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COVID-19 PANDEMIC: EVOLUTION OF THE DISEASE AND INPATIENT MORTALITY IN RELATION TO VACCINATION

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Summary Introduction: After the onset of the COVID-19 pandemic, different vaccines were developed, decreasing mortality according to retrospective studies or with computational modelling. The aim was to to compare mortality in hospitalised patients diagnosed with COVID-19 according to vaccination. **Methods**: Longitudinal observational comparative study. Patients hospitalised with COVID-19 from 17/12/21 to 23/02/2022 at the Hospital Nacional Prof. A Posadas and the Hospital Interzonal General de Agudos Eva Perón were included. **Results**: We analysed 245 patients and found a total mortality of 25.3%, 16.8% in those with complete vaccination (2 doses or more and less than 150 days since the last dose) and 31.9% with incomplete vaccination (not vaccinated, 1 or 2 doses and more than 150 days since the last dose) (p = 0.007), OR 2.31(IC95; 1.25-4.28). In those with pneumonia, mortality was 32.2%, 22.2% with complete vaccination and 38% with incomplete vaccination (p = 0.048), OR 2.15 (95%CI 1.01-4.58). Mortality was associated with older age (70 vs. 59 years; p < 0.001), female sex (54.8% vs. 37.7%; p < 0.02) and oncological disease (27.4 vs. 14.8%; p = 0.02). The PESI *score* was higher in those with incomplete vaccination (102.5 vs. 93, p = 0.05) and the SOFA *score* was lower (2 vs. 3, p = 0.01). The number needed to treat (NNT) to prevent one death was 7 patients for the total sample (95%CI 4-22) and 6 (95%CI 3-106) for those with pneumonia. **Discussion**: This work constitutes a starting point for further research, contributing to awareness of the beneficial effects of vaccination in professionals and patients.

Keywords: COVID-19, mortality, inpatients, vaccination

Abstract *COVID-19 pandemic: outcomes and mortality inpatients related to vaccination*

Introduction: Different COVID-19 vaccines were developed in a short time after the beginning of pandemics, reducing mortality, especially in high risk population. This was demonstrated in several studies, mostly retrospective or based in mathematical models. The objective was to compare mortality inpatients with COVID-19 related to vaccination. **Methods**: Longitudinal, prospective, comparative, observational study. Inpatients with COVID-19 diagnosis were included between 17/12/2021 and 23/02/22, in Hospital Nacional Prof. A Posadas and Hospital Interzonal General de Agudos Eva Perón. **Results**: Inpatients (245) were analyzed, finding an overall mortality of 25.3%, 16.8% in fully vaccinated patients (two or more doses with less than 150 days since the last dose until the COVID-19 test) and 31.9% in those with incomplete vaccination (unvaccinated, one dose or two or more doses with more than 150 days since the last dose) (p = 0.007), OR 2.31 (IC95; 1.25-4.28) for incomplete vaccination. Mortality was 32.2% in patients who developed pneumonia, 22.2% for fully vaccinated and 38% for incompletely vaccinated (p = 0.048), OR 2.15(IC95; 1.01-4.58). Mortality was associated with older age (70 vs. 59 years; p < 0.001), female sex (54.8% vs. 37.7%; p < 0.02) and oncologic disease (27.4 vs. 14.8%; p = 0.02). PESI score was higher in incompletely vaccinated (102.5 vs. 93, p = 0.05) and SOFA score was lower (2 vs. 3, p = 0.01). The necessary number to treat (NNT) to prevent one death was 7 patients for the overall sample (CI95;4-22) and 6 (CI95;3-106) for pneumonia. **Discussion**: This study constitutes a starting point for develop- ing other investigations and raising awareness of medical community and people about the beneficial effects of vaccination.

Key words: COVID-19, mortality, inpatients, vaccine

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KEY POINTS

- In hospitalised patients diagnosed with COVID-19, full vaccination reduced mortality in those with and without pneumonia by 15.8% and 15.1% respectively.
- This supports the results of previous studies showing a reduction in disease complications in vaccinated patients and highlights the importance of immunisation during the pandemic.

