


RESEARCH ARTICLE

Transmission dynamics of SARS-CoV-2 within families with children in Greece: A study of 23 clusters

Helena C. Maltezos¹ | Rengina Vorou¹ | Kalliopi Papadima¹ |
Athanasios Kossyvakis² | Nikolaos Spanakis³ | Georgia Gioula⁴ | Maria Exindari⁴ |
Symeon Metallidis⁵ | Athanasia N. Lourida⁶ | Vasilios Raftopoulos⁷  |
Elisavet Froukala³ | Beatriz Martinez-Gonzalez² | Athanasios Mitsianis⁸ |
Emmanuel Roilides⁹ | Andreas Mentis² | Athanasios Tsakris³ | Anna Papa⁴

¹Directorate of Epidemiological Surveillance and Interventions for Infectious Diseases, National Public Health Organization, Athens, Greece

²National Reference Laboratory for Influenza and other Respiratory Viruses, Hellenic Pasteur Institute, Athens, Greece

³Department of Microbiology, Medical School, National and Kapodistrian University of Athens, Athens, Greece

⁴Department of Microbiology, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece

⁵Infectious Diseases Division, First Internal Medicine Department, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece

⁶Infection Prevention and Control Committee, Aghia Sofia Children's Hospital, Athens, Greece

⁷Epidemiological Surveillance of HIV/AIDS Department, National Public Health Organization, Athens, Greece

⁸Internal Medicine Department, Mpodosakeio General Prefecture Hospital of Ptolemaida, Ptolemaida, Greece

⁹Third Department of Pediatrics, School of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece

Correspondence

Helena C. Maltezos, Directorate for Epidemiological Surveillance and Interventions for Infectious Diseases, National Public Health Organization, 3-5 Agrafon St, Athens 15123, Greece.

Email: helen-maltezos@ath.forthnet.gr

Abstract

There is limited information on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection clustering within families with children. We aimed to study the transmission dynamics of SARS-CoV-2 within families with children in Greece. We studied 23 family clusters of coronavirus disease 2019 (COVID-19). Infection was diagnosed by reverse-transcriptase polymerase chain reaction in respiratory specimens. The level of viral load was categorized as high, moderate, or low based on the cycle threshold values. There were 109 household members (66 adults and 43 children). The median attack rate per cluster was 60% (range: 33.4%-100%). An adult member with COVID-19 was the first case in 21 (91.3%) clusters. Transmission of infection occurred from an adult to a child in 19 clusters and/or from an adult to another adult in 12 clusters. There was no evidence of child-to-adult or child-to-child transmission. In total 68 household members (62.4%) tested positive. Children were more likely to have an asymptomatic SARS-CoV-2 infection compared to adults (40% vs 10.5%; $P = .021$). In contrast, adults were more likely to develop a severe clinical course compared with children (8.8% vs 0%; $P = .021$). In addition, infected children were significantly more likely to have a low viral load while adults were more likely to have a moderate viral load (40.7% and 18.6% vs 13.8% and 51.7%, respectively; $P = .016$). In conclusion, while children become infected by SARS-CoV-2, they do not appear to transmit infection to others. Furthermore, children more frequently have an asymptomatic or mild course compared to adults. Further studies are needed to elucidate the role of viral load on these findings.

KEYWORDS

children, cluster, COVID-19, family, SARS-CoV-2, viral load

1 | INTRODUCTION

Following the emergence of a new coronavirus named severe acute respiratory coronavirus 2 (SARS-CoV-2) in China in late December

2019 and subsequent global spread, a pandemic was declared by the World Health Organization on 11 March 2020.¹ As of 26 July 2020, more than fifteen million cases of the new respiratory disease named coronavirus disease 2019 (COVID-19) and 640 016 deaths have been

notified globally.¹ In Greece the first cases were diagnosed on 26 February 2020.² During the first weeks of the epidemic, most COVID-19 cases were travel-associated, while as the epidemic progressed, community transmission was established.² The first evidence that SARS-CoV-2 can be transmitted from person-to-person was set when a member of a family in China who did not travel to Wuhan, became infected by the virus after several days of contact with family members who traveled to Wuhan; all patients had radiological ground-glass lung opacities, with adults presenting respiratory symptoms, while a 10-year child remained asymptomatic.³ Soon after, it became evident that asymptomatic infection and mild clinical illness are more prevalent in children compared to adults.^{4,5} Herein, we studied the transmission dynamics of SARS-CoV-2 infection within families with children in Greece, focusing on the comparison of disease severity, outcome, and viral load between adults and children.

