RESEARCH ARTICLE

Case Series of 46 Covid-19 Breakthrough Infections in Vaccinated People with Vaccine Booster Shot in General Medicine for the Period December 2021 to February 2022, in Toledo, Spain

Jose Luis Turabian

Specialist in Family and Community Medicine, Health Center Santa Maria de Benquerencia, Regional Health Service of Castilla la Mancha (SESCAM), Toledo, Spain

ABSTRACT

Background: COVID-19 vaccines showed excellent efficacy until the end of December 2021 when the world registered the highest number of infections related to the Omicron variant. **Objective**: To describe the cases of covid-19 breakthrough infections in vaccinated people with vaccine booster. **Methodology:** An observational, longitudinal and prospective case series study of patients with covid-19 breakthrough infections in vaccinated people with vaccine booster in general medicine for the period December 2021 to February 2022, during the omicron variant contagion wave. **Results:** Forty-six cases were included, with a mean age of 53 years, 28% being >=65 years. 59% were women. 15% had presented previous symptomatic Covid-19. The mean time in days from Booster to COVID-19 in breakthrough infections was 27 days. 89% were symptomatic, with a mean duration of symptoms of 5 days, with ENT symptoms predominating. 28% were socio-health care workers. 76% had chronic diseases. The majority (85%) received heterologous booster doses, predominantly 2 doses of BNT162b2 mRNA vaccine with mRNA-1273 vaccine booster. **Conclusion**: The profile of Covid-19 breakthrough infections in vaccinated people with Vaccine Booster, in general medicine in Toledo, Spain, for the period December 1, 2021 to February 28, 2022, when the most intense wave of pandemic cases was experienced, due to to the predominance of the omicron variant, was a 50 year old woman, socio-health care worker, with two doses of BNT162b2 mRNA vaccine and a mRNA-1273 vaccine booster given in the previous 4 weeks, with mild ENT symptoms and chronic diseases.

Key words: COVID-19, SARS-CoV-2, COVID-19 Vaccine, Breakthrough Infection, Immunization, Secondary, General Practice, Case Series.

INTRODUCTION

From the extension of the corona virus disease (Covid-19) vaccination in December 2020 to the end of the summer of 2021, cases of breakthrough Infection in vaccinated people were rare. But in January 2022, the Omicron variant broke records for Covid-19 infection in Europe, North America, Africa, and Australia, and the world registered the highest number of Covid-19 infections in a week (1-3).

The introduction of safe and effective vaccines that were developed at an unprecedented scale and speed against severe

Address for correspondence:
Jose Luis Turabian, Specialist in Family and Community Medicine, Health Center Santa Maria de Benquerencia, Regional Health Service of Castilla la Mancha (SESCAM), Toledo, Spain.

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acute respiratory syndrome corona virus (SARS-CoV-2) have helped turn the tide of the pandemic by saving many lives, achieving an impressive decline of new cases in just over 2 months after the start of the vaccination campaign, reducing illnesses and hospital admissions (4-6). However, decreased vaccine-induced immunity and the emergence of worrying variants of SARS-CoV-2 with increased resistance to neutralization have limited the efficacy of currently available vaccines (5). The omicron variant (B.1.1.529) of SARS-CoV-2 shows substantial resistance to vaccine-induced serum neutralizing activity and is therefore of particular concern due to its high transmissibility and potential for evade immunity from neutralizing antibodies induced by vaccination or natural infection with wild-type virus (7, 8).

Although the risk of infection after vaccination, and even more so of severe disease, remains low, the gradual increase in clinical outcomes related to infection by the omicron variant suggested that booster vaccination should be accelerated (9, 10). In this way, the decision to vaccinate all people who received the second dose at least 5 months earlier, regardless of their age, was quickly implemented. However, the protection conferred by booster doses of vaccines (compared to the protection conferred by the primary series, which was previously shown to have high efficacy against Covid-19) in effectively neutralizing infection with the omicron variant, not clear (4, 11, 12).

The four vaccines available in Europe have managed to induce sufficient humoral and cellular immunity to neutralize SARS-CoV-2 and significantly reduce severe Covid-19. However, the omicron variant harbors 36 spike protein mutations that attenuate vaccine-driven immunity (13). Researchers evaluating the power of neutralizing antibodies against various variants of SARS-CoV-2 found that, after the third dose of the vaccine, the participants' antibodies were able to stop omicron from infecting cells, but not as well as they blocked the Delta variant (14).

Thus, scientists and the public have been closely monitoring the clinical effects of the wave of the omicron variant to estimate the relative transmissibility, immune evasion capacity, and severity in comparison with previous variants (15). This highlights the importance of infection tracing to understand the epidemiological evolution of the pandemic, which is even more important now that we are facing the challenge of the omicron variant. Thus, real-world data are urgently needed to fully understand the effect of the omicron variant and guide appropriate health policies (16) including on the serial use of homologous boosters (same as primary vaccine) and heterologous boosters (other than the primary vaccine) in fully vaccinated recipients (13). On the other hand, it is important to list the clinical symptoms of new variants, since not doing so is a threat to the control of the pandemic (17).

In this context, we present an observational, longitudinal and prospective case series study of patients with covid-19 breakthrough infections in vaccinated people with vaccine booster in general medicine for the period December 2021 to February 2022, during the omicron variant contagion wave.

