

## Coronavirus Pandemic

# Intrafamilial transmission and clustering of COVID-19: a socioepidemiological perspective

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### Abstract

**Introduction:** The dynamics of COVID-19 transmission occurring in familial clusters may be related to sociodemographic and epidemiological characteristics of cases and contacts. The aim of this study was to identify the dynamics of COVID-19 transmission in families with more than one documented case.

**Methodology:** Data of about 58 familiar clusters of COVID-19 was gathered and followed up clinically and by telephonic interview. Age, gender, social security plan, comorbidities, occupation, incubation, and symptoms were analyzed using Students' t-test and Chi squared test.

**Results:** The contacts were younger and healthier than cases, and students were predominant (28%). Among the symptomatic contacts, reverse transcription polymerase chain reaction yielded a positive rate of 69%. There were 2.93 contacts per case. Families with clustered cases had more family members when compared to families without clustered cases (4.2 vs. 3.3;  $p = 0.022$ ). Mean age of contacts in families with clustered cases compared to families without clustered cases also showed differences (29.5 vs. 35.7;  $p = 0.047$ ).

**Conclusions:** Characterization of cases and contacts amidst a pandemic is essential for the effective implementation of health policies and research perspectives.

**Key words:** Coronavirus; epidemiology; pandemics; COVID-19.

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### Introduction

Since the declaration of the coronavirus (COVID-19) pandemic by the World Health Organization on January 30th 2020 [1], knowledge about this viral infection has grown exponentially. Most healthcare professionals caring for COVID-19 patients continue to learn while working in the trenches.

In addition to the search for an effective treatment, efforts are being made to delineate the dynamics of transmission and the rate of SARS-CoV-2 infectivity. It has been postulated that with four independently introduced cases, there is > 50% possibility that the infection will be established within a population [2]. Only 37 days after the index case was reported in Wuhan, China (on December 8th 2019) there were indications of community spread where infected patients did not have a clearly identified source of exposure [3].

Dynamics and demographics (age and structure) of the population determined differences in progression of

the pandemic in different countries. It was predicted that lower-income countries with weaker health systems but younger populations would suffer a lesser impact of the disease [4].

Community, intra-family, and nosocomial transmission modes have been documented for COVID-19 [3]. Family dynamics are important in COVID-19 transmission, spread, and outcomes; for example, in many countries, one or both parents work distantly, while their children are brought up by grandparents [5]. The characteristics of informal economy, prevalent in some countries, such as irregular or inconsistent salaries or healthcare access, [6] may increase the rates of exposure to COVID-19 and introduction to the family households. It has been reported that among the potential exposure sites; e.g., public transport, healthcare facilities, and household, the risk of getting the infection at home is the greatest, with an incidence of 10.1% [7].

It has been estimated that close contacts who lived with an index case (patient) had a 12 times higher risk for infection (Relative Risk 12.5) [8]. Furthermore, some studies have found that children have not played a substantive role in the intrahousehold transmission of SARS-CoV-2, (incidence rate < 10%) [9]. This emphasizes the role played by adults that exit and re-enter the household. At the same time, family gatherings including funerals, birthday parties, and traditional celebrations might foster transmission of SARS-CoV-2 and its incidence in clusters.

More than one COVID-19 case in several families, and sometimes more than one casualty, have been observed anecdotally. Analysis of familial clustering helps to explain the source of exposure of the index case (e.g. job, occupation, type of social security), the social determinants of this exposure and the chain of transmission. We can use the reproduction number ( $R_t$ ) to determine the transmissibility of a disease:  $R_t$  is defined by the ratio of the index cases (first generation of contagion) divided by cases in the second generation, i.e. the number of positive contacts per index case.  $R_t$  can be different for symptomatic and asymptomatic patients [10].

A family model to establish the differences between the index case (the first documented case in a family) and secondary (positive contact) cases as well as the socio-epidemiological differences between cases with familial clustering and cases without familial transmission of the disease is presented [2,11].

## Methodology

A retrospective analysis was performed aided by prospective acquisition of epidemiological data. The study was conducted in a COVID-19 designated hospital in the Northern part of Mexico that serves a population of more than one million inhabitants with a population density of 15,712.5 inhabitants per square mile. The city is located at the border with California, U.S.A.

### *Study design and subjects*

The operational definitions we used were as follows:

**Case:** a patient with viral respiratory infection symptoms (fever, headache, malaise, asthenia, dyspnea, cough, myalgia) and a positive nasal swab RT-PCR (Reverse Transcription Polymerase Chain Reaction) [12].

