



# A Longitudinal Study of SARS-CoV-2 Secondary Infection Risks in Family Members: Psychosocial Factors May be More Important than Biological Ones

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## Abstract

**Background:** The factors of why some people get SARS-CoV-2 and others do not, after a primary case in families remains questionable.

**Objective:** To analyze some of the possible risk factors for contracting COVID-19 within families after there is a primary case.

**Methodology:** An observational, longitudinal and prospective study to analyze data of variables considered possible risk factors collected of 132 people in 39 families with at least one polymerase chain reaction (PCR) confirmed COVID-19 primary case, was conducted from March 15 to December 15, 2020, in a center of general medicine in Toledo (Spain). The Relative Risk (Incidence among the exposed population / Incidence among the population not exposed) for possible risk factors as predictors of secondary transmission were calculated.

**Results:** 39 families with 92 people were included with a primary case, of which 70 were sick (PCR positive) and 22 were healthy (PCR negative and asymptomatic). Age <45 years, being a woman and being a member of a low-income household, were the only variables that showed a weak and statistically significant risk for secondary infection in families; The high socio-occupational level was an effective and statistically significant protective factor against secondary contagion in families.

**Conclusion:** It is suggested that psychosocial factors can be more important vs. biological ones in secondary contagion within families.

**Keywords:** COVID-19; SARS-CoV-2; Epidemiological Characteristic; Family Characteristics; Prospective Studies; Risk Factors; Household Contact

**Abbreviations:** SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; COVID-19: Coronavirus Disease 2019; PCR: Polymerase Chain Reaction; RR: Relative Risk.

## Introduction

The proportion of risk factors for transmission and community spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), among household and non-

household contacts remains unclear. Carriers of SARS-CoV-2 occurred more frequently in middle-aged people who had close contact with infected relatives [1]. About half of adults with coronavirus disease 2019 (COVID-19) report they had no known close contact with an infected individual in the 2 weeks prior to their illness; among those who reported close contact with an infected person, that person was most often (45% of cases) a family member [2].

Household members who are older, have underlying medical conditions, or share a bed or vehicle with the index case appear to be the most susceptible to infection [3-5]. Children are probably less at risk of becoming infected [6]. However, your stool samples and nasopharyngeal swabs may remain positive for SARS-CoV-2 for more than two weeks after resolution of symptoms, although its role in transmission has not yet been established [7].

The number of people infected with COVID-19 receiving treatment at home is increasing every day. On many occasions, despite the fact that they must be hospitalized, due to the impossibility of ensuring the care of children, infected parents are receiving medical treatment at home [8]. Taken together, it can be said that currently the transmission of COVID-19 within families and close contacts accounts for most of the epidemic growth [9]. In China, more than 70% of person-to-person transmission of SARS-CoV-2 occurred in families. Household transmission in the presymptomatic or early symptomatic period of COVID-19 is a driver of epidemic growth and any measure aimed at reducing this can flatten the curve [9].

Decisions on the continued need for control measures to contain the spread of SARS-CoV-2 are based on information about the number of people who test positive for SARS-CoV-2 and factors of individual risk. But surveillance systems generally are not based on family samples and are not longitudinal in design. Furthermore, important questions remain about home transmission. Research should be conducted to identify the determinants of transmission in the home and the optimal strategies to isolate cases and protect household contacts. These strategies will be particularly important for those most at risk of adverse outcomes, including ethnic minority communities, people from low-income households, and those living in urban areas with overcrowded housing [10].

In this context, this article which is part of a set of research studies on COVID-19 in families, aims to study secondary cases in families to looking for some information on why some people have COVID-19 and others remain healthy after a primary case. In this way, some of the possible risk factors for contracting COVID-19 were studied within families, after there is a primary case, and these variables are compared between secondary cases (polymerase chain reaction [PCR] positive) and non-diseased cases (PCR negative and asymptomatic), calculating relative risks (RR).

## Materials and Methods

An observational, longitudinal and prospective that analyzes data of variables considered possible risk factors collected of 132 people in 39 families with at least one PCR

confirmed COVID-19 case, was conducted from March 15 to December 15, 2020, in a general medicine office in Toledo, Spain. PCR was performed on all family contacts/cohabiting after a primary case was declared in the family. The data was accumulated as part of a set of studies in 39 families with COVID-19, and in part the methodology has already been published [11].

