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Research Article

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Evolution of Risk Measures of COVID-19 from 2020 to 2022 Versus in 2023 in a General Medicine Office in Toledo (Spain)

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ABSTRACT

Background: The evolution of risk measures for COVID-19 infection from 2020 to 2023 is not clearly known.

Objective: To know the evolution of risk measures of cases of COVID-19 from March 15, 2020 to October 1, 2023 in a general medicine consultation in Toledo, Spain.

Methodology: Comparison of the COVID-19 incidence rate (IR), relative risk (RR) and attributable risk (AR) and in 2020, 2021 and 2022 and 2023 years versus covid-19 in 2023 (group with very broad hybrid immunity), based on data from previous longitudinal studies, all of them carried out in the same population of patients treated in a general medicine office in Toledo, Spain.

Results: 712 COVID-19 cases from March 15, 2020 to October 31, 2022 (3 years at risk) and 76 covid-19 cases from October 2022 to October 2023 (1 year at risk) were included, for a population at risk of 2,000 people. In 2023 vs. 2020-2022, the following statistically significant differences were found: a lower IR, a protective RR, and a negative AR for the entire at-risk population (IR= 36% x 3 Years; 12% on average for 1 year versus IR= 4% x 1 year; a RR of 0.33 [p= .037056], and an AR= -8); a lower IR in < 65 years [13% average x 1 year vs. 3%; p= .009149; RR= 0.23; RA= -10], and a lower IR in men [IR= 12% average for one year versus 4%; RR of 0.33 [p= .037056]; RA= -8. There was a lower IR in women, in cases with moderate-severe severity, and in socio-health workers, all with RRs that indicated protection factors, and negative ARs for the 2023 group vs. 2020-2022, but without statistical significance. However, the presence of chronic diseases meant a higher IR, a weak risk, and positive RA indicates that the incidence is greater for covid-19 in 2023 vs. in 2020-2022.

Conclusion: In general practice setting in Toledo, Spain, in 2023 the population at risk with greater hybrid immunity is better prepared in 2023 vs. 2020-22 to avoid cases of COVID-19, but people with chronic diseases pose a greater risk in 2023.

Keywords: COVID-19, SARS-CoV-2, Population Surveillance/Methods, Epidemiological Characteristic, Public Health Practice, General Practice

Introduction

During coronavirus disease 2019 (COVID-19) pandemic period, very detailed epidemiological surveillance measures were taken that were crucial. We are now in a likely endemic phase, where many of the community surveillance studies tracking infection levels have ended. Thus, COVID-19 case counts are no longer published, and it is not clear how many people are infected, nor can the evolution of new waves be assessed [1,2]. Furthermore, the patterns of emergence of variants for COVID-19 are largely unknown. To this we must add that is true short-term effectiveness of vaccines has been demonstrated with respect to the severity of SARS-CoV-2 infection, but the effectiveness of the vaccine is not yet fully understood in general population [3].

Four years after the start of the COVID-19 pandemic we find ourselves in a new scenario with high level population immunity. But COVID-19 will remain with us, threatening the health and well-being of millions of people around the world [4]. The new reality with this virus is that we will have repeat infections. It is estimated that at least 30% of the population could be re-infected in successive waves. Continuous waves of infection carry the risk of new variants emerging that can compete with the current ones and be more severe [1]. There is increasing scientific evidence that shows that the protection generated by vaccination decreases over time, although it is re-established with the inoculation of booster doses. Additionally, we must take into account the decline in immunity as a result of the new variants, and that despite vaccines, boosters and natural immunity, the variants appear to be capable of evading any protection that may have been obtained against SARS -CoV-2 [5-10].

In this scenario, knowing the evolution of the epidemiological measurements of the risk of COVID-19 infection is crucial to evaluate its trajectory and the factors of the infections. Ultimately, studying the evolution of infections will help researchers understand what the transition of SARS-CoV-2 to an endemic virus will look like [11].

