

Covid-19 Breakthrough Infections in Vaccinated People Versus Covid-19 Infections People without Vaccination: Secondary Data Analysis of Clinical-Epidemiological Characteristics in a General Medicine Practice in Toledo (Spain)

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ABSTRACT

Background: COVID-19 infections and COVID-19 breakthrough infections in vaccinated people appear to have different clinical-epidemiological characteristics. **Objective:** To determine the differential clinical-epidemiological characteristics between COVID-19 breakthrough infections in vaccinated people vs. patients with COVID-19 without vaccination in general medicine. **Methodology:** Secondary analysis of data from patients diagnosed with COVID-19 from March 1 to May 31, 2020, and from March 15 to November 15, 2020, which were compared with data of a study of COVID-19 breakthrough infections in vaccinated people carried out from February 1, 2021 to September 30, 2021, in a general medicine office at a health center in Toledo, Spain. **Results:** COVID-19 breakthrough infections in vaccinated people vs. COVID-19 in unvaccinated patients, were statistically significant older (65.5 years vs. 41.61 years of mean), with more patients ≥ 65 years (27% vs. 10%), presenting more ENT symptoms (33% vs. 10%), fewer psychiatric symptoms (0% vs. 10%), and more chronic musculoskeletal diseases (19% vs. 10%). There was no difference by sex. Mild cases predominated in both groups. **Conclusion:** In the context of general medicine in Toledo (Spain), this secondary analysis of data from the same office, from the onset of the pandemic to when the delta variant became dominant but before the rise of omicron, suggests that COVID-19 breakthrough infections in vaccinated people vs. COVID-19 in unvaccinated occurs in older people and with more ENT symptoms.

Key words: COVID-19, SARS-CoV-2, Vaccination, Breakthrough Infection, General Practice, Secondary Analysis

INTRODUCTION

As of the date of November 2021 when this document is written, we are at a point in the COVID-19 pandemic in which we have countries in which there are still

high rates of circulation of SARS-CoV-2. Despite vaccination has advanced far enough, COVID-19 cases have been reported in fully vaccinated people. Scientific evidence has consistently shown that vaccines reduce the possibility of severe COVID-19 or death from it, so understanding the changes in the clinical

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presentation and evolution of the disease in vaccinated people is of great importance (1).

Since the start of the vaccination campaign, the development of COVID-19 has been reported in people who have received one or both doses of the vaccine (2). In public health, a “breakthrough case” is when a fully vaccinated person later gets the disease they were vaccinated for. No vaccine provides 100 percent protection against infection, so breakthrough cases are not new, and not unique, to COVID-19 (3).

Generally speaking, it would appear that vaccinated people who contract COVID-19 and suffer from symptoms are prone to them in the same way that an unvaccinated person might experience them. These include fever, cough, and shortness of breath, fatigue, body aches, headache, sore throat, congestion, nausea, vomiting, and diarrhea. Loss of taste or smell can sometimes serve as a telltale clue, although it doesn’t happen to all. What is probably different is the severity of the symptoms. So while a person who is not vaccinated may experience a very bad headache, a very severe sore throat, or very serious gastrointestinal problems, those same symptoms would be less severe in a person who is vaccinated (4).

Since the onset of the pandemic, general practitioners (GPs) have been familiar with the distinctive symptoms of contagion, including loss of taste or smell, fever, cough, shortness of breath, and fatigue. But what happens now, more than a year later, when in many countries more than half the population is vaccinated? Have symptoms changed since delta is the most common variant in some countries? There is little data on that and much remains to be clarified (5).

In this context, a study is presented based on the secondary analysis of data previously collected, processed, analyzed and published, referring to the same population attended in a general medicine consultation, and collected by the same GP researcher, which are used to compare clinical-epidemiological characteristics of COVID-19 breakthrough infections in vaccinated people vs. patients with COVID without vaccination.

MATERIAL AND METHODS

A secondary analysis of data collected, processed, analyzed, and published for purposes other than this research objectives, was conducted to compare clinical-epidemiological characteristics of COVID-19 breakthrough infections in vaccinated people vs. patients with COVID-19 without vaccination. Thus, this current study uses data from patients diagnosed with COVID-19 who consulted in general medicine office at a health centre in Toledo, Spain, from March 1 to May 31, 2020, and from March 15 to November 15, 2020 (6, 7) and a study of COVID-19 breakthrough infections in vaccinated people carried out from February 1, 2021 to September 30, 2021 (8).