MATERIAL AND METHODS

An observational, longitudinal and prospective study of Covid-19 breakthrough infections in vaccinated people with vaccine booster was conducted from December 1, 2021 to February 28, 2022, in a general medicine office in Toledo, Spain, which has a list of 2,000 patients > 14 years of age (in Spain, the general practitioners [GPs] care for people > 14 years of age, except for exceptions requested by the child's family and accepted by the GP). The GPs in Spain work within the National Health System, which is public in nature, and are the gateway for all patients to the system, and each person is assigned a GP (18).

Criteria for Inclusion and Exclusion of Participants

Definition of Homologous or Heterologous Booster

Currently, the European Commission has authorized four vaccines: Comirnaty, from Pfizer/BioNTech, authorized December 21, 2020; Moderna vaccine, authorized on January 6, 2021; AstraZeneca vaccine, authorized on January 29 and Janssen/Johnson & Johnson vaccine, authorized on March 11, 2021. These four vaccines are currently available in Spain, all of them have been approved by the European Medicines Agency. These vaccines have been shown to be highly effective in preventing mild to severe COVID-19 (19). The original BNT162b2 mRNA vaccine (Comirnaty, Pfizer/BioNTech), mRNA-1273, and ChAdOx1 nCoV-19 vaccine (Vaxzevria, Oxford/AstraZeneca) regimens were homologous induction and booster regimens, whereas the original Ad26 vaccine regimen .COV2.S (Janssen vaccine; Johnson & Johnson vaccine) was a single injection regimen.

As of November 23, 2021, in Castilla La Mancha, the region where the study was carried out, booster doses against Covid-19 with messenger RNA (mRNA) vaccines began 6 months after completion the vaccination schedule and after 3 months in case of having received a dose of the Ad26.COV2.S vaccine (Janssen vaccine; Johnson & Johnson vaccine). Recruitment was carried out actively by age cohorts in a descending manner, beginning with those over 80 years of age and people inpatients in centers for the elderly and in other socio-health and health centers (including day centers and occupational centers), regardless of age, people who received a dose of Ad26.COV2.S vaccine (Janssen vaccine; Johnson & Johnson vaccine) as primary vaccination and those with a homologous schedule of Vaxzevria as primary vaccination (first and second dose of Vaxzevria, from AstraZeneca), followed by people aged between between 79 to 70 years old, from 69 to 65 years

old, 64 to 60 years old, 59 to 50 and 49 to 40 years old, etc. The booster dose was administered with mRNA vaccines (0.3 ml of Comirnaty or 0.25 ml of Spikevax – half the usual dose in primary vaccination).

Homologous or heterologous booster

Any mRNA vaccine was used to administer the booster dose, regardless of the vaccine used in the primary vaccination. In people with incomplete regimen (in vaccines that require two doses as primary vaccination) the regimen was completed first with mRNA vaccine (0.3 ml of BNT162b2 mRNA vaccine [Comirnaty, Pfizer / BioNTech] or 0.5 ml of mRNA- 1273 vaccine [Spikevax, formerly COVID-19 Vaccine Moderna]). The booster dose (0.3 ml Comirnaty or 0.25 ml Spikevax) was given 6 months later. In people for whom a booster dose was recommended who had a history of symptomatic or asymptomatic SARS-CoV-2 infection, a booster dose with mRNA (0.3 ml of Comirnaty or 0. 25 ml of Spikevax) at least 4 weeks after the diagnosis of the infection and from 6 months (subsequently modified on January 13, 2022 to 5 months) if the last dose administered in the primary vaccination was with mRNA vaccine (Comirnaty or Spikevax), and from 3 months if it was an adenovirus vector vaccine (ChAdOx1 nCoV-19 vaccine [Vaxzevria, Oxford / AstraZeneca] or Ad26.COV2.S vaccine [Janssen vaccine; Johnson & Johnson vaccine])(20).

To consider a person completely vaccinated with the booster, there are different definitions in the literature, which consider 3 possibilities: having passed 7 days after the booster dose against the corona virus (21), having passed 15 days, and having passed 29 days after the booster (13). For the data in this study, all Covid-19 cases in people fully vaccinated with the booster were included, regardless of time to Covid-19 diagnosis.

All possibilities of reinforcement were considered:

-Full homologous booster dose:

A. 2 doses of BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech) with Pfizer-BioNTech booster

B. 2 doses of mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna) with Moderna booster

-The 6 possible combinations of heterologous booster doses:

A. 2 doses of BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech) with mRNA-1273 vaccine booster (Spikevax, formerly COVID-19 Vaccine Moderna)

B. 2 doses of ChAdOx1 nCoV-19 vaccine (Vaxzevria, Oxford / AstraZeneca) with booster of mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna)

C. 2 doses of ChAdOx1 nCoV-19 vaccine (Vaxzevria, Oxford / AstraZeneca) with booster of BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech)

D. 1 dose of Ad26.COV2.S (Janssen vaccine; Johnson & Johnson vaccine) with mRNA-1273 vaccine booster (Spikevax, formerly COVID-19 Vaccine Moderna)

E. 1 dose of Ad26.COV2.S (Janssen vaccine; Johnson & Johnson vaccine) with booster of BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech)