Since the dawn of mankind, different diseases have occurred which, as they spread, have become pandemics, causing large numbers of deaths among the population and provoking changes in all areas of life1, 2. The first major epidemics were caused by smallpox, bubonic plague, followed by cholera and, at the end of the 19th century, by the appearance of those caused by the influenza virus3 . Epidemic diseases were brought under control thanks to the discoveries of Louis Pasteur and Robert Koch in microbiology and the invention of vaccines1 . In the light of history, the two most effective measures to prevent disease, disability and death from infectious diseases have been immunisation and environmental sanitation4 . Most early approvals of vaccines are based on interim results of efficacy trials, leading to authorisation for use in emergencies or conditional approval5. 5 While the decision to introduce proven effective COVID-19 vaccines may be a no-brainer for most countries due to the onerous burden of disease on public health and the economy worldwide, it is still essential to know the effectiveness of these vaccines in real-world settings after their introduction. COVID-19 vaccines reduce the risk of disease, severe disease, hospitalisation and death6. The objectives proposed by the World Health Organisation (WHO) for the evaluation of vaccine effectiveness include the assessment of outcomes of interest (e.g. severe illness, death, symptomatic or asymptomatic infection, transmission), their effectiveness in different population groups at risk (e.g. the very old, people with human immunodeficiency virus (HIV) infection), duration of vaccine protection, etc.6 One of the principles that has guided the evaluation of the effectiveness of vaccines in real-life settings since the introduction of COVID-19 vaccines has been to assess the effectiveness of vaccines in the field. One of the guiding principles behind the early introduction of vaccines was to prevent death from the disease, so measuring the effectiveness of vaccines against deaths caused by COVID-19 disease would be of great public health importance. The majority of the studies consulted on the analysis of mortality in children with COVID-19 disease are of great public health importance.

The main findings of this study are retrospective analyses of registries, model-based analyses or Intensive Care Unit (ICU) data7-11 , which demonstrated a decrease in hospitalisations, severe illness and death from COVID-19 in vaccinated patients compared to unvaccinated patients. The aim of this study was to compare mortality in hospitalised patients diagnosed with COVID-19 with complete vaccination (two or more doses and less than 150 days since the last dose) with those with incomplete vaccination (unvaccinated, 1 or 2 doses and more than 150 days since the last dose), describing the characteristics of these patients.

Material and methods

Prospective longitudinal observational comparative study. We included patients over 18 years of age admitted to the general ward and ICU with a diagnosis of COVID-19 disease at the Hospital Nacional Prof. A. Posadas and the Hospital Interzonal General de Agudos Eva Perón between 17/12/21 and 23/02/2022, including those whose cause of hospitalisation was COVID-19 disease and those admitted for another cause who presented symptoms during hospitalisation and whose swab result was positive. We excluded those admitted to the general ward under follow-up by surgical services, those not under follow-up by the medical clinic service and those whose follow-up was lost due to de- rivation or whose vaccination data were unreliable. The patients were assessed with the CURB-65 *score* (which evaluates the state of consciousness, uremia, respiratory rate and pressure on admission to the hospital and if the age was over 65 years), APACHE II (which evaluates vital signs heart rate, respiratory rate, temperature, mean arterial pressure, partial blood oxygen pressure, inspired oxygen fraction, arterial pH, natraemia, potassaemia, haematocrit, leukocyte count, state of consciousness -using the Glasgow Coma Score-, presence of chronic disease, and age), PESI *score* (includes age over 80 years, history of oncological disease, history of oncological disease, history of chronic disease, and age), PESI *score* (includes age over 80 years, history of oncological disease, history of chronic cardiovascular or pulmonary disease, systolic pressure less than 90 mmHg, heart rate greater than 110 beats per minute, and oximetry less than 90% on room air) and SOFA *score* (which takes into account partial pressure of oxygen in the blood, inspired fraction of oxygen, platelet count, platelet count, blood oxygen status, blood oxygen partial pressure, blood oxygen fraction, blood platelet count, blood platelet status, and blood oxygen status), platelet count, consciousness, bilirubinaemia, mean arterial pressure, and/or vasopressor requirement and renal function), and asked about vaccination data (number of doses and type of vaccine) by checking the data in SISA (Sistema Integrado de Información Sanitaria Argentino). History was recorded (diabetes mellitus, arterial hypertension, respiratory disease, coronary heart disease, heart failure, oncological disease, renal disease on dialysis, obesity, autoimmune disease, cerebrovascular disease) as reported by the patient. Clinical and laboratory data were recorded. The patient was followed up until discharge or death. Evolution and mortality were assessed in fully vaccinated (2 doses or more and less than 150 days since the last dose at the time of swabbing)[6] and incompletely vaccinated patients (unvaccinated or one or two doses and more than 150 days since the last dose).