**Contact:** those who lived in the same household, shared a meal, travelled, or socially interacted before airborne and contact precautions were instituted or

without the use of personal protective equipment (e.g., a high-efficiency mask), with an index case from 2 days before to 14 days after the onset of symptoms of the index case [13].

**Probable case:** a person who meets the clinical criteria (acute onset of fever and cough; or acute onset of three or more of the following signs or symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnea, anorexia/nausea/vomiting, diarrhea, altered mental status) and is also a contact of a case [14].

### *Time frame and data source*

The data was collected from the beginning of the pandemic to December 31st 2020. Clinical and demographic data was collected from the hospital records obtained during emergency department (ED) admission and during hospitalization. Each documented case was screened through examination of medical records and telephone interviews to identify other family members who were infected.

Cases and contacts with familial clustering (two or more documented cases in a same family) were compared to cases and contacts without familial clustering (only one documented case in a family). For each cluster, symptom onset after probable exposure to contagion was investigated [15]. The following data on sociodemographic and epidemiological characteristics were recorded: age (years) and gender, mean number of family members, male/female ratio, mean age of cases and contacts, occupation of cases and contacts, time from symptoms onset to RT-PCR positivity for the cases, time from suspicion of exposure to onset of symptoms for contacts, and type of social security or healthcare plan.

### *Statistical analysis*

Central tendency and dispersion for the whole sample, keeping cases and contacts separate, were calculated. Continuous variables were expressed as medians; Students' t-test was used to identify differences between means. Categorical variables were summarized as cumulative frequencies and percentages and differences were assessed by Chi-squared test. All statistical analyses were conducted with IBM SPSS statistics 24.0.

### *Ethical aspects*

The appropriate Ethics Committee approved the study protocol. The research was conducted according to the World Medical Association Declaration of

Helsinki and the participants provided written informed consent; anonymity and confidentiality were preserved.

**Results**

The first diagnosed case occurred on March 17th 2020. From the total population of 1439 patients designated as COVID-19 cases, 740 were excluded because of lack of a confirmatory positive RT-PCR test; of the remaining, 301 were excluded because their final outcome was death as inpatients and it was considered that respect for family bereavement was a priority. From the remaining 398 cases, 230 were excluded because of lack of contact number, 11 were excluded because they were underage and 68 were excluded because contact by telephone could not be achieved. Finally, 89 families agreed to be interviewed.

The proportion of males to females in the cases was 1.4:1 (52 males and 37 females). Six patients lived alone; the remaining 83 cases had household contact with at least one relative, resulting in a total of 243 people (2.93 contacts per case).

Demographic characteristics of cases and contacts are summarized in Table 1. All the patients were at least

**Table 2.** Epidemiological data of contacts and probable cases. \* March to December 2020.

Characteristics	Contacts (n = 243)	Probable cases (n = 117)
<b>Gender</b>		
Male	117	50
Female	126	67
<b>Age</b>	31.0 ± 20.7	35.5 ± 19.2
<b>Relation to case</b>		
Son/Daughter	100 (41%)	43 (37%)
Couple	50 (20%)	37 (32%)
Parents	13 (5%)	7 (6%)
Second degree	44 (18%)	11 (9%)
Political family	13 (5%)	11 (9%)
Average time of exposure to symptoms		6.0 days

\* Contacts of 89 patients were determined for each case in each household; their clinical evolution was determined after discharge of patients (cases) from hospital. Probable cases are those contacts who developed symptoms.

21 years old; the youngest contact was 8 months old. The proportion of male to female contacts was 1:1.07.

Among 89 cases or families, which included 243 contacts, clustered cases were identified in 58 families (65%), amounting to 117 probable cases. Of these, 39 (33%) were tested using RT-PCR resulting in a positivity rate of 69% (27 positive tests out of 39 tested probable cases). Reproduction numbers (Rt) ranged from 0 to 6 among families. Three of the six deceased contacts (probable cases) did not have a RT-PCR test performed, and in one of the three performed tests, the result was negative. Table 2 shows family relations among contacts; probable cases (contacts with symptoms) are also specified. Table 3 shows the comparison between 58 cases with clustering and 25 cases without clustering. There was no significant difference in gender, age, and occupation of cases. However, differences in age of contacts and number of family members were statistically significant for intrafamilial transmission; gender and occupation of contacts yielded non-statistically significant values.