2 | METHODS

2.1 | Surveillance and contact tracing of SARS-CoV-2 infections

SARS-CoV-2 infection is notifiable disease in Greece. Surveillance of SARS-CoV-2 infection is performed by the National Public Health Organization on a case basis. Data are notified daily by all laboratories testing for SARS-CoV-2 using real-time reverse-transcriptase polymerase chain reaction (RT-PCR). In addition, physicians notify all laboratory-confirmed COVID-19 cases using a standardized notification form. A passive comprehensive system for hospitalized cases is also in place, collecting data daily on admissions in intensive care unit (ICU), complications, and outcome. For every COVID-19 case admitted in ICU or COVID-19-associated death, information is also collected through telephone interview with the physician in charge.

Contacts of SARS-CoV-2 infected cases were traced. Close contacts were instructed to stay isolated for 14 days following the last contact with the COVID-19 case. In case of onset of symptoms, contacts were advised to attend a COVID-19 referral hospital for testing.

2.2 | Data collection

The study period extended from 26 February (first COVID-19 case diagnosed in Greece) to 3 May 2020 (last date of lockdown in Greece). Family clusters were identified through the national registry of SARS-CoV-2 infections. We studied family clusters diagnosed in three reference laboratories for SARS-CoV-2 (two in Athens and one in Thessaloniki) where most cases were diagnosed. Families with at least one child were included in the study. Demographic, epidemiological and clinical data were collected. An adult family member (preferably the mother) was contacted through telephone to collect

data about the possible source of infection of the first case, symptoms of household members and in-family contacts.

2.3 | Virological investigation

Patients' respiratory samples were tested by real time RT-PCR following commercial or in-house protocols. Based on the cycle threshold (C_t) value of the PCR, persons were categorized into three groups, those having high, moderate, or low viral load (C_t 25, 25-30, or 30, respectively). Each cluster was investigated in one laboratory.

2.4 | Definitions

Asymptomatic SARS-CoV-2 cases were defined as those with positive SARS-CoV-2 PCR in the absence of symptoms. COVID-19 cases were defined as those with positive SARS-CoV-2 PCR and compatible signs and symptoms. COVID-19 cases were classified as mild when patients were managed in the outpatient setting, moderate when patients were admitted to hospital and had a favorable outcome, while severe were classified those admitted to ICU or had a fatal outcome. Children were defined as persons <18 years of age. A family cluster was defined as the detection of at least two cases of SARS-CoV-2 infection within a family. Index case was defined as the first laboratory-diagnosed case in the family, which brought SARS-CoV-2 infection in the family under medical attention. In contrast, first case was defined as the first COVID-19 case in a family. Household contacts were defined as persons either living in the same residence or having close contacts with a family member for ≥ 4 hours daily in the family residence. Close contact was defined as a contact of >15 minutes within a distance of less than 2 m with a COVID-19 case.

2.5 | Statistical analysis

Categorical variables were compared by using the χ^2 test while for continuous variables t test was used. $P \leq .05$ were considered statistically significant. A logistic regression analysis was not performed due to the small sample size and the inadequate events per variable, given that small to moderate samples size such as less than 100 usually overestimate the effect measure.⁶ The results are presented mainly in a descriptive form, including total numbers, frequencies, or percentages. Analysis was performed by using IBM-SPSS 26 (IBM Corp. Released 2016).

2.6 | Ethical issues

Written consent was not required, given that the data were collected within the frame of epidemiological surveillance. Data were managed in accordance with the national and European Union laws.

