Prevalence of Asymptomatic COVID-19 Among Children Attending Elective Dental Surgeries Under General Anesthesia

Heba Altrawneh *, Basma Alsakarneh*, Liali Aladwan*, Oraib Ababneh*, Maram Batarseh**

ABSTRACT

Objective: The actual incidence of asymptomatic infection with SARS-CoV-2 in children is unknown, with variation in the estimated prevalence in the literature. Our study aimed to evaluate the prevalence of COVID-19 in asymptomatic children attending elective dental procedures under general anesthesia at a single institution.

Methods: The records for 128 patients, 68 males (53.1%) and 60 females (46.9%), aged between 3 and 12 years, who were selected for elective pediatric dental surgical procedures, were retrieved retrospectively from the available electronic medical records (Hakeem) at Queen Rania Al-Abdullah Hospital for Children from November 2020 to April 2021. Strict inclusion and exclusion criteria were applied for patient selection for elective surgeries to make the estimated prevalence of COVID-19 among the study population as reliable and valid as possible.

Results: The prevalence of asymptomatic SARS-CoV-2 infection among the study population was approximately 7% (nine out of 128 patients). Forty-one of 128 patients were medically compromised (have other medical conditions), and of those forty-one medically compromised, seven patients tested positive for SARS-CoV-2 infection. Only medical conditions significantly affected the real-time reverse transcription-polymerase chain reaction (RT-PCR) test results (p value<0.05), while gender, age groups, and parents' occupation did not.

Conclusion: Asymptomatic infection with SARS-CoV-2 is prevalent among children, making them a potential source of the spread of COVID-19. Therefore, healthcare providers should take precautions when dealing with children and perform the RT-PCR to detect infected children if applicable. Medically compromised children are more prone to SARS-CoV-2 infection. Although compromised children are at serious risk for severe disease, they may have no symptoms before the diagnosis.

Keywords

Asymptomatic children, Coronavirus, COVID-19, Prevalence of COVID-19, RT-PCR, SARS-CoV-2 infection.

JRMS August 2024; 31 (2): 10.12816/0061992

Introduction

In December 2019, multiple cases of acute respiratory illness of an unknown origin that share similar presentation, particularly fever, were reported in Wuhan city, Hubei province of China (1, 2). The intensive efforts directed to finding out the cause of the pneumonia showed that a novel single-stranded RNA virus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was the causative agent (2). Subsequently, this acute respiratory illness was named 'coronavirus disease 2019' COVID-19 (2).

From the departments of:

^{*}Pediatric Dentistry.

^{**} Pediatric Prosthodontics.

Correspondence should be addressed to: Dr. Heba Altrawneh.,Email: <u>Dr_heba_tarawneh@Yyahoo.com</u> Submission date: 26 August. 2021 , Acceptance date: 14 Feb. 2022 , Publication date: August,2024

Coronavirus is a single-stranded RNA, medium-sized (80 to 90 nm), enveloped, and round virus that gets its name from the club-shaped and peculiar fringe of widely spaced projections covering its surface (3). SARS-Cov-2 enters host cells by binding to the angiotensin-converting enzyme II (ACE2) receptor expressed in various human tissues, especially the respiratory tract (4). The majority of COVID-19 patients complain of fever, shortness of breath, and dry cough. Other patients may have rhinorrhea, sneezing, sore throat, or other upper respiratory tract or gastrointestinal symptoms (3, 5). Besides, a significant percentage of infected patients may not experience any symptoms. Thus, they are considered a potential source of substantial spread of the disease (6, 7).

The global outbreak of COVID-19 prompted the World Health Organization (WHO) to declare it as a pandemic in March 2020 (8). Jordan, like many countries, enforced a national lockdown for about two and a half months (between March 18 and June 4, 2020) in its attempt to contain and prevent the spread of the coronavirus. From September 1, 2020, the total number of daily-confirmed cases in Jordan increased rapidly from 68 up to 7,933 on November 19, 2020. This accelerated increase in confirmed cases forced policymakers to apply more strict precautionary measures. In July 2021, in Jordan, the number of confirmed cases with COVID-19 reached 756,923, with 9,836 deaths (9).

