadequate description of the methods can reduce the possibility of publication, regardless of the results. Almost 30% of rejection reasons are specifically related to this section[2].

Mistakes in the Materials and Methods section can occur at various levels, including the study design, methods employed, materials used in the research, description of measures, data analysis, and ethical approval[3,4].

In some articles, the research design does not adequately allow for testing the arguments presented. For instance, the use of cross-sectional study design is to test association rather than causality. Other frequent design issues include unsuitable sampling methods or insufficient sample sizes.

The authors often fail to clearly explain what they have done. For instance, a clinical trial of a surgical procedure may omit a step-by-step account of the clinical protocol, making replication impossible. Similarly, laboratory studies frequently lack adequate details of critical experimental steps, leaving readers unable to thoroughly understand the procedures. The reasons for this include the inexperience of authors, especially early career researchers, or their deep familiarity with the work, which may lead them to assume that the omitted details are self-evident. Whatever the reason, the authors are obligated to provide a clear and sufficient description of the validity and reliability of the methods and measures used in the study.

Another common mistake is the lack of essential details regarding the materials used, such as the active ingredient, trademark, manufacturer, and country of origin. The omission of such information undermines the reproducibility and integrity of the research. On the other hand, overemphasizing trademarks, for example, can unintentionally make a manuscript appear promotional.

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Statistical analysis is another frequent weakness in the Materials and Methods. The authors often provided insufficient details regarding the statistical techniques used. This issue is exacerbated by the authors' limited understanding of statistical methods, making it challenging to clearly articulate their decisions. To address this issue, collaboration with a statistician is essential. A statistician can provide a concise summary of the statistical methodology to ensure that the manuscript is both accurate and comprehensible.

A final significant oversight is the lack of reporting approval from the research ethics committee. Studies may sometimes be initiated without the committee's approval, which constitutes research misconduct. According to the International Committee of Medical Journal Editors, it is imperative to include a statement indicating that the research was approved by an independent review body, whether local, regional, or national (e.g., ethics committee, institutional review board)[5].

Many guidelines are available to help authors improve the completeness and transparency of their research articles. The Enhancing the QUAlity and Transparency Of health Research Network's online Library for Health Research Reporting (https://www.equator-network.org/) lists many reporting guidelines to increase manuscript quality[6]. In Clinical Innovations in Health Research-HJM, we suggest that authors consult these guidelines to maximize the value of their publications.

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ORIGINAL ARTICLE

COVID-19 vaccination effectiveness on survived in a mixed and incomplete schedule

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Abstract

Background: *Vaccines against SARS-CoV-2 were limited, and the recommended schedule was not available. Thus, government politics covered most of the at-risk population.* **Objectives:** *Analyzed the effectiveness on mortality of unvaccinated and vaccinated patients with any kind of schedule.* **Methods:** *This retrospective study included all confirmed COVID-19 hospitalized patients at a third-level hospital in Mexico City between October 2021 and February 2023. We analyzed the risk factors and number of vaccines, the types of vaccines and their effect on death, descriptive statistics, and U–Mann–Whitney, or X^2. We also have multiple logistic regressions for dead.* **Results:** *We included 567 patients; the risk factors for death were still male, age > 60, and unvaccinated, more so than any vaccine, and any kind of scheduled vaccination was better than unvaccinated. The regression showed that age, vaccination, SO2, and N/L index were the main factors that predicted death.* **Conclusions:** *Vaccinated patients with any schedule, with at least one dose of vaccine, could be the better option at the beginning. Nowadays, it is important to administer booster shots.*

Keywords: *COVID-19 vaccination. Effects on survived by mixed vaccines. Vaccination strategy in Mexico.*

Introduction

Since the emergency of SARS-CoV-2 in December 2019 in Wuhan, China, the virus has spread worldwide and has shaken our healthcare and economic systems. SARS-CoV-2 is the cause of coronavirus disease 2019 (COVID-19), an infection of the respiratory tract[1,2].

The pandemic also generated unparalleled amounts of genomic data for a single pathogen, which served to combat and understand the biology of this virus[3].