Statistical analysis

Numerical variables were described as mean and standard deviation or median and interquartile range according to their distribution. Nominal variables were expressed as percentages. Comparison of means was performed with Student's test and of medians with Wilcoxon Mann Whitney test. Chi-square and *odds ratio* were used to evaluate nominal variables. Infostat software version 2018 was used for the analysis. The sample size was 50 patients in each group (complete vaccination/incomplete vaccination), with a confidence level of 95% and a power of 80%, calculating a mortality rate of 16% in the unvaccinated and 1% in the vaccinated.

Ethical aspects

The work was approved by the Research Ethics Committees of the Hospital Nacional Prof. A. Posadas and the Hospital Interzonal General de Agudos Eva Perón San Martín.
This work was carried out in accordance with good clinical practice guidelines, respecting the principles established in the Helsinki Declaration regarding human rights and biomedicine, as well as data protection. The researchers undertook to protect the confidentiality of personal and institutional information, ensuring the anonymity of individuals as indicated by the ethics committees.

Results

A total of 250 patients were included, of which 5 were eliminated due to lack of swab data or lack of evolution. A total of 245 patients were finally analysed.

hospitalised with a diagnosis of COVID-19 by nasopharyngeal swabbing between 17/12/21 and 23/02/2022 at the Hospital Nacional Prof. Alejandro Posadas (n = 205) and at the Hospital Interzonal General de Agudos Eva Perón (n = 40). The median age was 61.5 years (47-73), and 58% (n = 142) were male. Regarding vaccination, 138 patients (53.2%) had incomplete vaccination and 107 (43.7% of the sample) had complete vaccination. Data on patient characteristics and clinical and laboratory parameters according to vaccination are described in Tables 1 and 2. Information on the type of vaccines given is given in Figure 1. Of the patients analysed, 168 (68.6%) were hospitalised for COVID-19 disease and 77 (31.4%) acquired the disease in hospital while hospitalised for another reason. One hundred and forty-six patients (59.6%) had pneumonia. Data on the characteristics of patients with pneumonia and their clinical and laboratory parameters according to vaccination are given in tables 3 and 4. Mortality of the included patients was 25.3% (n = 62). Those with complete vaccination had a mortality of 16.8% (n = 18) while the group with incomplete vaccination had a mortality of 31.9% (n = 44) p = 0.007, OR 2.31 (95%CI;1.25- 0.007). 4.28). Mortality by age group is depicted in figure 2. Mortality of patients with pneumonia was 32.2% (n = 47). Of the remainder, 92 (63.0%) left the hospital

TABLE 1.- *Characteristics of the patients analysed according to vaccination.*

Characteristics/background	Full vaccination (n = 107)	Incomplete vaccination (n = 138)	p
Age	61 (50-71)‡	61.5 (47-73)‡	0.81
Female sex	44 (41.1)¶	59 (42.8)¶	0.79
Arterial hypertension	52 (48.5)¶	59 (42.8)¶	0.63
Diabetes mellitus	27 (25.2)¶	22 (15.9)¶	0.06
Mild-moderate obesity 30 < BMI < 40	21 (19.6)¶	21 (15.2)¶	0.37
Morbid obesity BMI > 40	4 (3.7)¶	14(10.1)¶	0.055
Coronary heart disease	13 (12.1)¶	13 (9.4)¶	0.49
Collagenopathy/ immunosuppression	15 (14)¶	15 (10.8)¶	0.46
IRC	9 (8.4)¶	8 (5.8)¶	0.43
CKD in dialysis	0 (0)¶	3 (2.2)¶	0.25
Respiratory disease (COPD/asthma)	10 (9.3)¶	19 (13.7)¶	0.28
Oncology	19 (17.8)¶	25 (18.1)¶	0.92
Heart failure	22 (20.6)¶	24 (17.4)¶	0.53
Limitation of therapeutic effort	15 (14)¶	29 (21)¶	0.13
Positive on admission (hospitalised for other reason)	45 (42)¶	32 (23.2)¶	0.002

CKD = chronic renal failure
Complete vaccination: Vaccinated 2 or more doses less than 150 days since the last dose Incomplete vaccination: Not vaccinated or 1 dose or 2 or more doses more than 150 days since last dose

‡ *Median (Interquartile range)*
¶ *n (%)*

Clinical and laboratory parameters on admission of the patients analysed according to vaccination.