During the lockdown and for a long period afterwards, outpatients' clinics and elective operations were suspended. Even after their return, there were strict precautionary measures in the health sector to control the spread of infection among patients and healthcare providers. The Jordanian Royal Medical Services (RMS) have been one of the pioneers in this context. Many children attend outpatient clinics and undergo surgeries at the JRMS hospitals. Queen Rania Al-Abdullah Hospital for Children is an advanced tertiary and referral hospital that provides surgical and medical services for a large number of children annually. On a daily basis, close contact with children exposes the children themselves, parents, and healthcare providers to infection with SARS-CoV-2.

The actual incidence of infection with SARS-CoV-2 among children is unknown due to the lower percentage of children being tested than adults and patients with severe illness and the significantly lower hospitalization rate of children with COVID-19 than adults (10). In Jordan in 2020, children aged less than 14 years old comprise about 32.85% (3,351,730) of the total population (10,203,134) (11, 12).

Given the relatively limited publicly available data concerning the prevalence of COVID-19 in asymptomatic children in Jordan, urgent attempts should be directed to address this gap. This study aimed to assess the prevalence of COVID-19 in asymptomatic children attending elective dental procedures under general anesthesia at Queen Rania Al-Abdullah Hospital for Children.

Methods

A retrospective observational study was conducted at pediatric dental clinics at Queen Rania Al-Abdullah Hospital for Children, one of the Jordanian Royal Medical Services (JRMS) hospitals, located in Amman, the capital of Jordan, between November 2020 and April 2021. The data for 128 patients, 68 males (53.1%) and 60 females (46.9%), aged between 3 and 12 years (divided into two groups from 3 to 6 and from 7 to 12 years old), who were selected for elective pediatric dental surgical procedures, were obtained from the available electronic medical records (known as Hakeem) in the hospital. All patients had dental pain and were indicated for elective treatment under general anesthesia (uncooperative).

Patients were subjected to strict selection criteria due to the critical pandemic situation during the study period. The real-time reverse transcription-polymerase chain reaction (RT-PCR) test was ordered only for patients who met the inclusion criteria for elective surgeries. It was performed on the day before surgeries, and

results were obtained on the same day from the JRMS laboratory. Surgeries were postponed for four weeks for patients with positive RT-PCR test results, and the data for those patients were not included again in the study. During follow-up periods, all patients had no symptoms of COVID-19.

Inclusion criteria for patient selection for elective surgeries:

Patients without any features of COVID-19 aged between 3 and 12 years who had normal investigations (CBC, PT, PTT, INR) and had no contraindications for general anesthesia were included.

Exclusion criteria for patient selection for elective surgeries:

Patients who had one or more features of the disease (fever, respiratory symptoms (chest pain and tightness, and dyspnea), imaging evidence of pneumonia, general weakness, or fatigue, eye symptoms (lacrimation and conjunctivitis), GI symptoms (diarrhea and vomiting), dizziness, headache, and skin rash) were excluded.

The ethical committee (IRB) at the JRMS approved the study (ethical code number: 38 _ 6/2012). The study protocol adhered to the guidelines of the Declaration of Helsinki, as revised in Tokyo and Venice. The Statistical Package for the Social Sciences (SPSS; version 25) was used for statistical analysis.

Statistical analysis

The SPSS, version 25, was used for all computations and a p-value of less than 0.05 was considered statistically significant. Descriptive analysis was conducted for all variables using frequencies and percentages. The relationship between the RT-PCR test (dependent variable) and all other variables, including gender, age groups, parents' occupation (medical or non-medical), and the medical condition of patients (fit or compromised), was assessed by Fisher's exact test.

Results

A total of 128 subjects, 68 males (53.1%) and 60 females (46.9%), participated in the study with a mean age of 6 ± 2.3 . The characteristics of patients are shown in Table 1. Eighty-seven (68%) subjects were medically fit, while 41 (32%) were medically compromised. Patients who were considered compromised had a history medical illnesses, including cardiac, respiratory, endocrinological, haemato-oncological, of neurodevelopmental, and genetic disorders (Table 2). Only 119 (93%) patients underwent surgical procedures. Surgeries were cancelled for nine (7%) asymptomatic patients infected with SARS-CoV-2. Seven of these nine patients were medically compromised, and two of them were medically fit. The medical conditions with these seven patients are epilepsy, autism, diabetes mellitus, tetralogy of Fallot, acute lymphocytic leukemia, G6PD deficiency, and scleroderma (Table2). During the follow-ups, all patients were symptom-free, and no complications were reported.