Despite the unprecedented faster creation of many kinds of vaccines worldwide and the innovative technologies, COVID-19 still affects worldwide due to accelerated development, distribution of COVID-19, and distinct SARS-CoV-2 variants of concern (VOC) that modified transmissibility, severity, and immune evasion. However, the number of cases and deaths has declined globally thanks mainly to the large-scale deployment of effective vaccines; an estimated 14.4 million deaths were prevented globally because of vaccination[2-6].

Even though it is well known that only a vaccination policy based on rapid and massive vaccination of the population could combat the SARS-CoV-2-VOC in the lower-middle-income countries (LMIC) were unable to achieve at least 10% population coverage during initial vaccine rollouts, despite the rapid development of vaccines[4,5].

Mexico implemented a policy encompassing up to 15 vaccines to cover almost 160 million inhabitants[7].

However, the efforts of the government in collaboration between the Ministries of Foreign Affairs (procurement), Treasury (financing), Welfare (logistics and registry), Health (store, distribution, cold chain, application, and adverse event surveillance), and local governments,

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many factors limited the vaccination effectiveness such as mixed vaccines that are related to vaccine supply, storage, demand dynamics, distribution logistics, and cold chain management[8].

The studies about effectiveness were performed on a population with a full COVID-19 vaccination schedule or the side effects of mixing vaccination, but the real scenario on LMICs is that some people do not know if they were vaccinated with a mixed vaccine or not, and in many cases, they do not have the recommended schedule[2,9,10].

The pandemic still affects worldwide; on 19 December 2023, the World Health Organization confirmed more than 700 million confirmed cases and almost 7 million deaths from COVID-19[11].

The main objective of the study was to analyze the effectiveness on the mortality of unvaccinated and vaccinated patients with any kind of schedule and the main clinical and biochemical profile at hospitalization.

Methods

Study population

The study is a retrospective cohort, transversal. We include data from digital expedients of patients from a third-level hospital in Mexico City from "Secretaría de la Defensa Nacional" (SEDENA) between October 2021 and February 2023. The protocol was approved by the Research Committee of the Institution (043/2023) and attached to the guidelines of the Declaration of Helsinki.

The inclusion criteria were patients of both sexes, > 18 years old, with confirmatory diagnostic of COVID-19 by reverse transcription-polymerase chain reaction, that on the expedients include the vaccination data (type and doses), comorbidities (hypertension, diabetes, immunodeficiencies, kidney sick), symptoms (thoracic pain, asthenia, dyspnea, cough, headache, rhinorrhea), vital signs (heart rate, respiratory rate, SaO_2, temperature), laboratory test at hospitalization (leukocytes, erythrocytes, lymphocytes, neutrophils, neutrophil/lymphocyte index, hemoglobin, platelets, glucose, blood urea nitrogen (BUN), creatinine, urea, sodium, potassium).

Exclusion criteria were incomplete expedient, another kind of diagnosis, and outpatients.

The groups were divided into patients who died or survived. We analyzed whether they were vaccinated, how many doses (including booster), the kind of vaccine or combination they received, whether they were older or younger than 60, sex, comorbidities, hospitalization main symptoms, vital signs, and laboratory findings.

Data collection

We register the number of doses of COVID-19 vaccination, the type of vaccine, whether they die of COVID-19, comorbidities, vital signs and symptoms at ingress, hematic biometry, blood chemistry, and serum electrolytes at the beginning of the hospitalization. In this study, the sample size was not calculated; we only recorded the type of hospital discharge (survive or die).

Statistical analysis

The statistical analysis was using the SPSS v26, the Kolmoworov–Smirnof test was applied to the qualitative data, the data were expressed by the median and interquartile range (IQR), the qualitative data were expressed by frequency (n) and percentage (%), the inferential statistics was by U-Mann–Whitney or X^2. Furthermore, we included multiple logistic regression analyses for dead people, considering $p < 0.05$ as a significant statistic.

Results

We include 567 patients. Most were male (53.1%), 301 patients, and 266 were female (46.9%). The median age was 62 years (46 years - 73 years), with a minimum of 19 years and a maximum of 90 years. The majority, 53.6% (304 patients), were ≥ 60 years old, and 46.4% (263 patients) were < 60 years old.

