

Covid-19 Temporal Variations and Association with Risk Factors in Endemicity Time from October 2022 to October 2023, In A General Medicine Office, In Toledo (Spain): The Seasonal Pattern of Covid-19 Does Not Appear to Be Related to Climate Factors but to Human Activities

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Abstract

Background

The seasonal variations of covid-19 cases in the current endemic situation and their possible associations with risk factors are unknown.

Objective

To study covid-19 seasonal variations (those occurring regularly at certain times of the year and their temporal association with certain selected risk factors).

Methodology

An observational, longitudinal and prospective study of covid-19 infections was conducted from October 1, 2022 to October 1, 2023, in a general medicine office in Toledo (Spain).

Results

76 cases of covid-19 were included. The study of variations according to the seasons of the year showed two waves of increase in cases: 24% of the cases occurred in autumn (from October 2022 to December 2022 and 27% occurred in summer (between July and September 2023). In this second wave, 50% of the cases were in social-health workers.

Conclusion

In the general practice setting in Toledo, Spain, a seasonal pattern linked to meteorological changes is not clear. The seasonal variations found were probably temporally associated with: 1) In October-January 2022, the fourth dose of the covid-19 vaccine had not yet been given or had been given on those days; And 2) In August-September 2023, for having received the fourth dose more than 6 months before, because of travelling in summer holidays, and for the elimination of the mandatory use of masks in health centres. However, one should be cautious when extrapolating general rules because of few events and having a short observation time frame. In any case, general practitioner may be a better source of information on covid-19 seasonal variation in endemic time.

Introduction

In epidemiology, the study of variations in morbidity includes the study of seasonal variations (those occurring regularly at certain times of the year). Knowledge of these variations can be related to their associated causes or factors, such as agent ecology, climate and atmospheric phenomena, human activities, human concentration and dispersion, exposure to different agents, etc. This knowledge of the seasonal evolution of the morbidity allows to control or to manage its frequency, and to establish previsions and interventions [1-4].

It is considered that any biomedical variable has a seasonal behaviour, or shows seasonality when its presentation in the different times of the year defined as seasons (astronomical or climatologically) is not statistically uniform [5]. The study of seasonal variations has enough interest to know the environmental or personal factors that influence, or the variation in exposure to infectious agents due to the natural life cycle of the infectious agent, or the changes in the opportunity for exposure, or variations in habits, such as diet, or other environmental factors, or the possible Influence of sunlight, cold or heat, humidity, barometric pressure, exercise or physical inactivity in winter versus summer, the environmental pollution, the variations in neuroendocrine and metabolic function or seasonal movements of the population, etc. [6-12]. All of these are factors that are likely to be able to act on seasonal variations of diseases, also are reflected on morbidity which is attended in general practice, and it forces to adapting the services to the variability of demand [13].

For most illnesses, in many health systems, the general practitioner (GP) is the first point of contact in the health care system and he looks after a population whose age and sex composition are known. So, GP is a major source of information on health problems and their variation. GP is in an ideal position to conduct inquiries about seasonal variations of diseases [14].

It has been interpreted that if the patterns that have been observed so far in cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continue along this path, its post-pandemic evolution could become seasonal and resemble that of other respiratory infections like flu. In this scenario, immune-evading mutations of circulating variants, such as Omicron, could combine with drops in population-wide immunity to become key drivers of periodic waves of infection [15, 16]. While climate is not currently the dominant factor driving SARS-CoV-2 transmission, and factors such as human behaviour outweigh the influence of climate, experts say that in the future coronavirus disease 2019 (COVID-19) may become a seasonal winter disease, a circulating pattern observed among other pre-existing seasonal human coronaviruses [16, 17].

