PERIÓDICO TCHÊ QUÍMICA
ARTIGO ORIGINAL

SOROPREVALÊNCIA DE ANTICORPOS IGG COVID-19 NA CIDADE DE SHAHREKORD, IRÃ

SEROPREVALENCE OF COVID-19 IGG ANTIBODIES IN SHAHREKORD COUNTY, IRAN

شیوع سرمی آنتی بادی های IgG کووید 19 در شهرستان شهرکرد، ایران

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RESUMO

Introdução: A estimativa da soroprevalência de anticorpos covid-19 pode ser usada para prever com mais precisão a epidemia, estimar a vulnerabilidade da comunidade, obter informações sobre a progressão da doença e gerenciar o tratamento da doença. **Objetivos:** O presente estudo foi desenhado para avaliar a soroprevalência de anticorpos IgG contra o vírus COVID-19 na população urbana do município de Shahrekord (Irã). **Methods:** Neste estudo analítico-descritivo, foram identificadas 690 pessoas residentes no município de Shahrekord encaminhadas a laboratórios de diagnóstico médico entre Outubro e Dezembro de 2020, e os níveis séricos de IgG foram medidos através do teste ELISA. O teste estatistico Qui-quadrado e o teste de Spearman, executados no SPSS-20, foram utilizados para investigar a relação entre as variáveis. **Results:** Das 690 amostras, 190 foram positivas para anticorpos IgG contra COVID-19. A frequência de anticorpos positivos foi de 27,5% [IC 95%: 23,1-30 (26,9% em homens e 28% em mulheres)]. Não houve relação significativa entre a soroprevalência de COVID-19 e sexo, ocupação, estado civil e IMC (P > 0,05). A soroprevalência de COVID-19 foi significativamente maior em indivíduos com histórico de contato com pessoa infectada, indivíduos com sintomas de COVID-19 durante a pandemia, indivíduos com histórico de diagnóstico definitivo por PCR e indivíduos com idade superior a 60 anos (P < 0,05). **Discussões:** Com base nos resultados, a soroprevalência de anticorpos contra COVID-19 na população estudada foi de 27,5% e superior à prevalência da doença baseada em testes de triagem molecular.. **Conclusão:** A determinação da prevalência de anticorpos IgG contra COVID-19 na comunidade para ajudar na previsão mais precisa da epidemia pode ser utilizada no gerenciamento da doença.

Palavras-chave: *Coronavírus, COVID-19, Epidemiologia, Anticorpos, Sistema imunológico.*

ABSTRACT

Background: Estimation of seroprevalence of COVID-19 antibodies can be used to predict the epidemic more accurately and estimate the vulnerability of the community, gain information on disease progression, and manage disease treatment. **Aims:** The present study was designed to evaluate the seroprevalence of IgG antibodies against the COVID-19 virus in the urban population of Shahrekord county (Iran). **Methods:** In this descriptive-analytical study, 690 people living in Shahrekord county referred to medical diagnostic laboratories in the county between October to December 2020 were identified, and their serum IgG levels were measured using ELISA. Chi-square and Spearman's test in SPSS 20 were used to investigate the relationship between variables.

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Results: Out of 690 samples, 190 were positive for IgG antibodies against COVID-19. The frequency of positive antibodies was 27.5% [CI 95%: 23.1-30 (26.9% in men and 28% in women)]. There was no significant relationship between the seroprevalence of COVID-19 and gender, occupation, marital status, and BMI (P>0.05). Seroprevalence of COVID-19 was significantly higher in individuals with a history of contact with an infected person, individuals with COVID-19 symptoms during the pandemic, individuals with a history of definitive diagnosis based on PCR, and individuals aged over 60 years (P<0.05). **Discussion:** Based on the results, the seroprevalence of antibodies against COVID-19 in the study population was 27.5% and more than the prevalence of the disease based on molecular screening tests. **Conclusion:** Determination of IgG antibodies prevalence against COVID-19 in the community to help in more accurate prediction of the epidemic can be used in managing the disease.