We analyzed and compared confirmed cases of COVID-19 with positive polymerase chain reaction (PCR), with COVID-19 breakthrough infections in vaccinated people, all of them identified in same general practice clinic, and performed by the same investigator and GP, in order to determine the differential characteristics between COVID-19 breakthrough infections in vaccinated people vs. patients with COVID without vaccination. The methodology of the previous studies has already been published and It is presented here in summary form (6-8).

Study location

The study was conducted on data previously collected at a general medicine office in the Santa Maria de Benquerencia Health Centre, Toledo, Spain, which has a list of 2,000 patients >= 14 years of age. In Spain, GPs care for people >= 14 years of age, with exceptions requested by the child’s family and accepted by the GP).

Outcome of interest

The outcome of interest was determining the differential clinical-epidemiological characteristics between COVID-19 breakthrough infections in vaccinated people vs. patients with COVID-19 without vaccination.

Diagnosis of COVID-19 breakthrough infections in vaccinated people

To consider a person as fully vaccinated, it was required

1. That they have received 2 doses of vaccine separated by a minimum of 19 days if the first dose was BNT162b2 mRNA vaccine (Comirnaty, Pfizer / BioNTech), 21 days in the case of ChAdOx1 nCoV-19 vaccine (Vaxzevria, Oxford / AstraZeneca) or 25 days in the case of mRNA-1273 vaccine (Spikevax, formerly COVID-19 Vaccine Moderna), and that a minimum period of 7 days has elapsed since the last dose if the last dose was with BNT162b2 mRNA vaccine (Comirnaty), or 14 days if it was with ChAdOx1 nCoV-19 vaccine (Vaxzevria) or mRNA-1273 vaccine (Spikevax). People who received a dose of Janssen vaccine (Johnson & Johnson vaccine) more than 14 days ago were also considered fully vaccinated. In Spain, these four vaccines are currently available, all of which have been approved by the European Medicines Agency (9).
2. Or, that having passed the disease they have received a dose of any of the vaccines, after the minimum period equal to that established for the second doses.
3. In the heterologous regimen in which Vaxzevria (Oxford / AstraZeneca) is used in the first dose and mRNA vaccines in the second, it was considered fully vaccinated after 7 days if the second dose was with Comirnaty, or after 14 days if it was with the Moderna vaccine (10)

COVID-19 diagnosis

Diagnosis was performed with PCR oropharyngeal swab test (11) or antigen test for symptomatic patients with less than 5 days of evolution (from December, 2020). The PCR tests were performed both in symptomatic patients and in asymptomatic contacts. 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 (12).

Because of, since the outbreak began, diagnostic tests were not available at the primary care level, since the instructions were as of March 18, 2020, that diagnostic test for SARS-CoV-2 was performed at people admitted to the hospital, and in respiratory infection of any degree in health personnel. Since May 19, 2020 PCR began to be carried out on suspected COVID-19 cases and contacts in general medicine (13, 14). In the consultation object of the study, no population screening activity was carried out to detect COVID-19 positive people without symptoms and without suspected contacts. But PCR tests were carried out in asymptomatic people before their incorporation to social health work or hospital admissions or in programmed nursing homes.

Collected variables

Data on the index case and close contacts were extracted from the medical records of the general medicine practice under study. The following variables were collected: age, sex, socio-health worker, symptoms, severity of COVID-19 infections (mild cases: clinical symptoms are mild and no manifestation

of pneumonia could not be found on images; moderate cases: with symptoms such as fever and respiratory tract symptoms, and the manifestation of pneumonia can be seen on the imaging tests; and severe cases: respiratory distress, respiratory rate ≥ 30 breaths / min., pulse oxygen saturation $\leq 93\%$ with room air at rest, arterial partial pressure of oxygen / oxygen concentration ≤ 300 mmHg.) (15); to simplify comparison, moderate and severe cases were counted together, 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” (16), classified according to the International Statistical Classification of Diseases and Health-Related Problems, CD-10 Version: 2019 (16).