The prevalence of COVID-19 among the study population was approximately 7% (nine out of 128 patients). as demonstrated from the results of the RT-PCR test. All patients diagnosed with COVID-19 were asymptomatic.

Only medical conditions significantly affected the RT-PCR test results (p value<0.05). Of the nine positive cases, two patients were medically fit, while the rest of the patients were medically compromised

(Table 3). Other factors, including gender, age groups, and parents' occupation did not significantly affect the RT-PCR test results.

Variables	Frequency	Percentage					
Age groups							
3-6 years	82	64.1%					
7-12 years	46	35.9%					
Gender							
males	68	53.1%					
Females	60	46.9%					
Medical condition							
Compromised	41	32%					
Fit	87	68%					
Parents' occupation							
Medical	21	16.4%					
None-medical	107	83.6%					

Table I : Patients'	characteristics	(simple descrip	ptive analysis	of 128 subjects)
	enaraeteristies	(bimpie debein	per ve anar jois	01 120 540 0000

Table II: Patients' medical conditions (medically compromised patients).

Medical condition	Number of patients	RT-PCR test result
Epilepsy/cerebral palsy	8	Positive in 1 patient
Autism/ ADHD	5	Positive in 1 patient
VSD and ASD	3	Negative
Asthma	3	Negative
Diabetes mellitus	3	Positive in 1 patient
Hypothyroidism	3	Negative
Global developmental delay	2	Negative
Cleft palate	1	Negative
Tetralogy of Fallot	1	Positive
Apert syndrome	1	Negative
Acute lymphocytic leukemia	1	Positive
Down syndrome	1	Negative
Hypogammaglobulinemia	1	Negative
Osteogenesis imperfecta	1	Negative
G6PD deficiency	1	Positive
factor VIII deficiency	1	Negative
Tuberculosis	1	Negative
Scleroderma	1	Positive
Phenylketonuria	1	Negative
Epidermolysis bullosa	1	Negative
Chronic cholestatic diseases	1	Negative
Total	41 (100%)	7 (17.1%)

VSD: Ventricular septal defect, ASD: Atrial septal defect, ADHD: Attention deficit hyperactivity disorder, G6PD: Glucose-6-phosphate dehydrogenase.

Fisher's exact test was conducted to calculate the P-value for this sample.

	PCR re	PCR result		P-value
Gender				
	Negative	Positive		D 1 0 204
Females	54 (45.4%)	6 (66.7%)	60	P value=0.304
Males	65 (54.6%)	3 (33.3%)	68	
Total	119	9	128	
3- 6 years	76 (63.9%)	6 (66.7%)	82	P value=1.000
7-12 years	43 (36.1%)	3 (33.3%)	46	
Total	119	9	128	
Compromised	34 (28.6%)	7(77.8%)	41	P value=0.005*
Fit	85 (71.4%)	2 (22.2%)	87	
Total	119	9	128	
Parents' occupation				
Medical	21 (17.60%)	0 (0 %)	21	P value=0.354
Non-medical	98 (82.4)	9 (100%)	107	
Total	119	9	128	

Table III. The relationship between RT-PCR results and all other variables.

P-value<0.05* was considered statistically significant.

Discussion

To the best of our knowledge, this is the first study that aimed to estimate the prevalence of COVID-19 in asymptomatic children attending elective surgeries in Jordan. The current study revealed that the prevalence of SARS-CoV-2 infection among asymptomatic children is approximately 7%. The prevalence in the current study is very close to the prevalence reported in previous studies. A study conducted by Guo et al. found that the prevalence of asymptomatic children infected with SARS-CoV-2 was 5.9% (13). Another study carried out by Dong et al. revealed that 4.4% of children with COVID-19 were asymptomatic (14). However, the exact prevalence of asymptomatic infected children remains a subject of variation between studies. The prevalence of children infected with SARS-CoV-2 without symptoms, who were tested in 28 children's hospitals in the United States before clinic visits, surgery, or hospital admissions, varied from 0% to 2.2% (15). A systematic review and meta-analysis that evaluated the clinical characteristics and epidemiological spectrum of children with COVID-19 showed that approximately 23% of pediatric patients across 31 studies had no features of the disease before the diagnosis (16). A single-arm meta-analysis that included 29 studies with 4300 children infected with SARS-CoV-2 revealed that the estimated prevalence of asymptomatic cases was 18.4% (17). Another study reported that 15-35% of children could have no symptoms (18). This variation in the estimated prevalence among studies can be attributed to the difference in screening and testing strategies between the countries.