Keywords: *Coronavirus, COVID-19, Epidemiology, Antibodies, Immune system.*

چکیده

زمینه: *تخمین شیوع سرمی آنتی‌بادی‌های کووید-19 می‌تواند برای پیش‌بینی دقیق‌تر اپیدمی و تخمین آسیب‌پذیری جامعه، کسب اطلاعات در مورد پیشرفت بیماری و مدیریت درمان بیماری استفاده شود.* ***هدف:*** *مطالعه حاضر به منظور ارزیابی شیوع سرمی آنتی بادی های IgG علیه ویروس کووید-19 در جمعیت شهری شهرستان شهرکرد طراحی و اجرا شد.* ***روش کار:*** *در این مطالعه توصیفی-تحلیلی، تعداد 690 نفر از افراد ساکن در شهرستان شهرکرد که در فاصله مهر تا آذرماه سال 1399 به آزمایشگاه‌های تشخیص پزشکی شهرستان مراجعه کرده بودند، شناسایی و سطح سرمی IgG آنها با روش الایزا اندازه‌گیری شد. برای بررسی رابطه بین متغیرها از آزمون کای اسکوئر و اسپیرمن درنرم افزار SPSS- 20 استفاده شد.* ***یافته ها:*** *از 690 نمونه آزمایش شده، 190 نفر از نظر آنتی بادی IgG علیه کووید-19 مثبت بودند. میزان فراوانی آنتی بادی های مثبت 27.5 درصد (CI 95%: 23.1-30%)، در مردان 26.9 درصد و در زنان 28 درصد بود. بین شیوع سرمی کووید-19 با جنسیت، شغل، وضعیت تاهل و BMI رابطه معنی داری وجود نداشت (P>0.05). شیوع سرمی کووید-19 به طور معناداری در افراد با سابقه تماس با فرد آلوده، افراد دارای علائم کووید-19 در طی پاندمی، افراد با سابقه تشخیص قطعی بر اساس تست PCR و افراد بالای 60 سال بیشتر بود (P<0.05).* ***بحث:*** *بر اساس نتایج، شیوع سرمی آنتی بادی های ضد کووید-19 در جمعیت مورد مطالعه 27.5 درصد و بیشتر از شیوع بیماری بر اساس تست های غربالگری مولکولی بود.* ***نتیجه‌گیری:*** *تعیین میزان شیوع آنتی‌بادی‌های IgG علیه کووید-19 در جامعه می‌تواند برای پیش بینی دقیق تر اپیدمی و مدیریت بیماری استفاده شود.*

واژگان کلیدی: ویروس کرونا، کووید-19، اپیدمیولوژی، آنتی بادی ها، سیستم ایمنی.

1. INTRODUCTION:

Despite advances in the prevention and treatment of diseases, the emergence of viral diseases continues and is considered a serious public health issue. In the past 20 years, we have seen viral epidemics such as SARS-CoV in 2002-2003, H1N1 flu in 2009, and then MERS-CoV in 2012. Recently, in December 2019, an unknown epidemic was reported in Wuhan, China, with an unexplained infection of the lower respiratory tract (Wu *et al*., 2021; Alsamman and Zayed, 2020). The new virus was initially called nCoV-2019. Subsequently, the International Committee on Taxonomy of Viruses (ICTV) named the virus SARS-CoV-2 due to 80% similarity of its nucleotides to SARS's, which is a member of the coronaviridae family. As with the causative agent of SARS this virus belongs to the βCoV2 group and is therefore considered as a positive-stranded RNA virus coated with a helical nucleocapsid (Lupia *et al*., 2020). Approximately 30 types of coronaviruses have been identified in humans, mammals, and birds. So far, it has been established that seven types of viruses have caused infections in humans: alpha and beta. The genomes of these viruses encode four structural proteins, namely, nucleocapsid (N), membrane (M), envelope (E), and spike (S) (Walls *et al*., 2020; Ahmed *et al*., 2020). The human immune system produces two types of antibodies, namely IgM and IgG, against the virus. The presence of IgM antibodies against this virus indicates the acute phase of the disease, and the presence of IgG antibodies, as a stable response against this disease, indicates that immunity against this disease has developed (Bryant *et al*., 2020; Stadlbauer *et al*., 2020; Farnsworth and Anderson; 2020).