Clinical and laboratory parameters	Full vaccination (n = 107)	Incomplete vaccination (n = 138)	p
Pneumonia	54 (50.5)¶	92 (66.7)¶	0.02
Disease severity by COVID-19			
Slight	51 (48)¶	40 (30)¶	0.003
Moderate	35 (33)¶	44 (33)¶	
Serious	20 (19)¶	48 (36)¶	
Pesi score	93 (73-121)‡	102.5 (79-138)‡	0.05
SOFA	3 (2-5)‡	2 (1-4)‡	0.01
Quick SOFA	1 (0-1)‡	1 (0-2)‡	0.2
Apache II	19 (14-22)‡	18 (14-22)‡	0.76
CURB 65	2 (1-2)‡	2 (1-2)‡	0.31
Rto de Bcos*	8300 (5800-13 200)‡	7950 (5800-11 800)‡	0.41
Platelets	189 000 (135 000-274000)‡	185 500 (131 000-263 000)‡	0.74
Blood glucose (mgdl)*	125 (97-158)‡	115 (97-149)‡	0.27
Creatinine	0.90 (0.70-1.30)‡	1 (0.70-1.40)‡	0.53
Sodium* Sodium* Sodium* Sodium* Sodium* Sodium* Sodium* Sodium* Sodium	137 (134-139)‡	136.9 (134-140)‡	0.97
Potassium* Potassium* Potassium* Potassium* Potassium* Potassium* Potassium	4 (3.70-4.30)‡	3.9 (3.4-4.3)‡	0.1
TGO* TGO* TGO* TGO* TGO* TGO* TGO* TGO* TGO	28.5 (22-54)‡	33 (24-51)‡	0.51
TGP* TGP* TGP* TGP* TGP* TGP* TGP* TGP* TGP	28.5 (17-59)‡	30 (16-53)‡	0.59
PCR* PCR* PCR* PCR* PCR* PCR* PCR* PCR* PCR	8.90 (2.80-19.30)‡	9.90 (3.80-19.57)‡	0.51

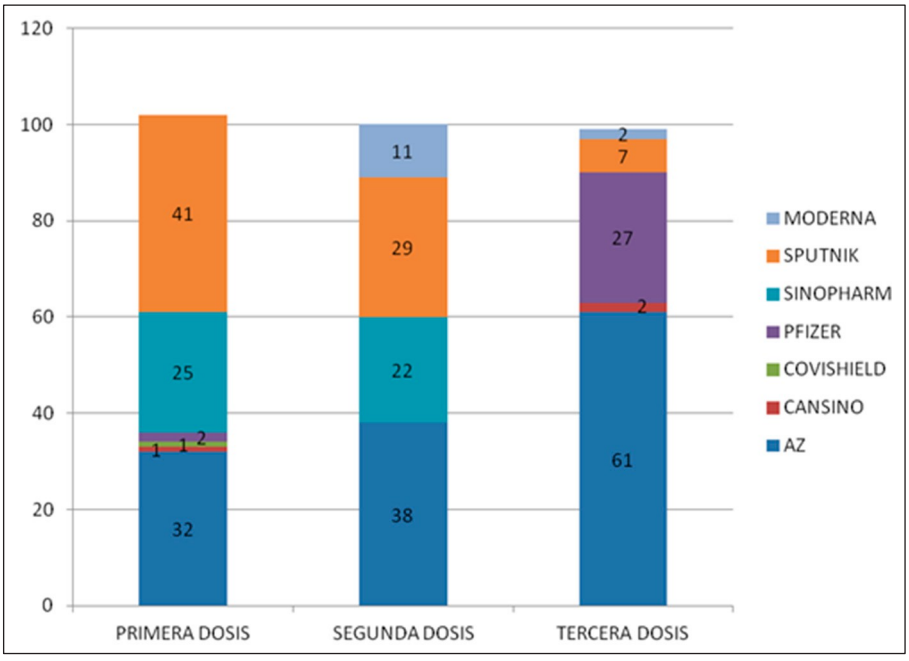
Complete vaccination: Vaccinated 2 or more doses less than 150 days since the last dose Incomplete vaccination: Not vaccinated or 1 dose or 2 or more doses more than 150 days since last dose

