RESEARCH ARTICLE

Transmissibility of Sars-Cov-2 within Families Comparing Fully Vaccinated Individuals in 2021 Versus Unvaccinated in 2020. Vaccine Prevents A Third of Contagions among Household Contacts

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: It is not clear whether vaccine against SARS-CoV-2 protects members within households. **Objective:** Evaluation of variation of the transmissibility of SARS-CoV-2 in vaccinated family members (in 2021) versus in not vaccinated (in 2020). **Methodology:** Comparison of secondary data from two observational, longitudinal, and prospective studies of families with unvaccinated secondary cases from March 15 to December 31, 2020, and secondary cases in vaccinated 2 doses people from February 1 to November 30, 2021, in the same population of patients treated in a general medicine office in Toledo, Spain. **Results**: In 2020, crude secondary attack rate (SAR) in total exposed people was 76%. In 2021, crude SAR in total people exposed and fully vaccinated was 53%. Vaccine effectiveness (VE) against transmission among household contacts [1− (SAR in vaccinated people/SAR unvaccinated people) ×100%] was 30%. Secondary cases in fully vaccinated family members in 2021 vs. Secondary cases of unvaccinated family members in 2020 differed statistically significantly in being more chronically ill and with more ENT and neurological symptoms. **Conclusion**: In the context of general medicine in Toledo (Spain), the VE against transmission among household contacts in 2021 (alpha and delta variants, with higher transmissibility than previous variants) vs. transmission in families without vaccination in 2020 (lineage A of the coronavirus and variant 20E/EU1) allowed to prevent a third of infections in the family. However, the small sample analyzed generates uncertainty in the estimates.

Key words: COVID-19, SARS-CoV-2, Epidemiological characteristic, Household contact, Secondary attack rate, Vaccination, Breakthrough Infection, General Practice.

INTRODUCTION

Familial infections of viral diseases are not usually studied, and thus studies that assess the probability of a pathogen spreading from an infected individual to a healthy one, that is, the transmissibility, within the family are not frequent. Therefore, the risk of secondary transmission given an index case in a household is unclear for most viral infectious diseases. Furthermore, classic chains of transmission may not fully explain transmission, as many respiratory viruses depend on time and proximity, and the context of the family is the classic scenario where these factors are found. Knowledge of these data could offer critical information on prevention and control decisions (1-3).

As the number of people vaccinated against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) increases around the world, population-level data on the ability of vaccines to reduce infection is generated. The studies that have accumulated both pre and post-marketing of the vaccines have

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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shown that they significantly reduce the symptoms of covid-19. However, little is known about its effects on transmission between individuals (4), and even less is known about whether vaccinating individuals against SARS-CoV-2 protects their family members (5). In addition, a variable degree of decreased immunity is known to occur after all vaccines studied to date, and this loss of protection was likely augmented by the increased prevalence of the delta variant(6).

Control of the SARS-CoV-2 pandemic requires interventions based on accurate estimates of transmission. The variables involved in transmission may vary depending on the interventions to reduce the disease and the structure of the population, as well as the properties of the SARS-CoV-2 variant (7). Although the prevention of serious illness and death remains the main public health goal in the acute phase of the pandemic, and this is being achieved with available COVID-19 vaccines despite the emergence of the delta variant, address the issue of the transmission of SARS-CoV-2 is an additional factor of paramount importance that must be taken into account: that is, it is necessary to reduce transmission to reduce the circulation of the virus in the community (8).

Therefore, assessing how well SARS-CoV-2 vaccines can reduce transmission has important epidemiological, social, and political implications, as ineffective reduction of transmission by vaccines would hamper efforts to achieve herd immunity (4). In this situation, households are an ideal setting to assess virus transmission and the effects of vaccination through the secondary attack rate (SAR) among household members (9,10).

In this context, the present study aimed to compare some selected variables in cases of covid-19 and the rate of home secondary transmission of SARS-CoV-2, using secondary data from the same population attended in a general medicine consultation in two time periods, one in 2020 where individuals had not yet received a covid-19 vaccine, and another in 2021 in relatives who had completed vaccination, and thus calculate the relative effectiveness of the vaccine in terms of intra-family transmission of cases primary to secondary.