TABLE 1 Characteristics of household members per family cluster, Greece, 26 February to 3 May 2020

Cluster member	Member (age ^a)	Onset of symptoms	Sample collection	Day of illness ^b	PCR	Hospital	Outcome	Clinical course	Viral load
1a	Mother (38)	25/02/20	25/02/20	1	Positive	Yes ^c	Alive	Mild	Moderate
1b	Son (9)	NA	26/02/20	NA	Positive	Yes ^c	Alive	Asymptomatic	Moderate
1c	Grandfather (69)	NA	26/02 & 2/3/20	NA	Negative	No	Alive	NA	NA
1d	Grandmother (62)	NA	26/02 & 2/3/20	NA	Negative	No	Alive	NA	NA
1e	Uncle (32)	NA	26/02 & 2/3/20	NA	Negative	No	Alive	NA	NA
1f	Father (41)	NA	26/02 & 2/3/20	NA	Negative	No	Alive	NA	NA
2a	Father (54)	29/02/20	06/03/20	7	Positive	Yes	Alive	Moderate	High
2b	Mother (48)	05/03/20	07/03/20	3	Positive	No	Alive	Mild	Moderate
2c	Son (16)	NA	07/03/20	NA	Positive	No	Alive	Asymptomatic	Moderate
3a	Father (48)	01/03/20	10/03/20	9	Positive	No	Alive	Mild	Moderate
3b	Son (12)	NA	11/03/20	NA	Positive	No	Alive	Asymptomatic	High
3c	Daughter (10)	NA	11/03/20	NA	Positive	No	Alive	Asymptomatic	Low
3d	Mother (43)	NA	11/03/20	NA	Negative	No	Alive	NA	NA
3e	Daughter (14)	NA	11/03/20	NA	Negative	No	Alive	NA	NA
4a	Mother (34)	02/03/20	08/03/20	7	Positive	No	Alive	Mild	Moderate
4b	Father (36)	03/03/20	08/03/20	6	Positive	No	Alive	Mild	High
4c	Son (2)	04/03/20	08/03/20	5	Negative	No	Alive	NA	NA
4d	Son (4)	NA	08/03/20	NA	Positive	No	Alive	Asymptomatic	High
5a	Father (56)	05/03/20	09/03/20	5	Positive	No	Alive	Mild	High
5b	Mother (54)	08/03/20	10/03/20	3	Positive	No	Alive	Mild	High
5c	Son (17)	NA	10/03/20	NA	Positive	No	Alive	Asymptomatic	Low
5d	Son (14)	NA	10/03/20	NA	Positive	No	Alive	Asymptomatic	High
6a	Mother (53)	07/03/20	11/03/20	5	Positive	No	Alive	Mild	Unknown
6b	Daughter (18)	08/03/20	11/03/20	4	Positive	No	Alive	Mild	Unknown
6c	Son (18)	NA	11/03/20	NA	Negative	No	Alive	NA	NA
6d	Daughter (22)	NA	11/03/20	NA	Negative	No	Alive	NA	NA
6e	Housemaid (25)	NA	11/03/20	NA	Negative	No	Alive	NA	NA
7a	Father (37)	08/03/20	11/03/20	4	Positive	No	Alive	Mild	Unknown
7b	Mother (46)	09/03/20	11/03/20	3	Positive	No	Alive	Mild	Unknown
7c	Son (6)	NA	11/03/20	NA	Negative	No	Alive	NA	NA
7d	Grandmother (80)	NA	11/03/20	NA	Negative	No	Alive	NA	NA
7e	Housemaid (55)	NA	11/03/20	NA	Negative	No	Alive	NA	NA
8a	Mother (40)	09/03/20	11/03/20	3	Positive	No	Alive	Mild	High
8b	Father (40)	14/03/20	12/03/20	-2	Positive	No	Alive	Mild	Low
8c	Daughter (8)	NA	12/03/20	NA	Positive	No	Alive	Asymptomatic	Low
8d	Son (6)	NA	12/03/20	NA	Positive	No	Alive	Asymptomatic	High
8e	Son (4)	NA	12/03/20	NA	Positive	No	Alive	Asymptomatic	Low
9a	Mother (40)	10/03/20	15/03/20	6	Negative	No	Alive	NA	NA
9b	Daughter (14)	11/03/20	14/03/20	4	Positive	No	Alive	Mild	Low
9c	Daughter (12)	12/03/20	14/03/20	3	Positive	No	Alive	Mild	Low

TABLE 1 (Continued)