### Diagnosis of COVID-19

The diagnosis was confirmed with PCR oropharyngeal. The cases included symptomatic cases and asymptomatic carriers. Information on COVID-19 patients and their contacts was registered in the system used by medical services in the consultation and a progressive follow-up was carried out until the end of the study.

### Diagnosis of Healthy Partners

Healthy partners were defined as such by presenting a negative PCR and being asymptomatic.

### Outcome of Interest

The outcome of interest was to study some of the possible risk factors for contracting COVID-19 within families, after there is a primary case, seeking information on why some people have disease and others remain healthy. In this sense, the variables collected were compared by calculating the RR as the Incidence among the exposed population / Incidence among the population not exposed to possible risk factors, in the sick (positive PCR) and non-ill (negative PCR).

The RR assumes the strength of the association; The RR expresses to the clinician the excess risk that a patient has for being exposed to the risk factor, and also serves to identify people at high risk, but does not measure the probability that someone with the risk factors will acquire the disease. The RR was interpreted as follows [12]:

- From 0 to 0.5: effective protection factor
- From 0.6.0.8: certain benefit
- From 0.9 to 1.1: not significant
- From 1.2 to 1.6: weak risk
- From 1.7 to 2.5: moderate risk
- Greater than 2.5: strong risk

### Household Contacts

Household contacts were defined as people who shared a residence with the COVID-19 index case. We defined family members as those who had lived with primary cases in a house 4 days before and for more than 24 hours after the primary cases developed illness related to COVID-19. Families with secondary transmission were defined as those where

some or all of the family members become infected within one incubation period (2 weeks) of symptom onset of the primary case. The onset date of a confirmed case was defined as the date of the first appearance of self-reported clinical symptoms [13]. Contacts were quarantined shortly after the index case was diagnosed, thereby reducing the risk of transmission (a provision not available in all circumstances).

### Collected Variables

Data on the index case and close contacts were extracted from the medical records of the general medicine practice under study. For the family members of the primary case the following variables were collected: age, 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” [14-16], classified according to the International Statistical Classification of Diseases and Health -Related Problems, CD-10 Version: 2019 [17], social-occupancy class (according to the Registrar General’s classification of occupations and social status code) [18,19], summarizing their groups in two: skilled and unskilled workers, students, problems in the family context and low income household based on the genogram and in the experience of the general practitioner 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) [20-24], belonging to an ethnic minority, and the number of family members.

For the primary cases, the following variables were collected: presence of symptoms (only cough and diarrhea, as they are symptoms of greater risk of infection) or being asymptomatic, and severity of the disease (mild cases: clinical symptoms are mild and no manifestation of pneumonia can 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  $\geq 30$  breaths/min; pulse oxygen saturation  $\leq 93\%$  with room air at rest; arterial partial pressure of oxygen/oxygen concentration  $\leq 300$  mmHg); to simplify comparison, moderate and severe cases were counted together.

### Sample

A convenience sampling was used. The families participating in the study were chosen because they had

their members in the same consultation and all medical information was available.

### Sample Size

Sample size was calculated for cohort studies, with a two-sided confidence level (1-alpha) of 95, a power (% probability of detection) of 80, a ratio of controls per case of 3, a hypothetical proportion of cases with 40% exposure and a hypothetical proportion of controls with 10% exposure. These parameters give a sample of 68 individuals, 17 cases and 51 controls (Kelsey) [25].

### Statistical Analysis

The bivariate comparisons were performed using the Chi Square test ( $X^2$ ),  $X^2$  with Yates correction or Fisher Exact Test when necessary, for percentages (according to the number the expected cell totals), and the Student t test for the mean.

### Results

39 families with 132 cohabitants were included, whose members were seen in the same consultation and all medical information was available. Family size was  $3.38 + -0.96$  members (arithmetic mean + -standard deviation). There were 92 family members, of which 22 had negative PCR ( $22/92 = 24\%$ ), one newborn who did not have PCR and was asymptomatic, and 70 secondary cases with positive PCR (Figure 1). The age in years (arithmetic mean and standard deviation) and the range was  $38.89 + -15.41$  (Range: 12-67) in the patients, and  $32.45 + -20.93$  (Range: 1-89) in the healthy ones ( $t = 1.68266$ .  $p = .047679$ . Significant at  $p < .05$ ).