MATERIAL AND METHODS

This study compares data from two previous studies:

1. An observational, longitudinal and prospective study of families in which there was one confirmed covid-19 case (primary case) and at least one subsequent secondary case within the family, that was conducted from March 15 to December 31, 2020 (11). In this period, from March to April, in Spain, the A lineage of the coronavirus predominated, especially the SEC7 and SEC8, and from summer to December, 2020, the 20E (EU1) variant (12, 13).

2. An observational, longitudinal and prospective study of all families in which there was one case of covid-19 (primary case), and at least one other member in the household with breakthrough infection with a full vaccination schedule (2 doses), that was conducted from February 1 to November 30, 2021 (before beginning with COVID-19 Vaccine Booster) (14). In this period, from January 2021 the alpha variant predominated, and from the summer-autumn of 2021 the delta variant (15, 16).

The two studies were conducted on the same population: patients seen 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 (17). The methodology of both studies has been previously published (11, 14). This methodology will only be partially mentioned here, to avoid repetition.

Outcomes of Interest

The outcomes of interest were:

1. Assess secondary transmission of SARS-CoV-2 from index cases in the family, comparing secondary transmission from people vaccinated with the complete regimen to other family members versus from unvaccinated people to other family members. In this way, the selected variables of the secondary cases of unvaccinated primary cases in the family (in 2020) are compared with the secondary cases of fully vaccinated primary cases in the family (in 2021).

2.-Calculate Vaccine effectiveness (VE) against infection among household secondary contacts (vaccinated) in 2021 vs. infection among household secondary contacts no vaccinated) in 2020.

Secondary Attack Rate

SAR was defined as the number of new cases (infection events) divided by the number of people exposed to a primary case during the follow-up time (18). The existence of second or third generation cases was not assessed. The cases for the determination of the attack rate included confirmed symptomatic cases and asymptomatic cases.

Household Contacts

Household contacts were defined as people who shared a residence with the covid-19 index case from 4 days before and for more than 24 hours after the primary cases developed illness. Presumed household transmission of an index case in households was considered when secondary transmission occurred from 1 to 14 days (19). The onset date of a confirmed

case was defined as the date of the first appearance of self-reported clinical symptoms, and in asymptomatic cases when a positive covid-19 PCR test was obtained (20, 21).

Calculation of VE Against Transmission Among Household Contacts

VE against transmission was calculated via SAR among close contacts of confirmed index cases (22-25):

[1 − (SAR in vaccinated people/SAR unvaccinated people)] × 100%

Collected Variables

Age, Sex, Symptomatic / asymptomatic covid-19, symptoms, severity of the disease (21), chronic diseases (26), classified according to the International Statistical Classification of Diseases and Health-Related Problems, CD-10 Version: 2019 (27), social-occupancy class (28), problems in the family context and low income household based on the genogram and in the experience of the general practitioner (GP) for their continuity of care and knowledge of the family (29), number of family members, and ethnic minority.

Sample

All families where a secondary case of covid-19 was diagnosed in each study, during the follow-up periods, in the consultation, were included.

Statistic analysis

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

RESULTS

In the 2020 study, 39 primary covid-19 cases not vaccinated in 39 families (92 people exposed in total families) and 70 secondary cases not vaccinated with covid-19 were included (Crude SAR in total people exposed: 70/92=76%). In the 2021 study, 13 primary cases of covid-19 breakthrough infection in fully vaccinated people in 13 families (33 people exposed in all families), with 20 secondary cases: 9 secondary cases of covid-19 breakthrough infection in fully vaccinated, 6 cases not fully vaccinated, and 5 not vaccinated were included (Crude SAR in the total number of exposed and fully vaccinated people: 9/17=53%). VE against transmission among household contacts [1− (SAR in vaccinated people/ SAR unvaccinated people) ×100%] = 30%.

Secondary cases in fully vaccinated family members in 2021 vs. Secondary cases of unvaccinated family members in 2020 differed statistically significantly in being more chronically ill and with more ENT and neurological symptoms. In addition, they were more male, older, higher income, with more members in the family, with fewer complex families, with less severity and mortality, more symptomatic, and shorter duration of symptoms; but all these differences were not statistically significant (**TABLE 1, TABLE 2, TABLE 3, TABLE 4**).