**Data from 238 patients*

¶ *n(%)*

‡ *Median (Interquartile range)*

Fig. 1.- Distribution of the type of vaccines in percentage according to application



AZ = AstraZeneca

TABLE 3.- *Characteristics of patients with pneumonia according to immunisation*

Characteristics/background	Full vaccination (n = 54)	Incomplete vaccination (n = 92)	p
Age	63.5 (49-78)‡	66 (48-75)‡	0.75
Female sex	30 (55.5)¶	39 (42.4)¶	0.12
Arterial hypertension	26 (48.1)¶	39 (42.3)¶	0.53
Diabetes mellitus	14 (25.9)¶	10 (10.8)¶	0.01
Mild - moderate obesity 30 < BMI < 40	11 (20.4)¶	17 (18.5)¶	0.80
Morbid obesity BMI > 40	2 (3.7)¶	9 (9.8)¶	0.63
Coronary heart disease	3 (5.6)¶	5 (5.4)¶	0.97
Collagenopathy/ immunosuppression	9 (16.7)¶	11 (11.9)¶	0.43
IRC	6 (11.1)¶	5 (5.4)¶	0.21
CKD in dialysis	0 (0)¶	1 (1.1)	0.99
Respiratory disease (COPD/asthma)	9 (16.7)¶	17 (18.5)¶	0.75
Oncology	8 (14.8)¶	19 (20.7)¶	0.36
Heart failure	9 (16.7)¶	12 (13.0)¶	0.55
Limitation of therapeutic effort	8 (14.8)¶	21 (22.8)¶	0.20
Positive on admission (hospitalised for other reason)	4 (7.4)¶	7 (7.6)¶	0.96

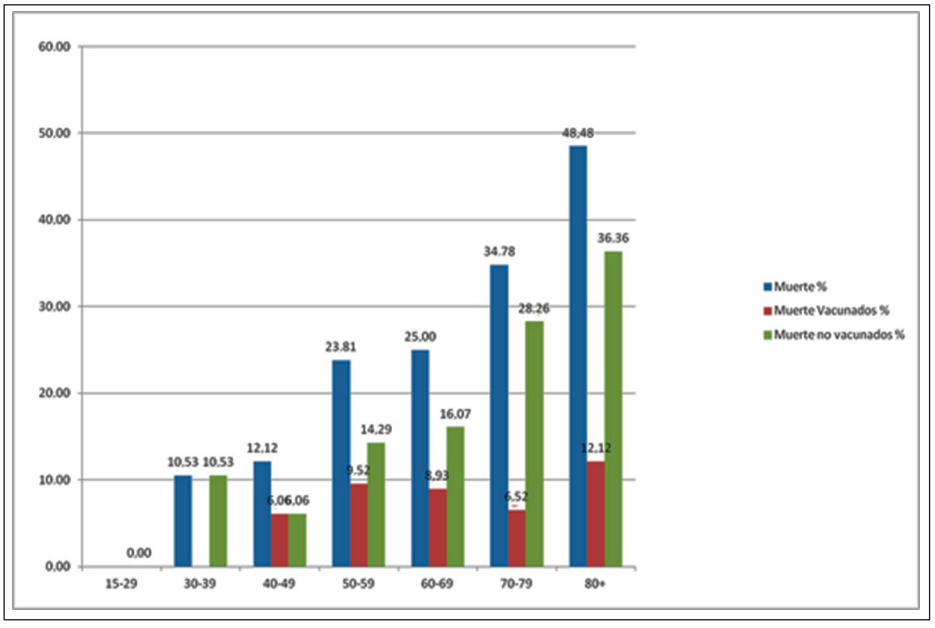
CKD = chronic renal failure
Complete vaccination: Vaccinated 2 or more doses less than 150 days since the last dose Incomplete vaccination: Not vaccinated or 1 dose or 2 or more doses more than 150 days since last dose
**Data from 143 patients*
‡ *Median (interquartile range)*
¶ *n (%)*

Clinical and laboratory parameters of patients with pneumonia according to vaccination.