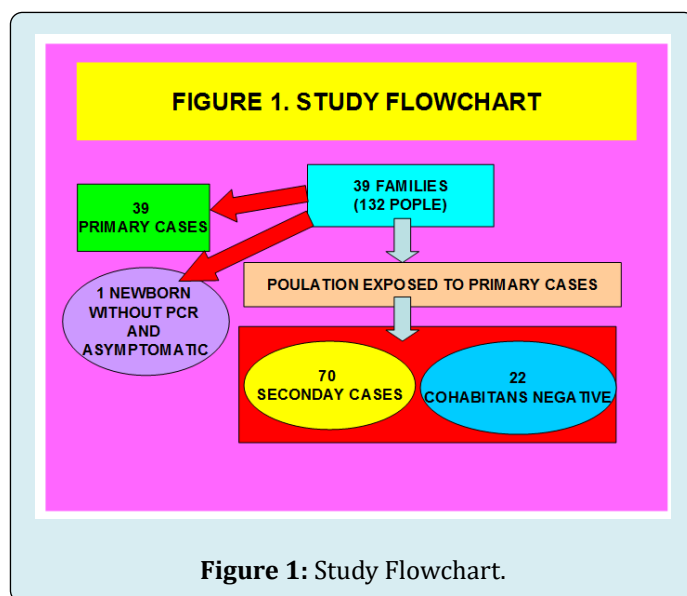


Figure 1: Study Flowchart.

The comparison between the variables studied and their Relative Risk (RR) in cases and non-cases are presented in Tables 1-3. The following risk factors for secondary infection were found in families: Age <45 years, being a woman and being a member of a low-income household, were the only variables that showed a weak and statistically significant risk; Age>65 years, being a student, being an ethnic minority, the presence of chronic diseases of the Respiratory system and Genitourinary, also showed a weak risk, but not statistically significant. The high socio-occupational level was a protective factor and statistically significant against secondary

contagion in families. The larger family size (Family with > = 4 members) was a factor of certain protective benefit but not statistically significant. The presence of chronic diseases of the Neoplasm group showed some protective benefit, and the diseases of the blood were an effective protection factor, but the latter two were without statistical significance. Regarding the characteristics of the primary case, the presence of cough and being asymptomatic were factors of certain protective benefit to become a secondary case in the family, but without statistical significance (Figure 2).

Risk Factors	Positive Secondary Cases (Patients) (N=70)	Negative Partners (Healthy) (N=22)	Statistical Significance	Relative Risk (Rr)
-Woman	51 (73)	9 (41)	X <sup>2</sup> = 7.5318. p= .006062. Significant at p < .05.	1.4 (CI 95 %: 1.08, 1.89); Weak risk
> = 65 years	6 (9)	0	Fisher exact test = 0.3296. NS	1.3 (CI 95%: 0.72, 2.48); Weak risk
< 45 years	52 (74)	10 (45)	X <sup>2</sup> = 6.3317. p= .01186. Significant at p < .05.	1.4 (CI 95%: 1.05, 1.87); Weak risk
-Workers with some type of specialization	20 (29)	20 (91)	x <sup>2</sup> = 12.1205. p= .000499. Significant at p < .05	0.5 (CI 95%: 0.79, 0.37); Effective protection factor
-Students	27 (39)	4 (18)	X <sup>2</sup> = 3.1148. NS	1.2 (CI 95%: 0.94, 1.64); Weak risk
-Ethnic minority	23 (33)	4 (18)	X <sup>2</sup> = 1.7386. NS	1.2 (CI 95%: 0.87, 1.61); Weak risk
-Low income household	23 (33)	2 (9)	X <sup>2</sup> = 4.7777. p= .028831. Significant at p < .05.	1.3 (CI 95%: 0.99, 1.73); Weak risk
-Complex family	12 (17)	3 (14)	X <sup>2</sup> with Yates correction= 0.0033. NS	1.1 (CI 95: 0.16, 7.11); Not significant
-Family with > = 4 members	38	17	X <sup>2</sup> = 3.6788. NS	0.8 (CI 95%: 1.04, 0.62); Certain protective benefit
-Presence of chronic diseases	24 (34)	8 (36)	X <sup>2</sup> = 0.0319. NS	1 (CI 95%: 1.61, 0.6); Not significant

( ): Denotes percentages of total in patients (positive PCR) and in healthy (negative PCR and asymptomatic)

NS: Not significant at p < .05.