Table 1. Comparison of the variables studied between positive secondary cases in 2020 (without vaccine) and positive fully vaccinated secondary cases in family in 2021

VARIABLES	POSITIVE SECONDARY CASES IN 2020 -WITHOUT VACCINE (N= 70)	POSITIVE FULLY VACCINATED SECONDARY CASES IN 2021 (N= 9)	STATISTICAL SIGNIFICANCE
-Woman	51 (73)	5 (56)	Fisher exact test= 0.4355. NS
> = 65 years	6 (9)	2 (22)	Fisher exact test= 0.2246. NS
< 45 years	52 (74)	5 (56)	Fisher exact test= 0.2551. NS
-Workers with some type of specialization	20 (29)	2 (22)	Fisher exact test = 1. NS
-Ethnic minority	23 (33)	3 (33)	Fisher exact test = 1. NS
-Low income household	23 (33)	1 (11)	Fisher exact test= 0.2632. NS
-Complex family	12 (17)	0	Fisher exact test= 0.3408. NS
-Family with > = 4 members	38 (54)	6 (67)	X2 with Yates correction= 0.1207. NS
-Symptomatic	45 (64)	9 (100)	Fisher exact test= 0.0508. NS
-Moderate-severe severity	15 (21)	0	Fisher exact test= 0.1947. NS

-Exitus	1	0	Fisher exact test = 1. NS
-Duration of symptoms in days (arithmetic mean +- standard deviation and range)	5.52+-8.00 (Range*: 0-34 days)	4.11+-1.36 (Range: 2-7 days)	t-value= 0.52723. p= .299774. NS
-Presence of crhonic diseases	24 (34)	8 (89)	X2 with Yates correction= 7.7306. p= .005429. Significant at p < .05.

( ): Denotes percentages; NS: Not significant at p< .05;
*Asymptomatic cases (N=25) were computed as zero days of symptom duration

Table 2. Comparison of chronic diseases between positive secondary cases in 2020 (without vaccine) and positive fully vaccinated secondary cases in family in 2021

CRHONIC DISEASES* ACCORDING TO WHO, ICD-10 GROUPS	POSITIVE SECONDARY CASES IN 2020 -WITHOUT VACCINE) (N= 70)	POSITIVE FULLY VACCINATED SECONDARY CASES IN 2021 (N= 9)	STATISTICAL SIGNIFICANCE
-II Neoplasms	1 (1)	0	Fisher exact test = 1. NS
-III Diseases of the blood	0	1 (4)	Fisher exact test= 0.2556. NS
-IV Endocrine	21 (31)	6 (26)	X2= 0.2253. p= .635053. NS
-V Mental	10 (15)	1 (4)	Fisher exact test= is 0.2773. NS
-VI-VIII Nervous and Senses	6 (9)	1 (4)	Fisher exact test= is 0.673. NS
-IX Circulatory system	5 (8)	4 (18)	Fisher exact test= 0.2258. NS
-X Respiratory system	3 (5)	2 (9)	Fisher exact test= 0.5989. NS
-XI Digestive system	5 (7)	3 (13)	Fisher exact test= 0.4162. NS
-XII Diseases of the skin	3 (5)	0	Fisher exact test= 0.5671. NS
-XIII Musculo-skeletal	8 (12)	5 (22)	X2 with Yates correction= 0.6556. p= .418129. NS
-XIV Genitourinary	5 (7)	0	Fisher exact test= 0.3231. NS
TOTAL*=	67 (100)	23 (100)	---

( ): Denotes percentages; NS: Not significant at p< .05; *Patients could have more than one chronic disease. The percentages are over the total of chronic disease

Table 3. Comparison of symptoms between positive secondary cases in 2020 (without vaccine) and positive fully vaccinated secondary cases in family in 2021