Cluster member	Member (age ^a)	Onset of symptoms	Sample collection	Day of illness ^b	PCR	Hospital	Outcome	Clinical course	Viral load
9d	Father (60)	NA	15/03/20	NA	Negative	No	Alive	NA	NA
9e	Housemaid (40)	unknown	not tested	NA	NA	No	Alive	Mild	NA
10a	Mother (48)	11/03/20	14/03/20	4	Negative	No	Alive	NA	NA
10b	Father (50)	12/03/20	13/03/20	2	Positive	Yes	Dead	Severe	Moderate
10c	Daughter (10)	NA	14/03/20	NA	Negative	No	Alive	NA	NA
10d	Daughter (7)	NA	14/03/20	NA	Negative	No	Alive	NA	NA
10e	Son (15)	24/03/20	27/03/20	4	Positive	No	Alive	Mild	Moderate
11a	Mother (37)	11/03/20	14/03/20	4	Positive	No	Alive	Mild	High
11b	Housemaid (62)	16/03/20	25/03/20	10	Positive	Yes	Alive	Moderate	Moderate
11c	Father (40)	16/03/20	14/03/20	-2	Negative	No	Alive	NA	NA
11d	Daughter (4)	27/03/20	14/03/20	-13	Negative	No	Alive	NA	NA
11e	Daughter (6)	28/03/20	30/03/20	3	Positive	No	Alive	Mild	Unknown
12a	Father (39)	11/03/20	13/03/20	3	Positive	No	Alive	Mild	Low
12b	Mother (36)	18/03/20	13/03/20	-5	Positive	No	Alive	Mild	High
12c	Daughter (5)	NA	13/03/20	NA	Positive	No	Alive	Asymptomatic	Low
12d	Son (2)	NA	13/03/20	NA	Negative	No	Alive	NA	NA
13a	Mother (40)	13/03/20	20/03/20	8	Positive	No	Alive	Mild	Unknown
13b	Daughter (10 d)	18/03/20	20/03/20	3	Positive	Yes	Alive	Moderate	Low
13c	Daughter (3)	19/03/20	23/03/20	5	Positive	No	Alive	Mild	Low
13d	Father (39)	19/03/20	23/03/20	5	Positive	No	Alive	Mild	Low
13e	Grandmother (71)	NA	23/03/20	NA	Negative	No	Alive	NA	NA
13f	Other (68)	NA	23/03/20	NA	Negative	No	Alive	NA	NA
13g	Other (74)	NA	not tested	NA	NA	No	Alive	Asymptomatic	NA
14a	Mother (40)	15/03/20	19/03/20	5	Positive	No	Alive	Mild	Moderate
14b	Son (3 mo)	18/03/20	19/03/20	2	Positive	Yes	Alive	Moderate	High
14c	Father (47)	NA	19/03/20	NA	Negative	No	Alive	NA	NA
14d	Daughter (4.5)	NA	19/03/20	NA	Negative	No	Alive	NA	NA
14e	Grandmother (67)	NA	26/03/20	NA	Positive	No	Alive	Asymptomatic	Unknown
15a	Aunt (27)	15/03/20	20/03/20	6	Positive	No	Alive	Mild	Unknown
15b	Son (17 d)	16/03/20	19/03/20	4	Positive	Yes	Alive	Moderate	High
15c	Mother (32)	NA	20/03/20	NA	Negative	No	Alive	NA	NA
15d	Father (29)	NA	20/03/20	NA	Negative	No	Alive	NA	NA
16a	Mother (32)	16/03/20	24/03/20	9	Positive	No	Alive	Mild	Unknown
16b	Daughter (1)	20/03/20	27/03/20	8	Positive	No	Alive	Mild	Unknown
16c	Father (37)	20/03/20	27/03/20	8	Positive	No	Alive	Mild	Unknown
16d	Babysitter (67)	08/04/20	10/04/20	3	Negative	No	Alive	NA	NA
16e	Grandmother (66)	NA	not tested	NA	NA	No	Alive	Asymptomatic	NA
17a	Father (54)	17/03/20	27/03/20	11	Positive	Yes	Alive	Moderate	Low
17b	Son (25)	20/03/20	not tested	NA	NA	No	Alive	Mild	NA
17c	Mother (50)	24/03/20	29/03/20	6	Positive	No	Alive	Mild	High