F. 2 doses of mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna) with booster of BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech)

Diagnosis of Covid-19

The diagnosis was performed with reverse transcriptase polymerase chain reaction (PCR) oropharyngeal swab tests or antigen testing. Rapid antigen tests began to be carried out for symptomatic patients with less than 5 days of evolution. The PCR tests were performed both in symptomatic patients and in asymptomatic contacts. The cases included confirmed cases and asymptomatic carriers. Information on Covid-19 patients and their contacts was obtained from the registry systems used by general medical services in the consultation. A symptomatic confirmed case with active infection was considered to be any person with a clinical picture of sudden onset acute respiratory infection of any severity that occurs, among others, with fever, cough or feeling of shortness of breath. Other symptoms such as odynophagia, anosmia, ageusia, muscle pain, diarrhea, chest pain or headache, among others, were also considered symptoms of suspected SARS-CoV-2 infection according to clinical criteria; and a positive PCR or rapid antigen test positive (22).

The onset date of a confirmed case was defined as the date of the first appearance of self-reported clinical symptoms (20). The onset date for an asymptomatic carrier was defined as the date a positive Covid-19 PCR test was obtained (23). Previous SARS-CoV-2 infection was defined as a positive result in the PCR assay or antigen test at least 90 days before a new positive result (24).

Collected variables

The following variables were collected:

-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" (25), classified according to the International Statistical

Classification of Diseases and Health-Related Problems, CD-10 Version: 2019 (26)

-Social-occupancy class (according to the Registrar General's classification of occupations and social status code) (27, 28)

-If they were Health Care Workers

-Problems in the family context (complex families) based on the genogram and in the experience of the GP for their continuity of care and knowledge of the family (genogram is a schematic model of the structure and processes of a family, which included the family structure, life cycle and family relational patterns. It was understood that "complex" genograms present families with psychosocial problems) (29-32)

-Ethnic minority

-Vaccine type: Comirnaty (Pfizer-BioNTech-BNT162b2 mRNA; Pfizer / BioNTech), Moderna-mRNA-1273 mRNA, Vaxzevria (AstraZeneca), and Janssen / Johnson & Johnson vaccine (Currently, the European Commission has licensed four vaccines: Comirnaty, Pfizer / BioNTech, licensed December 21, 2020; Moderna vaccine, licensed January 6; AstraZeneca vaccine, licensed 29 December and the Janssen / Johnson & Johnson vaccine, authorized on March 11. In Spain, these four vaccines are currently available, all of which have been approved by the European Medicines Agency) (33)

Sample

All patients with covid-19 breakthrough infections in vaccinated people with vaccine booster at the consultation of general medicine for the period December 2021 to February 2022, were included.

RESULTS

Forty-six cases were included, with a mean age of 53 years, 28% being >=65 years. 59% were women. 15% had presented previous symptomatic Covid-19. The median time in days from Booster to Covid-19 in breakthrough infections in vaccinated people was 27 days (range: 1-84 days). 89% were symptomatic, with a mean duration of symptoms of 5 days (range: 2-15 days), predominantly ENT symptoms (anosmia/ageusia, odynophagia, rhinorrhea, pharyngeal dryness-mucus), and 2% of cases with moderate or severe severity. Of the 46 cases, 28% were socio-health care workers. 76% had chronic diseases, predominantly the Endocrine and Genitourinary groups. Most (85%) received heterologous booster doses, predominantly 2 doses of BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech) with mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna) booster (TABLE1, TABLE 2, TABLE 3, and TABLE 4).

Table 1. Frequency of selected variables in the case series of covid-19 breakthrough infections in vaccinated people with vaccine booster

VARIABLES	COVID-19 BREAKTHROUGH INFECTIONS IN VACCINATED PEOPLE WITH VACCINE BOOSTER N=46
Age in years (Arithmetic mean + - Standard deviation; Range)	53.76+-13.61 (26-90 years)
>= 65 years	13 (28)
= <45 years	12 (26)
= <18 years (According to vaccination protocol only as of January 13, 2021, it was extended to everyone over 18 years of age)	0
Women	27 (59)
Men	19 (41)
Previous symptomatic COVID-19	7 (15)
Time in days from Booster to Covid-19 in breakthrough infections in vaccinated people (Arithmetic mean + - Standard deviation; Range)	27.34+-21.51 (1-84 days)
Symptomatic Covid-19 in breakthrough infections in vaccinated people	41 (89)
Duration of symptoms in days of Covid-19 in breakthrough infections in vaccinated people (Arithmetic mean + - Standard deviation; Range)	(Symptomatic N= 41) 5.82+-2.99 (2-15 days)
Covid-19 breakthrough infections in vaccinated people with severity moderate and severe	1 (2) [Pneumonia]

Social-occupancy class of patients (people with some type of labor specialization)	25 (53)
Health care workers with Covid-19 breakthrough infections in vaccinated people	13 (28)
Sick leave for Covid-19 breakthrough infections in vaccinated people	20 (43)
Ethnic minority with Covid-19 breakthrough infections in vaccinated people	3 (6)
Complex family with Covid-19 breakthrough infections in vaccinated people	4 (9)
Chronic diseases presence in Covid-19 breakthrough infections in vaccinated people	35 (76)