CI: Confidence Interval

**Table 1:** Comparison of the Variables Studied Between Positive Secondary Cases (Sick; N = 70) and Negative Partners in Families (Healthy; N = 22).

Chronic Diseases According To Who, Icd-10 Groups	Positive Secondary Cases (Patients) (N=70)	Negative Partners (Healthy) (N=22)	Statistical Significance	Relative Risk (RR)
-II Neoplasms	1 (1)	1 (7)	Fisher exact test = 0.3176. NS	0.6 (CI 95%: 18.95, 0.02); Certain protective benefit
-III Diseases of the blood	0	1 (7)	Fisher exact test= 0.1728. NS	0 (CI 95%: Infinity, 0); Effective protection factor
-IV Endocrine	21 (31)	2 (14)	X2 with Yates correction= 0.9244. NS	1.1 (CI 95%: 0.86, 1.53); Not significant
-V Mental	10 (15)	3 (22)	Fisher exact test statistic= 0.6885. NS	0.9 (CI 95%: 2.08, 0.41); Not significant
-VI-VIII Nervous and Senses	6 (9)	2 (14)	Fisher exact test = 0.6215. NS.	0.9 (CI 95%: 5.03, 0.16); Not significant
-IX Circulatory system	5 (8)	1 (7)	Fisher exact test = 1. NS	1 (CI 95%: 0.97, 1.05); Not significant
-X Respiratory system	3 (5)	0	Fisher exact test = 1. NS	1.2 (CI 95%: 0, Infinity); Weak risk
-XI Digestive system	5 (7)	1 (7)	Fisher exact test = 1. NS	1 (CI 95%: 1.99, 0.41); Not significant
-XII Diseases of the skin	3 (5)	1 (7)	Fisher exact test = 0.5393. NS	0.9 (CI 95%: 1.99, 0.41); Not significant
-XIII Musculo-skeletal	8 (12)	2 (15)	Fisher exact test = 0.6813. NS	1 (CI 95%: 1.43, 0.64); Not significant
-XIV Genitourinary	5 (7)	0	Fisher exact test = 0.5812. NS.	1.2 (CI 95%: 0.49, 3.09); Weak risk
TOTAL*=-	67*(100)	14*(100)	-	-

( ) : Denotes percentages of total in patients (positive PCR) and in healthy (negative PCR and asymptomatic)

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

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

CI: Confidence interval

**Table 2:** Comparison of Chronic Diseases between Cohabitants with Positive Secondary Cases (Sick; N = 70) and Negative Cohabitants (Healthy; N = 22) In Families.



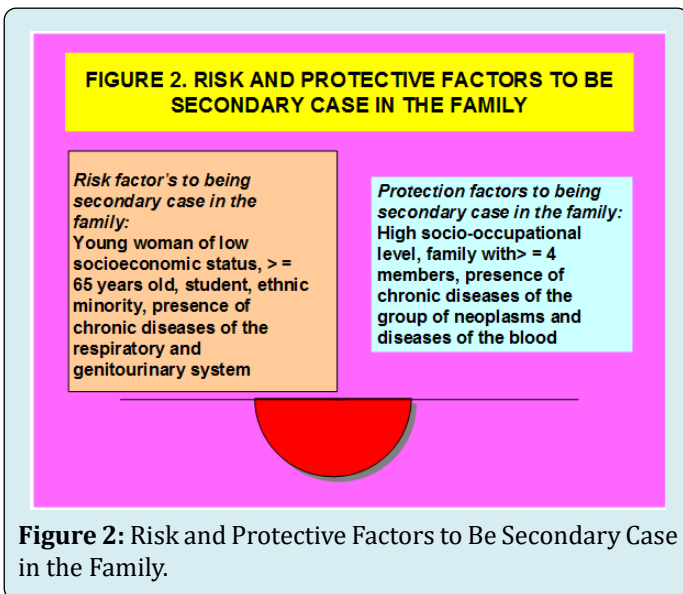
Characteristics of Primary Cases	Positive Secondary Cases (Patients) (N= 70)	Negative Partners (Healthy) (N=22)	Statistical Significance	Relative Risk (RR)
-Cough	40 (57)	17 (77)	X <sup>2</sup> = 2.8777. NS	RR=0.8 (CI 95%: 1.07, 0.63); Certain protective benefit
-Diarrhea	4 (6)	2 (9)	Fisher exact test= 0.6266. NS	RR=0.9 (CI 95%: 1.24, 0.74); Not significant
-With gravity	15 (21)	5 (23)	X <sup>2</sup> with Yates correction= 0.028. NS	RR= 0.9 (CI 95%: 1.24, 0.78); Not significant
-Asymptomatic	7 (10)	4 (18)	Fisher exact test= 0.4501. NS.	RR=0.8 (CI 95%: 1.48, 0.45); Certain protective benefit