SYMPTOMS*ACCORDING TO WHO, ICD-10 GROUPS	POSITIVE SECONDARY CASES IN 2020 -WITHOUT VACCINE)(N= 70)	POSITIVE FULLY VACCINATED SECONDARY CASES IN 2021 (N= 9)	STATISTICAL SIGNIFICANCE
General (discomfort, asthenia, myalgia, fever, artralgias)	38 (31)	6 (23)	X2= 0.7077. p= .400196. NS
Respiratory (cough, dyspnea, chest pain)	40 (33)	6 (23)	X2= 0.9916. p= .31935. NS
ENT (Anosmia / ageusia, odynophagia, rhinorrhea, pharyngeal dryness-mucus, epixtasis)	17 (14)	8 (31)	X2= 4.2387. p= .039513. Significant at p < .05.

Digestive (anorexia, nausea / vomiting, diarrhea, abdominal pain)	11 (9)	0	Fisher exact test= 0.3618. NS
Neurological (headache, dizziness, mental confusion -brain fog)	9 (7)	6 (23)	X2 with Yates correction= 4.1332. p= .04205. Significant at p < .05.
Psychiatric (Anxiety, insomnia)	3 (3)	0	Fisher exact test = 1. NS
Skin (chilblains, flictenas, rash)	3 (3)	0	Fisher exact test = 1. NS
Total symptoms*	121 (100)	26 (100)	---

( ): Denotes percentages; NS: Not significant at p< .05; * Patients could have more than one symptom. The percentages are over the total of symptoms

Table 4. Relative vaccine effectiveness against transmission among positive fully vaccinated secondary cases in family in 2021 versus positive secondary cases in 2020 (without vaccine)

POSITIVE FULLY VACCINATED SECONDARY CASES IN FAMILY IN 2021, REGARDING EXPOSED POPULATION FULLY VACCINATED	GROSS SAR	POSITIVE SECONDARY CASES IN 2020 (WITHOUT VACCINE), REGARDING THE EXPOSED POPULATION (WITHOUT VACCINE)	GROSS SAR
9/17	53%	70/92	76%
VE against transmission among household contacts [1 − (SAR in vaccinated people/SAR unvaccinated people) × 100%]= [1-(0.53/0.76)] x 100= 30%			

VE: Vaccine effectiveness; SAR: Secondary attack Rate

DISCUSSION

Vaccines have been shown to be effective in reducing the severity of SARS-CoV-2 infection (30-31), the risk of infection (32), and transmission (9), including within the household (33). There are several relevant features by which vaccine-induced immunity can reduce transmission: 1) Prevention of infection (34, 35); 2) viral replication (reduction of viral loads) (35-37); 3) Reduction of symptomatology (for example, coughing and sneezing); and 4) Induction of immune responses that reduce the infectivity of the virus released (4, 9, 38-40).

Vaccination effectiveness; Comparison with other studies The reduction in transmissibility can be evaluated by measuring the decrease in infections caused by vaccination. That is, counting the number of cases in the cohabitants of those who have been vaccinated, and comparing them with the number of cases in the cohabitants of unvaccinated people (41). The first effectiveness studies, which were carried out with the alpha variant, revealed a decrease in infections of around 30% (9, 40, and 42). Studies focused on vaccine efficacy against any SARS-CoV-2 infection caused by the delta variant showed estimates ranging from 18% to 85% approximately six months after completion of the primary vaccination course (43). On the other hand, vaccination has been reported to be associated with a smaller reduction in transmission of the delta variant than that of the alpha variant, and the effects of vaccination diminished over time (36, 44).

Although the vaccines that are currently available were not initially designed to prevent infection, it is now accepted that they do have that ability to some extent after the full course. It has been estimated that unvaccinated people would have a 12-fold higher risk of transmitting the virus than those who have been vaccinated (45); likewise, in a situation of the majority delta variant, fully vaccinated people would have a 50-60% reduction in the risk of infection (including asymptomatic people) compared to unvaccinated people (46, 47). Other studies show that vaccinated people have an 80-90% reduction in the risk of becoming infected (48) and an effectiveness against transmission between vaccinated people and close household contacts of around 70% (5, 24).