( ): Denotes percentages

Table 2. Symptoms in covid-19 breakthrough infections in vaccinated people with vaccine booster

SYMPTOMS * ACCORDING TO WHO, ICD-10 GROUPS	COVID-19 BREAKTHROUGH INFECTIONS IN VACCINATED PEOPLE WITH VACCINE BOOSTER N=46
General (discomfort, asthenia, myalgia, fever, arthralgias)	34 (31)
Respiratory (cough, dyspnea, chest pain)	24 (22)
ENT (anosmia / ageusia, odynophagia, rhinorrhea, pharyngeal dryness-mucus, epixtasis)	41 (37)
Digestive (anorexia, nausea / vomiting, diarrhea, abdominal pain)	3 (3)
Neurological (headache, dizziness, mental confusion -brain fog)	8 (7)
Total symptoms*	110 (100)

( ): Denotes percentages

* Patients could have more than one symptom. The percentages are over the total of symptoms

Table 3. Chronic diseases in covid-19 breakthrough infections in vaccinated people with vaccine booster

CHRONIC DISEASES* ACCORDING TO WHO, ICD-10 GROUPS	COVID-19 BREAKTHROUGH INFECTIONS IN VACCINATED PEOPLE WITH VACCINE BOOSTER N=46
-II Neoplasias	5 (3)
-III Diseases of the blood	1 (1)
-IV Endocrine	24 (16)
-V Mental	8 (6)
-VI-VIII Nervous and Senses	14 (10)
-IX Circulatory system	18 (12)
-X Respiratory system	8 (6)
-XI Digestive system	18 (12)
-XII Diseases of the skin	8 (6)
-XIII Musculo-skeletal	17 (12)
-XIV Genitourinary	23 (16)
TOTAL chronic diseases*	144 (100)

( ): Denotes percentages

* Patients could have more than one chronic disease. The percentages are over the total of chronic diseases

Table 4. Vaccine type in covid-19 breakthrough infections in vaccinated people

VACCINE TYPE	COVID-19 BREAKTHROUGH INFECTIONS IN VACCINATED PEOPLE WITH VACCINE BOOSTER N=46
HOMOLOGOUS booster dose	7 (15)
2 doses of BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech) with BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech) booster	5 (11)
2 doses of mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna) with mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna) booster	2 (4)
HETEROLOGOUS booster dose	39 (85)
2 doses of BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech) with mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna) booster	25 (54)
2 doses of ChAdOx1 nCoV-19 vaccine (Vaxzevria, Oxford / AstraZeneca) with mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna) booster	10 (22)
1 dose of Ad26.COV2.S (Janssen vaccine; Johnson &Johnson vaccine) with mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna)booster	3 (7)
2 doses of mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna)with BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech) booster	1 (2)
TOTAL	46 (100)

( ): Denotes percentages

DISCUSSION

In the course of the Covid-19 pandemic, SARS-CoV-2 has mutated enough to escape first-line immune defences, specifically antibodies. This is why we are seeing breakthrough infections even in highly vaccinated populations (33). The omicron variant of SARS-CoV-2 began spreading rapidly and outpacing other variants in late 2021. It broke records day after day, largely due to a series of mutations in the virus' spike protein that makes vaccines much less effective in stopping infection than earlier variants (34).

Most people with hybrid immunity against natural infection and vaccination have measurable neutralizing antibody activity against the omicron variant, albeit a lower level than against wild-type virus. In this context, a high incidence of progression cases and reinfections with the omicron variant was to be expected (8). Evidence of the high transmissibility of this highly infectious strain of SARS-CoV-2 has pushed covid-19 rates to the highest level ever seen (2, 17).

Eligibility for booster vaccination was initially restricted to older adults, immuno compromised persons, and persons with severe or multiple chronic diseases; but, it was later expanded, depending on age group, to the rest of the population. As booster vaccination was expanded, the omicron variant was introduced into the population, causing the largest epidemic wave of SARS-CoV-2 infections in Spain and the world. In what has been called "the sixth wave" in Spain, from mid-October 2021 to February 2022, despite high vaccination rate, there have been as many infections as the sum of all the previous waves since March 2020 (35).

Age

Older age is a key risk factor for morbidity and mortality associated with SARS-CoV-2 infection. Therefore, older adults have generally been prioritized for COVID-19 vaccination. In addition, the lower immunogenicity of the vaccine and the more pronounced decline in humoral immunity in older people than in younger people has prompted earlier booster campaigns (7). We found a mean age of the patients of 53 years, with 28% being >=65 years. It must be taken into account that the vaccine booster was carried out by age cohorts in descending order, beginning with those over 80 years of age, followed by people aged between 79 to 70 years, from 69 to 65 years, 64 to 60, 59 to 50 and 49 to 40 years, etc. As of January 13, 2021,

it was extended to everyone over 18 years of age. Thus, as of February 24, 2022, in Castilla-La Mancha, 80% of people >40 years of age had received a vaccine booster, but only 35% between 20-39 years of age (36). In short, the mean age of the cases in our study is biased by this fact.

Reinfection in vaccinated with booster doses

Natural infection with SARS-CoV-2 elicits strong protection against reinfection with B.1.1.7 (alpha), B.1.351 (beta), and B.1.617.2 (delta). However, the B.1.1.529 (omicron) variant harbors multiple mutations that can mediate immune evasion (37). In this line, we found that 15% had presented previous symptomatic Covid-19.