Although 350 patients (61.7%) have at least one vaccine, 217 (38.3%) have not been vaccinated.

Moreover, most patients had only one dose, and that is the main reason they did not have mixed vaccination, as described in table 1.

Most of the patients were vaccinated by AstraZeneca–AZD1222, followed by Pfizer – BNT162b2, as described in table 1.

There is a significant association between unvaccinated patients and the risk of death, as shown in table 2. We can see that 26.7% (58 patients) were not vaccinated, while 17.4% (61 patients) had at least one vaccine (Table 2). Moreover, the mortality rate decreases with more vaccine doses, as shown in table 2.

The vaccine with major protection was Pfizer – BNT162b2 alone, with less mortality. However, table 3 shows that any combination is better than a single dose.

Most of the patients survived 79% (448 patients), 21% (119 patients) died; patients who died (91 patients) were ≥ 60 years old, and 28 patients were younger than 60 years old (table 4).

Table 1. Type of vaccine combination and doses

Type of vaccine	n (%)					
One type	226 (64.6)					
Two types	68 (19.4)					
Tree types	2 (0.6)					
Unknown	54 (15.4)					
Type of vaccine received	**Total**	**Doses**				
	n (%)	**1 (n)**	**2 (n)**	**3 (n)**	**4 (n)**	**5 (n)**
Pfizer - BNT162b2	71 (20.3)	26	29	11	5	0
AstraZeneca - AZD1222	115 (32.9)	50	31	27	7	0
Sputnik V - Gam-COVID-Vac	9 (2.6)	6	3	0	0	0
Sinovac - CoronaVac	13 (3.7)	3	8	2	0	0
CanSino - Ad5-nCoV	15 (4.3)	14	0	1	0	0
Moderna - mRNA-1273	3 (0.9)	1	1	1	0	0
Unknow	54 (15.4)	52	0	1	1	0
Pfizer - BNT162b2/AstraZeneca-AZD1222	44 (12.6)	0	2	23	14	5
Pfizer - BNT162b2/Sputnik V-Gam-COVID-Vac	1 (0.3)	0	0	1	0	0
Pfizer - BNT162b2/Moderna	2 (0.6)	0	1	0	1	0
Pfizer - BNT162b2/CanSino-Ad5-nCoV	1 (0.3)	0	0	1	0	0
AstraZeneca - AZD1222/Sputnik V–Gam-COVID-Vac	7 (2)	0	2	2	3	0
AstraZeneca - AZD1222/CanSino-Ad5-nCoV	8 (2.3)	0	3	3	2	0
AstraZeneca - AZD1222/Moderna-mRNA-1273	2 (0.6)	0	1	1	0	0
AstraZeneca - AZD1222/Sinovac–CoronaVac	3 (0.9)	0	0	3	0	0
Pfizer - BNT162b2/AstraZeneca-AZD1222/Sputnik V-*Gam-COVID-Vac	1 (0.3)	0	0	0	1	0
Pfizer - BNT162b2/AstraZeneca-AZD1222/Unknown	1 (0.3)	0	0	0	1	0

Table 2. Vaccine doses decrease mortality

Vaccination status	Survival, n (%)	Dead, n (%)
Unvaccinated	159 (73.3)	58 (26.7)
Vaccinated	289 (82.6)	61 (17.4)
$X^2 = 6.986$, $p = 0.008$		
Doses		
None	159 (73.3)	58 (26.7)
One	128 (84.2)	24 (15.8)
Two	55 (67.9)	26 (32.1)
Three	67 (87)	10 (13)
Four	34 (97.1)	1 (2.9)
Five	5 (100)	0 (0)

$X^2 = 24.058$; $p < 0.0001$

Furthermore, male patients showed more mortality (25.6%) in comparison with females, who showed 15.8% deaths (Table 4).

The main comorbidities associated with death were hypertension, and the symptoms and vital signs associated with death were asthenia and dyspnea; there was an increase in heart rate and respiratory rate and a decrease in SaO_2, as shown in table 5.

As shown in Table 5, there was a significant increase in leukocytes, neutrophils, neutrophils/leukocytes ratio and a decrease in lymphocytes and platelets; and an increase in glucose, BUN, creatinine, urea, and potassium on dead patients in comparison with survival patients, there are not found significant differences on laboratory findings between vaccinated or not patients.