( ): Denotes percentages of total in patients (positive PCR) and in healthy (negative PCR and asymptomatic)

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

CI: Confidence interval

**Table 3:** Comparison of Characteristics of Primary Cases In Secondary Cases (Sick; N = 70) and Negative Cohabitants (Healthy; N = 22) In Families.



**Figure 2:** Risk and Protective Factors to Be Secondary Case in the Family.

## Discussion

Most people with COVID-19 receive care at home, increasing the likelihood of exposure for household members; however, less attention has been paid to family members [26]. Sometimes COVID-19 feels like a game of chance; like Russian roulette [27]. There are numerous reports where very close cohabitants with similar characteristics, including twin brothers with the same body mass index and cardiovascular risk, who work and live together, who share dietary habits, who would have been infected with SARS-CoV-2 from the same person, who had the same viral load

at diagnosis and who were treated by the same doctors, had a very different evolution of the disease [28]. The reasons for the different clinical paths are a mystery. Additional research (genetic, epigenetic, metabolic, immunological, and microbiological) is expected to improve understanding of the pathophysiological mechanisms of COVID-19. In addition, there are several reasons why risk factors can vary over time; the behavior and contact patterns of subgroups change over time; adherence to prevention measures may decrease more over time among subgroups with a low risk of hospital admission and death related to COVID-19, than among those who are more vulnerable; and subgroups of people who have been disproportionately affected in a first wave of SARS-CoV-2 infection may have acquired sufficient immunity [29].

## Factors beyond Genetic Variants that Contribute to COVID-19

One line of study is the search for genes that could explain why some people are victims of coronavirus infection, while others escape relatively unscathed or have few or no symptoms [30]. Previous research has discovered genetic variants that can alter a person's chances of contracting an infectious disease. The most famous example is a mutation in the CCR5 gene, which offers protection against HIV. It has also been shown that variants in the human leukocyte antigen genes, which influence the body's immune response, may explain why some people spontaneously clear hepatitis C infection, while others remain chronically ill [31,32]. Variants of five key genes responsible for antiviral immunity and lung inflammation have been found to be associated with severe

COVID-19. While there is no guarantee that when a gene is found, targeting that gene will result in therapeutic efficacy. What genetic studies do is help to finding very specific starting points for further research. There are likely many other factors beyond these genetic variants that contribute to the severity of COVID-19 disease. Part of the answer is in the genes, but it is unlikely that a single element is completely responsible for the development of COVID-19. It is more likely to be a combination of factors, which can include genetics and age, obesity, gender, and other characteristics [33].

### Superpropagation Events: The Importance of Biopsychosocial Factors

A “superspreader” refers to an unusually contagious organism infected with a disease. There is growing evidence that SARS-CoV2 has substantial transmission heterogeneity and that super-spread events have driven much of the local epidemics with consequent implications for mitigation strategies. The factors that contribute to overpredation are not fully understood and are probably multiple [34], including biological factors (characteristics possibly related to viral load), behavioral and social factors (certain people have a large number of contacts in relation to the general population), hazardous facilities (for example, confined spaces with poor ventilation), and what are called “opportunistic” situations (large events with many contacts), or temporary increases in transmissibility (such as occurs when speaking or singing in voice aloud). It has been considered that 70% of those infected do not infect anyone and 20% infect a single person, so only 10% participate in the epidemic process and transmit SARS-CoV-2 to several people [35,36].