Statistic analysis

The bivariate comparisons were performed using the Chi Square test (X²) or Fisher Exact Test, for percentages (according to the number the expected cell totals), and the Student t test for the mean.

RESULTS

COVID-19 breakthrough infections in vaccinated people vs. COVID-19 in unvaccinated patients, were statistically significant older (65.5 vs. 41.61 years), with more patients > 65 years (27% vs. 10%), presenting more ENT symptoms (33% vs. 10%), and fewer psychiatric symptoms (0% vs. 10%), and more chronic musculoskeletal diseases (19% vs. 10%). There was no difference by sex. Mild cases predominated in both groups (TABLES 1, 2, and 3)

Table 1: Comparison between covid-19 in unvaccinated people and covid-19 breakthrough infections in vaccinated people

VARIABLES	COVID-19 IN UNVACCINATED PEOPLE (symptomatic and asymptomatic) N=100	COVID-19 breakthrough infections in vaccinated people (symptomatic and asymptomatic) N=30	STATISTICAL SIGNIFICANCE
Age in years (arithmetic mean and standard deviation)	41.61+-17.65 (Range: 2-80 years)	65.5+-14.71 (Rango: 26-84 years)	t-value= -4.19869. p= .000025. Significant at p < .05.
> = 65 years	10 (10)	8 (27)	X2 with Yates correction= 4.0673. p= .04372. Significant at p < .05.
Children and adolescents <= 22 years	11 (11)	0	Fisher exact test= 0.0672. NS
Women	54 (54)	16 (53)	X2= 0.0041. p= .948778. NS

Socio-health workers	11 (11)	5 (17)	Fisher exact test= 0.5255. NS
Gravedad moderada-severa	3 (3) [3 neumonías]	2 (7) [2 neumonías y 1 trombosis venas ováricas en el mismo paciente]	Fisher exact test= 0.326. NS
Exitus	1 (1)	0	Fisher exact test= 1. NS
Chronic diseases presence	51 (51)	17 (57)	X2= 0.297. p= .585742. NS

(): Denotes percentages; NS: Not significant

Table 2: comparison of chronic diseases between covid-19 in unvaccinated people and covid-19 breakthrough infections in vaccinated people

CRHONIC DISEASES ACCORDING TO WHO, ICD-10 GROUPS*	COVID-19 IN UNVACCINATED PEOPLE (symptomatic and asymptomatic) N=100	COVID-19 breakthrough infections in vaccinated people (symptomatic and asymptomatic) N=30	STATISTICAL SIGNIFICANCE
-II Neoplasms	3 (3)	0	Fisher exact test= 0.2686. NS
-II Diseases of the blood	1 (1)	2 (2)	Fisher exact test= 0.5704. NS
-IV Endocrine	26 (23)	13 (16)	X2= 1.3022. p= .253809. NS
-V Mental	11 (10)	4 (5)	X2= 1.4493. p= .228646.
-VI-VIII Nervous and Senses	9 (8)	10 (13)	X2= 1.105. p= .293177. NS
-IX Circulatory system	16 (14)	10 (13)	X2= 0.1043. p= .746681. NS
-X Respiratory system	12 (10)	3 (4)	X2= 3.0626. p= .080114. NS
-XI Digestive system	11 (10)	12 (15)	X2= 1.2605. p= .261559. NS
-XII Diseases of the skin	3 (3)	0	Fisher exact test= 0.2686. NS
-XIII Musculo-skeletal	10 (9)	19 (24)	X2= 8.226. p= .004129. Significant at p < .05.
-XIV Genitourinary	10 (9)	6 (8)	X2= 0.1073. p= .743184. NS
TOTAL*	112 (100)	79 (100)	-

(): Denotes percentages; NS: Not significant; *Patients could have more than one chronic disease. The percentages of chronic diseases are over the total of chronic diseases

Table 3: Comparison of symptoms between covid-19 in unvaccinated people and covid-19 breakthrough infections in vaccinated people

