

Research Article

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Evolution of the Characteristics of Covid-19 Index Cases From the Year 2000 (Not Vaccinated) To 2021 (Vaccinated) Within the Families, in Toledo (Spain): The Importance of Psycho-Social Factors

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ABSTRACT

Background: It is not known whether there have been changes in the primary cases of covid-19, which are the gateway for SARS-CoV-2 in households and families, during the course of the pandemic.

Objective: Evaluate the variation of the clinical-epidemiological characteristics of the primary cases of covid-19 in households, in 2020 versus 2021.

Methodology: Comparison of secondary data from two observational, longitudinal, and prospective studies of families in 2020 and 2021 in the same population of patients treated in a general medicine office in Toledo, Spain.

Results: It was included 39 primary cases in 2020 unvaccinated and 25 primary cases vaccinated with one or two doses in 2021, within families. The 2020 family primary cases differed statistically significantly from the 2021 family primary cases in that they were younger and had fewer ethnic minorities. Also, the primary cases of 2020 were more women, with lower income and more complex families, compared to the primary cases of 2021, but without statistical significance. No statistically significant differences were found in the primary cases in families of 2020 and 2021 in symptoms or in chronic diseases.

Conclusions: In the context of general medicine in Toledo (Spain), the changes in the “gateway” (primary cases) of SARS-CoV-2 in families during the course of the pandemic (from 2020 to 2021) were basically due to psychosocial factors rather than biological factors.

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Introduction

Family infections of viral diseases, including respiratory ones, are not usually studied, so studies that assess the probability of spread of a pathogen from an infected individual to a healthy one, that is, 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. Much of our understanding comes from mathematical models [1].

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 provide information for disease transmission modelling and public

health policy [2-4].

For a communicable disease to appear and spread in the community a set of factors must concur that, interacting with each other, give rise to the disease process; This set of factors is called the triad or ecological/epidemiological chain: causal agent, route of transmission/environmental or contextual factors, and susceptible host [5].

In coronavirus disease 2019 (covid-19), its epidemiological chain can be broken down as follows [6]:

1. The agent is a virus called SARS-CoV-2. Like all viruses, it is constantly changing. These changes occur over time and can lead to the emergence of variants that may have new characteristics. In the course of the covid-19 pandemic, SARS-CoV-2 has mutated enough to escape first-line immune defences, specifically antibodies [7, 8].

2. The environment plays a very important role in the process of infection and propagation of diseases, since, depending on the environmental conditions, the infectious agents are capable or not of reaching the hosts. In covid-19, viral transmission occurs primarily between people via respiratory droplets and contact routes [9, 10].

3. Human beings and some animals can be considered as epidemiological hosts, whose mechanisms of susceptibility, resistance and/or immunity at the time of infection are deficient or favour contracting a disease. Any human being who does not have prior immune protection can be a host.

Households are an ideal setting to assess virus transmission and the effects of vaccination through the secondary attack rate among household members [11, 12]. A key element of the epidemiology of infectious diseases is to take into account spread in the home [13, 14]. The family affects the health of its members and is affected by them; that is why the family can be considered as a cause and consequence of infections. On the other hand, mild or some moderate patients with covid-19 without underlying chronic diseases can receive care from their relatives or caregivers [15, 16]. Informal caregivers are a critical extension of the health care system when patients are at home; during the covid-19 pandemic, they may also be the patient's closest contact and therefore their main source of risk for covid-19 infection [17].

In this scenario, domestic transmission of covid-19 is known to be important. In fact, the majority of SARS-CoV-2 transmission occurs in households [18]. SARS-CoV-2 is more transmissible in households than SARS-CoV and MERS-CoV, and the elderly ≥ 60 years are the most vulnerable to household transmission [19]. For example, in a study of household transmission in four US jurisdictions, Omicron infection resulted in high transmission among household contacts, particularly those living with index patients who were unvaccinated or without measures to reduce the risk of transmission to household contacts [20].