In the transition from epidemic to endemic (without relevant peaks in cases), it is timely and extremely important to understand the long-term future of SARS-CoV-2. Currently, the fate of COVID-19 remains unclear; Un-

derstanding potential seasonal profiles of infection risks will be critical to inform effective surveillance and control strategies [18]. Furthermore, after the fourth vaccination dose in autumn 2022, there is a lack of information on the real incidence of covid-19 cases. In this context, a longitudinal study is presented with the objective of describing the seasonal variations of covid-19 and its temporal association with certain relevant events (such as the withdrawal of the mandatory use of masks in health centers), for one year, from on October 1, 2022 (start of the fourth dose of covid-19 vaccine) until October 1, 2023, in a general medicine office in Toledo, Spain.

Material and Methods

Design and emplacement

An observational, longitudinal and prospective study of covid-19 infections was conducted from October 1, 2022 to October 1, 2023, in a general medicine office in the Santa Maria de Benquerencia Health Center, Toledo, Spain, which has a list of 2,000 patients > 14 years of age (in Spain, general practitioners [GPs] care for people > 14 years of age, except for exceptions requested by the child's family and accepted by the GP).

Outcome of Interest

Describe the seasonal variations of covid-19 and their temporal association with certain relevant events (such as the withdrawal of the mandatory use of masks in health-care facilities), for one year, from October 1, 2022 (start of the fourth dose of covid-19 vaccine) until October 1, 2023 in a general medicine office in Toledo, Spain.

Diagnosis of Covid-19

The diagnosis was performed with reverse transcriptase polymerase chain reaction oropharyngeal swab tests or antigen testing (19).

Collected Variables

- Date of covid-19 infection diagnosis
- Age and sex
- If they were Health Care Workers
- Vaccination with fourth dose against covid-19 at the date of acute infection

Ethical Issues

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

Results

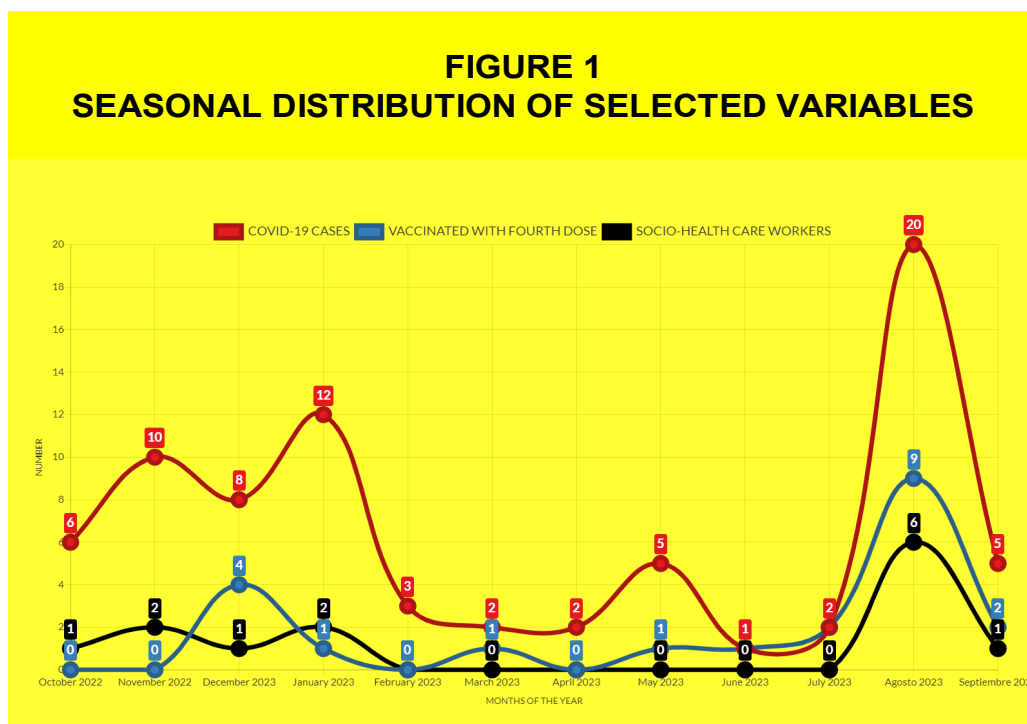
76 cases of covid-19 were included, 63% women, 28% ≥ 65 years, 17% socio-health care workers, 28% vaccinated with four doses. Covid-19 cases presented a seasonal increase between October-January 2022, and August-September 2023. In the first wave, 19% were vaccinated with the fourth dose. In the second wave, 50% of the cases were in social-health workers, and 61% were vaccinated with the fourth dose (TABLE 1, FIGURE 1).