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In summary, there is a lack of community data on the evolution of risk measures of COVID-19 from epidemic to endemic. In this context, we present a study carried out in a general medicine consultation, that compares data from previous observational, longitudinal and prospective studies of COVID-19 cases from March 15, 2020 to October 1, 2022 on the one hand, and it compares them with the data for the period from October 2022 to October 2023, which can be considered a "treatment" group, taking into account the very broad hybrid immunity in the population, and all this with the aim of knowing the evolution of risk measures (incidence rate, relative risk and attributable risk).

Material and Methods

Design and Emplacement

This study compares data from previous observational, longitudinal and prospective studies of COVID-19 infections from March, 2020 to October, 2023, already published:

1. A set of studies that included COVID-19 cases from March 15, 2020 to October 31, 2022 [12-19].
2. And a study of COVID-19 infections in 2023 [20,21].

In the current study, the comparison of COVID-19 incidence rates, relative risk and attributable risk in 2020, 2021, and 2022 years ("control" group) versus COVID-19 incidence rates in 2023 ("treatment" group with very broad hybrid immunity), was carried out, based on data from the previous longitudinal studies cited above. Descriptive epidemiological analyses In the current study, the comparison of COVID-19 incidence rates, relative risk and attributable risk in 2020, 2021 and 2022 years ("control" group) versus COVID-19 incidence rates in 2023 ("treatment" group: with very broad hybrid immunity), was carried out, based on data from the previous longitudinal studies cited above. Descriptive epidemiological analyzes considered selected demographic and clinical features.

Outcome of Interest

Know the evolution of risk measures (incidence rate, relative risk and attributable risk) of cases of COVID-19 from March 15, 2020 to October 1, 2023 in a general medicine consultation in Toledo, Spain.

Diagnosis of COVID-19

The diagnosis was performed with reverse transcriptase polymerase chain reaction (PCR) oropharyngeal swab tests or antigen testing performed in health services or at home [22].

Collected Variable

The following variables were collected:

- Date of COVID-19 infection diagnosis
- Age and sex
- Chronic diseases (defined as "any alteration or deviation from normal that has one or more of the following characteristics: is permanent, leaves residual impairment, is caused by a non-reversible pathological alteration, requires special training of the patient for rehabilitation, and / or can be expected to require a long period of control, observation or treatment" [23].
- If they were Health Care Workers
- Disease severity (classified according to: 1. mild cases: clinical symptoms are mild and no manifestation of pneumonia can be found on images; 2. moderate cases: with symptoms such as fever and respiratory tract symptoms and the manifestation of pneumonia can be seen on the imaging tests; and 3. severe cases: respiratory distress, respiratory rate ≥ 30 breaths / min., pulse oxygen saturation ≤ 93% with room air at rest, arterial partial pressure of oxygen / oxygen concentration ≤ 300 mmHg.) to simplify comparison, moderate and severe cases were counted together [24].

Calculation of Incidence Rates (IR)

Cumulative and density incidence rates were calculated at the GP's office by dividing the number of infection events during the study period divided by the individuals that could developed the event at start of the study (population at risk) and divided by the sum of the length of follow-up time of observation for all individuals (population-years at risk) [25,26].

Calculation of Relative Risk (RR)

The data group from 2023 was considered as the treated group (practically 100% of individuals were vaccinated and/or had previously had COVID-19 infection) and the group of cases from 2020 to 2022 as the control group. The RR was calculated by dividing the incidence in the treated group by the incidence in the control group. The RR was interpreted as follows: From 0 to 0.5: protection factor effectively; from 0.6 to 0.8: true benefits; from 0.9 to 1.1: not significant; from 1.2 to 1.6: weak risk; From 1.7 to 2.5: moderate risk; More than 2.5: strong risk [27].