As with many new respiratory pathogens, the main epidemiological, clinical, and virological parameters of SARS-CoV-2, as well as the dynamics of the outbreak, were initially unknown. At this time, the extent of infection, the route of transmission, the full clinical picture of the disease, and the viral dynamics of COVID-19 are better known. But, it is still essential to understand the epidemiological, clinical and virological characteristics of the first cases of COVID-19 and their direct contacts in relation to the transmission of the covid-19 virus in households, on which to base the guidance and specific measures to the public health response in each community [21].

In this context, it is worth asking: Are primary cases, as the gateway for SARS-CoV-2 in families, different between 2020 and 2021? How does epidemiological triad vary, when the primary host in the family is vaccinated with 1 or 2 doses? We present a study that evaluates the variation of the clinical-epidemiological characteristics of the primary cases of covid-19 in households in 2020 versus 2021, using secondary data from the same population attended in a general medicine consultation in these two time periods, with the goal of approaching the knowledge of the relative importance of primary case in the epidemiological triad of covid-19 (causal agent, environment, and host) within the family.

Material and Methods

This study compares data from two previous studies:

1. A study of families in which there was one confirmed covid-19 case (primary case) and at least one subsequent secondary case within the family, from March 15 to December 31, 2020 [22]. 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 [23, 24].

2. A 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 vaccination (1 or 2 doses), that was conducted from February 1 to November 30, 2021 (before beginning with COVID-19 Vaccine Booster) [25, 26]. In this period, from January 2021 the alpha variant predominated, and from the summer-autumn of 2021 the delta variant was predominant [27, 28].

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 [29]. The methodology of both studies has been previously published [22, 25, 26], and here only some specific aspects are mentioned for this study to avoid repetition.

Outcomes of Interest

Evaluate the variation of the clinical-epidemiological characteristics of the primary cases of covid-19 in households in 2020 versus 2021.

Collected Variables

Age, Sex, symptoms, severity of the disease, chronic diseases, classified according to the International Statistical Classification of Diseases and Health-Related Problems, CD-10 Version: 2019, social-occupancy class, problems in the family context and low income household based on the genogram and in the experience of the GP for their continuity of care and knowledge of the family, number of family members, and ethnic minority [30-34].

Statistics 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.

Results

It was included 39 primary cases in 2020 and 25 primary cases vaccinated with one or two doses in 2021 within families. The 2020 family primary cases differed statistically significantly from the 2021 family primary cases in being younger and having fewer ethnic minorities. The primary cases of 2020 were more female, with lower income and more complex families, compared to the primary cases of 2021, but without statistical significance. No statistically significant differences were found in the primary cases in families in 2020 vs. 2021, in symptoms, nor in chronic diseases (Table 1, Table 2, Table 3).

Table 1: Comparison of Selected Variables between Primary Covid-19 Cases in 2020 and Primary Covid-19 Cases (Vaccinated 1 or 2 Doses) In 2021 within Families

VARIABLES	PRIMARY COVID-19 CASES IN 2020 (N = 39)	PRIMARY COVID-19 CASES (VACCINATED 1 OR 2 DOSES) IN 2021 (N=25)	STATISTICAL SIGNIFICANCE
-Woman	20 (51)	7 (28)	X2= 3.3858. p= .06576. NS
> = 65 years	0	6 (24)	Fisher exact test= 0.0024. Significant at p < .05.
-Ethnic minority	8 (20)	11 (44)	X2= 4.0261. p= .044802. Significant at p < .05.
-Social-occupancy class of patients (people with some type of labor specialization)	21 (54)	8 (32)	X2= 2.9341. p= .086729. NS
-Low income household	7 (19)	1 (4)	X2 with Yates correction= 1.5848. p= .208076. NS
-Complex family	8 (20)	1 (4)	X2 with Yates correction= 2.2067. p= .137409. NS
-Severity moderate-severe	6 (15)	5 (20)	X2 with Yates correction= 0.019. p= .890286. NS
-Exitus	1 (3)	0	Fisher exact test = 1. NS

(): Denotes percentages of total in primary cases and in secondary cases

NS: Not significant at p< .05.