Clinical and laboratory parameters	Full vaccination (n = 54)	Incomplete vaccination (n = 92)	p
Disease severity by COVID-19			
Slight	13 (25)¶	14 (16)¶	0.15
Moderate	23 (43)¶	31 (36)¶	
Serious	17 (32)¶	42 (48)¶	
Pesi score	101.5 (78-126)‡	109 (88-143)‡	0.13
SOFA	3.5 (2-5)‡	3 (2-4)‡	0.09
Quick SOFA	1 (0-1)‡	1 (0-2)‡	0.41
Apache II	18 (12-24)‡	18 (14-22)‡	0.87
CURB-65	2 (1-2)‡	2 (1-3)‡	0.35
Rto. de Bcos.1	9650 (6100-16 000)‡	8000 (6300-12 500)‡	0.14
Platelets	180 000 (123 000-260 000)‡	180 500 (136 000-265 000)‡	0.79
Blood glucose (mg/dl)	132 (107-211)‡	119 (98-155)‡	0.08
Creatinine	0.9 (0.7-1.58)‡	1 (0.70-1.30)‡	0.91
Sodium	137 (135-139)‡	137 (134-140)‡	0.87
Potassium	4 (3.7-4.20)‡	3.90 (3.40-4.30)‡	0.36
TGO	28.5 (23-54)‡	37 (25-55)‡	0.21
TGP	26 (16-44)‡	31 (17-53)‡	0.58
PCR	12.7 (6.47-22.10)‡	12.35 (6.30-23.80)‡	0.98

Complete vaccination: Vaccinated 2 or more doses less than 150 days since the last dose Incomplete vaccination: Not vaccinated or 1 dose or 2 or more doses more than 150 days since the last dose
**Data from 140 patients. 1: white blood cell count.*
¶ *n(%)*
‡ *Median (Interquartile range)*

Mortality by age group of patients with COVID-19 according to vaccination.



At the time of discharge, 6 (4.1%) were still hospitalised at the end of the study and 1 (0.7%) left the hospital voluntarily. In patients with pneumonia and complete vaccination (n = 54) mortality was 22.2% (n = 12) and in those with incomplete vaccination (n = 92) it was 38% (n = 35) p = 0.048, OR 2.15 (95%CI 1.01-4.58).

Of the pneumonia patients who died (n = 47), 74.5% (n = 35) were not fully vaccinated at the time of illness. Among the characteristics of those who died, age was higher (70 years vs. 59 years; p < 0.001), a higher proportion of female sex was found among those who died (54.8% vs. 37.7%; p < 0.02), a higher percentage of oncology patients (27.4 vs. 14.8%; p = 0.02) and a lower percentage of those who were vaccinated (29% vs. 48.6%; p = 0.007). Among patients with diabetes who were vaccinated (n = 27; 55%), 7% (n = 2) died, compared with 27.3% (n = 6) of those with incomplete vaccination (n = 22; 45%), p = 0.06. Regarding the *scores* analysed, CURB-65, APACHE II and Quick SOFA showed no statistically significant differences between patients with complete or incomplete vaccination, while the PESI *score* was higher in those with incomplete vaccination and SOFA was lower (Table 2). The absolute risk reduction of death for vaccinated patients was 15.1% for the whole sample and 15.8% for patients with pneumonia and the NNT (number needed to treat) to prevent one death was 7 patients for the whole sample (CI95; 4-22) and 6 (CI95;3-106) for those with pneumonia.