**Discussion**

This study aimed to characterize the dynamics of COVID-19 transmission among cases and close contacts in familial clusters. A total of 89 COVID-19 cases were identified. Out of these, 58 cases (65%) had familial clustering according to the definition of a probable case. The number of symptomatic contacts (probable cases) with a positive RT-PCR test were 27, out of 39 tested.

To put this in context, as of June 15th 2022, the Johns Hopkins University Center for Systems Science and Engineering (JHU CSSE) reported 5,859,406 confirmed COVID-19 cases and 325,069 deaths in

**Table 1.** Demographic and clinical data of the studied population. \* Labels according to each category studied and the corresponding proportions are shown. March to December 2020.

Characteristics	Cases (n = 89)	Contacts (n = 243)
<b>Gender</b>		
Male	52	117
Female	37	126
<b>Age</b>	54.7 ± 13.5	31.0 ± 20.7
<b>Occupation</b>		
Housewife	30%	11%
Self-employed	23%	6%
Informal/manual	16%	10%
Formal employee	11%	15%
Student	1%	28%
Unemployed	3%	2%
Other	14%	28%
<b>Social security plan</b>		
None	22 (25%)	70 (29%)
INSABI	37 (42%)	64 (26%)
IMSS	11 (12%)	71 (29%)
ISSSTE	9 (10%)	15 (6%)
Other	10 (11%)	23 (9%)
<b>Comorbidities</b>		
High blood pressure	40 (44%)	35 (14%)
Diabetes	34 (38%)	19 (8%)
Obesity	33 (37%)	20 (8%)
Alcoholism	19 (21%)	30 (12%)
Other (thyroid disease, tuberculosis, heart disease, asthma, rheumatoid arthritis)	20 (22%)	21 (9%)

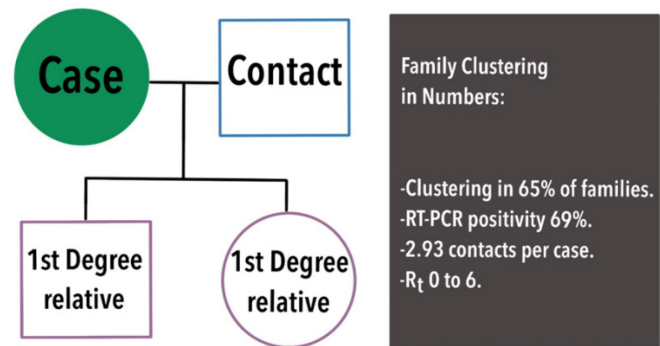
\* The sample corresponds to the families that agreed to answer a telephonic interview; 89 of 1439 COVID-19 cases.

Mexico [16]. The study was conducted in Baja California where the number of cases amounted to 137,167 with 12,306 deaths.

Among the population to which the sample belongs, contacts are younger, healthier, and mostly students. These characteristics are paramount considering that formal (schooled) education was suspended in our country since the beginning of the pandemic, and issues of proper isolation of cases and measures of social distancing are essential in view to the recent school reopening [17]. The sanitary measures concerning young adults, college and university students, are key to hinder transmission.

Some important considerations include: the proportion between asymptomatic and symptomatic contacts has been reported in the range from 1% to 50% [10,12]; this ratio varies if the infecting individual was in turn symptomatic or asymptomatic [10]. This variability in transmissibility indicates differences in the infecting and the infected individual as well as the context where transmission takes place. For example, aside from atypical manifestations, a rapid transmission, fast onset, and high infectivity occurs in groups of young people [18]. This difference (mean age of contacts) can explain the significant differences

**Figure 1.** Dynamics of COVID-19 transmission in a household. Characteristics correspond to the sample studied.



among families with clustering and families without clustering of cases in our study.

As expected, differences in number of persons sharing a household was statistically significant ( $p = 0.022$ ); nevertheless, based on the small difference among groups (3.3 vs. 4.2), we can assume that theoretically the transmission dynamics change after a certain subtle threshold (e.g. people per square area; restroom, bathroom, and kitchen sharing, as well as exiting and re-entering the household after work or after errands).

We consider that follow-up of cases and contacts must be emphasized; despite a contact being

**Table 3.** Comparison of cases and contacts between families with COVID-19 clustering and families without clustering; cases and contacts are analyzed separately. March to December 2020.