The high potential of this virus for human-to-human transmission on the one hand, and international travel, on the other hand, has increased the incidence of the disease in different countries. Besides this, many carriers are asymptomatic, which indicates the need for prevention and screening of patients to control the devastating effects of the disease. Reports suggest that 25-50% of people infected with the virus may never have symptoms, and some may only have mild illnesses (Rodriguez-Morales *et al*., 2020). However, to date, no accurate information has been reported on the number of asymptomatic patients, the rate of improvement in the immune system, or the likelihood of recurrence of COVID-19.

Tests based on the presence of antibodies in the serum of COVID-19 patients can identify people who have been exposed to the virus and help to gain insight into how the disease has spread and even become fatal, and understand the immune system's response rate to the disease and the likelihood of its recurrence appropriately. In addition, these tests are useful for identifying individuals who have exhibited a complete immune response to disease after recovery (Haveri *et al*., 2020; Xu *et al*., 2020; Infantino *et al*., 2020). In these experiments, the presence of antibodies is evaluated. Since the antigens and antibodies produced against the virus are substantially more stable than the virus RNA, they are less sensitive during sample transfer and storage. Therefore false negative tests are comparatively less likely.

This study aimed to determine the seroprevalence of IgG antibodies against COVID-19 in Shahrekord county and to compare the prevalence of the disease based on the serology and molecular tests in the community.

2. MATERIALS AND METHODS:

2.1. Study design and data collection

This descriptive-analytical study was performed cross-sectional between September and November 2020 in indigenous people referred to (public and private) medical diagnostic laboratories in Shahrekord for reasons other than COVID-19. The protocol of the study was approved by the Ethics Committee of Shahrekord University of Medical Sciences (IR.SKUMS.REC.1399.073), and informed consent to participate in the study was obtained from all participants, and the principles of data confidentiality were carefully observed by investigators. Based on the number of positive cases, available reports, and the statistical consultant's opinion, the sample size was considered at least 600 people during the study, and blood samples were taken from 690 patients, and their information was also collected.

Sampling was performed randomly and systematically. To this end, one out of every three who were referred to medical diagnostic laboratories in Shahrekord was randomly selected until the required sample size was achieved.

Complementary data were collected using a checklist of sociodemographic characteristics based on the information accessible through the Sib system of the Ministry’s Vice Chancellor for Health. This information included age, gender, occupation, marital status, history of molecular COVID-19 test, symptoms since the pandemic onset, history of hospitalization due to COVID-19, history of contact with an infected person, weight, and height.

2.2. Detection of SARS-CoV-2 IgG antibodies

Blood samples were transferred to the Virology Laboratory of Shahrekord University of Medical Sciences for serum isolation. The serum of the patients was centrifuged for 15 minutes at 3000 rpm and kept in the freezer at -20 °C until the experiments. This study evaluated the serum level of IgG antibodies against COVID-19 using an ELISA kit (Pishtaz Teb).

