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**ESTIMATION OF SEROPREVALENCE AND IMMUNITY OF
COVID-19 ANTIBODIES AMONG CHILDREN**

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ESTIMATION OF SEROPREVALENCE AND IMMUNITY OF COVID-19
ANTIBODIES AMONG CHILDREN

By Sarra Abdulrahım Assi AL-OBAIDI

August 2023

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ABSTRACT

ESTIMATION OF SEROPREVALENCE AND IMMUNITY OF COVID-19 ANTIBODIES AMONG CHILDREN

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Master of Science in Biology

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The COVID-19 pandemic, caused by the novel coronavirus SARS-CoV-2, has had a profound impact on global health and society. Understanding the dynamics of the virus's spread and its effects on different population segments is of utmost importance as the pandemic continues to evolve. While COVID-19 has predominantly affected adults, the susceptibility and role of children in its transmission have sparked significant interest and concern. The study aims to estimate the incidence of SARS-CoV-2 antibodies (Ab) in children. Also, to determine the naturally acquired immunity through examining recent and past infections of SARS-CoV-2 represented by the appearance of IgM and IgG antibodies in children. The study was conducted in Diyala, Iraq, from September 2022 to March 2023. During this time, a total of 180 samples were recorded and studied. The sample collected was divided into the patient group and the control group. The outcomes presented in this study provide a comprehensive comparative analysis between the patients and control groups regarding age, gender, and residence. Two age distribution classifications were used. The first one categorized the ages of the study groups into three groups. Statistical analysis showed a significant difference among these age categories ($P=0.034$). The second classification divided the age groups into fifteen segments, revealing another significant difference between the study groups ($P=0.012$). Moreover, the Mean $\pm$ SD in months within the control group showed a significantly higher value compared to the patient group, with values of $(76.4 \pm 51.7$ vs. 49.7 ± 44.9 , $P = 0.0001$), highlighting the age-based difference between the two groups. According to gender, the percentage of males within the patients' group was

substantially higher when compared to that of the controls, with a proportion of (63.41% vs. 47.95%). Conversely, the percentage of females in the control group was notably higher compared to the patients' group, with figures of (52.04% vs. 36.58%, $P=0.038$). Also, the findings revealed that the previous infection in children's families of the patient's group 63(76.8%) cases were significantly superior as compared with the control group 38 (38.8%) cases at P value (<0.0001). However, the findings showed that the number of cases infected with respiratory tract infection in the patient's group recorded 5(6.1%) cases, while 60(61.2%) no cases were monitored in the control group at P . value (<0.013). Specifically, the patient group exhibited markedly higher rates of several symptoms, including fever, sore throat, runny nose, rash, diarrhea, difficulty breathing, and coughing, compared to the control group ($P<0.0001$). Regarding the rate of anti-COVID-19 IgG, the results showed that out of 35 tested patients, 25 (74.28%) tested positive, while 9 (25.71%) tested negative. On the contrary, in the control group, among 74 healthy children who underwent testing, 56 (75.67%) were found to be positive, and 18 (24.32%) were negative for the antibody. Despite these variations, the difference between the two groups was statistically insignificant ($P=0.437$). Regarding anti-COVID-19 IgM, the analysis revealed that among the 82 tested patients, 63 (76.82%) were positive, while 19 (23.17%) were negative. In contrast, among the 24 tested individuals in the control group, 8.33% were positive, and 91.66% were negative for the antibody. This resulted in a statistically significant distinction between the two groups, with a P -value of 0.0001. In conclusion, this study found that children with respiratory tract symptoms had a higher rate of positive COVID-19 infection compared to controls. It also highlighted that COVID-19 infection in children cannot be differentiated from other respiratory diseases based on symptoms. Additionally, approximately 10% of apparently healthy children were found to be asymptotically infected with COVID-19. Furthermore, about 25% of patients and controls had protective immunity from previous infection or contact with positive cases.

2023, 58 pages

Keywords: COVID-19, Seroprevalence, Antibodies, Children, Immunity

ÖZET

ÇOCUKLAR ARASINDA COVID-19 ANTİKORLARININ SEROPREVALANS VE BAĞIŞIKLIĞININ TAHMİNİ

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COVID-19 pandemisi, yeni koronavirüs SARS-CoV-2 tarafından tetiklenen, küresel sağlık ve toplum üzerinde derin etkileri olan bir olaydır. Virüsün yayılma dinamiklerini anlamak ve farklı nüfus kesimleri üzerindeki etkilerini anlamak, pandeminin evrimleşmeye devam ettiği süreçte büyük önem taşımaktadır. COVID-19 özellikle yetişkinleri etkilemiş olsa da, çocukların duyarlılığı ve virüsün bulaşma süreçlerindeki rolü büyük ilgi ve endişe uyandırmıştır. Bu çalışma, çocuklarda SARS-CoV-2 antikorlarının (Ab) yaygınlığını tahmin etmeyi amaçlamaktadır. Ayrıca, IgM ve IgG antikorlarının çocuklarda görünümü aracılığıyla SARS-CoV-2'nin son ve geçmiş enfeksiyonlarını inceleyerek doğal kazanılmış bağışıklığı belirlemeyi hedeflemektedir. Çalışma, Eylül 2022'den Mart 2023'e kadar Diyala, Irak'ta gerçekleştirildi. Bu süre zarfında toplam 180 örnek kaydedildi ve incelendi. Toplanan örnek, hasta grubu ve kontrol grubu olarak ayrıldı. Bu çalışmada sunulan sonuçlar, yaş, cinsiyet ve ikamet yeri açısından hastalar ile kontrol grupları arasında kapsamlı bir karşılaştırmalı analiz sunmaktadır. İki yaş dağılımı sınıflandırması kullanıldı. İlk sınıflandırma, çalışma gruplarının yaşlarını üç gruba ayırdı. İstatistiksel analiz, bu yaş kategorileri arasında anlamlı bir fark olduğunu gösterdi ($P=0.034$). İkinci sınıflandırma ise yaş gruplarını on beş segmente böldü ve çalışma grupları arasında başka bir anlamlı farklılık ortaya çıktı ($P=0.012$). Ayrıca, kontrol grubundaki ortalama $\pm$ standart sapma değerleri, hasta grubuna kıyasla anlamlı derecede yüksek bir değer gösterdi ($76,4 \pm 51,7$ vs. $49,7 \pm 44,9$, $P = 0,0001$), bu da iki grup arasındaki yaşa dayalı farkı vurgulamaktadır. Cinsiyete göre, hasta grubundaki erkek yüzdesi, kontrol grubundakinin oranıyla karşılaştırıldığında

oldukça yüksekti ve oranlar (63,41% vs. 47,95%) şeklindeydi. Aksine, kontrol grubundaki kadın yüzdesi, hasta grubuna kıyasla belirgin şekilde daha yüksekti ve oranlar (52,04% vs. 36,58%, $P= 0,038$) olarak kaydedildi. Ayrıca, bulgular, hasta grubunun çocuklarının ailelerindeki önceki enfeksiyonun, hasta grubunda 63 (%76,8) vakayla karşılaştırıldığında kontrol grubunda 38 (%38,8) vakadan anlamlı şekilde üstün olduğunu ortaya koydu (P değeri $<0,0001$). Ancak, bulgular, solunum yolu enfeksiyonuna yakalanan hasta grubundaki vaka sayısının 5 (%6,1) olduğunu gösterirken, kontrol grubunda 60 (%61,2) vaka kaydedildiğini ortaya koydu. Özellikle, hasta grubu, kontrol grubuna kıyasla ($P<0,0001$) ateş, boğaz ağrısı, burun akıntısı, döküntü, ishal, nefes darlığı ve öksürük gibi birçok semptomun belirgin şekilde daha yüksek oranlarını gösterdi. Anti-COVID-19 IgG oranı bakımından, sonuçlar 35 test edilen hastadan 25'inin (%74,28) pozitif, 9'unun (%25,71) negatif olduğunu gösterdi. Bunun aksine, kontrol grubunda test edilen 74 sağlıklı çocuğun 56'sının (%75,67) pozitif olduğu ve 18'inin (%24,32) antikor bakımından negatif olduğu tespit edildi. Bu farklılıklara rağmen, iki grup arasındaki fark istatistiksel olarak anlamsızdı ($P= 0,437$). Anti-COVID-19 IgM bakımından yapılan analiz, test edilen 82 hastanın 63'ünün (%76,82) pozitif olduğunu, 19'unun (%23,17) ise negatif olduğunu ortaya koydu. Buna karşılık, kontrol grubundaki 24 test edilen bireyin %8,33'ü pozitif iken, %91,66'sı antikor bakımından negatif bulundu. Bu iki grup arasında istatistiksel olarak anlamlı bir fark vardı ve P değeri 0,0001 olarak kaydedildi. Sonuç olarak, bu çalışma solunum yolu semptomları gösteren çocukların COVID-19 enfeksiyonunun pozitif oranının kontrollerle karşılaştırıldığında daha yüksek olduğunu buldu. Ayrıca, bu çalışma COVID-19 enfeksiyonunun çocuklarda semptomlara dayalı olarak diğer solunum yolu hastalıklarından ayırt edilemeyeceğini vurguladı. Ek olarak, görünüşte sağlıklı çocukların yaklaşık %10'unun COVID-19 ile semptom göstermeksizin enfekte olduğu bulundu. Dahası, hastaların ve kontrollerin yaklaşık %25'inin önceki enfeksiyon veya pozitif vakalarla temas sonucu koruyucu bağışıklığa sahip olduğu belirlendi.

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Anahtar Kelimeler: COVID-19, Seroprevalans, Antikorlar, Çocuklar, Bağışıklık

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LIST OF SYMBOLS

-	Minus
%	Percent
**	Significant
/	Divide
+	Plus
<	Greater than
=	Equal
>	Less than
±	Plus minus
≤	Greater or equal to
≥	Less or equal to
L	Deciliter
g	Gram
kg	Kilogram
L	Liter
m ²	Square meter
μg	Microgram
Mg	Magnesium
mIU	Milli-international units
min	Minute
mL	Milliliter
mmol	Millimole
mol	Mole
ng	Nanogram
nm	Nanometer
NS	Non-significant
rpm	Revolutions per minute
μL	Microliter

LIST OF ABBREVIATIONS

ACE2	Angiotensin converting enzyme 2
AP	Alkaline phosphatase
E	Envelope
HCoV	Corona- viruses infecting humans
HRP	Horse radish peroxidase
M	Membrane
N	Nucleocapsid
PBS	Phosphate buffered saline
RBD	Receptor-binding domain
S	Spike
SARS	Severe acute respiratory syndrome
VOC	Variants of concern
WHO	World health organization

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1. INTRODUCTION

The Latin word "corona," which means "crown," is where the word "coronavirus" (CoV) originates (Weiss and Navas-Martin 2002). From a simple cold to severe respiratory distress syndrome, it causes a variety of respiratory tract diseases in people (Heymann and Shindo 2020). Newly developing viral infections have grown to represent a serious global danger to public health in recent years. There have been reports of a number of viral illnesses, the severe acute respiratory syndrome-causing coronavirus (COVID-19), among others (SARS-CoV) (Cheng *et al.* 2007).

In the early 20th century, viruses belonging to the order Nidovirales, which contains the family Coronaviridae, which includes the corona virus, were first found (Shchelkanov *et al.* 2020). The structural proteins nucleoprotein (N), membrane glycoprotein (M), and spike glycoprotein are crucial factors in viral virulence and function (Perlman 2020).

These positive-thread and single-thread coated RNAs with the largest genome size have the ability to infect a variety of wild and domestic animals as well as humans (Singh *et al.* 2020). COVID-19 is a zoonotic disease and the transitional animal host between a bat reservoir and humans is still unknown, and the first cases of the disease that were detected at the end of 2019 were related to the seafood market in Wuhan, China (Butola *et al.* 2020). Sadly, new coronaviruses are predicted to keep emerging and causing seasonal epidemics due to their high genetic diversity, frequent genome recombination, and rise in human-animal connections caused by modern agricultural practice (Zhu *et al.* 2020). As of 5 November 2020, there had been confirmed cases of COVID-19 infection in 48,539,872 people throughout 215 countries and territories, and 1,232,791 deaths (WHO 2020).

The Corona virus is characterized by the ability to rapidly transform and adapt to different epidemiological situations, and studies have shown that although there are differences in the virus genome sequence in the spike protein in coronaviruses, they are all similar to SARS and are able to use the same angiotensin-converting enzyme as the

human receptor (Idris and ELSanousi 2020). Symptoms of infection with the virus may be similar to those of a common cold or flu (Prasad *et al.* 2020). Symptoms also include loss of the sense of taste and smell, chest pain, shortness of breath, kidney failure in severe cases, and then death (Tripathi and Kumar 2020). 80.9% of the infections are mild and 40-45% are asymptomatic. Asymptomatic cases showed subclinical transfer, working from the virus for a period of more than 14 days, as proven by previous studies (Díaz-Vélez *et al.* 2021).