(Continues)

TABLE 1 (Continued)

Cluster member	Member (age ^a)	Onset of symptoms	Sample collection	Day of illness ^b	PCR	Hospital	Outcome	Clinical course	Viral load
17d	Daughter (15)	28/03/20	01/04/20	5	Positive	Yes	Alive	Mild	Moderate
17e	Son (19)	NA	30/03/20	NA	Negative	No	Alive	NA	NA
18a	Father (45)	19/03/20	25/03/20	7	Positive	Yes	Alive	Moderate	Moderate
18b	Daughter (7)	24/03/20	26/03/20	3	Positive	No	Alive	Mild	Low
18c	Mother (42)	24/03/20	not tested	NA	NA	No	Alive	Mild	NA
18d	Daughter (7)	25/03/20	26/03/20	2	Positive	No	Alive	Mild	High
18e	Son (7)	25/03/20	Not tested	NA	NA	No	Alive	Mild	NA
19a	Father (41)	22/03/20	27/03/20	6	Positive	Yes	Alive	Moderate	Unknown
19b	Son (3.5)	25/03/20	04/04/20	11	Negative	No	Alive	NA	NA
19c	Daughter (9)	26/03/20	04/04/20	10	Positive	No	Alive	Mild	Low
19d	Daughter (6)	26/03/20	04/04/20	10	Negative	No	Alive	NA	NA
19e	Mother (37)	30/03/20	01/04/20	3	Positive	Yes	Alive	Moderate	Moderate
20a	Mother (22)	24/03/20	02/04/20	10	Positive	No	Alive	Mild	High
20b	Son (15 d)	01/04/20	01/04/20	1	Positive	Yes	Alive	Moderate	High
20c	Father (32)	NA	Not tested	NA	NA	No	Alive	Asymptomatic	NA
21a	Uncle (47)	28/03/20	03/04/20	7	Positive	Yes	Alive	Moderate	Moderate
21b	Grandfather (76)	05/04/20	09/04/20	5	Positive	Yes	Dead	Severe	Moderate
21c	Father (45)	13/04/20	21/04/20	9	Positive	Yes	Alive	Moderate	Moderate
21d	Daughter (14)	19/04/20	25/04/20	7	Positive	No	Alive	Mild	High
21e	Son (2.5)	22/04/20	25/04/20	4	Positive	No	Alive	Mild	High
21f	Mother (38)	NA	25/04/20	NA	Positive	No	Alive	Asymptomatic	High
21g	Daughter (8)	NA	25/04/20	NA	Positive	No	Alive	Asymptomatic	Moderate
22a	Son (6 wk)	28/03/20	28/03/20	1	Positive	Yes	Alive	Moderate	High
22b	Mother (32)	NA	29/03/20	NA	Negative	No	Alive	NA	NA
22c	Father (43)	NA	02/04/20	NA	Negative	No	Alive	NA	NA
23a	Father (35)	11/04/20	20/04/20	10	Positive	Yes	Dead	Severe	Moderate
23b	Grandmother (50)	NA	23/04/20	NA	Positive	No	Alive	Asymptomatic	Moderate
23c	Mother (29)	NA	23/04/20	NA	Positive	No	Alive	Asymptomatic	Moderate
23d	Daughter (1)	NA	24/04/20	NA	Negative	No	Alive	NA	NA

Abbreviations: NA, does not apply; PCR, polymerase chain reaction.

^aAge is presented in years, unless specified.

^bOf sample collection.

^cThe first two cases were hospitalized for containment purposes.

3 | RESULTS

We studied 23 family clusters with a median number of 5 (range, 3-7) household members per family. In total there were 109 household members, including 66 adults and 43 children. An adult household member with COVID-19 was the first case in 21 (91.3%) family clusters and a child in 2 (8.7%). Among adults, fathers were identified as first cases in 9 clusters, mothers in 8,

both parents in 2 and other relatives in 2. In terms of source of infection of the first case, 11 were community-acquired, six travel-associated, three healthcare-associated, while in three the source of infection could not be identified. In six (26.1%) family clusters children constituted the index cases, including five infants ≤ 3 months (clusters 13,14,15, 20, 22) and one adolescent girl (cluster 9). The median number of days between the onset of symptoms and the date of sample collection for SARS-CoV-2 test