Calculation of Attributable Risk (AR)

El AR o risk difference was calculated by taking the incidence in the treated group (datos de 2023) and subtracting the incidence in the control group (data from 2020 to 2022). A positive difference indicates that the incidence is greater in the treated group, whereas a negative one means that the incidence is greater in the control group [25].

Calculation of the Number Needed to Treat (NNT)

The NNT was calculated as the inverse of absolute risk reduction (the opposite difference of AR: control minus treated). The NNT is how many patients would need to be treated with this intervention (vaccination or passing the COVID-19 infection) to give one more patient a positive outcome [25].

Calculation of Rate Numerators

All patients who consulted in the GP office object of the study with acute COVID-19 infection: Cases notified to the GP after a positive test at home, or diagnosed by the GP in health services, for the period March 2020 to October 2022, and from Octobre 2022 to October 2023 were included. The exception were data for the variables socio-health workers, m-oderate-severe severity, exitus, and presence of chronic diseases, which for the period from March 2020 to October 2022 were taken from a sample of 188 people based on previously published studies. [17-19].

Calculation of Rate Denominators

The total number of patients assigned to the consultation (2000 people) was used as an approximation to the denominator of rates. The denominator data for some variables were taken from different previous studies carried out in the same population treated in that general medicine consultation. The denominator data for prevalence of chronic diseases were taken from previous studies carried out in the same population treated in that general medicine consultation [28-30].

Epidemiological and Statistical Analysis

The calculation of the IR was performed as explained above (subsection "Calculation of incidence rates") by dividing the number of infection events by the person follow-up time (from March 15, 2020 to October 2022 on the one hand, and from October 2022 to October 2023 on the other hand) [26]. Data on the incidence were extrapolated to the entire population attended in the consultation (N=2,000 people) [27, 31].

To make the comparison of results easier and more intuitive, the years at risk were rounded: in the group from March 2020 to October 2023, it was rounded to 3 years at risk, and assigned to the period 2020 to 2022; in the group from October 2022 to October 2023, it was considered as 1 year at risk, and assigned to 2023.

The classes that classify the age groups were made taking into account > and < de 65 años [32]. As much as possible, excessive fragmentation of the data was avoided to avoid low numbers of classes to be compared. The age of 65 years was used as the beginning of old age [33].

The bivariate comparisons were performed using the Chi Square test (X2) with Yates correction or Fisher Exact Test when necessary (according to the number the expected cell totals). Data for equal time periods were compared: the average for 1 year in the group from 2020 to 2022, with the result for the year 2023. Figures with decimals were rounded to whole numbers for statistical comparison.

Ethical Issues

No personal data of the patients were used, but only group results, which were taken from the clinical history.

Results

712 cases of COVID-19 were included for a population at risk of 2,000 people, from March 15, 2020 to October 31, 2022 (years at risk) [IR= 36% x 3 years; 12% average for one year] versus 76 cases of COVID-19 for a population at risk of 2,000 people, from October 2022 to October 2023 [IR= 4% x 1 year], which represents a lower total incidence rate raw for 2023, with a RR of 0.33 (effective and statistically significant protection factor in 2023 vs. 2020-2022 [X2= 4.3478. p= .037056.]) and an RA= -8 (Table 1, Figure 1).

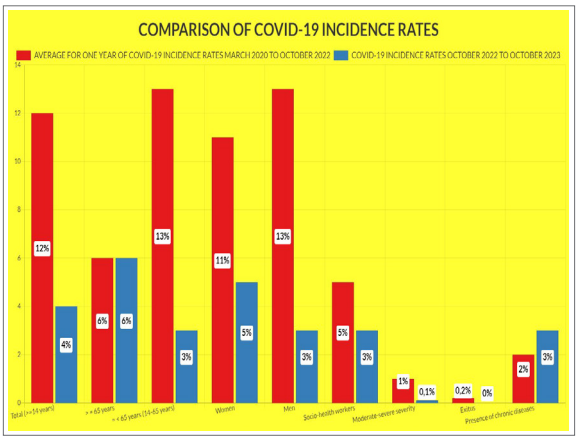

Figure 1: Comparison of covid-19 incidence rates between the period from march 2020 to october 2022 and the period from october 2022 to october 2023