Some patients with COVID-19 have also reported gastrointestinal symptoms, including diarrhea, vomiting, and abdominal pain, during the course of their illness. In the first case of COVID-19 to be reported in the United States. Before being admitted to the hospital, the patient experienced vertigo and vomiting for two days, followed by diarrhea and flatulence. The patient experienced abdominal distress beginning on the second day of hospitalization. Using reverse transcriptase-polymerase chain reaction, COVID-19 RNA was detected in the patient's feces on the seventh day of illness (Holshue *et al.*, 2020).

Children typically experience milder symptoms of COVID-19 and are at a lower risk of severe hospitalization and life-threatening outcomes (Dong *et al.* 2020). The presence of symptoms associated with SARS-CoV-2 increases the likelihood of transmission, whereas asymptomatic individuals pose a reduced transmission risk (Li *et al.* 2021). Initially, due to their milder symptoms, early studies indicated that children might not play a significant role in the spread of SARS-CoV-2. However, more recent research has raised questions regarding the potential for children to transmit the virus (DeBiasi and Delaney 2021).

1.1 Objectives of Study

1. To estimate the incidence of SARS-CoV-2 antibodies (Ab) overall in children.
2. To determine the natural acquired immunity through examining recent and past infections of SARS-CoV-2 represented by the appearance IgM and IgG antibodies in children.

3. To determine demographic and social parameters associated with SARS-CoV-2 infection..
4. To explore the proportion of unapparent infections with SARS-CoV-2 among asymptomatic children or with other clinical conditions.
5. To determine whether children play a role in transmitting infection to family members and the community.



2. LITERATURE REVIEW

2.1 Historical Review of COVID 19

COVID-19 is caused by SARS CoV-2, a positive-sense RNA virus with a single strand (Ge *et al.* 2020). The outbreak originated in the city of Wuhan, located in China, and then disseminated to numerous urban centers and nations globally (Wang *et al.* 2020). SARS-CoV-2 was isolated for the first time on December 26, 2019 in four Chinese patients with atypical pneumonia. On January 30, 2020, the World Health Organization (WHO) proclaimed it a "Public Health Emergency of International Concern," and on March 11, 2020, it was deemed a "Global Pandemic." (Cucinotta and Vanelli 2020).

Coronaviruses belong to a genus of viruses capable of infecting a diverse array of animals, leading to varying degrees of respiratory pathologies. Among these are the SARS-CoV and MERS-CoV types, both highly virulent zoonotic diseases. These viruses can strike unexpectedly and result in severe lung infections, often proving fatal (Krishnamoorthy *et al.* 2020).

The rapid and extensive movement of people facilitated the swift global spread of the disease within a matter of weeks. The United Arab Emirates was among the earliest countries in the Eastern Mediterranean region to identify COVID-19, detecting it in late January 2020, followed by Egypt and Iran. Subsequently, over the following weeks, every East Mediterranean nation recorded its inaugural cases. In Iraq, the first instance of COVID-19 was documented on February 24, 2020 (Ravelo and Jerving 2020). The initial documented case of COVID-19 in Iraq was reported in Najaf province on 24 February 2020, involving an Iranian student who had arrived from Iran. This was followed by four cases from a single family in Kirkuk province on 25 February, all of whom had also traveled to Iran. Another case was registered on 27 February in Baghdad, concerning a patient who had recently visited Iran (Sarhan *et al.* 2020). As of May 24, 2020, the confirmed COVID-19 cases had escalated to 4469,

with 160 reported fatalities, and a total of 2738 patients had successfully recovered from the infection (Alhilfi *et al.* 2020).

2.2 The Causative Agent

2.2.1 Nomenclature

The term "coronavirus" relates to the way these viruses appear under electron microscopy, which resembles a crown (Jin *et al.* 2020). The novel virus was given the name "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)" by ICTV on February 11, 2020. The virus was given this moniker because of its genetic similarity to the coronavirus that caused the 2003 SARS pandemic (WHO 2020).

On February 11, 2020, the World Health Organization (WHO) officially designated the name "COVID-19" for this novel disease, aligning with guidelines that had been collaboratively formulated with the World Organisation for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO) (WHO 2020).

2.2.2 Classification

The "Nidovirales" order of family members includes coronaviruses. The viruses that replicate utilizing a nested set of mRNAs are found in the Nidovirales order. Furthermore, the coronavirus subfamily has four genera (alpha, beta, gamma, and delta coronaviruses). From two of these genera, human coronaviruses (HCoV) are derived (alpha coronaviruses and beta coronaviruses) (Kesheh *et al.* 2022). Humans have alpha coronaviruses like HCoV-229E and HCoV-NL63, beta coronaviruses like HCoV-HKU1, HCoV-OC43 (Zumla *et al.* 2016).

2.2.3 Morphology and genomic structure

Under an electron microscope, coronaviruses have features that resemble crowns, thus their name. They have an outer envelope and positive-stranded RNA as their genomic material (McIntosh *et al.* 1967, Rabaan *et al.* 2020).

The greatest RNA genomes (27 to 32 kb) among RNA viruses are found in coronaviruses. The viral envelope, which is constructed from the host cell, contains spikes of glycoprotein. The nucleocapsid contains the viral genome, which is protected. When relaxed, the nucleocapsid has a helical structure; when inside the virus, it has a spherical shape. RNA from viruses replicates in a unique way. In the cytoplasm of the host cell (humans), the happen for coronavirus RNA replicates. When the viral genomic RNA's leader sequence is regularly attached to and detached from by the RNA polymerase, a nested collection of mRNAs with equivalent 3' ends is produced (Rabaan *et al.* 2020).

The genome of the coronavirus encodes for approximately four to five structural proteins, comprising the spike (S), membrane (M), envelope (E), nucleocapsid (N), and hemagglutinin-esterase (HE) proteins. The SARS-CoV-2, SARS CoV, HCoV-229E, and HCoV-NL63 genomes contain four genes that are responsible for producing the structural proteins S, M, N, and E. The coronaviruses HCoV-OC43 and HCoV-HKU1 contain an additional gene that encodes the HE protein (McIntosh and Peiris 2009). The evolutionary study reveals that the SARS-CoV-2 protein is deeply entrenched in the bat coronavirus genus lineage (Wan *et al.* 2020).

The entire genome of SARS-CoV-2 shares 80% of its sequence with SARS-CoV and 96% of its sequence with the bat coronavirus BatCoV-RaTG13 (Zhou *et al.* 2020). The spike protein sequences of SARS-CoV-2 and (SARS-CoV) share a 76-78% similarity. The RBD and RBM are similar in 73-76% and 50-53%, respectively. The human (MERS-CoV), on the other hand, is related to the Tylonycteris bat coronavirus HKU4, shares only around 54% of their sequence similarities, and chooses (DPP4) as its receptor (Yesudhas *et al.* 2021).

Sequence similarity between the (SARS-CoV-2) and (SARS-CoV) spike proteins explains their propensity to bind to the same receptor, angiotensin converting enzyme 2 (ACE2), in the host cell (Wan *et al.* 2020).

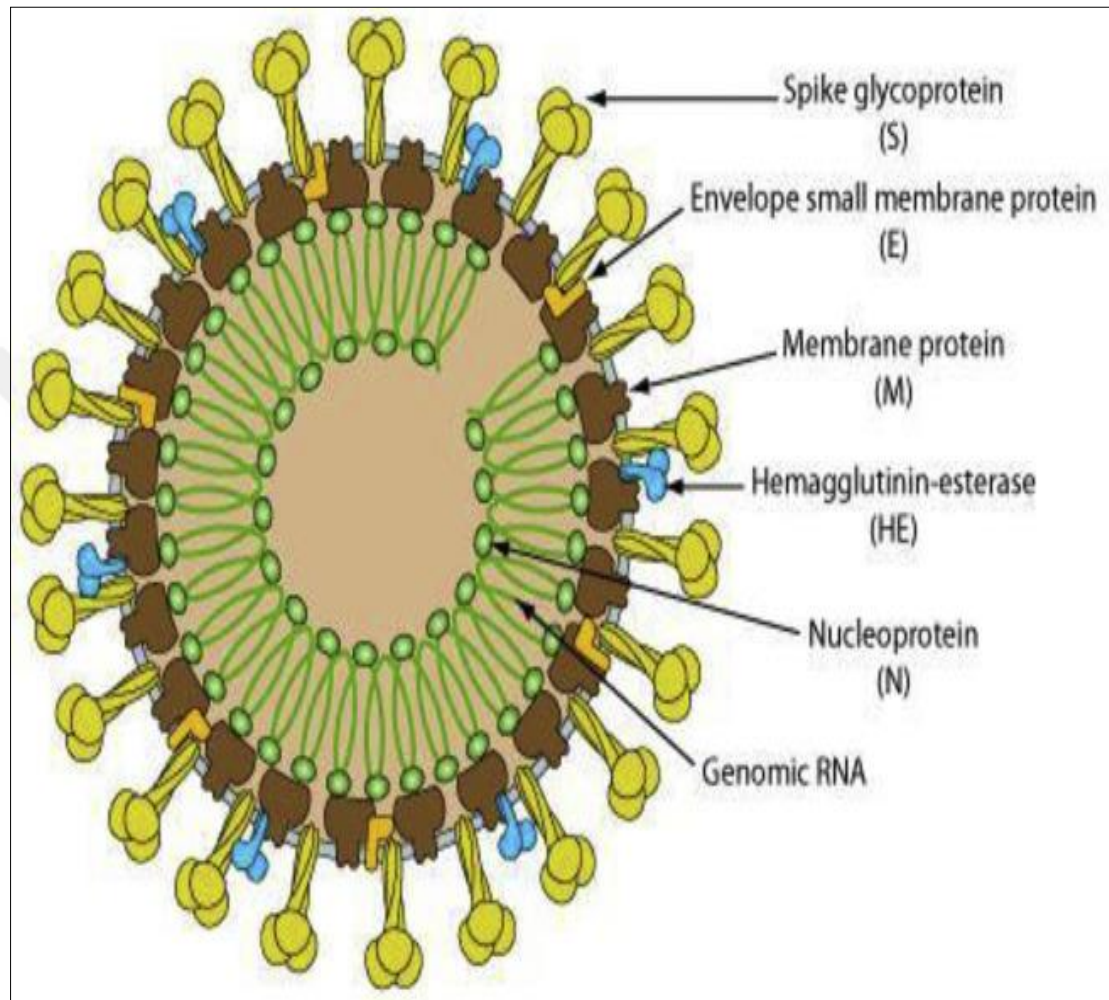


Figure 2.1 Schematic of a coronavirus (Mousavizadeh and Ghasemi 2021)

2.3 Replication of Virus

The spike of COVID-19 (SARS-CoV-2) attaches to the (ACE2), allowing COVID-19 to enter cells and cause infection. The spike protein must be activated by an enzyme known as a protease for the virus to effectively enter the cell following this initial stage. SARS-CoV-2 (COVID-19) completes this process similarly to SARS-CoV by employing the protease TMPRSS2 (Zhou *et al.* 2020, Hoffmann *et al.* 2020). Type-II

transmembrane serine proteases (TTSPs), specifically TMPRSS2, are considered promising pharmacological targets for inhibiting viral entry. These proteases play a crucial role in the life cycle of the virus by cleaving the viral spike protein, thereby exposing the fusion peptide required for cellular entry (Jackson *et al.* 2022).

The TMPRSS2 enzyme facilitates the activation, or priming, of the spike protein domain, a crucial glycoprotein present on coronaviruses. This activation process enables the virus to connect to ACE2 receptors on the respiratory epithelia of the cell surface, ultimately resulting in fusion. TMPRSS2, being a serine protease, facilitates the activation of the spike-domain (S) of SARS-CoV-2 by the cleavage of the S1/S2 sites, as depicted in Figure 2.2 (Zhou *et al.* 2020).