In one study, analyzing contact tracing data from 1,038 laboratory-confirmed cases of SARS-CoV-2 infection in Hong Kong between January and April 2020, the authors estimated that 80% of cases were seeded by only 19% of infected people; on the contrary, most of the patients failed to infect even one other person. Most of the contactor-infected transmission pairs identified (92 of 169) involved household contacts [37]. Thus, preliminary evidence points to SARS-CoV2 over-spread events that occur predominantly in closed environments with poor ventilation where people are very compact and exposed for prolonged periods, particularly with face-to-face contact (> 10 minutes) [38].

### Age

Although the elderly are more likely to suffer serious complications, thousands of young and previously healthy people have died from the disease [32]. Young adults, particularly those 17 to 24 years old, were a major early

driver of the rise in positivity rates in the second wave. For example, the estimated percentage of people who tested positive was more than six times higher in those aged 17 to 24 than in those aged 70 and over at the end of September 2020 [29]. Older people ( $\geq 60$  years) have been reported to be the most susceptible to domestic transmission of SARS-CoV-2. Compared with the older group ( $\geq 60$  years), the risk of infection at home was reported to be lower in the younger group (<20 years) and among adults aged 20 to 59 years [4]. Likewise, slightly greater differences in susceptibility have been reported between older ( $\geq 60$  years) and younger contacts [39].

We also found that the mean age of the sick (secondary cases) at home was higher than in the non-sick (negative PCR) ( $38.89 \pm 15.41$  in the sick, and  $32.45 \pm 20.93$  in healthy ones;  $t = 1.68266$ ,  $P < .05$ ). Being  $\geq 65$  years old was shown to be a weak risk (RR = 1.3; 95% CI: 0.72, 2.48; NS.). But being <45 years of age also represented a weak risk of being a secondary case in families (RR = 1.4; 95% CI: 1.05, 1.87;  $X^2 = 6.3317$ ,  $P < .05$ ).

### Sex

Female contacts have been reported to be slightly more susceptible than male contacts [39]. On average, women tend to have milder disease than men. Men are more likely to have serious complications [32]. Women also face a greater burden of chores and care at home [40,41]. In our study, being a woman represented a weak risk of being a secondary patient in the family (RR=1.4; 95% CI: 1.08, 1.89;  $p < .05$ ).

### Chronic Diseases

Although people with pre-existing conditions like heart disease are more likely to suffer serious complications, previously healthy people have died from the disease [32]. In a study in China, thirty percent of those who died had no comorbidities at all [42]. Regarding certain specific chronic diseases, asthma per se does not increase risk, perhaps because patients do not express substantial amounts of angiotensin-converting enzyme receptor 2 (coronavirus gateway); instead, there is growing evidence that patients with chronic obstructive pulmonary disease are at a moderately higher risk of a severe course of COVID-19, as are those with pulmonary fibrosis.

People who are obese or suffering from diabetes are particularly susceptible to severe cases of COVID-19 [43]. Diabetes may be an independent risk factor for the rapid progression and poor prognosis of COVID-19 through several known pathways and a possible new one: direct damage to the pancreatic islets [44,45]. We did not find that the

presence of chronic diseases in general showed a significant RR to become a secondary case in families. The presence of chronic diseases of the Respiratory system (RR = 1.2; 95% CI: 0, Infinity) and Genitourinary (RR = 1.2; 95% CI: 0.49, 3.09), showed a weak risk, but not statistically significant. And the presence of chronic diseases of the Neoplasm group showed a certain protective benefit (0.6 (95% CI: 18.95, 0.02), and the diseases of the blood being an effective protection factor (0; 95% CI: Infinity, 0), but also without statistical significance; in this regard, it can be thought that certain chronic diseases are valued as elements of greater risk, and thus motivate the family to increase preventive measures.

Ethnic minorities, people from low-income households, overcrowded housing and socio-occupational level Ethnic minority communities, people from low-income households, and those living in urban areas with overcrowded housing are at increased risk of adverse outcomes [10]. But, on the other hand, it has been reported that household overcrowding was not a significant factor [9]; there was also no connection between the risk of infection and the number of all people living in the same household. Has been communicated that secondary risk of infection for people living in the same household increased from 15% (one-person households) to 44% (2 people), 35% (3 people), and 18% (4 People;  $p < 0.001$ ); here the researchers expected higher values [46].