Table 1: Seasonal Distribution of Selected Variables

MONTHS OF THE YEAR	COVID-19 CASES N=76	VACCINATED WITH FOURTH DOSE N=21	SOCIO-HEALTH CARE WORKERS N=13
October 2022	6 (8)	0	1 (8)
November 2022	10 (13)	0	2 (15)
December 2023	8 (10)	4 (19)	1 (8)
January 2023	12 (15)	1 (5)	2 (15)
February 2023	3 (4)	0	0
March 2023	2 (3)	1 (5)	0
April 2023	2 (3)	0	0
May 2023	5 (7)	1 (5)	0
June 2023	1 (1)	1 (5)	0
July 2023	2 (3)	2 (9)	0
Agosto 2023	20 (26)	9 (43)	6 (46)
Septiembre 2023	5 (7)	2 (9)	1 (8)
Total	76 (100)	21 (100)	13 (100)

(): Denotes percentages

Figure 1: Seasonal Distribution Of Selected Variables



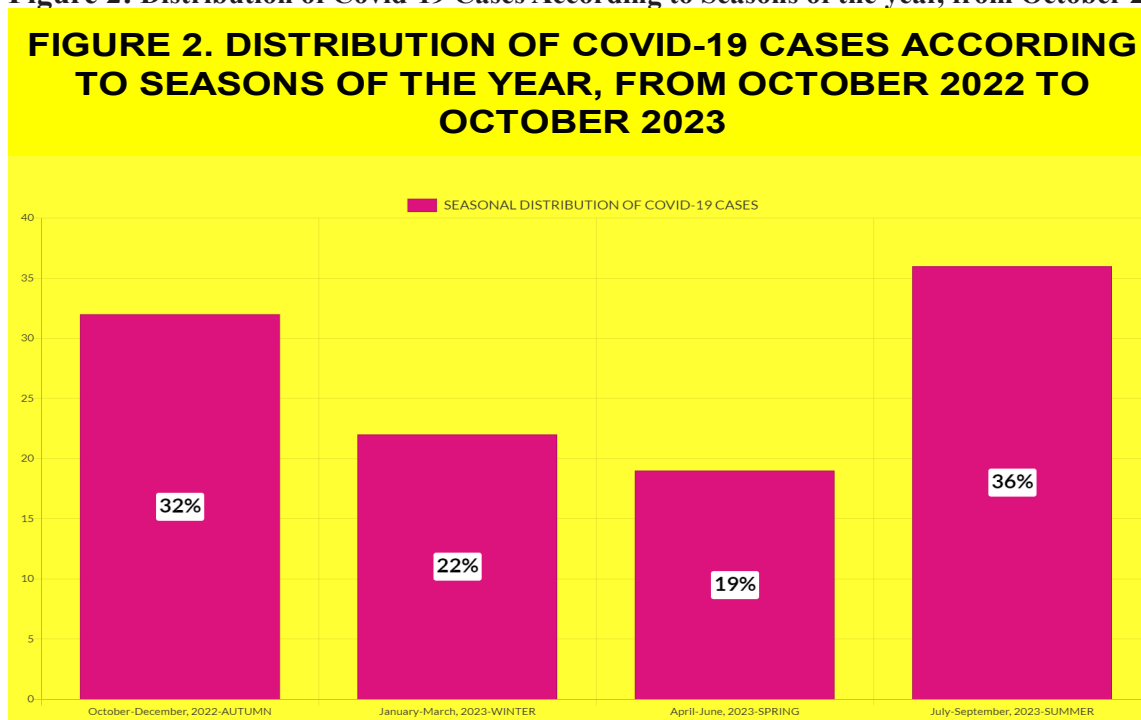
The study of seasonal variations according to the seasons of the year showed that 24% of the cases occurred in autumn (from October 2022 to December 2022; 17% of the cases occurred in winter (from January 2023 to March 2023; 8% occurred in spring (from April to June 2023); and 27% occurred in summer (between July and September 2023) (TABLE 2, FIGURE 2).