Gravity

The rise in population immunity complicates comparisons between the population-level severities of omicron (15). Furthermore, the likelihood that a person with pre-existing immunity will develop a productive infection and the clinical features of that infection are likely a function of both viral and host properties (15). In a small series of cases, the disease was classified as mild or moderate in all of them. And there seems to be agreement that vaccination has contributed to an appreciable reduction in the number of serious and critical clinical cases (2). In our series, all but one case (pneumonia) were also mild.

Symptoms

Models from the University of Washington estimate that 90% of omicron cases will be asymptomatic compared to 40% for previous variants (38). In our study, only 11% were asymptomatic (89% symptomatic) that were detected in the contact tracing process. But no screening activity was carried out to detect asymptomatic cases, and consequently this figure is probably underestimated.

Some findings suggest that Omicron does not target tissues associated with poorer disease outcomes. Factors such as vaccination may have cushioned omicron's blow, making it appear less severe than variants that emerged before Covid-19 vaccines were widely deployed (34). However, reports of a milder course are not necessarily applicable to chronically ill and immunocompromised patients (34). In our series, despite the mild nature of infections, the presence of chronic diseases was high, since 76% had chronic diseases.

The omicron variant appears to replicate rapidly in the upper respiratory tract (34, 38). The main symptoms of the omicron variant include a runny nose, headache, fatigue, sneezing, and sore throat (39), and generally other mild symptoms such as cough, congestion, and fatigue (40). In this way, the list of symptoms of previous infections, in which he stood out high temperature, a new continuous cough or a loss or change in the sense of smell or taste, has lost clinical validity (17). Along these same lines, we found a predominance of ENT symptoms (anosmia/ageusia, odynophagia, rhinorrhea, pharyngeal dryness-mucus). In any case, it must be taken into account that the symptoms may not depend so much on the variant, but on how the organism reacts to the virus (41). It may be that not everything depends on the pathogen, but also on the host and environment (42).

Covid-19 Vaccine Booster Options

It has been reported that mRNA boosters were highly effective against symptomatic delta infection, but less effective against symptomatic omicron infection. However, with both variants, the mRNA boosters led to strong protection against Covid-19-related hospitalization and death (11). Overall, the results suggest that neutralizing antibodies against omicron after a third dose of BNT162b2 mRNA vaccine (Comirnaty, Pfizer/BioNTech) are in a similar order as neutralizing antibodies against delta after a second dose of BNT162b2 mRNA vaccine. (Comirnaty, Pfizer/BioNTech) (43).

In an evaluation of seven boosters, the mRNA1273 (Moderna) vaccine yielded the greatest escalation of antibody and cellular immune responses (44). In this line, it has been shown that after the primary series of two doses of the mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna) the neutralization titers against the omicron variant were 35.0 times lower than those of the D614G (Malay; January 2020) variant. These lower titers could lead to a higher risk of serious infection. However, a booster dose of mRNA-1273 vaccine was associated with neutralizing titers against the omicron variant that were 20.0-fold higher than those assessed after the second dose of vaccine, and these titers may substantially reduce the risk of advanced infection (45).

In this regard, based on an analysis of 148,000 delta cases and 68,000 omicron cases in the UK up to 20 December 2021, booster injection protection against symptomatic Covid-19 caused by omicron variant seems to wear off in about 10 weeks . Among those who received two doses of the AstraZeneca vaccine, a booster of the BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech) or mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna) vaccine was 60% effective in preventing symptomatic disease 2 to 4 weeks after injection. But after 10 weeks, the Pfizer booster was 35% effective and the Moderna booster was 45% effective. Among those who received three doses of Pfizer, the vaccine's effectiveness was 70% about a week after the booster, but dropped to 45% after 10 weeks. At the same time, those who received an initial two-dose series of Pfizer vaccine and then a Moderna booster appeared to be 75% effective for up to 9 weeks (46, 47). In our study, the majority (85%) received a heterologous booster dose, predominantly 2 doses of Pfizer-BioNTech with a Moderna booster.

Time from booster to infection

A laboratory study suggests that vaccination against Covid-19 followed by breakthrough SARS-CoV-2 infection months later offers greater protection against the Omicron variant than vaccination with infection soon after (48). Booster shots of Covid-19 vaccines of BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech) and mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna) lost some effectiveness after four months, but still did a good job of keeping people out of the hospital during the omicron wave: they reduced 91 % hospitalizations at two months, and two months later the figure dropped to 78%, according to a study by the United States Centers for Disease Control and Prevention between August 2021 and January 22, 2022 (49). In another small case series, breakthrough infections occurred 22 to 59 days after the vaccine booster (10). Again, our data is similar: the mean time in days from booster to Covid-19 in breakthrough infections was 27 days (range: 1-84 days).

LIMITATIONS AND STRENGTHS OF THE STUDY

1. The sample was not random, although by including all with covid-19 breakthrough infections in vaccinated people with vaccine booster, because of the characteristics of the GP consultation, it can be assumed that the data is not far from real life.

2. The sample was small, so some data may cause misinterpretation.

3. May have been overlooked asymptomatic cases that did not attend in GP consultation, as no surveillance or systematic screening was done.