Characteristics of cases	No-familiar clustering	Familiar clustering	p value
	n = 25 cases	n = 58 cases*	
Gender (male/female)	(13/12)	(37/21)	0.313
Age	56.2 ± 14.6	53.0 ± 13.1	0.323
Occupation			0.283
	Housewife 32%	Housewife 26%	
	Self-employed 4%	Self-employed 9%	
	Informal/manual 12%	Informal/manual 15%	
	Formal employee 4%	Formal employee 21%	
	Student 0%	Student 1%	
	Unemployed 28%	Unemployed 17%	
	Sales 20%	Sales 9%	
	Other 0%	Other 3%	
Characteristics of contacts (n = 243)	n = 58 contacts	n = 185 contacts	
Gender (male/female)	(33/25)	(84/101)	0.126
Age	35.7 ± 20.4	29.5 ± 20.7	0.047**
Occupation			0.073
	Housewife 12%	Housewife 15%	
	Self-employed 3%	Self-employed 5%	
	Informal/manual 15%	Informal/manual 5%	
	Formal employee 13%	Formal employee 20%	
	Student 26%	Student 31%	
	Unemployed 10%	Unemployed 3%	
	Sales 2%	Sales 3%	
	Other 17%	Other 18%	
<b>Number of family members</b>	3.3 ± 1.6	4.2 ± 1.6	0.022**

\* 6 cases did not have contact with any family member; 6 + 83 = 89 total cases. \*\* p value < 0.05; Categorical variables compared using Chi-squared ( $\chi^2$ ) test; numerical variables compared using Student's t test.



asymptomatic she/he can develop symptoms and aggravate, or otherwise infect others even while asymptomatic.[13] Our study was based on the analysis of medical records, and a theoretical mode of transmission based on family dynamics of a household composed of four members could be established. The mode of transmission in the case of a housewife or an employee, and the close contacts who are younger and at least one of them is a student is represented in Figure 1.

A mean incubation period (time from exposure to symptoms) of 6.01 days was found (95% CI 4.55 to 7.47) in those cases where the data was established unambiguously; this value is consistent with other reports (Figure 2) [19].

Except for clear categories such as “student” and “housewife”, the wide range of occupations reported does not allow easy determination of the potential interactions of the cases (and contacts) in their workplace and the expected compliance with social distancing measures. In this regard, “employee” may signify isolated work with limited interactions, as well as constant traffic and multiple interactions.

The reproduction number (Rt) was heterogeneous among families. Some of them showed a Rt of 6, six probable or infected contacts per case, while other families had a Rt number of 0 where 8 persons shared a household (one case and seven asymptomatic contacts). The reason for these differences could not be interpreted. One probable reason for this was the almost absolute lack of RT-PCR tests in asymptomatic contacts. Data analysis during the early phase of the pandemic has established that the mean estimate of Rt ranges from 2.24 to 3.58 [11]. Theoretically, if a number of families with COVID-19 transmission among two or more members is analyzed, we would be

dealing with a cohort having a reproduction number of at least 1. Variations in the Rt can signal differences in transmission owing to different familial characteristics.

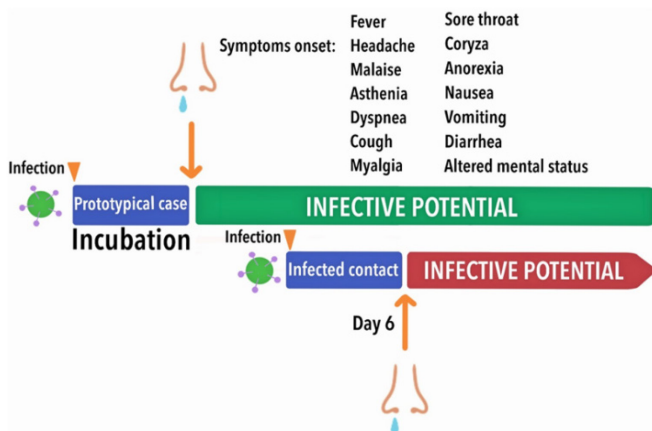
We must acknowledge that some patients suffer from COVID-19 with negative SARS-CoV-2 swabs. This can be due to the quality of the test, sampling location, volume, transportation, storage, as well as laboratory personnel and infrastructure conditions. In addition, there are likely incompletely known characteristics of this new virus [20]. The importance of operational definitions of case, contact, probable case, and other epidemiological terms, based on historical criteria and defined by experts in the field for each context must be emphasized.