To evaluate the level of IgG antibodies in serum samples isolated from patients' blood cells, serum samples, and all materials and reagents were first brought to room temperature. IgG kit controls were ready to use and did not require dilution. However, serum samples were diluted at 1:101 using a sample dilution solution. Two wells for blank, two wells for negative control (containing phosphate buffer solution and 0.05% protective substance and negative human serum for IgG antibody against SARS-CoV-2), and then positive control (containing buffer solution, containing protein as stabilizer and 0.05% protective substance and inactivated human serum, containing IgG antibody against SARS-CoV-2) was poured in duplicate, and other wells were used for samples. One hundred µl of positive control, 100 µl of negative control, and 100 µl of diluted samples were introduced into the corresponding wells of the ELISA kit covered with N antigens (N-coating, one of the most abundant antigens of virus) of SARS-CoV-2. The wells were then covered with a special plate label and left at 37 °C for 30 minutes. Afterward, the contents of the wells were emptied, and the wells were washed five times with a ready-to-use washing solution. Then, 100 µl of ready-to-use conjugated enzyme solution (containing human anti-IgG antibody solution bound to horseradish peroxidase) was added to the wells except for the blank wall. The wells were covered again with a special plate label and left at 37 °C for 30 minutes. Next, the contents of the wells were emptied, and the wells were washed five times with a ready-to-use washing solution. After washing, 100 µl of ready-to-use dye solution (containing tetramethylbenzidine and oxygenated water) was poured into all wells, and the wells were left at room temperature in the dark for 15 minutes. In this step, 100 µl of stopper solution (containing 1

normal hydrochloric acid) was added to each well to stop the enzymatic reactions and turn the blue color into yellow. Finally, the optical absorbance of the wells was read by an ELISA reader using a 450 nm filter up to half an hour after adding the stopper solution, and a 630 nm filter was used as a reference filter.

To calculate the results, the cut-off value was obtained by Equation 1:

Cut off value = Average optical absorbance of negative control + 0.15 (Eq. 01)

Then, the index value was calculated by dividing the sample's optical absorbance by the cut-off value to determine the positive and negative results. According to Equation 1, values higher than 1.1 and those lower than 0.9 negatives are considered positive. Therefore, samples with an index value of 0.9-1.1 were considered suspicious and retested using fresh serum or plasma after some time.

It should be noted that based on the information mentioned in the kit instructions, the sensitivity of the kit for measuring IgG antibodies against SARS-CoV-2 is 94.1%, and its specificity is 98.3%.

2.3. Statistical analysis

Qualitative variables were described using frequency and percentage, and quantitative variables were described using mean and standard deviation. The relationship between variables was assessed using Chi-square and Spearman's correlation tests. The analysis was done by SPSS 23 and significantly defined as $P<0.05$.

3. RESULTS AND DISCUSSION:

3.1. Results

Of the 690 studied individuals, 301 (43.6%) were male. The mean age of participants was 45.3±19.5 years (range; 5 months-92 years). Overall, 190 were positive for COVID-19-specific IgG. The prevalence of positive antibodies in our participants was 27.5% [CI 95%: 23.1-30 (26.9% in men and 28% in women)] (Table 1). Among the participants in the study, PCR test using nasal swabs was reported positive in 110 patients (15.9%) up to the time of sampling. There was no significant relationship between the seroprevalence of COVID-19 and gender, occupation, marital status, and BMI ($P>0.05$). However, the seroprevalence of COVID-19 (positive antibody) was significantly higher in people with a history of contact with an infected person, people with COVID symptoms during the pandemic, people with a history of definitive diagnosis based on PCR, and people over 50 years of age ($P<0.05$) (Table 1).

Of patients with positive antibodies, 23.6% had a history of hospitalization due to COVID-19. The mean antibody titer in patients with a positive antibody with a history of hospitalization was 10.95±6.35, and in patients with a positive antibody without a history of hospitalization, 9.5±6.1 ($P=0.199$).

In individuals with positive antibodies, Spearman's correlation coefficient showed a statistically significant relationship between age and IgG antibody titer, so with increasing age, the amount of antibody titer increased ($r=0.187$, $P<0.01$).

The mean BMI was 26.5±5.17 kg/m² in individuals with positive antibodies and 26.2±4.9 kg/m² in negative-antibody subjects ($P>0.05$).