Another study has reported that one in four (25%) vaccinated people living in households with a COVID-19 case become infected, compared to 38% of unvaccinated contacts (between September 13, 2020 and September 15, 2021) (49, 50). Along the same lines, another study showed that the number of transmissions from unvaccinated controls was three times higher than that from fully vaccinated patients (during the first 8 months of 2021) (51). In other words, fully vaccinated people are less contagious than unvaccinated people (52,

53), and vaccinated people clear the virus from their bodies much faster and are less contagious than unvaccinated people; this even in the presence of the predominant delta variant (52, 54, 55). But a person vaccinated with a delta infection was almost twice as likely to transmit the virus as a person infected with alpha (56, 57). Therefore, transmission of SARS-CoV-2 between vaccinated persons is possible (58).

We found an EV against transmission between household contacts [1− (SAR in vaccinated persons/SAR in unvaccinated persons) × 100%] of 30%. It should be noted that our comparison of covid-19 cases in the two studies compares different time periods with prevalence of different variants of SARS CoV-2: During 2020, the A lineage of the coronavirus predominated first, especially SEC7 and SEC8, and from summer to December variant 20E (EU1) (12, 13). In the year 2021, from January the alpha variant predominated, and from the summer-autumn the delta variant (15, 16). In this regard, several scientific publications and technical reports report an increase in the transmissibility of the alpha variant with estimates of between 30% and 70% higher than the previously circulating variants (59-61). And after the appearance of the Delta variant, a marked reduction in vaccine efficacy against susceptibility to infection has been observed compared to the pre-Delta period (39, 62).

These data are also consistent with the highest secondary attack rate found by the Public Health Service in England: 12.9% for the new variant, confirmed or probable, compared to 9.7% for other variants (59). However, comparative conclusions should be taken with caution. The risk of infection after a vaccine may be modulated by patient characteristics (eg, age), circumstances (eg, time since vaccination), and virus characteristics (eg, lineage) (4). However, in this context of increased transmissibility, vaccination in our study managed to prevent a third of cases due to contact with a primary case in the family. On the other hand, we did not find a reduction in symptomatic infection in vaccinated cases, as has been reported in other studies (52), although with a shorter duration of symptoms. But it should be kept in mind, again, that we are comparing different variants of SARS CoV-2. In addition, preventive behaviour changes in vaccinated can be considered. Individuals with symptomatic infection will be more likely than those with asymptomatic infection to self-isolate, which could reduce the degree of transmission from them, despite the higher potential for transmissibility of these individuals (4). But this behaviour can be modified in vaccinated people considering that they will not be contagious.

In our study, secondary cases vaccinated in 2021 had more NCD symptoms than secondary unvaccinated cases in 2020. Data show that the virus can thrive in the respiratory tract of vaccinated individuals (64).

STUDY LIMITATIONS

1. Surveillance and genomic classification were not performed. Therefore, the estimation of the SARS CoV-2 variant could only be presumptive,

2. The sample of families included was not a probabilistic sample, but included all cases that consulted with their GP.

3. Preventive behaviours associated with transmission were not analyzed and could have been different during the study periods.

4. Third-generation cases were not identified, so all were considered secondary cases; thus, there could have been errors when classifying a tertiary case as a secondary case.

5. The sample was small, thus the statistical significance of some variables could be obscured and an imprecise determination of vaccine effectiveness could be obtained.

CONCLUSION

In the context of general medicine in Toledo (Spain), the relative VE against transmission among household contacts in 2021 (alpha and delta variants, with greater transmissibility of previous variants) vs. transmission in families without vaccination in 2020 (lineage A of the coronavirus and variant 20E/EU1) managed to prevent a third of infections in the family. These results support the key message that vaccinated contacts are better protected than unvaccinated contacts. But these results also highlight that breakthrough infections continue to occur in the vaccinated, with an attack rate of 53%. Our study unfortunately also highlights that the relative effect of the vaccine in reducing transmission is minimal in the context of alpha and delta variant circulation (2021 vs. 2020). However, the small sample analyzed generates a high degree of uncertainty in the estimates of the effectiveness of the vaccine against infectiousness. It can be concluded that vaccination reduces but does not eliminate the risk of covid-19 transmission within households. These findings have immediate implications for public health.

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