Children experience milder symptoms than adults do, and in some children, symptoms may be unrecognized before the diagnosis (19-21). However, severe disease has been reported in children (19, 21). In our study, the prevalence of asymptomatic infection in children was estimated at 7%, which was higher than the prevalence among asymptomatic adults in another study (1%) (22). This difference in the prevalence of asymptomatic infection in children than adults. The ACE2 receptors' maturity and function were speculated to be lower in children than in adults. Besides, children have higher levels of antibodies against the virus than adults since they encounter more respiratory tract infections in winter.

In addition, the developing immune system in children may respond differently to pathogens than in adults (14). In contrast to adults, children are usually kept at home and are therefore less likely to be exposed to the virus or infected people (14).

Unhealthy older people, people who are immunocompromised, and those with underlying medical disorders such as cardiovascular and chronic respiratory illnesses, diabetes mellitus, and cancer are more liable to develop severe disease with acute injury to the lungs, heart, liver, and kidneys (4, 23, 24). In contrast, the younger population and the elderly who are healthy experience fewer symptoms and are at a lower risk of encountering severe symptoms (24, 25). The symptoms of COVID-19 in paediatrics and adults are similar, with a difference in the frequency of symptoms (26, 27). In this study, medically compromised children were found to be more liable to get the infection. However, all patients were asymptomatic and recovered without complications. A study conducted by Shekerdemian et al. revealed that comorbidities in children appeared to be an important factor in acquiring the disease. Also, it confirmed that severe illness was less frequent in children with significant preexisting comorbidities, with better hospital outcomes than in adults (28).

We found that age and gender were not correlated to the RT-PCR test results among the study population. Hu et al. conducted a study that included data on the total number of confirmed incident and death cases from SARS-CoV-2 infection in 177 countries. The study aimed to recognize the age groups with higher susceptibility and fatality. They found that the incidence and mortality rate of COVID-19 were negatively correlated to age and gender in patients aged from 0 to 24 years (29).

As far as we know, this is the first study that evaluated the prevalence of SARS-Cov-2 infection among asymptomatic children attending elective surgeries in a single institution in Jordan through a critical period of the pandemic. We excluded children with symptoms similar to symptoms of COVID-19 from performing the RT-PCR test to avoid any interference in the results, suspecting that SARS-CoV-2 infection was the primary cause of their illness. This method made the results of our study very realistic. However, the current study has some limitations. First, the study had an observational retrospective design conducted in a relatively short period. Second, the prevalence may be affected by the low probability of false positive and false negative results of the RT-PCR test.

Conclusion

Asymptomatic infection with SARS-CoV-2 is prevalent among children, making them a potential source of the spread of COVID-19. Therefore, healthcare providers should take precautions when dealing with children and should perform the RT-PCR to detect infected children if applicable. Medically compromised children are more prone to SARS-CoV-2 infection.

Acknowledgements

None.

References

1- Bogoch II, Watts A, Thomas-Bachli A, Huber C, Kraemer MUG, Khan K. Pneumonia of unknown aetiology in Wuhan, China: potential for international spread via commercial air travel. J Travel Med. 2020 Mar 13; 27(2):taaa008. doi: 10.1093/jtm/taaa008. PMID: 31943059; PMCID: PMC7107534.

2- Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. J Med Virol. 2020 Apr; 92(4):401-402. doi: 10.1002/jmv.25678. Epub 2020 Feb 12. PMID: 31950516; PMCID: PMC7166628.

3- Neuman BW, Adair BD, Yoshioka C, Quispe JD, Orca G, Kuhn P, et al. Supramolecular architecture of severe acute respiratory syndrome coronavirus revealed by electron cryomicroscopy. J Virol. 2006 Aug; 80(16):7918-28. doi: 10.1128/JVI.00645-06. PMID: 16873249; PMCID: PMC1563832.