3.2. Discussion

The outbreak of coronavirus has become a major concern across the world. Studies have shown that the prevalence of the disease has not been accurately reported due to the mild form of the disease, which causes many people with COVID-19 to be unaware of their disease or their molecular test results to be false-negative, necessitating serology-based procedures for a more acceptable estimate of the disease. For example, a report from the Chinese Center for Disease Control and Prevention, including 445,500 people, stated that the disease was mild in 81% of patients, with only 14% having a severe form of the illness and 5% having a critical form; asymptomatic infections have also been reported, indicating the high number of asymptomatic patients and the need for serological tests (Wang *et al*., 2020). In another study on the prevalence of COVID-19 on a cruise ship, in which almost all passengers and crew were screened for the virus, approximately 17% of the participants had a positive report. However, about half of the 619 confirmed cases were asymptomatic at the time of diagnosis (Mizumoto *et al*., 2020). Besides this, a study of the seroprevalence of antibodies in Santa Clara, California, showed that the infection caused by the virus was much wider than the number of cases confirmed using clinical findings and

molecular tests (Bendavid *et al*., 2020). Also, a study (2020) on the serological characteristics of SARS-CoV-2 infection from the time of exposure to the onset of symptoms showed the need for tests based on the evaluation of antibodies against the coronavirus (Lou *et al*., 2020). In this regard, several teams around the world have begun testing population samples for SARS-CoV-2 antibodies, whose initial findings show uncertainty about the exact prevalence of the disease in the current situation (Stadlbauer *et al*., 2020, Haveri *et al*., 2020; Xu *et al*., 2020; Infantino *et al*., 2020).

In the present study, which was conducted to investigate the seroprevalence of IgG antibodies against COVID-19 in the urban population of Shahrekord County, the seroprevalence of COVID-19 was 27.5%, which is higher than the prevalence of the disease based on molecular evaluations (15.9%). In a study (2020) on the seroprevalence of anti-SARS-CoV-2 IgG antibodies in the general Indian population, the serum level of IgG antibodies was determined by ELISA, and the results indicated a low seroprevalence in India so that by mid-May 2020, less than 1% (0.73%) of the population had been exposed to infection. The low prevalence of antibody levels in most regions of India indicates that India is in the first phase of the epidemic, and most of the population is still susceptible to the disease (Murhekar *et al*., 2020). In Iran, only one study, conducted from March to 20 May 2020, examined the prevalence of antibodies against SARS-CoV-2 in 18 cities from 17 provinces using ELISA. The study included 9,181 people, including 5,372 ones from high-risk populations (including front-line physicians and nurses, non-front-line health workers, pharmacy staff, taxi drivers, bank employees, and cashiers in supermarkets and chain stores) and 3,530 individuals from the general population (including those registered in the Iranian electronic health system or health care centers). That study showed a 17.1% and 20% prevalence of SARS-CoV-2 specific antibodies in the general and high-risk populations. According to these results, it can be estimated that the prevalence of SARS-CoV-2 specific antibodies is higher than the number of cases confirmed by PCR tests in the reports. The reason for the difference in the prevalence reported in the study conducted in Iran and that in the present study could be the time of the study, causing more people to be exposed to the virus and the prevalence to increase. Also, in the study conducted in Iran, after estimating population-based prevalence, the cities of Rasht, Qom, Gorgan, and Babol, with seroprevalence of 72.6%, 58.5%, 43.9%, and 22.4%, respectively, had the highest prevalence (Poustchi *et al*., 2021). The difference in prevalence in different areas can be due to reasons such as weather conditions and differences in the concentration and movement of people in public places, as well as the characteristics of mass communication among people.