Discussion

Two years after the start of the pandemic caused by the SARS-CoV-2 virus, multiple strategies are being rethought on a daily basis to reduce contagiousness and the adverse results of the disease (hospitalisation, admission to the ICU, need for mechanical ventilation, etc.). Among these, the development of different vaccines was achieved in record time, reducing mortality, especially in the population at increased [risk6]. The effectiveness of vaccines after their implementation has been the subject of several studies, including transmission models, in which a reduction in adverse events such as hospitalisations, ICU admissions and death has been [calculated7-11]. This study was carried out during the third wave of COVID-19 in Argentina, which began in December 2021, following up patients hospitalised with positive swabs for SARS-CoV-2, showing an absolute risk reduction of 15% in mortality in those hospitalised.1% reduction in mortality in hospitalised patients with complete vaccination versus those not vaccinated or incompletely vaccinated, indicating not only the importance of presenting a primary vaccination schedule with respective boosters, but also of being within the deadlines suggested by the different recommendations of health [organisations6]. At the beginning of our study, 84.2% of the national population was vaccinated with 1 dose, 71.4% with 2 doses and 11.1% with 3 [doses7]. In the work of Zhou

et al.[13], one of the first to describe the risk factors that affect the evolution of the disease and carried out before the appearance of vaccines, studied 191 patients, showing a total mortality of 28% in hospitalised patients, associated with a higher prevalence of diabetes, arterial hypertension and coronary heart disease in patients who died. In our study, the overall mortality rate was 25.3%, a figure similar to that of the article cited, but after vaccination had been implemented. The similarity in mortality between the two studies, despite the fact that Zhou's work was before vaccination, could be explained by the fact that the comorbidities of the patients who were hospitalised in our study were higher (diabetes in 25.2% vs. 19% in Zhou's article, hypertension in 48.5% vs. 30%, oncology 17.8% vs. 1%, coronary heart disease 12.1% vs. 8%) and older (61.5 vs. 56 years). This implies a higher risk population and for this reason there was no evidence of a reduction in total mortality in the hospitalised patients in our study after vaccination was implemented. Another study carried out in hospitalisation before [vaccination14], where 2199 patients were analysed, describes a mortality of 29%, although at the time of analysis, 49% of the sample remained hospitalised without knowing the subsequent outcome, implying a higher mortality than indicated. Mortality was associated with older age, as evidenced in our study. On the other hand, at the beginning of the pandemic, all positive patients were hospitalised regardless of their severity and this may be one of the reasons for the low mortality in hospitalised patients in the pre-vaccine era studies. However, the mortality in those vaccinated in our study was 16.8%. A study published in 2019 calculated the impact of vaccination based on a model of transmission, comorbidities and population immunity, concluding that vaccination reduces adverse events such as hospitalisations and death by 60-70% and that the impact would be greater in patients over 65 years of age. In our study, which was conducted in inpatients only, vaccination achieved a minor decrease in mortality (15.1%), but indeed the greatest impact is seen in those over 60 years of age and this difference becomes more pronounced with increasing age as depicted in Figure 2. Given the sample size, the differences were not statistically significant in terms of comparing absolute risk reduction in the different age groups. In a systematic review by Huang et [al15] in 2022, 7 articles were analysed showing a relative risk of serious events of 0.12 (95%CI; 0.04-0.36) $p < 0.05$ in vaccinated vs. unvaccinated patients also demonstrating the protective effect of any type of vaccine. In an Argentinean study by the Argentinean Society of Intensive [Care8], the characteristics of the vaccination were analysed in a study of the bed occupancy in intensive care, describing some aspects related to the patients. Fifty percent of the patients had incomplete or no vaccination, similar to the findings of our study (53%). Of these, 62% required mechanical ventilation, compared to 28% in vaccinated patients. A retrospective study in the [USA16] estimated, after analysis of 41552 hospitalisations, an effectiveness of more than 80% for different vaccines on hospitalisation and intensive care requirement. Another observational study analysing data from 48 US [states17] in 30643778 patients showed an 8% reduction in mortality for every 10% increase in vaccination coverage. The advantages of this study include its prospective nature, longitudinal follow-up with low sample loss, confirmation of the dates and types of vaccines and swabs in SISA, the participation of two reference centres in the Buenos Aires metropolitan area, the analysis of different *scores*, clinical and laboratory aspects, which confirm the findings and estimates of other types of studies mentioned above (observational, mathematical models) on the reduction of adverse events in COVID-19 disease. Limitations are related to the sample size, which does not allow to assess differences in age groups and risk groups (e.g. patients with diabetes) and the lack of analysis of other laboratory parameters such as d-dimer among others. This article is a starting point for further national and international research on the effect of vaccination on adverse events of COVID-19 disease, contributing to the awareness of both the population and the scientific community about the beneficial effects of vaccination.

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Conflict of interest: None to declare

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