4- Ni W, Yang X, Yang D, Bao J, Li R, Xiao Y, et al. role of angiotensin-converting enzyme 2 (ACE2) in COVID-19. Crit Care. 2020 Jul 13; 24(1):422. doi: 10.1186/s13054-020-03120-0. PMID: 32660650; PMCID: PMC7356137.

5- Peiris JSM. Coronaviruses. Medical Microbiology. 2012:587–93. doi: 10.1016/B978-0-7020-4089-4.00072-X. Epub 2012 May 24. PMCID: PMC7170185.

6- Al-Qahtani M, AlAli S, AbdulRahman A, Salman Alsayyad A, Otoom S, Atkin SL. The prevalence of asymptomatic and symptomatic COVID-19 in a cohort of quarantined subjects. Int J Infect Dis. 2021 Jan; 102:285-288. doi: 10.1016/j.ijid.2020.10.091. Epub 2020 Nov 3. PMID: 33157290; PMCID: PMC7607262.

7- Sayampanathan AA, Heng CS, Pin PH, Pang J, Leong TY, Lee VJ. Infectivity of asymptomatic versus symptomatic COVID-19. Lancet. 2021 Jan 9; 397(10269):93-94. doi: 10.1016/S0140-6736(20)32651-9. Epub 2020 Dec 18. PMID: 33347812; PMCID: PMC7836843.

8- WHO announces COVID-19 outbreak a pandemic. https://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/news/2020/3/who-announces-covid-19-outbreak-a-pandemic. (Accessed on 12 June, 2020).

9-WHO Coronavirus Disease (COVID-19) Dashboard/ Jordan. https://covid19.who.int/region/emro/country/jo. (Accessed on July 12, 2021).

10- Centers for Disease Control and Prevention. Information for Pediatric Healthcare Providers. https://www.cdc.gov/coronavirus/2019-ncov/hcp/pediatric-hcp.html

(Accessed on 15 July, 2021).

11- Statistica. Jordan: Age structure from 2010 to 2020. https://www.statista.com/statistics/385468/age-structure-in-jordan/ (Accessed on 15 July, 2021).

12- Worldometers. https://www.worldometers.info/world-population/jordan-population/ (Accessed on 15 July, 2021).

13- Guo CX, He L, Yin JY, Meng XG, Tan W, Yang GP, et al. Epidemiological and clinical features of pediatric COVID-19. BMC Med. 2020 Aug 6; 18(1):250. doi: 10.1186/s12916-020-01719-2. PMID: 32762696; PMCID: PMC7408975.

14- Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiology of COVID-19 Among Children in China. Pediatrics. 2020 Jun; 145(6):e20200702. doi: 10.1542/peds.2020-0702. Epub 2020 Mar 16. PMID: 32179660. 15- Sola AM, David AP, Rosbe KW, Baba A, Ramirez-Avila L, Chan DK. Prevalence of SARS-CoV-2 Infection in Children Without Symptoms of Coronavirus Disease 2019. JAMA Pediatr. 2021 Feb 1; 175(2):198-201. doi: 10.1001/jamapediatrics.2020.4095. Erratum in: JAMA Pediatr. 2021 Feb 1; 175(2):212. PMID: 32840605; PMCID: PMC7851725.

16- Li B, Zhang S, Zhang R, Chen X, Wang Y, Zhu C. Epidemiological and Clinical Characteristics of COVID-19 in Children: A Systematic Review and Meta-Analysis. Front Pediatr. 2020 Nov 2; 8:591132. doi: 10.3389/fped.2020.591132. PMID: 33224909; PMCID: PMC7667131.

17- Liu C, He Y, Liu L, Li F, Shi Y. Children with COVID-19 behaving milder may challenge the public policies: a systematic review and meta-analysis. BMC Pediatr. 2020 Sep 1; 20(1):410. doi: 10.1186/s12887-020-02316-1. PMID: 32873269; PMCID: PMC7459157.