Lower socioeconomic status is associated with an increased risk of contracting COVID-19 [47]. In addition, it has been shown that preventive behaviors are associated with educational and economic level [48]. We found that being a member of a low-income household showed a weak and statistically significant risk for becoming a secondary patient in the family (RR = 1.3; 95% CI: 0.99, 1.73.  $P < .05$ ). The high socio-occupational level was a protective factor against secondary contagion in families (RR = 0.5; 95% CI: 0.79, 0.37.  $P < .05$ ). Belonging to an ethnic minority also posed a weak risk of become secondary ill in the family (1.2; 95% CI: 0.87, 1.61), but not statistically significant. But being a "complex family" was not a significant risk (1.1; CI 95: 0.16, 7.11). The larger family size (family with  $> = 4$  members) was a factor of certain protective benefit (RR = 0.8; 95% CI: 1.04, 0.62) but not statistically significant.

### Relationship with Variables of the Index Case

The greater severity of the disease in the index case has been reported to be an increased risk of transmission, which ranged from 0.3% in asymptomatic contacts to 6.2% in severe / critical case contacts. In Guangzhou, China, secondary infection rates increased with the most severe disease in index cases and were very low with asymptomatic index cases [49]. In Wuhan asymptomatic individuals were much less likely to infect others than symptomatic cases [39].

When the index case patients had expectoration, they were associated with almost five times the risk of secondary transmission (14% vs 3% for the index cases without expectoration [49,50]. The risk of home transmission was 18 times higher with frequent daily close contact with the primary case, and four times higher if the primary case had diarrhea [9]. The lack of symptoms that could facilitate transmission (sneezing / coughing) may explain the low transmission rate of asymptomatic cases despite similar viral loads. However, super-spreader events have been associated with presymptomatic individuals [49,51]. In our study, the presence of cough (RR = 0.8; 95% CI: 1.07, 0.63) and being asymptomatic (RR = 0.8; 95% CI: 1.48, 0.45) in the primary case were factors of certain protective benefit, but without statistical significance, to become secondary case in the family. Again it can be hypothesized that knowledge of this risk leads families to increase their preventive measures, which makes risk a protective factor.

### Study Limitations

Some limitations of our study must be taken into account:

- Genetic analyzes of the infected were not carried out and the identification of the viral strain that circulated among them was not carried out, so that the transmission and causal extension of the infection from index cases to other family members, was only presumptive based on in the timing of onset of symptoms and / or dates of PCR, in a situation of community transmission [52,53].
- The detection of antibodies against SARS-CoV-2 was not carried out systematically, so it cannot be excluded that a healthy family member had previously had the disease.
- On the other hand, children may develop symptoms of COVID-19 and specific antibodies against SARS-CoV-2, but never test positive for the virus in a standard PCR test, which can confuse the results [54].
- The sample of included families was not a probabilistic sample; it was a convenience sample (the families participating in the study were chosen because their members were treated in the same consultation and all medical information was available). However, there are no logical reasons to think that the current research sample was different from the ideal, randomly selected sample (from the entire population), nor that there might be under- or over-represented people in the sample.

### Conclusion

Our results suggest that there are biological, psychological and social factors (associated with being a young woman or older than 65 years, of low socioeconomic status, student, ethnic minority, presence of chronic diseases of the respiratory and genitourinary system) that increase the risk and that probably they reduce the motivation to



comply with preventive measures to become a secondary case in families. Other biological, psychological and social factors (associated with occupational specialization, larger family size, presenting chronic diseases of the groups and neoplasms and of the blood, primary case with cough or asymptomatic) may have a preventive effect and complying with the public health advice for prevention and so, to avoid being a secondary case in families, probably by increase knowledge and motivation.

Public health councils recommend isolation of PCR-positive household members, but this can be difficult, especially in small apartments with shared facilities. Motivation to overcome these difficulties may be greater in larger families and with members with chronic diseases that can increase risk, such as neoplasms and blood diseases. The effective possibilities of doing isolation and the motivation for it, may be lower in young people, students or with low occupational level and ethnic minorities. In addition, the presence of certain diseases or known risk factors (cough in the index case, larger family size, etc.) may pose an added risk or, on the contrary, may be factors to more strictly comply with preventive measures. In summary, our results suggest that psychosocial factors (associated with the female gender, being young, ethnic minority, low socioeconomic and employment status, and related knowledge, beliefs and behaviors) are probably most important vs. biological ones (age, sex, and chronic diseases).

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