SYMPTOMS * ACCORDING TO WHO, ICD-10 GROUPS	COVID-19 IN UNVACCINATED PEOPLE (symptomatic) N=15	COVID-19 breakthrough infections in vaccinated people (symptomatic) N=30	STATISTICAL SIGNIFICANCE
General (discomfort, asthenia, myalgia, fever, artralgiás)	24 (31) [Fever 10, myalgia 6, asthenia 4, discomfort 4]	15 (21) [Fever 10, asthenia 2, discomfort 3]	X2= 1.7847.p= .181576. NS
Respiratory (cough, dyspnea, chest pain)	19 (25) [chest pain 2, cough 10, dyspnea 7]	19 (27) [chest pain 1, cough 18]	X2= 0.1165. p= .732893. NS
ENT (Anosmia / ageusia, odynophagia, rhinorrhea, pharyngeal dryness-mucus, epixtasis)	8 (10) [Anosmia / ageusia 4, rhinorrhea 1, odynophagia 3]	23 (33) [Anosmia 1, rhinorrhea 3, odynophagia 11, pharyngeal mucus 3, nasal congestion 5]	X2= 11.1224. p= .000853. Significant at p < .05.

Digestive (anorexia, nausea / vomiting, diarrhea, abdominal pain)	9 (12) [Anorexia 1, vomiting, 4, diarrhea 3, dysphagia 1]	5 (7) [Anorexia 2, vomiting, 1, diarrhea 2]	X2= 0.8792. p=.348425. NS
Neurological (headache, dizziness, mental confusion -brain fog)	7 (9) [Headache 6, Upper limb tremor 1]	8 (12) [Headache 6, dizziness 2]	X2= 0.2187. p=.640049. NS
Psychiatric (Anxiety, insomnia)	8 (10)[Anxiety 4, insomnia 4]	0	Fisher exact test= 0.0068. Significant at p < .05.
Skin (chilblains, flictenas, rash)	2 (3) [Chilblains 1, petechiae 1]	0	Fisher exact test= 0.4977. NS
Total symptoms*	77 (100)	70 (100)	-

(): Denotes percentages; NS: Not significant; *Patients could have more than one symptom; the percentages are over the total of symptoms

DISCUSSION

The benefits of COVID-19 vaccines are substantial, and their rapid implementation is a major public health achievement (17). COVID-19 cases after vaccination are rare (when the Delta variant was becoming predominant and before the arrival of Omicrom); So, we found in the population of this study, in a previous investigation, an incidence rate of COVID-19 breakthrough infections in vaccinated people > 14 years in GP consultation of 1.5% cases x 8 months (18).

Unfortunately, given that a proportion of COVID-19 patients after vaccination are asymptomatic, it is challenging to know the true prevalence of the disease after vaccination. It has been reported that in this 1.5% of vaccinated people the presence of the virus is limited to the nose and nasopharynx, while the lungs are free; therefore: those vaccinated in rare cases can become infected and, in an additional subgroup, have a high viral load, as can the unvaccinated. The difference is that, while an unvaccinated person remains infected, and therefore is contagious, for several days and can become seriously ill, the vaccinated person has a short time (1-2, maximum 3 days) to transmit the infection and is also very rare to have severe symptoms (19).

A link has also been shown between higher levels of neutralizing antibodies and a lower probability of progressive infection (20). Four out of 10 people (including hematologic and solid organ cancers, end-stage liver and kidney disease, organ transplants, and immune-mediated inflammatory disease such as inflammatory bowel disease, vasculitis, or rheumatoid arthritis) who are clinically vulnerable generate lower levels of antibodies than healthy recipients after two injections of the SARS-CoV-2 vaccine, according to one study (21).

Gravity

So far we know (when the Delta variant was becoming predominant and before the arrival of Omicrom) that the

majority of patients with COVID-19 after vaccination tend to have mild disease, of shorter duration, or even remain asymptomatic, reducing associated infectivity, severe disease, hospitalization and death; even with respect to the delta variant. Thus, the majority of people admitted to hospital after vaccination became infected before immunity could develop (5, 17, 22-30). Likewise, in black adults and Hispanic adults, who have been disproportionately affected by COVID-19, mRNA-based vaccines were equally effective with respect to hospitalization associated with COVID-19 (31).