Table 1: Comparison of COVID-19 Risk Measures Between the Period from March 2020 to October 2022 and the Period from October 2022 to October 2023

Variables	Population of the General Medicine Office (Population at Risk) n=2.000	Acute COVID-19 Cases from March 15, 2020 to October 31, 2022 (Years at Risk) n=712	COVID-19 Incidence Rates from the Period of March 2020 to October 2022 (for the Population and Years at Risk at Risk)	October 2022 to October 2023 COVID-19 Cases (Year at Risk) n=76	COVID-19 Incidence Rates from the Period of October 2022 to October 2023 (for the Population and Year at Risk at Risk)	Relative risk (Incidence in 2023 Divided by Incidence in 2020-2022)	Attributable Risk (Incidence in 2023 Minus Incidence in 2020-2022)	Number Needed to Treat (the Inverse of Absolute Risk Reduction)	Statistical Significance (comparison of Equal Time Periods: Average for 1 Year in the 2020 to 2022 Group, with 1 Year in the 2023 Group)
Total (>=14 years)	2.000	712 (100)	36% x 3 years [12% average x 1 year]	76 (100)	4% x 1 year	4/12= 0.33 (protection factor effectively)	4-12= -8 (the incidence is greater in the control group)	1/12-4= 0.125	X2= 4.3478. p= .037056. Significant at p < .05.
> = 65 years	349 (17)	67 (9)	19% x 3 years [6% average x 1 year]	21 (28)	6% x 1 year	6/6= 1 (not significant)	6-6= 0	1/6-6= infinito [NaN]	X2= 0. p= 1. NS
= < 65 years (14-65 years)	1651 (83)	645 (91)	39% x 3 years [13% average x 1 year]	55 (72)	3% x 1 year	3/13= 0,23 (protection factor effectively)	3-13= -10 (the incidence is greater in the control group)	1/13-3= 0,1	X2= 6.7935. p= .009149. Significant at p < .05.

Women	1020 (51)	340 (48)	33% x 3 years [11% average x 1 year]	48 (63)	5% x 1 year	5/11= 0,45 (protection factor effectively)	5-11= -6 (the incidence is greater in the control group)	1/11-5= 0,16	X2= 2.4457. p= .117851. NS
Men	980 (49)	372 (52)	38% x 3 years [13% average x 1 year]	28 (37)	3% x 1 year	3/13= 0,23 (protection factor effectively)	3-13= -10 (the incidence is greater in the control group)	1/13-3= 0,1	X2= 6.7935. p= .009149. Significant at p < .05.
Socio-health workers	NA	31 (16)*	16% x 3 years [5% average x 1 year]	31 (41)	3% x 1 year 3/5= 0,6 (true benefits)	3/5= 0,6 (true benefits)	3-5= -2 (the incidence is greater in the control group)	1/5-3= 0,5	X2 with Yates correction= 0.1302. p= .718216. NS
Moderatesevere severity	2000 (100)	8 (4)*	4% x 3 years [1% average x 1 year]	2 (3)	0.1% x 1 year	0.1/1= 0,1 (protection factor effectively)	0.1-1= -0,9 (the incidence is greater in the control group)	1/1-0.1= 1,11	Fisher exact test= 1. NS
Exitus	NA	1 (0.5)*	0.5% x 3 years [0.2% average x 1 year]	0	0 % x 1 year	0/0.2= 0 (protection factor effectively)	0-0.2= -0,2 (the incidence is greater in the control group)	1/0.2-0= 5	Fisher exact test= 1. NS
Presence of chronic diseases	1459 (73)	108 (7)*	7% x 3 years [2% average x 1 year]	48 (63) sobre una muestra de N=76	3% x 1 year	3/2= 1,5 (weak risk)	3-2=1 (A positive difference indicates that the incidence is greater in the treated group)	1/2-3= -1	Fisher exact test= 1. NS