TABLE 2 SARS-CoV-2-associated morbidity by age group in 23 family clusters

Characteristic	Adults (n = 66)	Children (n = 43)	P value
SARS-CoV-2 infection ^a	38 (57.6%)	30 (69.8%)	.256
Asymptomatic	4 (10.5%)	12 (40.0%)	.021
COVID-19	34 (89.5%)	18 (60.0%)	.171
Mild	23 (67.7%)	13 (72.2%)	.021
Moderate	8 (23.5%)	5 (27.8%)	
Severe	3 (8.8%)	0 (0%)	
Death	3 (8.8%)	0 (0%)	.173

Abbreviations: COVID-19, coronavirus disease 2019; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

^aOf 60 (90.9%) adults and 42 (97.7%) children tested by PCR.

was 5 days, with significant difference between children (3.67 ± 2.35 days) and adults (5.92 ± 3.00 days) ($P = .019$).

Table 1 shows the characteristics of household members and the timeline of transmission of infection per family cluster. There was a median of 3 (range, 1–7) infected persons per cluster. The median attack rate per family cluster was 60% (range: 33.4%–100%). Transmission of infection occurred from an adult to a child in 19 clusters; in 12 clusters transmission occurred from an adult to another adult. There was no evidence of child-to-adult or child-to-child transmission, although in 14 clusters there was close contact between infected children and noninfected adult household members.

Table 2 summarizes the COVID-19 associated morbidity in the 109 household members by age group. In total 68 household members tested positive for SARS-CoV-2 infection. Children were more likely to have an asymptomatic infection compared with adults (40% vs 10.5%; $P = .021$), accounting for 75% of all asymptomatic infections. In contrast, adults were more likely to develop a severe clinical course compared with children (8.8% vs 0%; $P = .021$). Three men aged 35, 50 and 76 years died because of COVID-19. No fatal case was seen among children.

Regarding viral load, 11 (40.7%) children had high viral load, 5 (18.6%) moderate, and 11 (40.7%) low viral load, while the respective frequencies and percentages for the adults were 10 (34.5%), 15 (51.7%), and 4 (13.8%) ($P = .016$). No child presented severe disease. Among the 18 children with COVID-19, 13 (72.2%) presented mild symptoms and five (27.8%) presented a moderate clinical course. Of note, all five children with moderate clinical course were ≤ 3 months old; four were males and had high viral load, while low viral load had the female infant (Table 1).

4 | DISCUSSION

We studied 23 family clusters of SARS-CoV-2 infection that occurred in Greece. We found a median attack rate of 60% (up to 100% in some clusters), which demonstrates the high transmission dynamics of SARS-CoV-2. Attack rates up to 75% have been also reported in other family

clusters.^{7,8} In line with studies from Switzerland and China,^{7,9} in our study adults accounted for almost all virus importations within families. Of note, five clusters were brought under attention because a young infant became ill and hospitalization was required. In terms of timing, the complete lockdown had an exceptional impact on the onset of family clusters, given that less than one-fifth of identified clusters occurred after that date.

We found no case of transmission of SARS-CoV-2 infection from an infected child to another child or an adult. In a cluster of COVID-19 that occurred in the French Alps, one infected, symptomatic child had many close contacts within three different schools, yet no case of transmission was identified despite an exhaustive epidemiologic and virologic investigation.¹⁰ This may be attributed to the fact that children with SARS-CoV-2 infection more often have an asymptomatic infection or a mild course compared to adults.^{5,7-9,11} In our study infected children were significantly more likely to have an asymptomatic infection or a mild disease and a favorable outcome, compared to adults. The shorter time period that elapsed between the onset of symptoms and testing in children compared with adults, may be attributed to the increased awareness and high rate of healthcare seeking for ill children. It has been reported that patients with severe COVID-19 tend to have a higher viral load than those with mild disease.¹² Although the number of children in the present study was low, it was found that one-third (4 out of 12) of asymptomatic children presented high viral load. High viral load has been detected in children with no severe symptoms.⁹ In our study, children were either asymptomatic or presented mild symptoms, and only infants presented a moderate form of the disease, and none presented a severe form of the disease. Most probably these findings are related with the immune response in the various age groups rather than the viral load.