Table 2: Comparison of Symptoms between Primary Covid-19 Cases in 2020 and Primary Covid-19 Cases (Vaccinated 1 or 2 Doses) In 2021 within Families

SYMPTOMS	PRIMARY COVID-19 CASES IN 2020 (N = 39)	PRIMARY COVID-19 CASES (VACCINATED 1 OR 2 DOSES) IN 2021 (N=25)	STATISTICAL SIGNIFICANCE
General (discomfort, asthenia, myalgia, fever, artralgiás)	46 (38)	30 (45)	X2= 1.0681. p= .301386. NS
Respiratory (cough, dyspnea, chest pain)	38 (31)	14 (21)	X2= 2.113. p= .146056. NS
ENT (Anosmia / ageusia, odynophagia, rhinorrhea, pharyngeal dryness-mucus, epistaxis)	18 (15)	14 (21)	X2= 1.2647. p= .260764. NS
Digestive (anorexia, nausea / vomiting, diarrhea, abdominal pain)	7 (6)	5 (8)	X2 with Yates correction= 0.0322. p= .85751. NS
Neurological (headache, dizziness, mental confusion -brain fog)	11 (9)	3 (5)	X2 with Yates correction= 0.6782. p= .410217. NS
Psychiatric (Anxiety, insomnia)	2 (1)	0	Fisher exact test = 1. NS
Skin (chilblains, flictenas, rash)	0	0	Fisher exact test = 1. NS
Total symptoms*	122 (100)	66 (100)	---

(): Denotes percentages of total in primary cases and in secondary cases

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

NS: Not significant at p< .05.

Table 3: Comparison of Chronic Diseases between Primary Covid-19 Cases in 2020 and Primary Covid-19 Cases (Vaccinated 1 or 2 Doses) In 2021 within Families

CHRONIC DISEASES ACCORDING TO WHO, ICD-10 GROUPS	PRIMARY COVID-19 CASES IN 2020 (N = 39)	PRIMARY COVID-19 CASES (VACCINATED 1 OR 2 DOSES) IN 2021 (N=25)	STATISTICAL SIGNIFICANCE
-II Neoplasms	3 (10)	2 (4)	Fisher exact test = 0.3538. NS
-III Diseases of the blood	0	2 (4)	Fisher exact test = 0.5278. NS
-IV Endocrine	7 (23)	9 (17)	X2= 0.3853. p= .53478. NS
-V Mental	5 (17)	3 (6)	X2 with Yates correction= 1.4051. p= .235865. NS
-VI-VIII Nervous and Senses	2 (7)	5 (10)	Fisher exact test statistic value= 1. NS
-IX Circulatory system	4 (13)	6 (12)	X2 with Yates correction= 0.0203. p= .886701. NS
-X Respiratory system	3 (10)	2 (4)	Fisher exact test statistic value= 0.3538. NS
-XI Digestive system	1 (3)	11 (21)	X2 with Yates correction= 3.637. p= .05651. NS
-XII Diseases of the skin	1 (3)	0	Fisher exact test statistic value= 0.3704. NS
-XIII Musculo-skeletal	2 (7)	6 (12)	Fisher exact test statistic value= 0.7035. NS
-XIV Genitourinary	2 (7)	5 (10)	Fisher exact test statistic value= 1. NS
TOTAL	30 (100)	51 (100)	---

(): Denotes percentages of total in primary cases and in secondary cases

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

NS: Not significant at $p < .05$.

Discussion

Main Findings

No statistically significant differences were found in primary cases in families of 2020 and 2021, or in symptoms, or in chronic diseases. Some specific population groups, mainly men, the elderly and people with comorbidities, have been more aggressively affected by covid-19 [35]. Comorbidities are the host factors that most contribute to the severity of covid-19; and among these, the ones that have contributed the most have been cardiovascular diseases, diabetes, and chronic respiratory diseases [36]. But the results of our study seem to indicate that the host in the primary cases between 2020 and 2021 did not present biological variations.