( ): Denotes percentages; NS: Not significant; NaN: No es un número (representa el resultado de operaciones matemáticas indefinidas); RR: Relative Risk; AR: Attributable risk; NNT: number needed to treat; NA: Not available; * On a sample of N=188

In 2023 vs. 2020-2022 the following statistically significant differences were found:

- Lower IR in < 65 years [13% average x 1 year vs. 3%; X2= 6.7935. p= .009149; RR= 0.23 (effective protection factor); AR= -10]
- A lower IR in men [IR= 12% average for one year versus 4%; RR of 0.33 (effective protection factor); RA= -8 [X2= 4.3478. p= .037056.]

There was a lower IR in women, in cases with moderate-severe severity, and in socio-sanitary. All these RRs indicated protective factors, and negative ARs (the incidence was higher in the control group), for the 2023 group vs. 2020 -2022. However, the presence of chronic diseases had a higher IR, a weak risk, and positive AR in 2023 vs. in 2020-2022 (Indicating greater incident in cases of COVID-19 with chronic diseases in 2023 vs. 2020-2022).

By sex, it was observed that its frequency was reversed: from a higher IR in men in 2020-2022 to a higher rate in women in 2023 (Table 1, Figure 1).

Discussion

Main findings

The main findings of our study were:

1. In 2023, the population at risk with greater hybrid immunity presented lower IR (with a RR indicating protection factor and negative RA indicating lower IR, in a statistically significant manner), than the average for the 2020-2022 period. This also occurred, in a statistically significant way, in men and in <65 years.
2. In women, in cases with moderate-severe severity, and in socio-health workers, although there was a lower IR, with protective RRs and negative ARs, statistical significance was not reached. By sex, it was observed that its frequency was reversed: from a higher rate in men in 2020-2022 to a higher rate in women in 2023.
3. Finally, the presence of chronic diseases meant a higher IR, risk factor according their RR, and positive AR, although without statistical significance.

Comparison with other Studies

COVID-19 is at a tipping point, meaning that high levels of immunity to SARS-CoV-2 are beginning to limit its impact and reach. Currently, many countries do not test all symptomatic patients, nor do they systematically collect the number of cases or their clinical-epidemiological characteristics [2,34].

In Spain, the surveillance and control strategy against COVID-19 after the acute phase of the pandemic, in force since March 28,

2022, indicates the need to perform PCR or antigen testing only in specific situations that fundamentally include people with vulnerability criteria, of vulnerable areas, and those that require hospital admission. The reported cases therefore represent these groups and not the total number of SARS-CoV-2 infections, so the evolution of the pandemic monitoring indicators must be adapted to this circumstance and the data from these reports cannot be compared with those of prior reports [35]. In this situation, many people with symptoms in the community choose to perform individual tests at home [36].

In this way, the official figures imply significant under-reporting and the incidence of COVID-19 and other risk measures such as RR and AR, and their evolution over time in the community, are truly unknown. But, frequently, people with a positive test at home do communicate this circumstance to their family doctor, to seek treatment and/or sick leave. In this way, the data on COVID-19 cases in general medicine has been proposed as an indicator of the variation in incidence in the community, and as a complement to the data on mortality and hospitalizations [21,37].

Our study, carried out on the same at-risk population seen in a general medicine consultation from 2020 to 2023, and including cases of COVID-19 with tests carried out in health services and those carried out at home, and reported to the GP overcomes these limitations of official reports, allowing comparisons between time periods.

Based on incomplete official data, the current situation is usually classified as "low incidence" [38].