Here, we analyzed the effectiveness of vaccination and number with the other well-known risk factors by multiple logistic regression analysis. We found that age, SO2, N/L index, and vaccination influenced death (Table 6), related to specificity was 96.4%, but the sensitivity was 32.5%.

Table 3. Vaccine combination effectiveness

Type of vaccine received	Total, n (%)	Survival, n (%)	Dead, n (%)
Pfizer - BNT162b2	71 (20.3)	60 (84.5)	11 (15.5)
AstraZeneca - AZD1222	115 (32.9)	86 (74.8)	29 (25.2)
Sputnik V - Gam-COVID-Vac	9 (2.6)	7 (77.8)	2 (22.2)
Sinovac - CoronaVac	13 (3.7)	7 (53.8)	6 (46.2)
CanSino - Ad5-nCoV	15 (4.3)	12 (80)	3 (20)
Moderna - mRNA-1273	3 (0.9)	1 (33.3)	2 (66.7)
Unknown	54 (15.4)	49 (90.7)	5 (9.3)
Pfizer - BNT162b2/AstraZeneca-AZD1222	44 (12.6)	44 (100)	0 (0)
Pfizer - BNT162b2/Sputnik V-Gam-COVID-Vac	1 (0.3)	1 (100)	0 (0)
Pfizer - BNT162b2/Moderna	2 (0.6)	2 (100)	0 (0)
Pfizer - BNT162b2/CanSino-Ad5-nCoV	1 (0.3)	1 (100)	0 (0)
AstraZeneca - AZD1222/CanSino-Ad5-nCoV	7 (2)	5 (71.4)	2 (28.6)
AstraZeneca - AZD1222/Moderna-mRNA-1273	8 (2.3)	7 (87.5)	1 (12.5)
AstraZeneca - AZD1222/Sinovac-CoronaVac	2 (0.6)	2 (100)	0 (0)
Pfizer - BNT162b2/AstraZeneca-AZD1222/Sputnik V-Gam-COVID-Vac	3 (0.9)	3 (100)	0 (0)
AstraZeneca - AZD1222/CanSino-Ad5-nCoV	1 (0.3)	1 (100)	0 (0)
Pfizer - BNT162b2/AstraZeneca-AZD1222/Unknown	1 (0.3)	1 (100)	0 (0)

$X^2 = 32.605$; $p = 0.008$

Discussion

It is well known that the global administration of COVID-19 vaccines has dramatically decrease the infection rate, severity, and mortality. However, there are many factors that modified the effectiveness such as that in low-and-middle-income countries (LMICs) could not secure enough vaccines for vulnerable populations and apply perishable vaccines in large territories[6,7].

As in other countries, the primary strategy was for most of the population to receive at least one dose. More importantly, vaccinating more people with lesser doses may reduce the transmission of the virus, which might reduce the incidence and occurrence of the disease[12].

Our results showed that most vaccinated patients received only one dose, and there were many mixed combinations.

The report of Hernandez-Avila at IMSS found that most of the symptomatic patients were vaccinated (73.3%), like our findings of 61.7% 8.

In comparison, the majority of our population's patients were vaccinated by AstraZeneca-AZD1222, while the report at IMSS stated that most patients were vaccinated by Sinovac-CoronaVac[8].

In a study on Mexican pensioners covered by the Mexican Institute of Social Security (IMSS), the median age was 70 years, like our population, which involves all the patients covered at a third-level hospital in Mexico City from SEDENA[8].

As described, the main risk factors for infection were old age and male sex, similar to our findings[13].

Furthermore, the well-established risk factors for severity and mortality of COVID-19 disease progression are older age, male sex, pre-existing comorbidities, and laboratory indices, as our findings suggest. The main protective factor is vaccine[13].

Moreover, the most common symptoms reported are fever, fatigue, and dry cough. Furthermore, headache, sore throat, myalgia, diarrhea, vomiting, chills, and loss of smell and taste were reported. Here, we found that the most common symptoms were asthenia, dysphonia, and cough, showing that the presence of asthenia and dyspnea was more common in dead patients in comparison with the survival patients[2].