CONCLUSION

The profile of Covid-19 breakthrough infections in vaccinated people with vaccine booster, in general medicine in Toledo, Spain, for the period December 1, 2021 to February 28, 2022, when the most intense wave of pandemic cases was experienced, due to the predominance of the omicron variant, it was a female, socio-Health care worker, with two doses of BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech) and a mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna) booster given in the previous 4 weeks, with mild ENT symptoms, lasting 5 days and with chronic diseases of Endocrine and Genitourinary.

REFERENCES

1. Taylor L (2022) Covid-19: Omicron drives weekly record high in global infections. BMJ; 376: o66. https://www.bmj.com/content/376/bmj.o66
2. Turabian JL (2022) Implications for general practitioner of evolution of incidence rates of COVID-19 breakthrough infections in vaccinated people as of December 2021 with the highest spike of infections of the entire pandemic. Arch Community Med Public Health; 8(1): 008-012. https://www.peertechzpublications.com/articles/ACMPH-8-268.pdf
3. Kupferschmidt K, Vogel G (2022) Omicron cases are exploding. Scientists still don't know how bad the wave will be. Early data suggest the new variant may cause less severe disease and death—but hospitals are stretched to their limits. Science; 4 JAN. https://www.science.org/content/article/omicron-cases-are-exploding-scientists-still-don-t-know-how-bad-wave-will-be
4. Gilboa M, Mandelboim M, Indenbaum V, et al. (2022) Early Immunogenicity and Safety of the Third Dose of BNT162b2 Messenger RNA Coronavirus Disease 2019 Vaccine Among Adults Older Than 60 Years: Real-World Experience. J Infect Dis; 225(5): 785–92. https://doi.org/10.1093/infdis/jiab584
5. Kaku CI, Champney ER, Normark J, et al. (2022) Broad anti–SARS-CoV-2 antibody immunity induced by heterologous ChAdOx1/mRNA-1273 vaccination. Science; 375(6584): 1041-7. https://doi.org/10.1126/science.abn2688
6. Stokel-Walker C (2022) What do we know about covid vaccines and preventing transmission? *BMJ*; 376: o298. https://www.bmj.com/content/376/bmj.o298?utm_source=etoc&utm_medium=email&utm_campaign=tbmj&utm_content=weekly&utm_term=20220211
7. Vanshylla K, Tober-Lau P, Gruell H, et al. (2022) Durability of omicron-neutralising serum activity after mRNA booster immunisation in older adults. Lancet Infect Dis. https://doi.org/10.1016/S1473-3099(22)00135-9
8. Madhi SA, Kwatra G, Myers JE, et al. (2022) Population Immunity and Covid-19 Severity with Omicron Variant in South Africa. N Engl J Med. https://www.nejm.org/doi/full/10.1056/NEJMoa2119658?query=TOC&cid=NEJM%20eToc,%20February%2024,%202022%20DM758850_NEJM_Non_Subscriber&bid=842598181
9. Corrao G, Franchi M, Cereda D, et al. (2022) Persistence of protection against SARS-CoV-2 clinical outcomes up to 9 months since vaccine completion: a retrospective observational analysis in Lombardy, Italy. Lancet Infect Dis. https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00813-6/fulltext?rss=yes&utm_campaign=update-laninf&utm_medium=email&_hsmi=202580813&_hsenc=p2ANqtz-_LmRul0qxJzDZu3UfWgCcWs-yxNk3q9qv7f04xu0yLVbq-MRZCyKyy1wfAbA0JOdLRr5wEoWSdrfTTWT_ZEYOQLNczfw&utm_content=202580813&utm_source=hs_email
10. Kuhlmann C, Mayer CK, Claassen M, et al. (2022) Breakthrough infections with SARS-CoV-2 omicron despite mRNA vaccine booster dose. Lancet; 399(10325): 625-6. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00090-3/fulltext?dgcid=raven_jbs_etoc_email