We also find a lower crude IR for 2023 compared to the 2020-2022 period, with a RR of 0.33 and an RA= -8. These risk measures seem to indicate that the risk population is better prepared in 2023 vs. 2020-22 to avoid cases of COVID-19; this is probably due to their higher level of hybrid immunity. It must be taken into account that in Spain 93% of people over 12 years of age are vaccinated with 2 doses, and 56% with a booster dose [39]. Vaccination against COVID-19 has substantially altered the course of the pandemic, saving tens of millions of lives around the world [40].

In our study it was found in 2023 vs. 2020-2022 a lower IR in < 65 years (young people), with a RR indicating protection factor and negative AR. On the other hand, the presence of chronic diseases meant a higher IR, a RR indicating risk factor, and positive AR, although without statistical significance; Moreover the IR in the elderly (> 65 years) did not change. Patients at risk are known to be the elderly, those with multiple illnesses, fragile health or immunocompromised. The association of infection with comorbidities (diabetes mellitus, arterial hypertension, obesity, chronic kidney disease and chronic obstructive pulmonary disease) darkens the prognosis and causes complications [41-45]. These populations will likely need vaccine annual reinforcements. For younger, healthier patients, probably the recommendation is an annual booster, similar to the flu [34].

In our study, by sex, it was observed that its frequency was reversed: from a higher rate in men in 2020-2022 to a higher rate in women in 2023. At the peak of the coronavirus crisis, men still made up the majority of all COVID-19 deaths even though women accounted for a larger proportion of confirmed cases, which was blamed on biology and behaviour [46].

In summary, everything seems to indicate that the risk population is better prepared in 2023 vs. 2020-22 to avoid cases of COVID-19, which is homogeneous with other studies, and quite reasonable from common sense, but people with chronic diseases have a greater risk in 2023, and a trend seems to be observed to increase IR in women vs. men. But, these results should be interpreted with caution given that the number of tests carried out in the community is currently probably low, which suggests an indeterminate COVID-19 situation [47].

Although at this point in COVID-19 infection the incidence levels is low meaning regarding the values prior to 2023 (due to vaccination and hybrid immunity), they are still very relevant for policy formulation. For example, they correlate with the risk of long COVID-19, determine the effectiveness of test, and predict the proportion of severe cases requiring hospitalization [48].

Limitations and Strengths of the Study

1. The use of databases collected for specific purposes in the primary analysis, other than the secondary analysis, limits the analysis and interpretation of results.
2. The sample size may not meet the needs of the secondary analysis performed. The sample was small, so some data may cause misinterpretation.
3. Rounding the years at risk may imply a small calculation error, but it helps to better understand the results
4. Asymptomatic cases were missing because they did not attend in GP consultation, as no surveillance or systematic screening was done.
5. There may be an underreporting of infections to GP of patients with a positive test at home. But given the situation of the GP as the gateway to the health system, the vast majority of positive COVID-19 tests at home, is likely to be reported in GP office.
6. The study has the strength of its longitudinality, characteristic of work in general medicine.
7. All the studies were carried out in the same general medicine practice and carried out by the same researcher, which gives coherence to the results.

Conclusion

In the general practice setting in Toledo, Spain, we found that in 2023 the population at risk with greater hybrid immunity presented lower IR, with their RR indicating protection factor and negative RA (indicating lower IR) in a statistically significant way versus the average for the period 2020-2022. This also occurred in a statistically significant way in men and in <65 years. In women, cases with moderate-severe severity, and in socio-health workers, although there was a lower IR, with protective RRs and negative ARs, statistical significance was not reached. By sex, it was observed that its frequency was reversed: from a higher rate in men in 2020-2022 to a higher rate in women in 2023. Finally, the presence of chronic diseases meant a higher IR, a RR of risk factor RR, and a positive AR , although without statistical significance. In summary, the risk population is better prepared in 2023 vs. 2020-22 to avoid cases of COVID-19, but people with chronic diseases pose a greater risk in 2023, and a trend seems to be observed to increase IR in women vs. men.

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