18- Alsohime F, Temsah MH, Al-Nemri AM, Somily AM, Al-Subaie S. COVID-19 infection prevalence in pediatric population: Etiology, clinical presentation, and outcome. J Infect Public Health. 2020 Dec;

13(12):1791-1796. doi: 10.1016/j.jiph.2020.10.008. Epub 2020 Oct 20. PMID: 33127335; PMCID: PMC7574780.

19- Han MS, Choi EH, Chang SH, Jin BL, Lee EJ, Kim BN, et al. Clinical Characteristics and Viral RNA Detection in Children With Coronavirus Disease 2019 in the Republic of Korea. JAMA Pediatr. 2021 Jan 1; 175(1):73-80. doi: 10.1001/jamapediatrics.2020.3988. PMID: 32857112; PMCID: PMC7455883.

20- Liguoro I, Pilotto C, Bonanni M, Ferrari ME, Pusiol A, Nocerino A, et al. SARS-COV-2 infection in children and newborns: a systematic review. Eur J Pediatr. 2020 Jul; 179(7):1029-1046. doi: 10.1007/s00431-020-03684-7. Epub 2020 May 18. Erratum in: Eur J Pediatr. 2021 Jul;180(7):2343. PMID: 32424745; PMCID: PMC7234446.

21- Mehta NS, Mytton OT, Mullins EWS, Fowler TA, Falconer CL, Murphy OB, et al. SARS-CoV-2 (COVID-19): What Do We Know About Children? A Systematic Review. Clin Infect Dis. 2020 Dec 3; 71(9):2469-2479. doi: 10.1093/cid/ciaa556. PMID: 32392337; PMCID: PMC7239259.

22- Wu Z, McGoogan JM. Characteristics of and Important Lessons from the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020 Apr 7; 323(13):1239-1242. doi: 10.1001/jama.2020.2648. PMID: 32091533.

23- World Health Organization (WHO). Statement: Older people are at highest risk from COVID-19, but all must act to prevent community spread. 2020. http://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/statements/statement-older-people-are-at-highest-risk-from-covid-19,-but-all-must-act-to-prevent-community-spread. (Accessed on 15 July, 2021).

24- Liu K, Chen Y, Lin R, Han K. Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. J Infect. 2020 Jun; 80(6):e14-e18. doi: 10.1016/j.jinf.2020.03.005. Epub 2020 Mar 27. PMID: 32171866; PMCID: PMC7102640.

25- Gardner W, States D, Bagley N. The Coronavirus and the Risks to the Elderly in Long-Term Care. J Aging Soc Policy. 2020 Jul-Oct; 32(4-5):310-315. doi: 10.1080/08959420.2020.1750543. Epub 2020 Apr 3. PMID: 32245346.

26- Stokes EK, Zambrano LD, Anderson KN, Marder EP, Raz KM, El Burai Felix S, Tie Y, Fullerton KE. Coronavirus Disease 2019 Case Surveillance - United States, January 22-May 30, 2020. MMWR Morb Mortal Wkly Rep. 2020 Jun 19; 69(24):759-765. doi: 10.15585/mmwr.mm6924e2. PMID: 32555134; PMCID: PMC7302472.

27- Poletti P, Tirani M, Cereda D, Trentini F, Guzzetta G, Sabatino G, et al. Association of Age With Likelihood of Developing Symptoms and Critical Disease Among Close Contacts Exposed to Patients With Confirmed SARS-CoV-2 Infection in Italy. JAMA Netw Open. 2021 Mar 1; 4(3):e211085. doi: 10.1001/jamanetworkopen.2021.1085. PMID: 33688964; PMCID: PMC7948061.

28- Shekerdemian LS, Mahmood NR, Wolfe KK, Riggs BJ, Ross CE, McKiernan CA, et al. Characteristics and Outcomes of Children With Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units. JAMA Pediatr. 2020 Sep 1; 174(9):868-873. doi: 10.1001/jamapediatrics.2020.1948. PMID: 32392288; PMCID: PMC7489842.

29- Hu D, Lou X, Meng N, Li Z, Teng Y, Zou Y, et al. Influence of age and gender on the epidemic of COVID-19: Evidence from 177 countries and territories - an exploratory, ecological study. Wien Klin Wochenschr. 2021 Apr; 133(7-8):321-330. doi: 10.1007/s00508-021-01816-z. Epub 2021 Feb 5. PMID: 33547492; PMCID: PMC7864622.