Table 2: Distribution Of Covid-19 Cases According to Seasons of The Year

SEASONAL DISTRIBUTION OF COVID-19 CASES	COVID-19 CASES N=76
October 2022-December 2023-AUTUMN	24 (32)
January-March-WINTER	17 (22)
April-June-SPRING	8 (10)
July-September-SUMMER	27 (36)
Total	76 (100)

(): Denotes percentages

Figure 2: Distribution of Covid-19 Cases According to Seasons of the year, from October 2022 To October 2023



Discussion

Main Findings

We found two seasonal increases, one in October-January 2022, and another in August-September 2023. This seasonal pattern does not appear to be related to climatic factors such as temperature, humidity, or winter conditions (since one occurred in autumn and beginning of winter, and the other in summer). The first wave was probably temporally associated with not having received, or having received in those days without time to achieve an adequate level of immunity, the fourth dose of the covid-19 vaccine; And the second wave, from August-September 2023, to having received the fourth dose more than 6 months before, travel for the summer holidays, and the elimination of the mandatory use of masks in health centers, which in Spain occurred from July 4 of 2023 [20]. This last factor may be, in our study, behind the peak of cases in social-health workers in that seasonal period. This situation has occurred in other places such as the United States, where on May 11, 2023 the 2020 declaration that qualified the coronavirus as a public health emergency expired and from that moment on covid-19 was treated like any other respiratory disease; More than three months after that date, a wave of coronavirus infections in late summer hit schools, workplaces and local governments [21].

In any case, the results must be evaluated with caution. Since April 28, 2022 there was in Spain a new "Surveillance and Control Strategy Against Covid-19" that included the non-performance of diagnostic tests, which were focused only on those over 60 years of age [22]. This means that in our study positive cases have been recorded with tests carried out in health services and with tests carried out at home and later communicated to the GP. In this way, the existence of

under-recording is likely.

On the other hand, the evolution of the predominant SARS-CoV-2 variants in the context of our study must be taken into account. The omicron variant was the dominant one in Spain (in the week of November 21 to 27, 2022), the omicron percentage stood at 100% [23]. In Spain, the replacement of BA.2 with BA.5 occurred in mid-June 2022. From that moment on, a period of great diversification of the BA.2, BA.4 and BA.5 lineages began, with mutations that could be related to greater escape from the immune response against previously circulating variants. The XBB.1.5 lineage became the dominant one globally in February 2023 (in March in Spain) [24]. The EG.5 strain, already popularly known as Eris, has spread rapidly since the end of July in the United States, Europe and Asia, and in Spain in August 2023 [25-27]. However, it is possible that some of these infections are occurring with few symptoms or symptoms that can be confused with other mild conditions. The reality is that in Spain covid-19 is already considered as another respiratory infection [25].

Comparison with other Studies

A season is a specific period of time and one of the ways in which a year can be divided, in this case into four parts, with duration greater than the month, characterized by the typical behaviour of some meteorological variable (temperature, precipitation, winds, etc.). They occur in a cyclical and inverted manner between one hemisphere and another. The succession of the seasons is caused by astronomical characteristics of the planet [28].

It has long been accepted that morbidity patterns in general practice vary seasonally, which depends mainly on the acute pathology of infectious origin, mainly respiratory infections. General medicine is an important source of information about health problems and their variations. For most diseases, the GP is the first point of contact in the healthcare system [13].

It is unclear what trajectory SARS-CoV-2 transmission will follow after the initial pandemic wave. One of the speculations is that SARS-CoV-2 will adapt to seasonal circulation like the 2009 H1N1 pandemic influenza virus, and it following the same seasonal patterns as human coronaviruses [16]. It has been suggested that while climate is not currently the dominant factor driving SARS-CoV-2 transmission, experts say that in the future covid-19 may

become a winter disease. It has been reported that the transmissibility of SARS-CoV-2 is certainly modulated by climatic factors such as temperature, humidity, and winter conditions in some places facilitate airborne transmission, but these factors are not currently the dominant factors driving it. [17]. Time series analysis of new daily covid-19 cases revealed both long-term (waves) and short-term (cycles) variations. This cyclical nature provides an innate defense of the herd through a type of temporal distancing [29].