However, COVID-19 breakthrough infections in vaccinated people could be due to vaccination failure, which means that the vaccine did not provide the person with immunity; a fact that is not unexpected, since vaccines are not 100% effective (32). So far, factors associated with suffering from severe COVID-19 after vaccination have not been clearly identified, although it is considered that age over 65 years, a history of chronic diseases or immunocompromise could be associated with serious conditions. In a study 14 cases of severe COVID-19 were reported after vaccination, with a mean age of 80.5 years and all with comorbidities (obesity, cardiovascular disease, lung disease, cancer and type 2 diabetes); On the other hand, others researchers identified certain risk factors: Down syndrome, kidney transplant, sickle cell anemia, chemotherapy, nursing home residence, HIV / AIDS, liver cirrhosis, neurological conditions, recent transplantation bone marrow or ever solid organ transplant, dementia, and Parkinson's disease (33).

In our study, mild cases prevailed in both COVID-19 breakthrough infections in vaccinated people and COVID-19 in unvaccinated people, and there was more chronic musculoskeletal diseases in COVID-19 breakthrough infections in vaccinated people vs COVID-19 in unvaccinated people (19% vs. 10%), probably related to the fact that the cases of COVID-19 breakthrough infections in vaccinated people were older.

Age and gender

As of April 2021, in the United States, the population infected with vaccination was constituted by 63% of women (proportional to the proportion of vaccinated); the median age was 58 years (34). Data suggest that the risk of SARS-CoV-2 infection after vaccination is reduced in older age groups (35). And the effectiveness of the vaccine against hospitalization has been reported to be significantly lower among adults 75 years and older (23). Along the same lines, our study shows that COVID-19 breakthrough infections in vaccinated people vs. COVID-19 in unvaccinated patients were statistically significant older and with more patients ≥ 65 years.

Symptoms of COVID-19 breakthrough infections in vaccinated people vs. infections in not vaccinated people

COVID-19 presentations in not vaccinated people have ranged from mild / asymptomatic symptoms to severe illness and mortality. While a wide range of symptoms can accompany COVID-19, the CDC says that a vast majority of patients in a recent study exhibited one of three symptoms: fever, cough, and shortness of breath. Centers for Disease Control and Prevention study involved 164 people in 16 states who had confirmed cases of the corona virus between January 14 and April 4, 2020; Researchers found that 96% of patients had a fever, cough, or difficulty to breathe. About 45% had all three symptoms. The most common symptom was cough (84%) followed by fever (80%). The COVID-19 patients also showed other symptoms, such as chills, muscle pain, headaches, fatigue, and digestive problems such as nausea, abdominal pain, vomiting, or diarrhea. About half of the patients reported one or more gastrointestinal symptoms; among these, diarrhea was reported more frequently (38%) and vomiting less frequently (13%) (36).

Other more recent reports have identified a variety of symptoms associated with COVID-19. These include fever or chills, cough, shortness of breath or shortness of breath, fatigue, muscle or body aches, headache, new loss of taste or smell, sore throat, stuffy or runny nose, nausea or vomiting and diarrhea, and others such as malaise (37-40). Anosmia, ageusia, fever, new persistent cough, chills, loss of appetite, and muscle pain have been reported to be the seven symptoms that (out of a total of 26) best predict a positive test result for SARS-CoV infection. 2 in adults, based on a British analysis of more than 1 million participants studied between June 2020 and January 2021 (41, 42).

Symptoms are similar in children, although headache replaces persistent cough in the top 7 symptoms and the presence of rhinorrhea slightly decreases the probability of a positive test (41, 42).

We report in a study in the population of the GP consultation,

from March 9 to April 3, 2020, where COVID-19 diagnostic test was not initially performed, the patients who should be considered as probable COVID-19: 1) presence of fever, dyspnea, diarrhea, nausea / vomiting, or physical signs of pneumonia, with long duration of symptoms, in male patients or over 65 years; and / or 2) presence of chronic diseases of the circulatory system, the self-communication of possible contact with a COVID-19 patient, the visit to the services of emergency or hospital, or being healthcare personnel / working in healthcare settings (43).