Furthermore, our study finds that primary cases in families in 2020 were younger, more female, lower income, with fewer ethnic minorities. These data suggest that the differences between the primary cases in 2020 and 2021 are basically influenced by socio-psychological factors, rather than biological factors. Adherence to preventive behaviours plays a crucial role regarding the control of covid-19. The psychological characteristics and risk perception of different individuals result in various forms of response to preventive behaviours. A key factor is perceived susceptibility. Although covid-19 is highly contagious, it has a relatively low mortality rate and milder symptomatology with the latest variants [37].

In addition, a large part of the population (although with an unequal distribution between high and low income countries) is vaccinated with at least one dose, which has been estimated as of June 2022 in more than 5,200 million people -the 67% of the world population, which can also influence the reduction of risk perception [38].

Another important factor associated with personal preventive behaviours is gender: being a woman is a significant factor that affects preventive behaviours. Given that women are more likely to be health conscious and risk averse, women tend to be more compliant with preventive behaviours towards infectious diseases than men [37, 39, 40].

In addition, people with a higher educational level tend to have preventive behaviours. This may be due to the fact that people with higher levels of education are more likely to have a better risk management assessment and are more likely to be exposed to information related to preventive behaviours [37].

Relevance of Characteristics of Primary Hosts in Families for Foreseeable Future Patterns of Presentation of Covid-19

The emergence of multiple variants of SARS-CoV-2 with increased transmissibility/virulence and immune escape capacity is an unfortunate turn in the course of the pandemic. The wide spread of the first wave of covid-19 would have created an immunological barrier in the infected population against the wild-type strain of SARS-CoV-2, which, it was hoped, would limit recurrent waves. Paradoxically, new massive waves of covid-19 driven by emerging variants of SARS-CoV-2 occurred in the years 2020-2021 worldwide [41]. Evidence has emerged that may explain better virus-host interaction and greater immune escape capacity of variants, and this has dashed hopes of a quicker end to the pandemic [42-45].

The variants, known as BA.4 and BA.5, are slightly more transmissible than earlier forms of Omicron and can bypass some of the immune protection conferred by previous infections and vaccinations. The increase in BA.4 and BA.5 could mean

that SARS-CoV-2 waves are beginning to establish themselves in predictable patterns, with new waves periodically emerging from circulating strains [46]. If SARS-CoV-2 continues down this path, its course could resemble that of respiratory illnesses that are seasonal (like the flu) and come in waves. The pattern of coronavirus infection may also become more predictable, as new mutations in the virus take advantage of vulnerabilities in population-wide immunity, leading to periodic waves of infection [47].

In this scenario, immune-evading mutations in circulating variants, such as Omicron, could combine with declines in population-wide immunity to become the key drivers of periodic waves of infection [46]. In most cases, previous vaccination or infection still appears to provide protection against severe disease. The new strains would be “an added nuisance,” but there is no evidence that they are more dangerous or more pathogenic [48, 49]. Knowledge of the variation in psychosocial factors associated with covid-19 cases over the course of the pandemic, and in view of the possible evolution towards a pattern of seasonal waves, may be relevant for preventive interventions and management of risks in families.

Strengths and Weaknesses 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 samples were small, thus statistical significance of some variables could be obscured.
3. Diagnosis of covid-19 was made in the same community and general medicine practice, and carried out by the same researcher, which gives coherence to the results.

Conclusions

The gateways (primary cases) of SARS-CoV-2 in families during the course of the pandemic (from 2020 to 2021) changed in the sense of being older individuals, with fewer women, with more income, with less complex families, and with a greater presence of ethnic minorities, but without differences in symptoms or chronic diseases. These data suggest that the differences between the primary cases in 2020 and 2021 are basically influenced by socio-psychological factors, rather than biological factors. It could be hypothesized that although the new variants are highly contagious, the relatively low mortality rate and the relatively milder symptomatology with the latest variants, together with the high vaccination rate in individuals, would be factors that modify the perception of risk of infection. Knowledge of these data may be relevant regarding preventive interventions in the future if the evolution of SARS-CoV-2 tends to resemble that of respiratory diseases that are seasonal and come in waves.

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