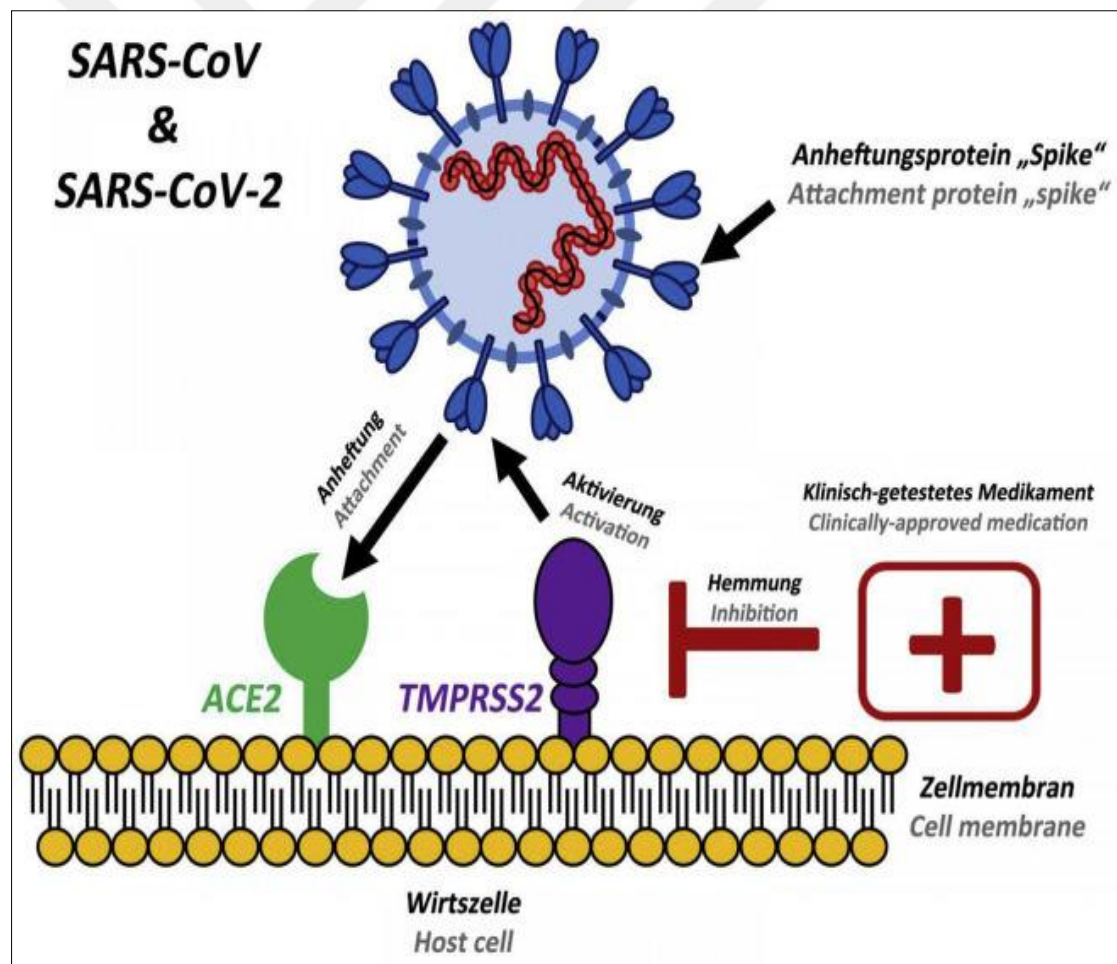


Figure 2.2 The attach virus receptor (Hoffmann *et al.* 2020)

Once the virus enters the host cell and sheds its coat, the genome undergoes transcription, followed by translation. The replicase gene, spanning 20 kb, encodes the viral replicase—a substantial protein complex that orchestrates the continuous and discontinuous RNA synthesis processes during coronavirus genome transcription and replication on cytoplasmic membranes (Sola *et al.* 2015). The completed particle arises by budding from the interior cell membranes, where the proteins are formed, and genomic RNA is integrated (Sanjuán and Domingo-Calap 2016).

2.4 Mutations

According to Sanjuán and Domingo-Calap (2016), virus-related pandemics are frequently characterized by varying levels of mutation that result in particular variations (many viral strains). The "receptor-binding domain" (RBD) of the SARS-CoV 2 spike-protein interacts with the ACE2 receptor to enter host cells. This suggests that modifications to the viral spike protein, in particular those that impact RBD, affect the virus' capacity to infect cells, and that modifications to the virus' capacity to bind to host cells affect both the virus' capacity to infect cells and the clinical course of infection (Kirby 2021).

The genetic drift of the influenza virus can produce a different type of antibody, which led to the seasonal or annual update of influenza vaccines, and since viruses have a more aggressive adaptation strategy, which is that they can change the bulk of the genome, which leads to an increase in infection and transmission of typing to another person. Corona viruses can stimulate genetic recombination through the coexistence of two or more strains of the virus in the same host, so that the strains can mix their genes to form a hybrid virus (SARS) (Neagu *et al.* 2021).

The World Health Organization has identified four strains from the beginning of the pandemic, namely alpha, beta, gamma and delta. These strains are responsible for the occurrence of different waves of the disease, and they are more deadly than the first strain of the virus that originated in China at the beginning of the epidemic (Roy *et al.* 2021).

2.5 Epidemiology

The disease varies epidemiologically with race, sex and age (Elibol 2021). And due to the fact that the virus is highly contagious and has the ability to transmit from one person to another, it has spread to more than 196 countries in the world. Among the factors affecting the spread of the viral disease SARS-CoV-2 are age, health status, immunity, diabetes, and previous disease records (Srivastava *et al.* 2020).

At the present time, the number of diagnosed infections and deaths is still increasing rapidly in most countries of the world, despite the uneven geographical distribution. These cases differ in different countries and continents depending on the aforementioned factors and determinants, in addition to environmental pollution and some weather factors such as humidity and temperature (Neagu *et al.* 2021).

2.6 Mode of Transmission

2.6.1 Animal to human transmission

According to current research, other intermediary species presumably purchased, for this reason may have transferred COVID-19 to humans (Chan *et al.* 2020). This is due to the fact that bat-derived CoVs seldom infect people, making an intermediate host necessary for SARS-CoV-2 transmission to humans. According to the study, SARS-CoV-2-like coronaviruses were found in the majority of the wild pangolins from Malaya and China. It's important to note that a single (one) (RBD) in the Pangolin-CoV spike-protein was found to differ slightly from the SARS-CoV-2 RBD by just one amino acid. The Pangolin-CoV and Bat-nCoV viral recombination may have been the source of the (SARS-CoV-2) virus before it was transmitted to body humans, according to these studies (Xiao *et al.* 2020).

2.6.2 Human to human transmission

As respiratory droplets emitted by an infected individual are now understood to be the major means of human-to-human transmission, coughing and sneezing cause SARS-CoV-2 to become airborne, increasing the risk of infection for those who are not already ill (Carlos *et al.* 2020, Ather *et al.* 2020). Furthermore, the research has demonstrated that contact with contaminated inanimate objects can lead to fomite transmission, also known as SARS-CoV-2 transmission (Cai *et al.* 2020).

2.7 Clinical Features

COVID-19 symptoms are numerous and extremely diverse in their distribution. Fever (83-99%), cough (59-82%), fatigue (44-70%), anorexia (40-84%), shortness of breath (31-40%), sputum production (28-33%) and myalgia (11-35%) are hence symptoms that the vast majority of patients suffer (Guan *et al.* 2020*et al.*, Pan *et al.* 2020).

The most typical signs include a fever, a dry cough, and exhaustion. Aches and pains, a sore throat, diarrhea, conjunctivitis, headaches, a loss of taste or smell, a skin rash, or a change in finger or toe color are less frequent symptoms. It can progress into the following significant symptoms in certain people: pneumonia, breathing problems (acute respiratory distress syndrome), pressure in the chest, trouble speaking or moving, and chest discomfort, dysfunction of various organs, and people with heart disease, lung disease, cancer, aging diabetes, immunosuppressants, and pregnant women are so far the most vulnerable to infection in the world, and asymptomatic carriers of the virus can transmit the virus and thus play a decisive role in the spread of the disease. Severe symptoms cause pneumonia due to an exaggerated systemic inflammatory response, leading to multi-organ failure and death (Hou *et al.* 2020, Potere *et al.* 2020).

2.7.1 Children infected with corona virus

Although they are susceptible to (SARS-CoV-2) infection, children or/and adolescents have considerably lower incidence of severe COVID-19 disease than adults (Buonsenso *et al.* 2021). Research revealed that young children probably played a smaller role in transmission than adults before variants of concern (VOC) were created because many children only exhibit mild or no symptoms of infection (Tönshoff *et al.* 2021, Stringhini *et al.* 2020).

Children who have SARS-CoV-2 symptoms that are more severe may exhibit acute infection signs including fever or cough (Swann *et al.* 2020, Irfan *et al.* 2020). Other children may develop an acute inflammatory condition known as paediatric inflammatory syndrome temporally related with SARS-CoV-2 following the initial infection (PIMS-TS; also known as multisystem inflammatory syndrome connected to COVID-19) (Toubiana *et al.* 2020, Whittaker *et al.* 2020). Children and teens with moderate or no symptoms in the early stages of the disease were also shown to have a pediatric multiorgan immune syndrome, which manifested weeks to months after SARS-CoV-2 infection (Davies *et al.* 2020). Recent research has connected PIMS to the presence of (SARS-CoV-2) antibodies, and some authors have hypothesized that high levels of these antibodies may actually contribute to the development of the full-blown disease (Rothan and Byrareddy 2021). These findings suggest that immunological responses to SARS-CoV-2 exposure may vary between children and adults, at least in terms of intensity.

2.7.2 Seroprevalence rate

The ailment was referred to as corona virus disease after the pathogen, (sARS) Corona Virus-2 (SARS-CoV-2), a new beta coronavirus, was found to be the cause (COVID-19). Nearly every continent in the world has recorded cases of COVID-19 within a few months (Cucinotta and Vanelli 2020). Only 1% to 2% of COVID-19 instances that have been identified globally in people under the age of 18 are believed to be caused by children.

An earlier study from China that examined a cohort with 391 COVID-19 infections and 1286 close contacts found that children were equally likely to catch the virus as adults were (Bi *et al.* 2020). However, a significant Icelandic analysis found that children were less likely than adults to have an acute SARS-CoV-2 infection (Gudbjartsson *et al.* 2020). Similar to this, a serological study from Switzerland discovered that young children (5 to 9 years old) had a lower seroprevalence of (SARS-CoV-2) than adults did (Stringhini *et al.* 2020).

Children were also found to have a lower risk of infection in Israeli research on the dynamics of family transmission, an Italian investigation on the spread of SARS-CoV-2 using nasopharyngeal swabs, and a Spanish population-based seroepidemiological study (Somekh *et al.* 2020, Lavezzo *et al.* 2020, Pollán *et al.* 2020).

Although the respective contributions of each to the lower reported rates are not apparent, there is evidence that children may be infected at lower rates than adults (Yasuhara *et al.* 2020, Cui *et al.* 2020). They are also less likely to have severe symptoms. Up to 50% of SARS-CoV-2 infections appear to be in asymptomatic people, and the rate may potentially be greater in youngsters (Mizumoto *et al.* 2020), Nishiura *et al.* 2020). Children and those who are asymptomatic have substantial viral shedding, which is proof of their involvement in the disease's rapid spread (Furukawa *et al.* 2020, Dimeglio *et al.* 2020).

2.8 Diagnosis

1. Polymerase Chain reaction PCR: It is a screening method based on the polymerase reaction to examine the mucous smear from the nose and mouth of patients and suspects, and it is the main method of diagnosis (Wiersinga *et al.* 2020, Goyal *et al.* 2020).
2. Chest CT scans were chosen as the COVID-19 imaging method of choice (Yang and Yan 2020).

3. Immunodiagnosis: An antibody test can examine the presence and concentration of IgG and IgM levels in blood, serum, and plasma samples to determine whether the body is defending against a disease, such as an infectious virus. These artificial viruses can be used to produce "recombinant" antibodies with specific target binding affinities and antigens that imitate the virus (Loeffelholz and Tang 2020).

2.9 Disease Control

The epidemic is controlled by adopting public health measures to prevent infection, such as restricting movement, using alcohol-based hand sanitizer, using disposable personal protective equipment such as gloves (Neagu *et al.* 2021), and wearing face masks in public, crowded, Places, and social distancing and quarantine (Zhang *et al.* 2020).

With guidance on warning signals, mild illnesses should be treated at home. The standard guidelines include keeping hydrated, eating well, and managing cough and fever. Additionally, individuals with severe pneumonia need to be hospitalized and given access to intensive care units with adequate mechanical ventilation (Chen *et al.* 2020a, Jin *et al.* 2020).

2.10 Vaccines

There are three main types of vaccines, either the whole virus or parts of the virus or the genetic material of the virus is used, and in all cases the immune system is stimulated (WHO 2020). Among the authorized and recommended vaccines are:

1. Pfizer-BioNTech: The vaccine can be taken by people aged 12 years and over.
2. Moderna: The vaccine can be taken for people aged 18 and over.
3. Johnson and Johnson's Janssen: The vaccine can be obtained for people aged 18 and over.

2.11 Immune Response

The function of the immune system in response to infection with COVID-19 It is the counterattack of viral infection and the elimination of pathological factors, cellular homeostasis, tissue repair and the generation of memory cells that are reactivated when the virus is encountered again (Neagu 2021).