Table 4. Age, sex, comorbidities, symptoms, and vital signs associated with dead

Clinical and demographic variables	Total, n (%)	Survival, n (%)	Dead, n (%)	X^2, p
Age				
< 60 years old	263 (46.4)	235 (89.4)	28 (10.6)	31.634, < 0.0001
≥ 60 years old	304 (53.6)	213 (70.1)	91 (29.9)	
Sex				
Men	301 (53.1)	224 (74.4)	77 (25.6)	8.165, 0.004
Women	266 (46.9)	224 (84.2)	42 (15.8)	
Comorbidities				
Without comorbidities	129 (22.8)	110 (24.6)	19 (16)	3.945, 0.047
With comorbidities	438 (77.2)	338 (75.4)	100 (84)	3.985, 0.046
Hypertension	259 (45.7)	195 (43.5)	64 (53.8)	5.129, 0.024
Diabetes	180 (31.7)	132 (29.5)	48 (40.3)	0.680, 0.409
Immunodeficiencies	73 (12.9)	55 (12.3)	18 (15.1)	0.055, 0.815
Kidney sick	54 (9.5)	42 (9.4)	12 (10.1)	1.457, 0.227
Other	325 (57.3)	251 (56)	74 (62.2)	
Symptoms				
Thoracic pain	138 (24.3)	107 (24)	31 (26.1)	0.216, 0.642
Asthenia	344 (60.7)	260 (58)	84 (70.6)	6.209, 0.013
Dyspnea	325 (57.3)	235 (52.6)	90 (76.3)	21.458, < 0.0001
Cough	309 (54.5)	235 (52.6)	74 (62.2)	3.503, 0.061
Headache	265 (46.7)	208 (46.4)	57 (47.9)	0.082, 0.775
Rhinorrhea	191 (33.7)	151 (33.7)	40 (33.6)	0.0001, 0.985
Vital signs				
Heart rate (beats per minute)	84 (74, 98)	83 (74, 96)	89 (77, 106)	p = 0.002
Respiratory rate (breaths per minute)	20 (18, 21)	19 (18, 20)	21 (19, 24)	p < 0.0001
SaO_2 (%)	93 (88.5, 95)	93 (91, 95)	87 (75.3, 93)	p < 0.0001
Temperature	36.4 (36.1, 36.8)	36.4 (36.1, 36.8)	36.5 (36, 36.9)	p = 0.637

Table 5. Laboratory

Blood test panel	Total median (IQR)	Survival median (IQR)	Dead median (IQR)	p
Hematic biometry				
Leukocytes ($10^3/\mu L$)	7 (5.5, 9.8)	6.6 (5.2, 8.6)	10.1 (7.3, 14)	< 0.0001
Erythrocytes ($10^3/\mu L$)	4.6 (3.9, 5.1)	4.6 (4, 5.1)	4.5 (3.9, 5)	0.375
Lymphocytes ($10^3/\mu L$)	1.21 (0.74, 1.95)	1.4 (0.9, 2.1)	0.72 (0.42, 1.09)	< 0.0001
Neutrophils ($10^3/\mu L$)	5.32 (3.52, 9.13)	4.61 (3.32, 7.18)	9.63 (6.59, 16.13)	< 0.0001
N/L	4.1 (2.2, 10.2)	3.3 (1.9, 6.4)	13.1 (8.2, 26.1)	< 0.0001
Hemoglobin (g/dL)	14 (12, 15.5)	14 (11.8, 15.6)	13.8 (12, 15.4)	0.943
Platelets ($10^3/\mu L$)	242 (183, 311)	250 (187.5, 316.5)	214 (161, 281)	0.003
Blood chemistry test				
Glucose (mg/dL)	110 (91, 151)	105 (89.5, 137.5)	139 (106, 196)	< 0.0001
BUN (mg/dL)	19 (14, 29)	17 (13, 24.5)	31 (22, 54)	<0.0001
Creatinine (mg/dL)	0.8 (0.7, 1.1)	0.8 (0.6, 1.1)	1.1 (0.8, 2)	<0.0001
Urea (mg/dL)	38.5 (30, 62.1)	36.4 (27.8, 51.4)	64.2 (44.9, 115.6)	<0.0001
Serum electrolytes				
Na (mmol/L)	139 (135, 142)	139 (135, 141)	139 (135, 143)	0.115
K (mmol/L)	4.25 (3.9, 4.7)	4.2 (3.8, 4.6)	4.5 (4.1, 5.1)	< 0.0001

BUN: blood urea nitrogen; IQR: interquartile range.