Limitations of the study were the relatively low number of clusters tested and the fact that the clinical samples were taken from different sites and on different days after symptoms' onset in each patient; thus any conclusion on association of the viral load and severity of the disease cannot be drawn.

In conclusion, the present study provides an insight into transmission dynamics of SARS-CoV-2 within families with children indicating that the prevalent direction of transmission is adult-to-child than child-to-adult. Contact tracing showed that in most cases the adults had contact with a confirmed COVID-19 case, thus, they were the primary source of the family infection. However, since the tracing was based on the dates of the PCR test and given that adults present symptoms in a higher proportion than children, it may happen that more adults have been identified first and the positive children were assessed as secondary cases. Therefore, a conclusion about the index case cannot be drawn with certainty and the role of children in virus transmission needs further investigation.

ACKNOWLEDGMENTS

The authors thank all patients and healthcare personnel for their assistance in data collection. The authors also thank Anastasia Tentoma for technical assistance. The opinions are those of the authors and do not necessarily represent those of their institutions. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. The Reference

Laboratories were financially supported by the National Public Health Organization (Greece).

AUTHOR CONTRIBUTIONS

HCM: Conception and design of the study, investigation, writing of the manuscript. RV, KP, AK, NS, GG, ME, SM, ANL, EF, AM, and BMG: Investigation, review and editing. VR: Statistical analysis and review. ER, AM, and AT: Investigation, review and editing. AP: Conception and design of the study, investigation, review, writing, and editing.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Vasilios Raftopoulos  <http://orcid.org/0000-0003-0395-7820>

REFERENCES

- World Health Organization. Coronavirus disease (COVID-19) pandemic. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>. Accessed July 27, 2020.
- National Public Health Organization. Daily report of epidemiological surveillance of COVID-19. www.eody.gov.gr. Accessed July 27, 2020.
- Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet*. 2020;395:514-523.
- Du W, Yu J, Wang H, et al. Clinical characteristics of COVID-19 in children compared with adults in Shandong Province. *China. Infect*. 2020;48:445-452.
- Zhen-Dong Y, Gao-Jun Z, Run-Ming J, et al. Clinical and transmission dynamics characteristics of 406 children with coronavirus disease 2019 in China: a review. *J Infect*. 2020;81(2):e11-e15.
- Bujang MA, Sa'at N, Tg TMI, Sidik AB, Lim CJ. Sample size guidelines for logistic regression from observational studies with large population: emphasis on the accuracy between statistics and parameters based on real life clinical data. *Malays J Med Sci*. 2018;25:122-130.
- Jiang XL, Zhang XL, Zhao XN, et al. Transmission potential of asymptomatic and paucisymptomatic SARS-CoV-2 infections: a three-family cluster study in China. *J Infect Dis*. 2020;221:1948-1952.
- Wolf GK, Glueck T, Huebner J, et al. Clinical and epidemiological features of a family cluster of symptomatic and asymptomatic SARS-CoV-2 infection. *J Pediatric Infect Dis Soc*. 2020;9:362-365.
- Posfay-Barbe KM, Wagner N, Gauthey M, et al. COVID-19 in children and the dynamics of infection in families. *Pediatr*. 2020;146:e20201576. <https://doi.org/10.1542/peds.2020-1576>
- Danis K, Epaulard O, Bénet T, et al. Cluster of coronavirus disease 2019 (COVID-19) in the French Alps, 2020. *Clin Infect Dis*. 2020;71:825-832.
- Song R, Han B, Song M, et al. Clinical and epidemiological features of COVID-19 family clusters in Beijing, China. *J Infect*. 2020;81(2):e26-e30.
- Liu Y, Yan LM, Wan L, et al. Viral dynamics in mild and severe cases of COVID-19. *Lancet Infect Dis*. 2020;20:656-657.

How to cite this article: Maltezou HC, Vorou R, Papadima K, et al. Transmission dynamics of SARS-CoV-2 within families with children in Greece: A study of 23 clusters. *J Med Virol*. 2021;93:1414-1420. <https://doi.org/10.1002/jmv.26394>