An increase in the levels of IgM antibodies was previously observed in the first week (2-6) days after infection with the virus, and it reached its peak in two weeks, and after that it began to decline. It is considered the first line of defense of the humoral immunity in the body in most patients except those with immunodeficiency, and IgM levels decrease rapidly in recovered patients. As for the IgG antibody, it can be detected after about a week (8 days) of infection, and its level remains relatively high for a period of time that reaches approximately 48 days (Assaid *et al.* 2022).

It was found to be lower in critical cases compared to mild cases of infection with the virus, either because the disease is active or the response is weak. In critical cases, the IgG antibody plays a major role in the long-term immune memory. The immune response leads to an increase in the activity of T-cell immune cells (Hou 2020)

3. MATERIALS AND METHODS

3.1 Design of Study

The study was conducted in Diyala, Iraq, from September 2022 to March 2023. During this time, a total of 180 samples were recorded and studied. This study aimed to explore the rate of COVID-19 infection among children by detecting anti-COVID-19 IgG and IgM antibodies and identifying sociodemographic risk factors. To our knowledge, this is the first study of its kind conducted in Iraq.

The significance of this study is underscored by the global impact of the hazardous novel coronavirus pandemic. The World Health Organization (WHO) declared it a public health emergency of international concern, and by May 13, 2023, the pandemic had resulted in 8 million confirmed cases and 7 million confirmed deaths, marking it as the most devastating global crisis in the last century. Moreover, approximately 35% of recovered patients developed long COVID-19 syndrome. Additionally, the WHO reported that nearly 80–85% of COVID-19 infections exhibit mild or asymptomatic symptoms, particularly among children who may contribute to the transmission of the virus within the community (Liu *et al.* 2020).

3.2 Study Groups

In the present study, a total of 180 subjects were collected, constituting two distinct study groups: the patient group and the group of healthy children. Blood samples were collected from all participants at Al-Batoul Teaching Hospital for Maternity and Children. Subsequently, the serum was separated and stored in deep freezers at a temperature of -20°C until testing. A dedicated questionnaire form was designed for this study, encompassing sociodemographic and clinical information. The questionnaire was completed by the students through brief interviews conducted with the parents or guardians of the participants.

3.2.1 Patient Group

A total of 82 children aged between (1-168) months were participated in this study.. They were suffering from various symptoms, including fever, sore throat, rash, bowel disorder, difficulty breathing, cough, and runny nose.

3.2.2 Control Group

This group includes ninety-eight children aged between (1-168) months who enjoy fairly good health. Most of them were attend the health facility for vaccination. They were included as a control group for comparison with patients group.

3.3 Sample Collection

About 3 milliliters of venous blood was drawn aseptically from each participant of the two study groups. 70% ethanol was used to sterile the suction area. Blood samples were then aspirated using disposable syringes and then, 0.5 milliliters of the blood were placed in EDTA (ethylenediaminetetraacetic acid) anticoagulant tubes for determination of complete blood count (CBC). The remaining 2.5 milliliters of blood were placed into gel tubes and left at room temperature for 30 minutes to clot. Then centrifuged at 3000 rotation/minutes for 15 minutes. Separate serum samples were placed in eppendorf tubes, labelled, and kept at -20°C for serological examination.

3.4 Equipment and Tools

Following Table 3.1 Many research instruments and equipment were used.

Table 3.1 A list of the study's instrumentation

No.	Instruments	Company	Country
1	Micropipettes (different volumes)	Eppendorf	Germany
2	Multichannelpipette(50-300 μL)	Biohit	U.K
3	Absorbance Microplate Reader	Karl Kolb	Germany
4	Capped plastic tubes	Afco-Dispo	Jordan

Table 3.1 A list of the study's instrumentation (Continuous)

5	Centrifuge	Kokusan	Germany
6	Ependroff tubes	Sigma	England
7	Deep Freezer (-80 °C)	Angel Antoni	Italy
8	Gel Tubes	Afco	Jordan
9	Incubator	Memmert	Germany
10	Spectrophotometer	Shimadzu	Japan
11	Water bath	Kottermann	Germany
12	Refrigerator	Arjelic	Turky
13	ELISA washer	Seri	Italy
14	ELISA recorder	Seri	Italy

3.5 Laboratory Kits

An enzyme linked immunosorbant assays (ELISA) kits were employed for detection of anti-COVID 19 IgM and IgG antibodies in the serum in both study groups.

3.5.1 Detection of anti-COVID 19 IgM antibody

The ELISA kit (DIA-pro/Italy) was used to detect the anti-COVID-19 antibody in serum samples of both study groups. Microplates were coated with recombinant COVID-19-specific recombinant nucleocapsid and spike antibodies. Distribution of samples and components was monitored by the DiaPro Sample Addition Monitoring System (“SAMS”) in which correct addition of samples and assay reagents was visually followed by a stepwise color change.

Assay principal

The anti-COVID 19 IgM, if present in the serum, was collected after all other components had been swept away by antigens during the initial treatment of the solid phase with the diluted (Prepare) sample in the presence of a radiofrequency blocking (Solution) reagent. The addition of a polyclonal vector-specific, horseradish peroxidase (HRP)-labeled IgM antibody to the sample allowed for the detection of bound antibodies from the sample during the second incubation. The visual signal made

by the enzyme working on the substrate/chromogen mixture while it was captured on the solid phase was proportional to the amount of anti-COVID-19 IgM present in the serum. The cut-off (CO) value can be used to translate photointensities into COVID-19 IgM negative and positive readings. To avoid these types of manipulations, IgG anti-COVID and RF neutralization were performed in the experiment right away in the well.

Assay procedure

1. In the appropriate test tubes, 400 microliters of sample diluent were dispensed, then 10 microliters of sample were added to obtain a final dilution. The sample was mixed on a vortex. The color transition from light green to bluish green.
2. The microwell holder was filled with the necessary number of wells, but the first well was left unfilled for the blanking procedure.
3. Each well of the plate was received 50 microliters of neutralizing reagent, with the exception of well A.
4. Two hundred microliters of negative control were dispensed in triplicate and 200 microliters of positive control were dispensed into properly defined control wells. These control reagents were provided in the kit as ready to use reagents.
5. Finally; 200 microliters of the diluted samples were dispensed onto all sample wells.
6. The microtiterplate was mixed by slab gently by hand, avoiding flooding and contamination of neighboring wells.
7. The microplate was incubated for 45 minutes at
8. Then, the microplate was washed an automatic washer by delivering and aspirating 350 microliters/well of diluted washing solution as reported previously.
9. Except for the well of A, pipette 100 microliters of enzyme conjugate were added into each well, which were then sealed with sealant. With the exception of A1, the pink/red component was dispersed throughout all wells.
10. The microplate was incubated for 45 minutes at 37°C.
11. The microwells were washed as in step 8.
12. One hundred of the chromogen/substrate solution were added into each well, including the empty well. The microplate was then incubated for 15 minutes at room temperature (18 to 24 °C.).

13. The enzymatic reaction was stopped by adding 100 microliters of sulfuric acid into each well using the same pipette order as in step 10. The positive control and positive samples were blue before the addition of acid, but they were turned to yellow/brown.
14. The color intensity of the solution in each well was measured as described in section 1.5 at 450 nm.

Interpretation of results

The test results were interpreted as OD_{450nm}/620-630nm sample ratio and cut-off value, or S/Co, according to Table 3.1. In the case of probable COVID-19 infection, the following interpretation is pertinent: 0.9 -1.1 > 1.1 A positive area is determined when S/Co is negative and 0.9 gray. The absence of COVID-19 IgM from the individual is indicated by a negative result.

Table 3.2 Sample ratio and cut-off value

S/Co	Interpretation
<0.9	(-)
0.9-1.1	Gray-zone
>1.1	(+)

If the outcome is negative, it indicates that the subject's IgM to COVID-19 has not increased. If the outcome is affirmative, COVID-19 IgM is present.

3.5.2 Detection of the anti- COVID-19 IgG antibody

The ELISA kit (SUNLONG/CHINA) was used for detection of the anti-COVID-19 IgG antibody in both patents and control groups.

Assay Principle

This kit was developed using the indirect enzyme-linked immunosorbents screening method. On a 96-well plate, recombinant 2019-nCoV nucleocapsid protein (antigen) was pre-plated. Test samples were poured into the wells, and wash buffer was used to remove any unbound conjugates.

If there is any anti-2019-nCoV(N)-IgG in the samples, it will form a complex when HRP conjugated anti-human IgG is added. It was possible to see the HRP enzymatic process using TMB substrates. It was catalyzed by HRP to create a blue product that changed to yellow when the acid stop solution was added. A suitable photometer is used to measure the optical density of the created color at 450 nm, with a reference wavelength set to within 650 nm.

Assay procedure

Samples and reagents were diluted, and mixed thoroughly and evenly. Before adding TMB into the wells, we equilibrated the TMB substrate for 30 min at 37 °C.

1. Before use, all reagents were brought to room temperature.
2. Two negative controls, two positive controls, and one blank well are assigned in the microplate wells. Before adding the serum sample and control wells, the plate underwent two washes.
3. Each sample well received 49 microliters of sample buffer. To the blank well, add 50 microliters of sample buffer.
4. One microlitter of serum sample was added in sample wells. In order to fine-tune the controls, 50 microliters of both positive and negative controls were added, and gently squeezed the plate to ensure thorough mixing. The plate was covered with a lid, and it was incubated for 30 minutes at 37 °C.
5. After removing the coverlid, the plate was washed with washing buffer three times, each time leaving the wash buffer in the wells for 1-2 minutes.

6. Then 50 microliters of an anti-human factor IgG solution that was HRP conjugated.
7. The plate was covered with a coverlid, and it was then incubated for 30 minutes at 37 °C.
8. Then the plate was washed five times with wash buffer after the lid had been removed, each time being left in the wells for 1-2 minutes.
9. The 50 microliters of TMB substrate were added. On ensure full mixing, little pressure was applied to the plate for 10 minutes, the plate was covered and incubated at 37 °C in the dark. Clear blue tones were seen in the positive controls. Wells that were empty lacked any recognizable color.
10. The reaction was stopped by adding 50 microliters of stop solution and thoroughly mixed them. The color instantly turned yellow.
11. The optical density (OD) of all wells were read at 450 nm in a microplate reader immediately following the addition of the stop solution; the blank well was used as the reference point.

Interpretation of results

The anti-COVID IgG antibody was determined via an enzyme-linked immunoassay (ELISA) test. An index of 1 was considered positive, 0.9 to 1.1 was borderline, and 1 was considered negative. All test batches contained both positive and negative controls. By using the enzyme-linked immunoassay method for the qualitative detection of IgG antibodies, calculate the concentration of IgG antibodies using the COVID-19 IgG.

3.6 Statistical Analysis

An analysis of the accumulated data was carried out in order to determine the significances using the statistical package available from SPSS-28 (Statistical Packages for Social Sciences- version 28). Data were presented in simple measures of frequency, percentage, mean, standard deviation, and range (minimum-maximum values). Using the Students' t-test for difference between two independents, the significance of the differences between the means (quantitative data) was examined. When necessary,

Yate's adjustment or the Fisher Exact test were applied to the Pearson Chi-square test (c2-test) to determine the significance of differences between distinct percentages (qualitative data) when the P value was ≤ 0.05 .



4. RESULTS AND DISCUSSION

4.1 Distribution of Age, Gender and Residence in Study Groups

The outcomes presented in Table 4.1 and Figures (Figure 4.1, Figure 4.2) provide a comprehensive comparative analysis between the patients and control groups in terms of age, gender, and residence. Addressing the aspect of age distribution, two classifications were employed. The first classification grouped the ages of the two study groups into three categories. The statistical assessments conducted revealed a notable discrepancy among these age categories, with a calculated significance of ($P=0.034$). The second classification further refined the age categories into fifteen segments, once again displaying a statistically significant distinction between the two study groups, indicated by a significance level of ($P=0.012$).

Furthermore, the Mean $\pm$ SD in months within the control group demonstrated a significantly higher value in contrast to that observed within the patient group, with values of (76.4 ± 51.7 Vs 49.7 ± 44.9 , $P = 0.0001$), emphasizing the age-based variation between the groups.

Shifting the focus to gender, the percentage of males within the patients' group was substantially higher when compared to that of the controls, with a proportion of (63.41% vs 47.95%). Conversely, the percentage of females in the control group was notably higher in comparison to the patients' group, with figures of (52.04% Vs 36.58%, $P=0.038$).

In terms of residence, the children within both study groups were categorized based on their living environment, namely urban (city) and rural (village). The subsequent statistical analysis revealed that there was an insignificantly minor variation in the residence distribution between the two study groups, with a calculated p-value of ($P=0.658$). This underscores that the geographic distribution of the children, whether

urban or rural, did not play a substantial role in the observed variations between the patients and control groups.