As was described in other populations, severe disease and death occurred predominantly in the unvaccinated population. With one, two, or three doses, the risk of death decreases significantly even though there are mixed vaccinations that it is similar to the previous reported on Hong Kong with a single type of vaccine (Pfizer - BNT162b2 or Sinovac-CoronaVac[14].

Table 6. Factors influencing death

Factor	B	Standard error	Sig.	Exp (B)	Inferior limit	Superior limit
Age	0.056	0.008	< 0.0001	1.057	1.041	1.074
SO_2	–0.058	0.006	< 0.0001	0.944	0.932	0.955
N/L index	0.039	0.008	< 0.0001	1.039	1.024	1.055
Vaccination	–0.549	0.248	0.027	0.578	0.356	0.938

Nowadays, there are SARS-CoV-2 variants that could have immunity evasion to the vaccines performed at the beginning of the COVID-19 pandemic; the better protection still vaccinated it is well demonstrated that is the main protective factor, here we found that at least one dose could prevent death, also as described on Hong-Kong. Third doses of either BNT162b2 or CoronaVac provide substantial additional protection against severe COVID-19 and should be prioritized, particularly in older adults older than 60 and others in high-risk[5,14-16].

As described, even though one dose of either type of vaccine induces immune protection to death on COVID-19, administration of newly developed bivalent mRNA COVID-19 vaccines, as booster shots, would be decisive to avoid further circulation of the newly developed variants[16].

Heterologous prime-boost ("mix-and-match") regimens, which involve combinations of mRNA and Ad26 vaccines, are a plan for refining the magnitude and durability of humoral and cellular immunity compared with either type alone. In addition, the development of pan-sarbecovirus and pan-betacoronavirus vaccines is under way[17].

Booster plans should, therefore, be based on robust scientific data that evidence substantial and sustained increases in the anticipation of severe disease rather than on short-term intensifications in neutralizing antibody titers. Improved community engagement and implementation research may also reduce vaccine misinformation[17].

Ideally, COVID-19 boosters should be recommended at most annually and preferably less frequently, and a diversity of booster options should be accessible to the public. The use of vaccine platforms with improved durability would be highly desirable[17].

In the present study, the population was vaccinated with different vaccines, reporting protection from complications from COVID-19. A meta-analysis including AstraZeneca, Pfizer, Moderna, Bharat, and Johnson & Johnson reports that after the first dose of the vaccine, the total efficacy of all COVID-19 vaccines was 71% (95% CI: 0.65, 0.78). The total efficacy of vaccines after the second dose was 91% (95% CI: 0.88, 0.94)). The total effectiveness of vaccines after the first and second doses was 81% (95% CI: 0.70, 0.91) and 71% (95% CI: 0.62, 0.79), respectively[18].

Some vaccines' overall or variant-specific effectiveness and efficacy are unobtainable after the first or second dose. mRNA-based vaccines against COVID-19 showed the highest total efficacy and effectiveness, and administering the second dose produced a more consistent response and higher effectiveness than a single dose[18].

Conclusion

In Mexico, the strategy to reduce severity and mortality at the beginning of the pandemic was to protect the care staff following the persons with significant risk, that was, older adults. Due to this strategy, many persons do not have a complete schedule of vaccinations to vaccinate more people; our findings showed that either complete or not the vaccination schedule or mixed vaccines, it is still better to have at least one dose that unvaccinated to prevent dead, regardless other risk factors and it is better to have more than two doses to reduce death risk.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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BRIEF COMMUNICATION

Hyperglycemia as a predictor for no-reflow phenomenon in patients with acute ST-segment elevation myocardial infarction