Covid-19 has not shown clear seasonal patterns since the pandemic began in 2020. Since 2021 there have been peaks in summer, but they have also been frequent in the autumn-winter season and spikes have also been recorded in spring. Being a relatively new virus that is fought with massively injected vaccines, it does not have cycles as clear as others, such as the flu, which is much more regular (almost always in the coldest of winter). No one has a clear answer to how the virus will behave in the coming months, neither its expansion nor its severity. It will depend on their mutations and the response to the vaccination campaigns of the vulnerable population [30].

Our results are in line with the fact that the variations in the number of covid-19 cases in this endemic time do not follow a clear pattern of climatic seasons of the year as astronomical characteristics of the planet, having found a wave in autumn and early winter, but also in summer.

The rise of BA.4 and BA.5, as well as that of another branch of Omicron in North America, could mean that SARS-CoV-2 waves are beginning to settle into predictable patterns, with new waves periodically emerging from circulating strains. These are the first signs that the virus is evolving differently compared to the first two years of the pandemic. In this scenario, immune-evading mutations in circulating variants, such as Omicron, could combine with drops in population-wide immunity to become key drivers of periodic waves of infection [15, 24-26, 30-34].

Since the international emergency due to the covid-19 pandemic was declared in 2020, Spain has gone through seven waves. Currently, it seems to have been stabilized. In April 2022, the end of masks outdoors and in transport came into force and the elimination of the mandatory use of masks in health centers on 4 July 2023 (35, 20). Our results suggest that the observed waves are related to tem-

porary factors (reduction in vaccination immunity, travel for summer vacations, and elimination of mandatory use of masks in health centres, and spread of new strains). Other authors have drawn attention to decisions made to end the universal use of face masks in hospitals and doctors' offices that are placing patients and staff at greater risk of Covid-19 infection [36].

On the other hand, in our study, the two waves of cases found, in autumn and summer, are associated with the highest percentage of vaccinated with 4 doses. This is simply because since a large part of the population is vaccinated with 4 doses, infections occur in those vaccinated. In any case, more time is needed, perhaps many more years of observation, before this can be known with certainty [17].

In short, whether a seasonal pattern emerges and what it will look like will depend on many factors that have not yet been understood, including how long immunity lasts, how long recovery takes, and how likely it is that people can be re-infected, and the public behaviours and government decisions [37, 38].

Study limitations

1. The small number of covid-19 cases may make analysis difficult
2. There may be underreporting of infections
3. In our study, only Pizfer / BioNTech, Spikevax (mRNA-1273- Moderna), Vaxzevria, Oxford / Astra-Zeneca and Janssen (Johnson & Johnson) vaccines were used for the first and second doses. For the first booster, only messenger RNA (mRNA) was used. And only Moderna and Pfizer-BioNTech's bivalent covid-19 vaccines were used for the second booster. Thus, our results may not directly apply to other covid-19 vaccine platforms.

Conclusion

In the general practice setting in Toledo, Spain, we found two seasonal increases: one in autumn (and early winter) from October 2022 to December/January 2023, and another in summer, from July to September 2023. There is no clear seasonal pattern which could be linked to meteorological changes; These seasonal variations were probably temporarily associated with: 1) In October-January 2022, the fourth dose of the covid-19 vaccine had not yet been given or had been given on those days; And 2) In Au-

gust-September 2023, to having received the fourth dose more than 6 months before, the travel for the summer holidays, and the elimination of the mandatory use of masks in health centers. However, one should be cautious when extrapolating general rules because of the occurrence of few events and having a short observation time frame. In any case, GP may be a best source of information on covid-19 seasonal variation in endemic time.

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