Table 4.1 The age, gender, and residence of groups

		Respiratory tract infection		Control		P value
		No	%	No	%	
Age (years)	<1year	18	21.95	12	12.24	0.034*
	1---4	32	39.02	30	30.61	
	5---9	22	26.82	29	29.59	
	10---14years	10	12.19	27	27.55	
Age (years)	<1year	18	21.95	12	12.24	0.012*
	1---	13	15.85	8	8.16	
	2---	9	10.97	4	4.08	
	3---	4	4.87	5	5.10	
	4---	6	7.31	13	13.26	
	5---	7	8.53	2	2.04	
	6---	1	1.21	7	7.14	
	7----	7	8.53	7	7.14	
	8---	1	1.21	5	5.10	
	9---	6	7.31	8	8.16	
	10---	5	6.09	7	7.14	
	11---	1	1.21	6	6.12	
	12---	3	3.65	3	3.06	
	13---	-	-	5	5.10	
	14---	1	1.21	6	6.12	
	Mean±SD months (Range)	49.7±44.9 (1-168)		76.4±51.7 (1-168)		0.0001#
Gender	Male	52	63.41	47	47.95	0.038*
	Female	30	36.58	51	52.04	
Residence	Urban (city)	37	45.12	41	41.83	0.658
	Rural (village)	45	54.87	57	58.16	
*Significant difference between percentages using Pearson Chi-square test (χ^2 -test) at (0.05) level.						
(#)Sig. between 2 independent means-Students-t-test at 0.05 level.						

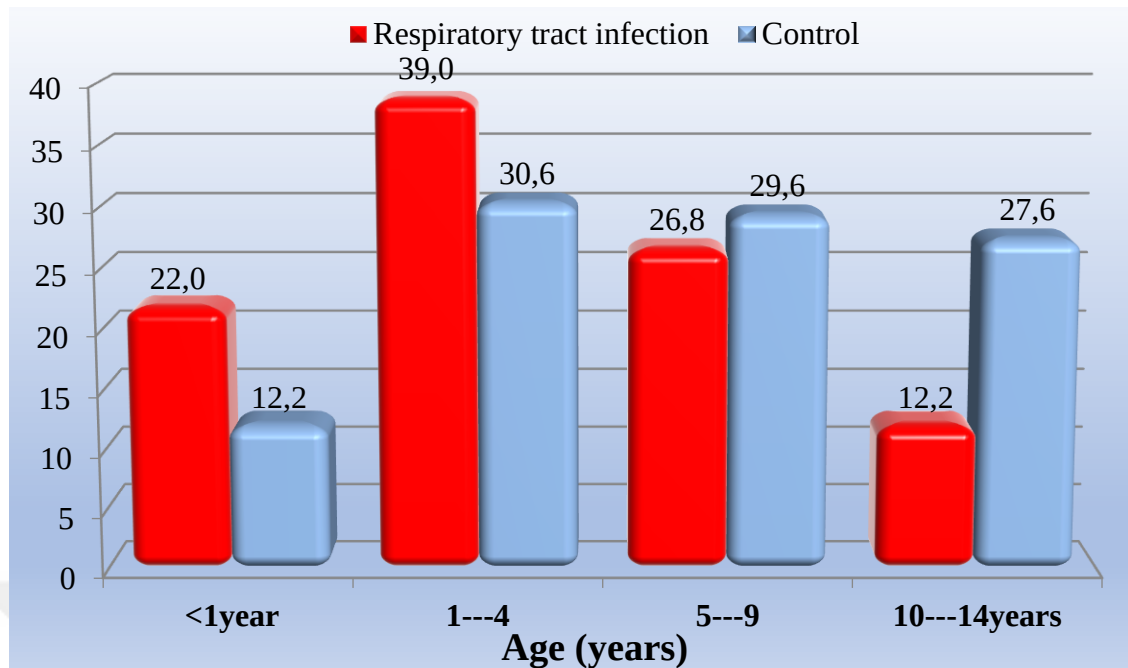


Figure 4.1 The distribution of age among children in the study groups

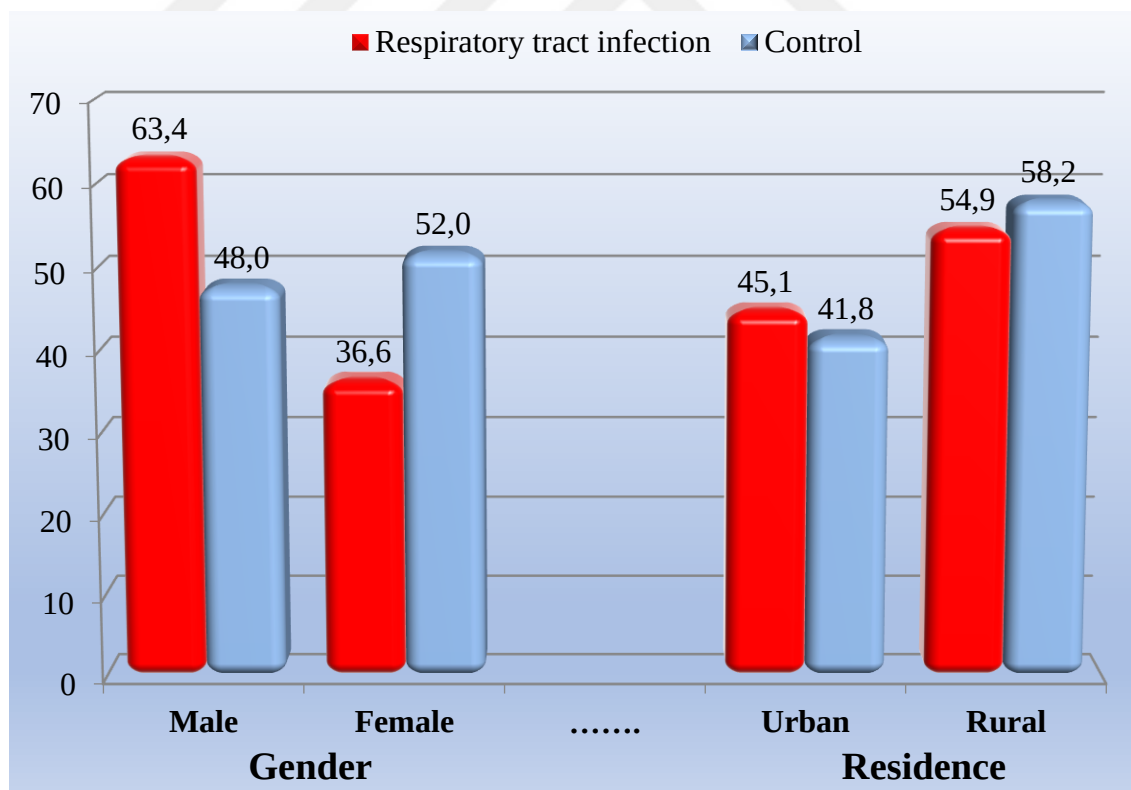


Figure 4.2 The distribution of gender among children in the study groups

The observed significant age difference between the two study groups is consistent with the random selection process employed for this study. It's worth noting that this age discrepancy is specific to certain age categories. For instance, the proportion of children under 1 year old was higher among patients compared to the control group (21.95% vs. 12.24%). On the other hand, in the 10-14 age category, children in the control group outnumbered those in the patients group (27.55% vs. 12.19%). In contrast, age categories 1-4 and 5-9 were fairly evenly distributed between both study groups.

Additionally, the distribution of gender revealed that the percentage of males was higher in the patients group compared to the control group (63.41% vs. 47.95%). Conversely, the percentage of females in the control group was greater than that in the patients group (52.04% vs. 36.58%). Lastly, when examining the distribution of study participants based on their place of residence, there was almost no discernible difference between the two groups, and this disparity was considered statistically insignificant.

The results of this study are consistent with the research conducted by Zinszer *et al.* (2021). Their study revealed that out of the 95 children who tested positive for SARS-CoV-2 antibodies, 82% tested negative. Among the positive cases, 52% exhibited mild symptoms, while the remaining 48% showed no clinical symptoms. Zinszer *et al.* (2021) concluded that the seroprevalence of SARS-CoV-2 antibodies increased from 4.8% among children aged 2-4 years to 7.2% among children aged 15-17 years, suggesting a higher rate of seropositivity in older age groups.

While Ulyte *et al.* (2020) It is assessed how common severe acute respiratory syndrome is. Cov-2 antibodies were examined in school-age children, their parents, and school staff, along with infection risk factors and the link between seropositivity and Cov-2 symptoms. They found that seroprevalence rates are always site- and time-specific, and that a longitudinal strategy will allow them to look at different pandemic stages. Additionally, they found that the wide age range of 6 to 16 years old will allow them to

detect age-based variation in seroprevalence, and that this variation can be expected to be driven by risk factors as the natural course of infection may vary by age.

In contrast, Smith *et al.* (2021) conducted a study in Missouri, USA, revealing distinct patterns of seropositivity among children. The findings indicated that seropositivity rates in children under 5 were significantly lower compared to adults. Interestingly, none of the children under the age of 4 exhibited seropositivity. This discrepancy in seropositivity rates among different age groups led researchers to explore potential factors contributing to children's resilience against COVID-19 and other coronaviruses.

A multitude of factors may contribute to children's relative protection from COVID-19 and coronaviruses in general. These factors encompass differences in both innate and adaptive immunity, increased instances of recurrent and concurrent infections in children, preexisting immunity developed through previous exposure to other coronaviruses, variations in microbiota composition, higher levels of melatonin, the protective impact of live vaccines on other infections, and lower levels of SARS-CoV-2 exposure intensity among children. These elements collectively suggest a complex interplay of factors that could potentially shield children from severe outcomes of COVID-19 and coronaviruses in general (Zimmermann and Curtis 2021).

In their study, Yamayoshi *et al.* (2022) observed that the infection spread among children who were not eligible for vaccination during the waves prompted by the SARS-CoV Delta and Omicron variants. They specifically highlighted that among children aged less than 5 years, the seroprevalence remained as low as 10% by March 2022. This finding sheds light on the transmission dynamics of these variants in younger age groups and emphasizes the challenges of safeguarding children below the age of 5 through vaccination strategies.

4.2 Distribution of Study Groups According to Family History and Presence of Chronic Diseases

The data of Table 4.2 showed a significant difference between percentages using the Pearson Chi-square test at 0.05 level of groups studied, revealed that the previous infection in children's families of patients group was significantly superior as compared with healthy children in the control group, where the patients group recorded 63(76.8%) cases compared with 38(38.8%) cases in the control group at P value (<0.0001). But the findings of Table 4.2 also showed that the no. of cases infected with respiratory tract infection in the patient's group recorded 5(6.1%) cases, while 60(61.2%) no cases were monitored in the control group at P. value (<0.013).

Also it seems that the presence of chronic diseases were associated with no. of children infected with respiratory tract infection which appear from the low value of percentage of infection in patients group which recorded 5(6.1%) while the absence of chronic disease lead to increase the percentage of children infected with respiratory tract infection 77(93.9%).

Table 4.2 Previous infection in the family and Presence of chronic diseases of patients and healthy children groups

		Respiratory tract infection		Control		P value
		No	%	No	%	
Previous infection in the family	Yes	63	76.8	38	38.8	0.0001*
	No	19	23.2	60	61.2	
Presence of chronic diseases	Yes	5	6.1	-	-	0.013*
	No	77	93.9	98	100	
*Significant difference between percentages using Pearson Chi-square test (χ^2 -test) at 0.05 level.						