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Abstract

Introduction: *The no-reflow phenomenon (NRP) is a complication associated with in-hospital mortality in patients undergoing percutaneous coronary intervention (PCI) for acute ST-segment elevation myocardial infarction (STEMI). Hyperglycemia in these patients can be observed regardless of diabetes mellitus.* **Objective:** *Determine the association between NRP and hyperglycemia.* **Methods:** *All patients with STEMI who underwent PCI at the ISSEMyM Medical Center from March 1st, 2019, to March 1st, 2020, were identified, and of these those who presented NRP. A cutoff value of glucose index > 140 was used for the development of the non-reflux phenomenon. The data evaluated with a normal curve, averages, and standard deviation were obtained, and with an asymmetric curve, median, and 25th and 75th percentile. The association of variables was applied with Pearson's χ^2 test and OR values according to the statistical significance obtained, taking P as a criterion < 0.05.* **Results:** *NRP was present in 32 cases (20.1%), and glucose index value ≥ 140 mg/dL was found, with statistical significance OR 2.27 (95% confidence interval: 1.01, 5.1).* **Conclusion:** *A glucose index > 140 mg/dL during a STEMI is a common finding and an adverse prognostic marker that increases the risk of NRP.*

Keywords: *No-reflow phenomenon. Acute myocardial infarction. Hyperglycemia.*

Introduction

Acute ST-segment elevation myocardial infarction (STEMI) is considered the leading cause of death due to cardiovascular diseases[1], most of the time because of a thrombotic event ascribed to cardioembolic etiology.

Percutaneous coronary intervention (PCI) was described for the first time by Grüntzig et al.[2] getting to be nowadays the gold standard in STEMI treatment as a mode of restoring the anterograde blood flow of the infarct-related artery (IRA)[3,4].

To perform successful revascularization of an infarct-related coronary artery, diverse aspects must be considered among which we can list[5]: (1) initial myocardial ischemic damage. (2) Elapsed time from the start of ischemia to reperfusion. (3) Reperfusion injury risk. (4) Initial permeability of the IRA. (5) Distal atherothrombotic embolization. (6) No-reflow phenomenon (NRP).

The NRP refers to a failure to restore normal blood flow in certain myocardial areas despite epicardial coronary artery recanalization after acute myocardial infarction (AMI), mainly attributed to functional and structural alteration of the coronary microcirculation[6,7].

NRP incidence ranges from 2.3% to 10% in a PCI due to AMI. It is important to underline the NRP's clinical relevance since it is pointed out as a cause of heart failure, malignant arrhythmias, and even in-hospital mortality.

Studies have shown that hyperglycemia is a commonly encountered issue in patients at the time of STEMI

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Table 1. Association between qualitative variables versus no-reflow phenomenon

Characteristics	Present n (%)	Absent n (%)	Total n (%)	p
Gender				
Male	27 (17)	105 (66)	132 (83.0)	0.819
Female	5 (3.1)	22 (13.8)	27 (17.0)	
Cutoff point for age				
> 78 years-old	5 (3.1)	6 (3.7)	11 (6.9)	
< 78 years -old	27 (17)	121 (76)	148 (93.1)	0.030
Cutoff point for glucose				
> 140 mg/dL	21 (13.2)	58 (36.4)	79 (49.7)	0.044
< 140 mg/dL	11 (7)	69 (43.3)	80 (50.3)	
Diabetes	20 (12.5)	62 (39)	82 (51.6)	0.166
Hypertension	17 (10.7)	65 (41)	82 (51.6)	0.844
Smoking	20 (12.6)	57 (36)	77 (48.4)	0.075

hospitalization with a prevalence from 51% to 58%, might be associated with impaired microvascular function after AMI, resulting in larger infarct size and worse functional recovery, being a predictor of mortality[8-10].

Although the association between hyperglycemia and NRP has been extensively studied in both retrospective and prospective ways even defining a prognostic value, there is no cutoff value yet that should be used as a diagnostic marker of hyperglycemia in Mexican patients suffering from IAM, just as there is no calculated patients' rate that will develop NRP because of it.

In this context, this article performs a retrospective analysis in a tertiary care center in Mexico State with respect to patients that developed NRP and its possible correlation with high glucose index value at hospitalization time.

Methods/Design

We performed a retrospective analysis of the Centro Médico ISSEMyM Toluca database from March 1st, 2019, to March 1st, 2020, including 159 patients with a diagnosis of STEMI treated with PCI.