One of the obstacles we faced was the heterogeneous definition of a “case” and the varied methods of laboratory confirmation used in our community; e.g. the diversity of molecular, serological (antibodies) and antigen tests authorized in our country [21]. Conversely, the resources needed to properly follow a case and screen its contacts can easily overwhelm the healthcare system infrastructure; the necessity of screening more than 60 contacts for a case of viral respiratory illness (medical and exposure history, health care-seeking behaviors, job-related activities, and social activities during the 14 days before illness onset) has been documented [22]. This endeavor is hard to accomplish in third-world countries since a great proportion of the population lives in crowded and impoverished cities where personal hygiene and social distancing are more difficult to implement; informal jobs (trade or commerce), as a common source of income adds to this situation.

From a community standpoint, environmental disinfection procedures such as testing, isolation, contact tracing, and quarantine are harder to implement in low-income neighborhoods [2,12]. In this respect, an important consideration is the difference between our operational definitions and those of the Guideline on Diagnosis and Treatment of COVID-19 (National Health Commission of the People's Republic of China) and other related documents [20]. Nevertheless, they are adequate for the analysis of our population [3,4,13,14].

A useful perspective for research in familiar clustering of COVID-19 is the possibility of differentiated humoral and cellular immune responses; a recent paper showed that even though some contacts did not seroconvert, T cells specific to SARS-CoV-2 were detected [23]. As far as we know, this approach is not undertaken in our country, at least not in non-research contexts. Clinical manifestations are another

**Figure 2.** Interactions and COVID-19 transmission from case to contact.



area of research; for example, although recorded anecdotally by our team, psychiatric manifestations developed in late convalescence were noted in several cases. This can be due to anxiety or mood disorders in relation to bereavement or post-traumatic reaction (prolonged intensive care) or a hint towards viral neurotropism [24,25]. At the same time, evidence on asymptomatic people as a source of transmission is lacking; the infective potential is considered to exist only in the presence of symptoms [26].

Another comment can be made on the access to social security of cases as well as contacts; health services are provided through several social security programs or National Health Institutes in our country: the Instituto Mexicano del Seguro Social (IMSS) for private sector employees, Instituto de Seguridad y Servicios Sociales para los Trabajadores del Estado (ISSSTE) for public employees, and Instituto de Salud Para el Bienestar (INSABI) for others [27]. The institution where the data was gathered usually serves individuals with no social security, but this situation was modified according to federal government indications as the pandemic was evolving. If this situation emerges in times of crisis, it is useful evidence supporting the claim that countries need to reduce health system fragmentation in order to achieve effectiveness and efficiency [28].

Finally, not having performed a Logistic Regression analysis is a limitation of our study; a decision was made to gather more data (clustered cases) before performing such analysis considering that, apart from sample size, the assumption of linearity between the dependent variable and the independent variables is a limitation of this technique [29]. Other limitations of our study are its retrospective nature, the quality of medical records, and a non-randomly selected sample. Repeated RT-PCR tests were not available to determine periods of virus shedding. Virus cultures or detailed sequencing analysis were not performed; this could have helped to clarify the transmission chains within the families.

## Conclusions

Medical records help to delineate the patterns of transmission along with the socioepidemiological characteristics of cases and contacts; it can also help in the design of health policies to stop the spread of the virus. One clear example of this can be the decisions around school reopening. These strategies are more effective when deployed in a timely and well-informed manner.

The characteristics and traits of this virus, and the disease caused by it, are still being defined; however, some characteristics of cases and/or contacts might explain the dynamics of transmission (e.g., young age and its inherent features).

Aggressive strategies for careful data collection and monitoring are essential for proper allocation of resources and evidence-based decision-making.

## Authors' contributions

Hiram Javier Jaramillo-Ramírez: conception and design of the work, theoretical framework, analysis and interpretation of data, drafting and revisions. Beatriz Hatsue Kushida-Contreras: design of the work, theoretical framework, analysis and interpretation of data, substantial revisions. Aranza Elena García-Aréstegui: conception of the work, acquisition and interpretation of data, substantial revisions. Gisel Viviana Licón-Martínez: conception of the work, acquisition and interpretation of data, substantial revisions. Miguel Angel Gaxiola-García: corresponding author, conception and design of the work, analysis and interpretation of data, drafting and substantial revisions.

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