11. Abu-Raddad JJ, Chemaitelly H, Ayoub HH, et al. (2022) Effect of mRNA Vaccine Boosters against SARS-CoV-2 Omicron Infection in Qatar. N Engl J Med. https://www.nejm.org/doi/full/10.1056/NEJMoa2200797?query=TOC&cid=NEJM%20eToc,%20March%2010,%202022%20DM809401_NEJM_Non_Subscriber&bid=866514643
12. Nemet I, Kliker l, Lustig Y, et al. (2022) Third BNT162b2 Vaccination Neutralization of SARS-CoV-2 Omicron Infection. N Engl J Med; 386:492-4. https://www.nejm.org/doi/full/10.1056/NEJMc2119358?query=TOC&cid=NEJM%20eToc,%20February%203,%202022%20DM684340_NEJM_Non_Subscriber&bid=805311301
13. Atmar RL, Lyke KE, Deming ME, et al (2022) Homologous and Heterologous Covid-19 Booster Vaccinations. N Engl J Med. https://www.nejm.org/doi/full/10.1056/NEJMoa2116414?query=TOC&cid=NEJM%20eToc,%20January%2027,%202022%20DM662764_NEJM_Non_Subscriber&bid=797873248
14. Mallapaty S (2022) Fourth dose of COVID vaccine offers only slight boost against Omicron infection. Israeli trial shows a fourth vaccination raises antibody levels but provides little extra protection against SARS-CoV-2 infection. Nature; 23 February. https://doi.org/10.1038/d41586-022-00486-9
15. Bhattacharyya RP, Hanage WP (2022) Challenges in Inferring Intrinsic Severity of the SARS-CoV-2 Omicron Variant. N Engl J Med. https://www.nejm.org/doi/full/10.1056/NEJMp2119682?query=WB&cid=NEJM%20Weekend%20Briefing,%20February%2013,%202022%20DM721905_NEJM_Non_Subscriber&bid=822107755
16. Castagnoli R, Marseglia GL (2022) Tracing and vaccinating: how to REACT to COVID-19 pandemic. Lancet Resp Med. https://doi.org/10.1016/S2213-2600(22)00016-9
17. Rae M (2022) Official list of covid-19 symptoms must be updated. *BMJ*; 376: o121. https://www.bmj.com/content/376/bmj.o121?utm_source=etoc&utm_medium=email&utm_campaign=tbmj&utm_content=weekly&utm_term=20220204
18. Turabian JL (1995) [Notebooks of Family and Community Medicine. An introduction to the principles of Family Medicine]. Madrid: Díaz de Santos. http://www.amazon.co.uk/Cuadernos-medicina-familia-y-comunitaria/dp/8479781920
19. Sablerolles RSG, Rietdijk WJR, Goorhuis A, et al. (2022) Immunogenicity and Reactogenicity of Vaccine Boosters after Ad26.COV2.S Priming. N Engl J Med. https://www.nejm.org/doi/full/10.1056/NEJMoa2116747?query=WB&cid=NEJM%20Weekend%20Briefing,%20January%2029,%202022%20DM668841_NEJM_Non_Subscriber&bid=802068212
20. [Update 10 Vaccination strategy against COVID-19 in Spain. Recommendations agreed upon in the Public Health Commission after review and proposal made by the Vaccination Program and Registry Report together with the COVID-19 Vaccination Technical Working Group and the COVID-19 Vaccination Working Group in the Child Population December 2021]. https://www.sanidad.gob.es/profesionales/saludPublica/prevPromocion/vacunaciones/covid19/Actualizaciones_Estrategia_Vacunacion/docs/COVID-19_Actualizacion10_EstrategiaVacunacion.pdf
21. Demonbreun AR, Sancilio A, Vaught LA, et al. (2021) Antibody titers before and after booster doses of SARS-CoV-2 mRNA vaccines in healthy adults. medRxiv2021.11.19.21266555. https://doi.org/10.1101/2021.11.19.21266555
22. Ministerio de Sanidad (2021) [COVID-19 early detection, surveillance and control strategy. Updated December 1, 2021]. https://www.mscbs.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/documentos/COVID19_Estrategia_vigilancia_y_control_e_indicadores.pdf
23. Mao S, Huang T, Yuan H, Li M, Huang X, Yang C, et al. (2020) Epidemiological analysis of 67 local COVID-19 clusters in Sichuan Province, China. BMC Public Health; 20: 1525. https://doi.org/10.1186/s12889-020-09606-4
24. Ayoub HH, Tomy M, Chemaitelly H, et al. (2022) Estimating protection afforded by prior infection in preventing reinfection: applying the test-negative study. MedRxiv 2022.01.02.22268622. https://www.medrxiv.org/content/10.1101/2022.01.02.22268622v1). preprint.
25. Strauss AL (1984) Chronic illness and the quality of life. St Louis: The C.V. Mosby Company.
26. WHO. International Statistical Classification of Diseases and Health-Related Problems. ICD-10 Version:2019. https://icd.who.int/browse10/2019/en
27. Royal Collage of General Practitioners (1986) The Classification and Analysis of General Practice Data. Occasional Paper 26.
28. Donaldson RJ, Donaldson LJ (1983) Essential Community Medicine. Lancaster: MTP Press.
29. Turabian JL (2017) Family Genogram in General Medicine: A Soft Technology that can be Strong. An Update. Res Med Eng Sci; 3(1). http://crimsonpublishers.com/rmes/pdf/RMES.000551.pdf
30. Russell LT (2020) Capturing Family Complexity in Family Nursing Research and Practice. J Fam Nurs; 26(4):287-293. 10.1177/1074840720965396
31. Watts C, Shrader E (1998) How to do (or not to do)… The genogram: a new research tool to document patterns of decision-making, conflict and vulnerability within households. Health Policy Plan; 13: 459-64. https://academic.oup.com/heapol/article/13/4/459/596227
32. McIlvain H, Crabtree B, Medder J, Stange KC, Miller WL (1998) Using practice genograms to understand and describe practice configurations. Fam Med; 30: 490-6. https://pubmed.ncbi.nlm.nih.gov/9669161/
33. Consejería de Sanidad Castilla La Mancha (2021). https://sanidad.castillalamancha.es/ciudadanos/enfermedades-infecciosas/coronavirus/preguntas-frecuentes-sobre-el-coronavirus-covid-19/campa%C3%B1a-vacunacion
34. McNamara D (2022) [Could the omicron wave hasten the transition from pandemic to endemic?[. Medscape; 6 de enero. https://espanol.medscape.com/verarticulo/5908352?uac=3