Exclusion criteria were non-ST-elevation myocardial infarction (NSTEMI), diagnosis of unstable angina, pregnancy, and final diagnosis of type 2 myocardial infarction according to the fourth universal definition of myocardial infarction.

Afterward, all patients who developed NRP during the coronary angiography and suffered hyperglycemia according to the operational definition (glucose index value > 140 mg/dL) were included.

On this basis, we defined the group with the highest probability of presenting NRP demonstrated by coronary angiography.

Descriptive statistics were applied according to conventional methods. Qualitative variables were described with absolute and relative frequencies and were represented in frequency tables and cross tables to elaborate bar charts.

Regarding quantitative variables, normality of distribution was evaluated. In the presence of normal distribution, means and standard deviation were calculated. In contrast, when an asymmetric curve was observed, the median and 25th and 75th percentiles were determined.

Pearson's Chi-square test and odds ratio (OR) were applied to make the variables association considering statistically significant $p < 0.05$. Full analyses were performed using the statistical software SPSS v.22.

Results

A total of 159 patients were selected at database review time and none of them were excluded or eliminated. The age range was from 29 to 86 years with a mean age of 60.1 years. Among 50% of the participants (p25-p75) registered a high glucose index. In terms of patient comorbidities, we observed a high percentage of diabetes (51.6%), hypertension (51.6%), and smoking habits (48.4%). Only 20.1% of the patients developed NRP whereas the rest (79.9%) did not. Among 83% (132) of the patients were male and 84.4% of these (27) developed NRP; however, these data were not statistically significant. In reference to age,

we found the cutoff point at 78 years old, that is patients who are 78 years and older are 3.73 times (OR: 95%; confidence interval [CI]: 1.06, 13.14) more likely to develop NRP (p = 0.030).

The cutoff point for glucose index value was 140 mg/dL, which means 65.6% of patients (21) with NRP have an OR of 2.27 (95% CI: 1.01, 5.1) times (p = 0.044). In contrast, the group glucose index value and its association with NRP was not relevant, even though 49.7% of patients (79) presented with hyperglycemia (Table 1).

Discussion

At present, the incidence of NRP as a complication of STEMI in this medical center has not been determined.

Hyperglycemia has been reported in medical literature as a predictor of NRP. On this basis, it is advisable to measure the glucose index of patients at hospitalization time since it is easy to access data to evaluate as in most of the medical centers it represents a routine measurement.

Foreign references have reported a RPN frequency from 2.3% to 10% which is lower in comparison with our result (20.1%), which at the same time is also lower than national references (28.1%)[9].

The mean age of patients who developed NRP was 60.1 years. It is important to highlight that we observed that age over 78 years increases the risk of NRP (OR 3.7, p = 0.030), which differs from Rivera-Linares et al. analysis which reported that age over 60 years was not statistically significant[9].

Even when diabetes (51.6%), hypertension (51.6%), and smoking habit (48.4%) reported a high incidence and these have been widely associated with coronary disease, they have not been related to the presence of NRP. About 50% of participants (p25-p75) recorded a high glucose index. The relevant cutoff point was 140 mg/dL, which means 65.6% (21) of our NRP cases have 2.27 times (OR [p = 0.044]).

In this context, hyperglycemia has been confirmed as an independent predictor of NRP even if the patient has no previous diabetes diagnosis. Our cutoff point turns out to be lower than reported in previous studies where the cutoff point of glucose index values was > 160 mg/dL[9], 216.19 mg/dL, and 231.6 mg/dL[9].

Conclusion

Hyperglycemia (glucose index > 140 mg/dL) during a STEMI is a common finding and an adverse prognostic marker that increases the risk of NRP. Prospective studies are needed to test whether intensive glucose control in patients with AMI will result in improved survival. Bigger sample size studies are required for this result to be significant.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of human and animal subjects. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidencialidad, consentimiento informado y aprobación ética. The authors have obtained approval from the Ethics Committee for the analysis of routinely obtained and anonymized clinical data, so informed consent was not necessary. Relevant guidelines were followed.

Use of artificial intelligence for generating text. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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