In the present study, a statistically significant relationship was observed between age and IgG antibody titer, so the amount of antibody titer increased with increasing age. Reports from some countries have suggested the role of age as a risk factor for disease severity (Jiang *et al*., 2020; Hossain *et al*., 2021). Studies have also shown that the rate of inflammation is higher in older people, and with increased inflammation in the body, the rate of systemic response of the immune system increases, and consequently, the level of antibodies in the blood will increase (Hotamisligil *et al*., 2006; Gonzalez-Quintela *et al*., 2008), being, in fact, one of the reasons for the relationship between aging and increased antibody titer in the present study. In addition to age, in the current study, the seroprevalence of COVID-19 was significantly higher in individuals with a history of contact with an infected person, individuals with COVID symptoms during the pandemic, and individuals with a history of definitive diagnosis based on PCR. These results are all in line with the higher risk of the disease and a higher likelihood of immune response in such individuals and confirm the need to follow health protocols and social distancing to reduce its incidence (Hossain *et al*., 2021).

4. CONCLUSIONS:

In the present study, the seroprevalence of IgG antibodies against COVID-19 in the urban population of Shahrekord county was 27.5%, higher than the prevalence of the disease based on molecular screening tests. Therefore, serological tests can be suggested for a more accurate prediction of the epidemic and for better management of the prevention and treatment of the disease.

5. DECLARATIONS

5.1. Study Limitations

Since the study is cross-sectional, the study is limited to a time of evaluation.

5.2. Acknowledgements

We would like to thank the Vice Chancellor for Research and Technology of the University, all

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5.3. Funding source

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5.4. Competing Interests

There were no conflicts of interest in conducting this research.

6. HUMAN AND ANIMAL-RELATED STUDIES

6.1. Ethical Approval

The protocol of this research has been approved by the Ethical Committee of Shahrekord University of Medical Sciences (ethics code: IR.SKUMS.REC.1399.073).

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Table 1. *Demographic characteristics of study participants*

Variables	Total number	Number of positive serology cases (%)	OR (95% CI) based on the univariable model	Significance level (P value)
Age groups				
Under 20 yr	45	13(28.9)	0.637 (0.306-1.328)	0.025
20-29 yr	93	18(19.4)	0.376 (0.202-0.702)	
30-39 yr	95	27(28.4)	0.623 (0.353-1.099)	
40-49 yr	106	29(37.9)	0.591 (0.340-1.027)	
50-59 yr	87	33(37.9)	0.959 (0.549-1.674)	
Over 60 yr	131	51(38.9)	1.0 [Reference]	
Gender				
Male	301	81(26.9)	0.946 (0.675-1.325)	0.764
Female	389	109(28)	1.0 [Reference]	
Marital status				
Single	64	13(20.3)	0.583 (0.198-1.71)	0.223
Married	344	114(33.1)	1.133 (0.453-2.832)	
Widow/widower-divorced	49	17(34.7)	1.214 (0.418-3.524)	
Under 15 yr	23	7(30.4)	1.0 [Reference]	
Occupation				
Housewife	176	53(30.1)	1.077 (0.323-3.589)	0.552
Student	51	11(21.6)	0.688 (0.18-2.62)	
Laborer	24	10(41.7)	1.786 (0.434-7.353)	
Civil servant	113	40(35.4)	1.37 (0.404-4.649)	
Jobless	36	10(27.8)	0.962 (0.244-3.783)	
Self-employed	68	24(35.3)	1.364 (0.386-4.816)	
Under 6 yr	14	4(28/6)	1.0 [Reference]	
History of definitive diagnosis by PCR				
Yes	110	71(64.5)	5.882 (3.728-9.279)	<0.001
No	385	91(23.6)	1.0 [Reference]	
Having symptoms during the pandemic				
Yes	169	95(56.2)	4.963 (3.308-7.445)	<0.01
No	326	67(20.6)	1.0 [Reference]	
History of contact with an infected person				
Yes	99	61(61.6)	4.736 (2.977-7.533)	<0.001
No	395	100(25.3)	1.0 [Reference]	
Working outside the home				
Yes	205	74(36.1)	1.441 (0.979-2.122)	0.064
No	277	78(28.2)	1.0 [Reference]	