27178AR&faf=1&sso=true&impID=3937062&src=mkm_latmkt_220111_mscmrk_mdsms_excnws_nl#vp

35. Robitzski D (2922) How Mild Is Omicron Really? Early reports that Omicron causes less-severe disease than Delta seem to be borne out, but it's not yet clear to what extent that's due to the variant itself versus the populations it's infecting. The Scientist; Jan 14. https://www.the-scientist.com/news-opinion/how-mild-is-omicron-really-69610?utm_campaign=TS_Newsletter_RAN_Immunology&utm_medium=email&_hsmi=203515489&_hsenc=p2ANqtz-8IBMdW-YHi_kxeZTMgpzQQd7c8-fsHiXPf0kZfauj24i3Bv4-cx6XcV0-gLex42atOj4UGY3tSwGyyDNhrWnpC7sbPHg&utm_content=203515489&utm_source=hs_email
36. Alonso S (2022) [As many infections in the sixth wave as the sum of all the previous ones]. La Razón; 31-01-2022. https://www.larazon.es/sociedad/20220131/65vs3mav25c47byyt3mgmrrsfa.html
37. Informe ejecutivo vacunación COVID19. Ministerio de Sanidad. Gobierno de España.
38. https://www.sanidad.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/documentos/Informe_GIV_comunicacion_20220225.pdf
39. Altarawneh HN, Chemaitelly H, Hasan HR, et al. (2022) Protection against the Omicron Variant from Previous SARS-CoV-2 Infection. N Engl J Med. https://www.nejm.org/doi/full/10.1056/NEJMc2200133?query=WB&cid=NEJM%20Weekend%20Briefing,%20February%2019,%202022%20DM740450_NEJM_Non_Subscriber&bid=838573606
40. Gray GE, Collie S, Garrett N, et al. (2021) Vaccine effectiveness against hospital admission in South African health care workers who received a homologous booster of Ad26.COV2 during an Omicron COVID19 wave: Preliminary Results of the Sisonke 2 Study. MedRxiv2021.12.28.21268436. https://doi.org/10.1101/2021.12.28.21268436
41. Shuai H, Chan JFW, Hu B, et al. (2022) Attenuated replication and pathogenicity of SARS-CoV-2 B.1.1.529 Omicron. Nature(2022). https://doi.org/10.1038/s41586-022-04442-5
42. ZOE COVID Study (2021) What are the new top 5 covid symptoms? https://covid.joinzoe.com/post/new-top-5-covid-symptoms#part_1
43. Roy M (2021) Most Reported U Omicron Cases Have Hit the Fully Vaccinated: CDC. Medscape; December 13. https://www.medscape.com/viewarticle/964600?uac=327178AR&faf=1&sso=true&impID=3926846&src=wnl_tp10n_220106_mscpedit
44. Iacobucci G (2021) Covid-19: Runny nose, headache, and fatigue are commonest symptoms of omicron, early data show. BMJ; 375: n3103. https://doi.org/10.1136/bmj.n3103
45. Ledford H (2021) How severe are Omicron infections? As cases spread and countries plan their response, researchers await crucial data on the severity of the disease caused by the coronavirus variant. Nature; 600: 577-8. https://doi.org/10.1038/d41586-021-03794-8
46. Wu M, Wall EC, Carr EJ, et al. (2022) Three-dose vaccination elicits neutralising antibodies against omicron.Lancet; 399(10326): 715-7. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00092-7/fulltext?dgcid=raven_jbs_etoc_email
47. Munro APS, Janani L, Cornelius V, et al. (2021) Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK (COV-BOOST): a blinded, multicentre, randomised, controlled, phase 2 trial. *Lancet*. https://doi.org/10.1016/S0140-6736(21)02717-3
48. Pajon R, Doria-Rose NA, Shen X, et al (2022) SARS-CoV-2 Omicron Variant Neutralization after mRNA-1273 Booster Vaccination, N Engl J Med. https://www.nejm.org/doi/full/10.1056/NEJMc2119912?query=TOC&cid=NEJM%20eToc,%20January%2027,%202022%20DM662764_NEJM_Non_Subscriber&bid=797873248
49. Crist C (2021) COVID Booster Protection May Wane in About 10 Weeks, New Data Show. Medscape; Dec 27. https://www.medscape.com/viewarticle/965612?spon=34&uac=327178AR&impID=3915076&sso=true&faf=1&src=WNL_mdpls_211231_mscpedit_fmed
50. Segura A (2021) [Another (plausible) account of the pandemic is possible]. Salud, dinero y atención primaria: Viernes, 31 de Diciembre. https://saludineroap.blogspot.com/2021/12/es-posible-otro-relato-verosimil-de-la.html
51. Sidik SM (2022) Immunity against Omicron from breakthrough infection could be a matter of timing. Laboratory studies hint that a longer interval between vaccination and infection is better than a shorter one. Nature; 07 January. https://www.nature.com/articles/d41586-022-00004-x?utm_source=Nature+Briefing&utm_campaign=c5806cbdf7-briefing-dy-20220110&utm_medium=email&utm_term=0_c9dfd39373-c5806cbdf7-42937943
52. Ellis R (2022) Booster Effectiveness Wanes After 4 Months, Study Shows. Medscape; Feb 15, https://www.medscape.com/viewarticle/968512

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