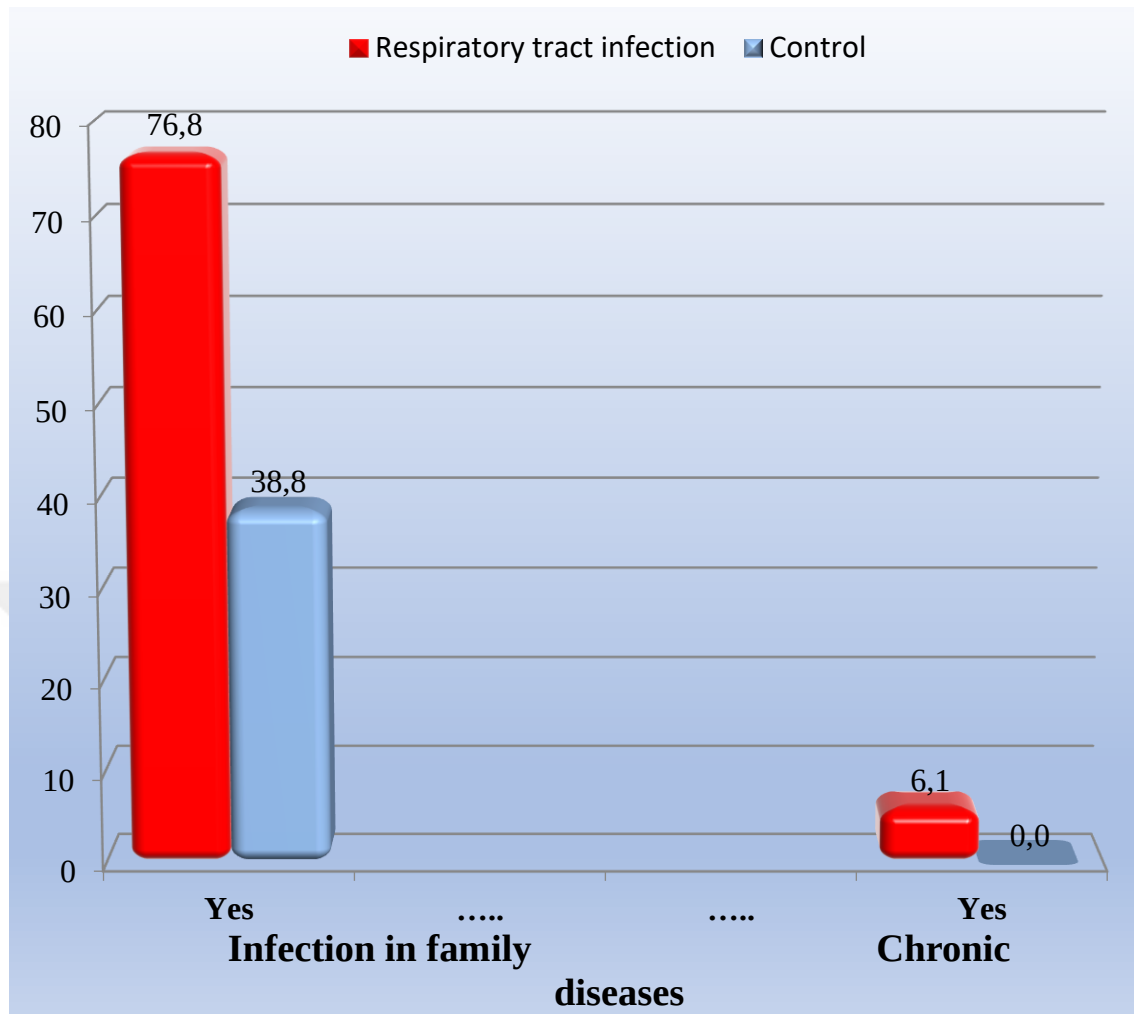


Figure 4.3 Previous infection in the family and Presence of chronic diseases of groups

The results unveiled a substantial disparity between the patients' group and the control group in terms of the prevalence of a family history of COVID-19 infection. This outcome was to be anticipated given the similar clinical manifestations of COVID-19 and other upper or lower respiratory tract infections (RTIs) (Garg *et al.*, 2020). Given that these infections are efficiently transmitted through the air, it follows that the familial environment serves as an optimal conduit for transmission (Chan *et al.*, 2021; Miller *et al.*, 2021). Consequently, the clustering of respiratory tract infections within families emerges as a shared characteristic.

Moreover, the presence of chronic ailments such as type 1 diabetes, thyroid disorders, and hematological disorders amplifies the risk of COVID-19 and other RTIs (Li *et al.*, 2020). This association stems from the observation that chronic conditions compromise the effectiveness of protective immunity, encompassing both humoral and cellular responses (Saeidi *et al.*, 2018).

Boey *et al.* (2022) conducted a study involving 362 primary and lower secondary school students (ages 6 to 15) from two Belgian cities, Pelt (a low transmission region) and Alken (a high transmission region). The research revealed that 4.4% of children in the low transmission area and 14.4% in the high transmission area had anti-SARS-CoV-2 antibodies. Interestingly, no primary school pupils in the low transmission region showed seropositivity, whereas in the high transmission region, no notable distinction in seroprevalence was observed between primary and secondary school students. Out of the 362 children, it was reported by the parents of 43 children that they were uncertain about the impact of COVID-19 on their child. On the other hand, 294 individuals stated that they had no documented history of COVID-19 infection. Interestingly, only four out of the 362 children were confirmed to have had a COVID-19 infection.

The study also unveiled that 5.8% of children had chronic illnesses, 14.1% had family members with conditions that increase the risk of severe COVID-19 infections (such as hypertension, diabetes, lung, heart, kidney, and immune deficiencies), and 3% lived in households where at least one resident was aged 65 or older.

Furthermore, a study carried out by Sorg *et al.* (2022) revealed that the prevalence of SARS-CoV-2 antibodies was observed in 28 cases out of 519 children, accounting for 5.4% of children under the age of 3. Similarly, among children aged 3 to 11 years, there were 28 cases out of 1955 children, representing a prevalence of 1.4%. These findings were obtained from data collected in Germany during the year 2020.

In another study conducted by Naeimi *et al.* (2023), a group of children was examined, and the findings demonstrated varying seroprevalence rates. These rates were 7.3% during the first wave of COVID-19, 37.6% during the fifth wave, and 56.6% during the

sixth wave. Notably, the highest seroprevalence was observed in the South East Asia region, ranging from 17.9% to 81.8% among older children. The study concluded that a significant portion (50-70%) of children globally remained susceptible to SARS-CoV-2, the coronavirus causing COVID-19.

While Simeni Njonnou *et al.* (2021) concluded that the prevalence among children is low worldwide and much lower in Sub-Saharan Africa, they suggested that this may be due to the action of immunomodulatory factors such as viral infection and the BCG vaccine.

4.3 Distribution of Clinical Signs and Symptoms of Study Groups

The findings from Table (4.3) and Figure (4.4) clearly illustrate a noteworthy disparity in the occurrence of various signs and symptoms between the patient group and the control group. Specifically, the patient group exhibited markedly higher rates of several symptoms, including fever, sore throat, runny nose, rash, diarrhea, difficulty breathing, and coughing, in comparison to the control group ($P < 0.0001$). This divergence in symptom prevalence highlights the distinct clinical manifestations associated with COVID-19 infection in children as opposed to the control subjects.

The results revealed that children with fever symptom in patient group was 76(92.7%) case compared with control group 7(7.1%), children without sore throat in patient group were 43(52.4%) compared with control group 93(94.39%). According to children without runny nose were 73(89.0%) compared with control group 74(75.5%), children without rash were 76(92.7%) compared with control group 98(100). According to children with diarrhea were 56(68.3%) compared with control group 16(16.3%), children without difficulty of breathing were 69(84.1%) compared with control group 98(100), and children without cough were 65(68.3) compared with control group 98(100).

Table 4.3 Data of respiratory tract infection symptoms of groups studied

		Respiratory tract infection		Control		P value
		No	%	No	%	
Fever	Yes	76	92.7	7	7.1	0.0001*
	No	6	7.3	91	92.9	
Sore throat	Yes	39	47.6	5	5.1	0.0001*
	No	43	52.4	93	94.9	
Runny nose	Yes	9	11.0	24	24.5	0.020*
	No	73	89.0	74	75.5	
Rash	Yes	6	7.3	-	-	0.006*
	No	76	92.7	98	100	
Intestinal diseases (diarrhea)	Yes	56	68.3	16	16.3	0.0001*
	No	26	31.7	82	83.7	
Difficulty of breathing	Yes	13	15.9	-	-	0.0001*
	No	69	84.1	98	100	
Cough	Yes	26	31.7	-	-	0.0001*
	No	56	68.3	98	100	

*Significant difference between percentages using Pearson Chi-square test (χ^2 -test) at 0.05 level.

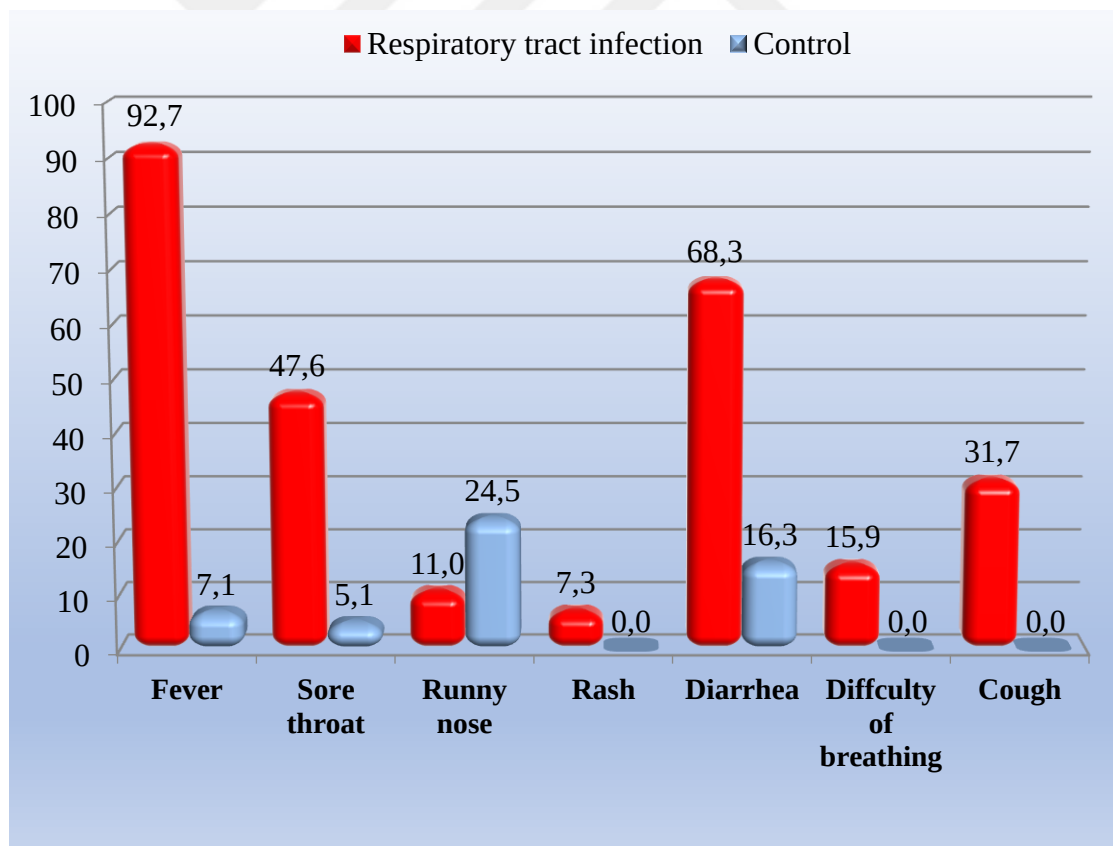


Figure 4.4 Respiratory tract infection symptoms of groups

These results concurred with the results of Melo *et al.* (2022) which examined the Covid-19 symptoms in children discovered that the most common symptoms were fever, cough, diarrhea, vomiting, sore throat, dyspnea, headache, abdominal pain, malaise, and weakness or exhaustion.

Zhou *et al.* (2022) discovered that the primary symptoms were headaches, sinusitis, a sore throat, nausea, and abdominal pain, vomiting, and diarrhea, and that testing positive for Covid-19 in children was either not associated with them or had a weaker association. 88.9% of the children studied had negative results for Covid-19.

4.4 Distribution of IgG and IgM Antibodies in Study Groups

The distribution of anti-COVID-19 IgG and IgM in the study groups is detailed in Table (4.4) and Figures (Figure 4.5, Figure 4.6). Regarding the rate of anti-COVID-19 IgG, the results showed that out of 35 patients who were tested, 25 (74.28%) tested positive while 9 (25.71%) tested negative. On the contrary, in the control group, among 74 apparently healthy children who underwent testing, 56 (75.67%) were found to be positive and 18 (24.32%) were negative for the antibody. Despite these variations, the difference between the two groups was determined to be statistically insignificant ($P=0.437$).

In terms of the anti-COVID-19 IgM, the analysis of the data showed that out of 82 patients who were tested, 63(76.82%) tested positive while 19(23.17%) tested negative. In comparison, among the 24 individuals tested in the control group, 8.33% were found to be positive for the antibody, whereas 91.66% tested negative. This discrepancy led to a statistically significant difference between the two groups, with a P-value of 0.0001.

Table 4.4 IgG and IgM antibodies and groups studied

		Respiratory tract infection		Control		P value
		No	%	No	%	
IgG	Positive	26	31.7	56	57.1	0.0001*
	Negative	9	11.0	18	18.4	
	Not done	47	57.3	24	24.5	
IgM	Positive	63	76.8	2	2.0	0.0001*
	Negative	19	23.2	22	22.4	
	Not done	-	-	74	75.6	
*Significant difference between percentages using Pearson Chi-square test (χ^2 -test) at 0.05 level.						