Symptoms in COVID-19 breakthrough infections in vaccinated people

So far we know that the majority of patients with COVID-19 after vaccination usually have mild disease or even remain asymptomatic (1). The symptoms with which COVID-19 manifested at the beginning of the pandemic are no longer the same as in the vaccinated population. The symptoms of COVID-19 change for those vaccinated. Fever is no longer the most permanent symptom, neither is the loss of taste and smell, and rhinorrhea, sore throat or dry cough and headache appear as very frequent symptoms in people with the vaccine (44).

In a study conducted in Israel, of 1,497 health workers fully vaccinated, 39 (2.6%) were positive for SARS-CoV-2, of which 69% were tested solely for having had contact with someone positive. Of the 39 patients who had COVID-19 after vaccination, 33% remained asymptomatic and among the symptomatic, 36% reported nasal congestion, 28% myalgia, 28% loss of smell or dysgeusia, and 21% fever. None were hospitalized. This report shows that COVID-19 symptoms after vaccination are usually mild and the proportion of asymptomatic adults is probably higher in vaccinated versus unvaccinated people (1).

Researchers from the ZOE COVID Symptom Study say that the five most common symptoms experienced by people vaccinated against SARS-CoV-2 are headache, runny nose, sneezing, sore throat and loss of smell. Additionally, those on the vaccine experience fewer symptoms in a shorter period of time, suggesting that they became less seriously ill and improved more quickly (45).

Among vaccinated adults symptoms are more closely related to the common cold; There are coughing, but also a higher prevalence of runny noses and sneezes; Headaches and sore throats are other top complaints. Fever and loss of taste and smell are being reported to a lesser extent (5). Researchers began to see milder symptoms when the delta variant became prevalent in the UK in late spring, which also coincided with the country's mass vaccination program (5).

It was communicated almost all of the individual symptoms of COVID-19 were less common in vaccinated participants

than unvaccinated ones, and more people in vaccinated than unvaccinated groups were completely asymptomatic. This increased incidence of asymptomatic or minimally symptomatic infection in vaccinated participants underscores the importance that individuals who interact with unvaccinated or clinically vulnerable groups (eg, healthcare workers and social care workers) continue to be tested for SARS-CoV-2 regularly, even if vaccinated (35).

Again, our results support the previous data. We found that COVID-19 breakthrough infections in vaccinated people vs. COVID in non-vaccinated patients presented statistically significantly more ENT symptoms (33% vs. 10%)

Comorbidities

Several comorbidities, including heart disease and lung disease, were significantly associated with post vaccination infection after one dose in older adults; although associations of marginal importance should be interpreted with caution, many of these comorbidities confer an increased risk of severe disease, hospitalization, mechanical ventilation, and mortality from COVID-19 (35). We found that COVID-19 breakthrough infections in vaccinated people vs. COVID in non-vaccinated patients had statistically significant more chronic musculoskeletal diseases. This finding is possibly related to the older age of COVID-19 breakthrough infections in vaccinated people, as well as health behaviours and seeking medical attention (46, 47). In this regard, it has been reported that patients with inflammatory rheumatic disease were more likely to be admitted with COVID-19 than the general population, and patients admitted for COVID-19 with rheumatoid arthritis could be at higher risk of a serious outcome. (48); and lupus patients have an increased susceptibility to infections due to autoimmune dysregulation and use of immunosuppressive therapy (49).

Healthcare workers

The risk of reporting a positive SARS-CoV-2 test is higher among frontline healthcare workers than the general population likely reflecting increased exposure and testing (35). But, we did not find statistically significant differences between healthcare workers with COVID-19 breakthrough infections in vaccinated people vs. COVID in unvaccinated.

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.
3. 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 context of general medicine in Toledo (Spain), this secondary analysis of data, from the onset of the pandemic to when the delta variant became dominant but before the rise of omicron, in the same office, suggests that COVID-19 breakthrough infections in vaccinated people vs. COVID in unvaccinated occur in older people and with more ENT symptoms, fewer psychiatric symptoms (possibly a variable associated with younger people and / or with the distress of the first wave of the pandemic) and more chronic musculoskeletal diseases (possibly a variable associated with older people), and in both cases mild symptoms predominate.

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