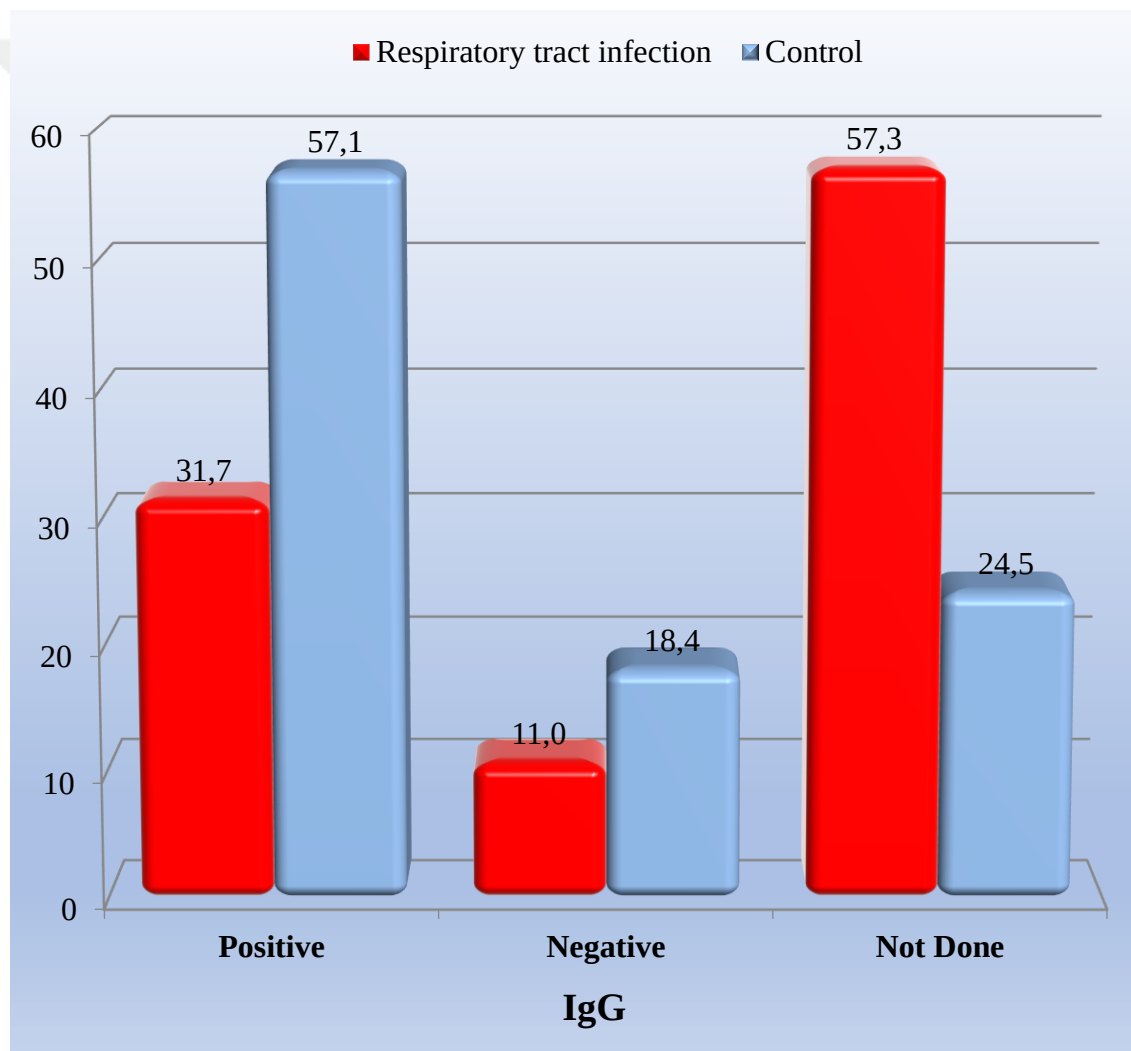


Figure 4.5 Seroprevalence of Covid-19 IgG of groups studied

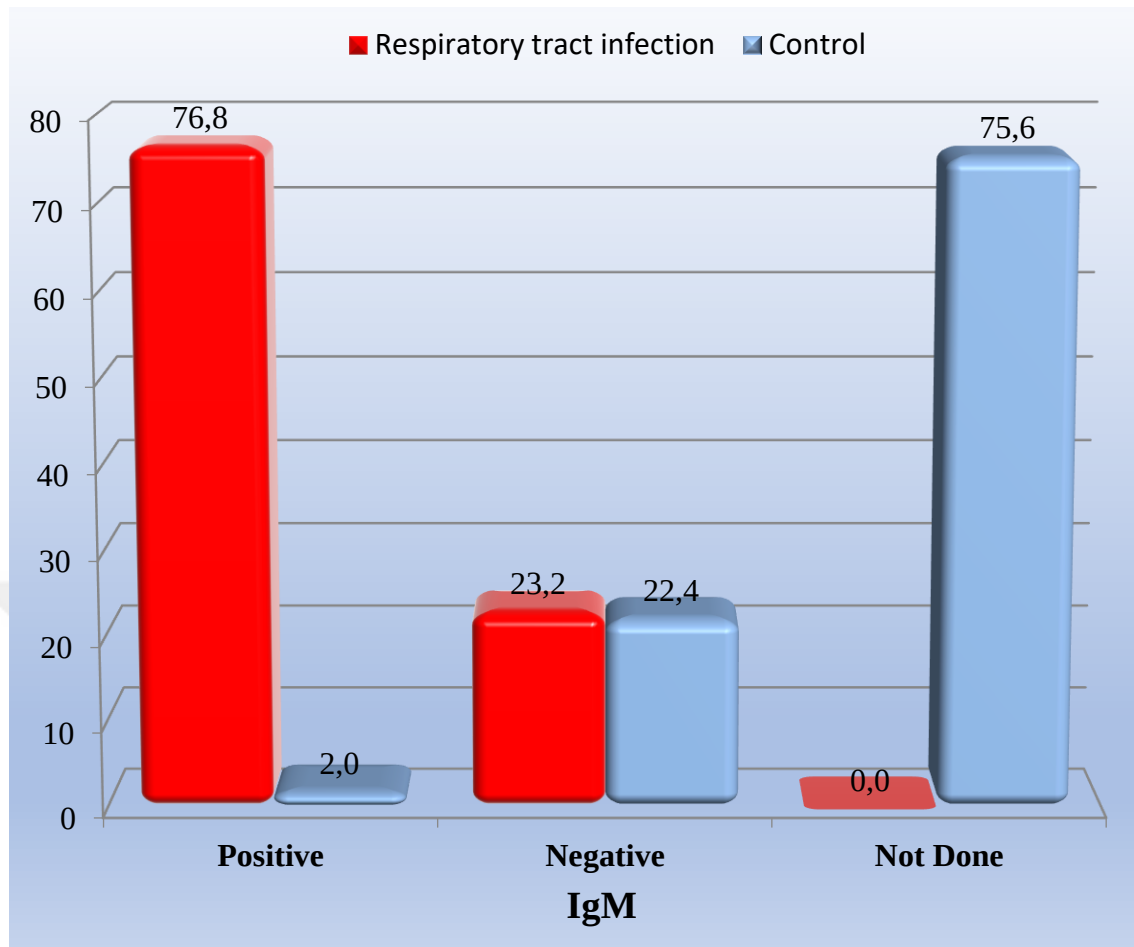


Figure 4.6 Seroprevalence of Covid-19 IgM of groups studied

In a study conducted by Lyimo *et al.* (2022) in two rural communities in Tanzania, the investigation focused on the seroprevalence of IgG antibodies to SARS-CoV-2. The study revealed that the seroprevalence of SARS-CoV-2 IgG was recorded at 30.7% and 32.5% in two villages of Tanzania. Notably, the researchers observed a significant increase in seroprevalence with age in both villages. Additionally, the study findings indicated a marked increase in the prevalence of SARS-CoV-2 symptoms, such as fever, cough, headache, and diarrhea, among the children in these two villages.

Smith *et al.* (2021) conducted a study in Missouri, USA, to estimate the seroprevalence of IgG antibodies against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in children. The study findings revealed that the seropositivity was significantly lower in children under the age of five compared to adults. However, the seroprevalence rates between children and adults aged five or older were similar. Interestingly, children

under the age of four had no instances of seropositivity. The IgG of the children at age ranged between 1-9 years old recorded 32.9 to 39.2%. The region of residence recorded the IgG positive was ranged from 24.8% in Norte region to 31.0% in Madeira region antibodies IgG. The IgG and IgM antibodies of covid-19 may be detected around the same time after infection, IgM is most useful in determining recent infection with corona virus or respiratory tract infection and it usually becomes undetectable weeks to months following infection, and IgG is usually detectable for longer period. Responses of IgG antibody was waned after 180 days of infected children with SARS-COV-2 and in the same time, their parents revealed a different antibody response to the virus and they concluded that serological tests should be used with caution in surveillance strategies among the general population (Bloise *et al.* 2021).

4.5 Association of Anti-COVID 19 IgG with Sociodemographic Parameters

The results presented in Table (4.5) illustrate the correlation between anti-COVID 19 IgG and various sociodemographic factors (age, gender, residence, family history, and presence of chronic diseases) within both the patient and control groups. Within the patient group, the highest anti-COVID 19 IgG positivity (34.6%) was observed among individuals aged 5-9 years. However, upon statistical analysis, this difference was found to be insignificant ($P= 0.364$). Similarly, in the control group, the highest IgG positivity rate was among those aged 10-14 years (35.7%), yet the difference did not reach statistical significance ($P= 0.070$). Regarding gender distribution, within the patient group, the highest anti-COVID 19 IgG positivity was among males (61.5%) compared to females (38.5%), but this difference was not statistically significant ($P= 0.391$). Similarly, within the control group, the highest IgG positivity rate was among males (53.6%) compared to females (46.4%), and once again, this difference was statistically insignificant ($P= 0.432$).

Regarding the residence, the results of patients showed that patients residing in rural areas had the highest IgG positivity rate compared to those who resided in urban areas, but the difference was still insignificant (57.7% Vs. 42.3%, $P= 649$). In the control children, the highest IgG positivity rate was among those who resided in rural areas

compared to those who resided in urban areas, but the difference was statistically insignificant (60.7% vs. 39.3%, $P = 0.725$). The presence of positive COVID-19 infection in the family increased the rate of IgG among patient children to 88.5% versus 11.5% among families without a positive history; however, the difference was statistically insignificant ($P = 0.110$). In the control group, families without previous history of COVID-19 infection had a higher IgG positivity rate (69.6%) versus (30.4%) among children in families without positive history, yet the difference failed to reach the level of statistically insignificant ($P = 0.063$).

Furthermore, the results indicated that patients with chronic diseases exhibited a IgG positivity rate of (7.7%), whereas those without chronic diseases demonstrated a rate of (92.3%). However, this difference was statistically insignificant ($P = 0.064$). Among the control children, all individuals (100%) with positive IgG had no chronic diseases, rendering statistical analysis unfeasible.

Table 4.5 Correlation between parameters of groups studied

		Respiratory tract infection						Control					
		IgG						IgG					
		Positive		Negative		Not done		Positive		Negative		Not done	
		No	%	No	%	No	%	No	%	No	%	No	%
Age (years)	<1year	6	23.1	2	22.2	10	21.3	8	14.3	2	11.1	2	8.3
	1---4	8	30.8	2	22.2	22	46.8	15	26.8	3	16.7	12	50.0
	5---9	9	34.6	2	22.2	11	23.4	13	23.2	8	44.4	8	33.3
	10---14	3	11.5	3	33.3	4	8.5	20	35.7	5	27.8	2	8.3
	P value	0.364						0.070					
Gender	Male	16	61.5	4	44.4	32	68.1	30	53.6	7	38.9	10	41.7
	Female	10	38.5	5	55.6	15	31.9	26	46.4	11	61.1	14	58.3
	P value	0.391						0.432					
Residence	Urban	11	42.3	3	33.3	23	48.9	22	39.3	9	50.0	10	41.7
	Rural	15	57.7	6	66.7	24	51.1	34	60.7	9	50.0	14	58.3
	P value	0.649						0.725					
Previous infection in the family	Yes	23	88.5	5	55.6	35	74.5	17	30.4	11	61.1	10	41.7
	No	3	11.5	4	44.4	12	25.5	39	69.6	7	38.9	14	58.3
	P value	0.110						0.063					
Presence of chronic diseases	Yes	2	7.7	2	22.2	1	2.1	-	-	-	-	-	-
	No	24	92.3	7	77.8	46	97.9	56	100	18	100	24	100
	P value	0.064						-					
*Significant difference between percentages using Pearson Chi-square test (γ^2 -test) at 0.05 level.													

4.6 Association of Anti-COVID 19 IgG with Clinical Manifestations

Table (4.6) provides insights into the relationship between anti-COVID 19 IgG and the clinical manifestations observed in the children included in this study. Among patients, those who exhibited fever showed a IgG positivity rate of 96.2%, compared to 88.9% in those who tested negative for IgG. However, the difference was not statistically significant ($P=0.687$). In the control group, 5.4% of children with fever were IgG positive, while 11.1% were negative, showing a statistically insignificant difference ($P=0.688$). Interestingly, only one child (3.8%) without fever tested positive for IgG, whereas a significant 94.6% of control children without fever displayed IgG positivity.

The IgG positivity rate was 61.5% among patients who had sore throat versus 55.6% who were negative, with statistically insignificant difference ($P=0.143$). In the control children, 3.6% who had sore throat were positive but none were negative for IgG, the difference was statistically insignificant ($P= 0.139$). Furthermore, 38.5% of patients without sore throat were positive for IgG versus 96.4% of control children without sore throat were positive for IgG.

The results also found that 3.6% of patients complaining skin rash were positive for IgG versus 11.1% who were negative for IgG, with a statistical insignificant difference ($P=0.687$). None of control children with skin rash. On the other side, 96.2% of patients without skin rash were positive for IgG while 100% of control children without skin rash were positive for IgG.

Patients complaining difficult breathing had 26.9% IgG positivity rate versus 11.1% who were negative for IgG, so the difference was statistically insignificant ($P=0.174$). None of control children complaining difficult breathing. Additionally, 73.1% of patients without difficulty breathing were positive for IgG versus 100% of control children were positive for IgG.

Regarding the presence of cough, patients with cough had 50% positivity rate for IgG versus 55.5% of patients with cough were negative for IgG with a statistically significant difference (P=0.004). On the other hand, 50.0% of patients without cough were positive for IgG against 100% of control children were positive for IgG.

Other fascinating results showed that 73.1% of patients who were positive for anti-COVID IgM were also positive for anti-COVID 19 IgG versus 66.7% who were positive for IgM but negative for IgG, the difference was statistically insignificant (P=0.561). Furthermore, 26.9% of patients who were negative for IgM were positive for IgM versus 33.3% of patients who were negative for both antibodies.

Table 4.6 Association of anti-COVID IgG with clinical manifestations

Variables		patients			Control		
		IgG			IgG		
		Positive No. (%)	Negative NO. (%)	Not done No. (%)	Positive No. (%)	Negative No. (%)	Not done No. (%)
Fever	Yes	25(96.2)	8(88.9)	43(91.5)	3(5.4)	2(11.1)	2(8.3)
	No	1(3.8)	1(11.1)	4(8.5)	53(94.6)	16(88.9)	22(91.7)
	P value	0.687			0.688		
Sore throat	Yes	16(61.5)	5(55.6)	18(38.3)	2(3.6)	-	3(12.5)
	No	10(38.5)	4(44.4)	29(61.7)	54(96.4)	18(100)	21(87.5)
	P value	0.143			0.139		
Skin Rash	Yes	1(3.8)	1(11.1)	4(8.58.5)	-	-	-
	No	25(96.2)	8(88.9)	43(8.5)	56(100)	18(100)	24(100)
	P value	0.687			-		
Diarrhea	Yes	20(76.9)	6(66.7)	30(63.8)	10(17.9)	3(16.7)	3(12.5)
	No	6(23.1)	3(33.3)	17(36.2)	46(82.1)	15(83.3)	21(87.5)
	P value	0.512			0.837		
Difficulty breathing	Yes	7(26.9)	1(11.1)	5(10.6)	-	-	-
	No	19(73.1)	8(88.9)	42(89.4)	56(100)	18(100)	24(100)
	P value	0.174			-		
Cough	Yes	13(50.0)	5(55.6)	8(17.0)	-	-	-
	No	13(50.0)	4(44.4)	39(83.0)	56(100)	18(100)	24(100)
	P value	0.004*			-		
Anti-COVID IgM	Positive	19(73.1)	6(66.7)	38(80.9)	-	-	2(8.3)
	Negative	7(26.9)	3(33.3)	9(19.1)	-	-	22(91.7)
	Not done	-	-	-	-	-	-
	P value	0.561			-		

*Significant difference between percentages using Pearson Chi-square test (χ^2 -test) at 0.05 level.

4.7 Association of IgM with Sociodemographic Variables

Table (4.7) summarize the association of anti-COVID 19 IgM with sociodemographic variables. Among patients, the highest IgM positivity rate (38.1%) was among age group 1-4 years versus 42.1% were negative. The difference was statically insignificant compared to other age groups ($P=0.861$). Of note, all patients were tested for anti-COVID 19 IgM. In the control children, 50% of those positive for IgM were in the age group 1-4 years, with statistically significant difference ($P=0.048$). Regarding gender, 61.9% of males versus 38.1% of females were positive for IgG with a statistically insignificant difference ($P=0.605$). On the other side, 100% of control children were positive for IgM with a statistically insignificant difference ($P=0.176$). The results also found that 41.3% of patients with positive IgM were from urban areas versus 58.7% from rural areas, with a statistically insignificant difference ($P=0.202$). On the other side, 100% of control children who were positive for IgM were from urban areas, with a statistically insignificant difference ($P=0.217$).

Table 4.7 Association of anti-COVID IgM with sociodemographic variables

Variables		Patients (IgM)		Control (IgM)		
		Positive No. (%)	Negative No. (%)	Positive No. (%)	Negative No. (%)	Not done No. (%)
Age (Ys)	<1	15(23.8)	3(15.8)	1(50.0)	1(4.5)	10(13.5)
	1---4	24(38.1)	8(42.1)	1(50.0)	11(50.0)	18(24.3)
	5---9	17(27.0)	5(26.3)	-	8(36.4)	21(28.4)
	10---14	7(11.1)	3(15.8)	-	2(9.1)	25(33.8)
	P value	0.861		0.048*		
Gender	Male	39(61.9)	13(68.4)	2(100)	8(36.4)	37(100)
	Female	24(38.1)	6(31.6)	-	14(63.6)	37(100)
	P value	0.605		0.176		
Residence	Urban	26(41.3)	11(57.9)	2(100)	8(36.4)	31(41.9)
	Rural	37(58.7)	8(42.1)	-	14(63.6)	43(58.1)
	P value	0.202		0.217		

4.8 Association of IgM with Family Variables

The data presented in Table 4.8 highlight the correlation between anti-COVID 19 IgM and family history. In terms of past infection with COVID-19 within the family, the

results revealed that patients with a positive history exhibited a 77.8% IgM positivity rate, while those with a positive history but negative for IgM showed a rate of 73.7%. This difference was statistically insignificant ($P=0.711$). Conversely, patients without a history of COVID-19 infection displayed a 22.2% IgM positivity rate. On the control side, the findings indicated that 100% of children with a positive history of COVID-19 infection tested positive for IgM, whereas 36.4% with a positive history but negative for IgM displayed IgM positivity. However, this difference was statistically insignificant ($P=0.198$). Concerning the presence of chronic diseases, the results showed that 7.9% of patients with chronic diseases were positive for IgM, while 92.1% of patients with negative history of chronic diseases were positive for IgM. Of note none of control children had positive history of chronic diseases.

Table 4.8 Association of anti-COVID IgM with family variables

Variables		Patients (IgM)		Control (IgM)		
		Positive No. (%)	Negative No. (%)	Positive No. (%)	Negative No. (%)	Not done No. (%)
Family history	Yes	49(77.8)	14(73.7)	2(100)	8(36.4)	28(37.8)
	No	14(22.2)	5(26.33)	-	14(63.6)	46(62.2)
	P value	0.711		0.198		
Chronic diseases	Yes	5(7.9)		-	-	-
	No	58(92.1)	19(100)	2(100)	22(100)	74(100)
	P value	0.205		-		

4.9 Association of IgM with Clinical Manifestations

Table 4.9 shows the results of the association of anti-COVID-19 IgM and clinical manifestations of the study groups. 90.5% of patients with fever were positive for IgM versus 100% who were negative for IgM, with a statistically insignificant difference ($P=0.162$). However, 9.5 of the patients without fever were positive for IgM. In the control group, 50% and 4.5% of children with fever were positive and negative for IgM, respectively, with a statistically insignificant difference ($P=0.056$). Furthermore, 50.0% of children without fever were positive for IgM. Regarding the sore throat, the patients with sore throat had a 44.4% IgM positivity rate versus 57.9% who were negative, with a statistically insignificant difference ($P=0.303$). Additionally, 55.5% of patients without sore throats were positive for IgM. In the control group, only two children

without sore throats were positive for IgM. For the skin rash, only 9.5% of patients were positive for IgM versus 90.5% without skin rash; the difference was statistically insignificant ($P=0.162$). The results also showed that 14.3% of patients with difficult breathing were positive versus 21.1% without difficulty breathing, with a statistically insignificant difference ($P= 0.479$). On the other hand, 85.7% of patients without difficulty breathing were positive for IgM. On the control side, there were only 2(100%) of children without difficulty breathing were positive for IgM. Concerning the cough, 31.7% and 31.6% of patients were positive for IgM, with a statistically insignificant difference ($P= 0.898$). Furthermore, 68.3% of patients without cough were positive for IgM. In the control children, only 2 (100%) without cough were positive for IgM. The results also found that 30.2% of patients who were positive for anti-COVID-19 IgG were also positive for IgM versus 36.8% who were positive for IgG but negative for IgM, with a statistically insignificant difference ($P= 0.561$). Moreover, 9.5% of patients who were negative for IgG were positive for IgM. Of the control children, only 2(100%) of those with negative IgG were positive for IgM.

Table 4.9 Association of anti-COVID IgM with family variables

Variables		Patients (IgM)		Control (IgM)		
		Positive No. (%)	Negative NO. (%)	PositiveNo. (%)	NegativeNo. (%)	Not done No. (%)
Fever	Yes	57(90.5)	19 (100)	1(50.0)	1(4.5)	5(6.8)
	No	6(9.5)	-	1(50.0)	21(95.5)	69(93.2)
	P value	0.162		0.056		
Sore throat	Yes	28(44.4)	11(57.9)	-	3(13.6)	2(2.7)
	No	35(55.6)	8(42.1)	2(100)	19(86.4)	72(97.3)
	P value	0.303		0.117		
Skin Rash	Yes	6(9.5)	-	-	-	-
	No	57(90.5)	19(100)	2(100)	22(100)	74(100)
	P value	0.162		-		
Diarrhea	Yes	41(65.1)	15(78.9)	-	3(13.6)	13(17.6)
	No	22(34.9)	4(21.1)	2(100)	19(86.4)	61(82.4)
	P value	0.255		0.744		
Difficult y breathin g	Yes	9(14.3)	4(21.1)	-	-	-
	No	54(85.7)	15(78.9)	2(100)	22(100)	74(100)
	P value	0.479		-		
Cough	Yes	20(31.7)	6(31.6)	-	-	-
	No	43(68.3)	13(68.4)	2(100)	22(100)	74(100)
	P value	0.989		-		
Anti-COVID IgG	Positive	19(30.2)	7(36.8)	-	-	56(75.7)
	Negative	6(9.5)	3(15.8)	-	-	18(24.3)
	Not done	38(60.3)	9(47.4)	2(100)	22(100)	-
	P value	0.561		-		

5. CONCLUSIONS AND RECOMMENDATION

5.1 Conclusions

- Patient children with respiratory tract signs and symptoms had a higher rate of positive COVID 19 infection which was significantly higher compared to controls.
- The COVID 19 infection in children cannot be differentiated from other respiratory infection on the clinical ground.
- About one tenth of apparently healthy children are actively infected with COVID 19 virus asymptotically.
- About one quarter of patients as well as controls had protective immunity derived either from previous COVID 19 infection or through contact with positive cases (Hared immunity).
- The ELISA kit for anti-COVID 19 IgM was efficiently detected recent or active cases, while COVID 19 IgG was efficiently detect past infection (Seroprevalence) or hared immunity.

5.2 Recommendations

- The COVID 19 infection should be introduce in the differential diagnosis of children with respiratory tract infection.
- Vaccination of Iraqi children against COVID 19 should be mandatory for all children.
- Ensuring a clean and healthy environment for children in both their homes and schools is essential in safeguarding them from COVID-19. This includes implementing measures such as the use of face masks when necessary.
- A future study will investigate the prevalence of COVID-19 infection within families.

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APPENDICES

APPENDIX 1. Ethical approval in Arabic

APPENDIX 2. Ethical approval in Turkish



APPENDIX 1. Ethical approval in Arabic



APPENDIX 2. Ethical approval in Turkish



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