

Immunological Evaluation of Covid-19 Vaccine in Babylon Population

Baidaa Shaheed Tuama¹, Abeer Fauzi Murad Al-Rubaye², Amal Merza³

^{1,2}Department, of Biology Science for Women, University of Babylon/Iraq

³Immunologist in Al-Sadiq Hospital/Babylon/Iraq

Email: baidaa.abed.gsci78@student.uobabylon.edu.iq

Abstract

The study was conducted in Babylon governorate on vaccinated person about (85) with or without previous infection as a test group, in comparison with (35) person recovering from Covid-19 which mentioned as positive (+ve) control with (30) healthy population as a negative (-ve) control groups. Different parameters were studied to evaluation of immunological status after receiving complete doses of different vaccine. low level of anti Sars-cov2 –IgM Ab of both vaccinated and control groups, while increased of Sars-cov2 –IgG in vaccinated population in comparison with control, at Mean \pm SD (33.21 \pm 16.06, 20.36 \pm 14.0, 21.47 \pm 13.77) in respective manner at P. Value < 0.01. There was a highly increased in IL-12, IL-15 and INF - γ levels in comparison with control groups. The cytokines level among infected population after receiving vaccine were higher than non-infected person as well as in control groups.

Keywords: covid-19; anti Sars-cov2 –IgM, IgG Ab; Cytokines; vaccine

1. Introduction

The cause of coronavirus sickness in 2019 is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (COVID-19). Since December 2019, SARS-CoV-2 has been spreading around the world, causing the COVID-19 pandemic, which would result in 234 million illnesses and 4.8 million fatalities by 30 September 2021. The COVID-19 pandemic has put tremendous pressure on the development of vaccines worldwide.

Coronavirus disease 2019 (Covid-19) must be prevented, and those who are vulnerable to complications must be protected, using vaccines (1). The immune mechanisms triggered by SARS-CoV-2 vaccines in healthy populations are not well-known. Studies are limited, especially from laboratories not directly related to the manufacture of vaccines or research teams leading the evaluations of phase 2 or 3 clinical trials (2). Recently, a prospective national cohort study reported that using this vaccination schedule, CoronaVac is effective for preventing hospitalization (87.5%), Intensive Care Unit (ICU) admission (90.3%), and Covid-19-related death (86.3%) (3). Vaccines that stimulate an immune response against the spike protein necessary for SARS-CoV-2 binding, fusion, and cell entry. As a result, vaccination causes anti-S and anti-RBD binding and neutralizing antibodies to be produced in the blood, but not anti-N antibodies. Vaccines cause early synthesis of serum IgA, IgM, and IgG antibodies, similar to infection (4; 5). As well as long-lasting memory B- and T- cell responses (6; 7).

2. Methodology

The duration of sampling in the study was during the period from 11/11/2021 to 29/1/2022 on people vaccinated with the corona vaccine in all area of Babylon government with two doses at different intervals after give the vaccine ranging from (2 W - 1 Mon, 2 Mon - 3 Mon, 4 Mon - 5 Mon, > 5 Mon) and

were also collected from unvaccinated people as control include (Healthy and Cured).

Five ml of venous blood was obtained from each participant. The blood was placed in gel tube and let to stand for 30 minutes, and then samples were centrifuge (3000rpm / 15 min). The serum collected divided into 3 Eppendorf (200 ml each) and kept in the freezer (-20 c) until it was used for the laboratory assays.

The VIDAS SARS –COV-2IgG is an automated assay using the ELFA Enzyme Linked Fluorescent Assay technique intended for qualitative detection of IgG antibodies to SARS-Cov-2 in human serum or plasma lithium heparin on instruments of the VIDAS family. The immunosorbent assay linked to the enzyme ELISA test known IL-15, IL-12 and IFN- γ in the serum were tested.

3. Result and Discussion

There was a low level of anti Sars-cov2 –IgM antibodies of both vaccinated and control groups, while increased of Sars-cov2 –IgG in vaccinated population in comparison with curried patients and healthy control, at Mean \pm SD (33.21 \pm 16.06, 20.36 \pm 14.0, 21.47 \pm 13.77) in respective manner at P. Value < 0.05 (P value < 0.012) Table (3-1)

This result might be refer to that vaccination might induce specific IgG production rather than IgM. During viral infection with SARS-CoV-2, the production of specific antibodies against the virus is consistent in most patients, except for immune deficient patients. IgM can be detected as early as 3 days after infection and provides the first line of humoral immunity defense, after which high-affinity IgG responses are initiated and play a key role in long-term immune memory (8).

The significance of antibody response in COVID-19 is important, not only in the diagnosis but also prognosis. Specific antibodies, including IgG antibodies and neutralizing antibodies, are important for protecting the

host from infection by blocking viral entry into host cells after viral infection(9).

There was a highly increased in IL-12, IL-15 and INF - γ levels in comparison with control groups (Curried and healthy) at Mean \pm SD of IL-12 (26.24 \pm 4.78, 6.0 \pm 0.9 2, 6.04 \pm 0.95) The IL-15 level(596.84 \pm 60.62 , 294.53 \pm 37.06 , 292.80 \pm 39.11) , and INF - γ (143.29 \pm 50.92 , 54.92 \pm 12.81 , 54.72 \pm 11.92) respectively at P value (< 0.05)(P value 0.001>). As shown in Table (3 - 2). This result might be refer to that the increased in cytokine level expressed on cellular activity of immune system more effective against vaccine particles used instead of natural virus component. cytokines that promote innate and adaptive immune response IFN- γ , IL-15, IL- 12/IL-23p40, tumor necrosis factor alpha TNF- α , IL-3, and IL-7 (10).

The IL-12 has also been shown to be very effective as a vaccine adjuvant for enhancement of protective antibody responses against pulmonary bacterial and viral infections, and is particularly effective when administered locally to mucosal surfaces, i.e., intranasally together with vaccine (11). The IL-15 immunotherapy may be a viable strategy for COVID-19, as it promotes innate immune responses via the induction of NK cells, CD8+ T cells, and T regulatory cells to neutralize Th2 cytokine storms, resulting in decreased levels of IL-4, IL-5, and IL-13(12). The gamma interferon has role in the prevention of COVID-19 to study and identify its role and mechanism to prevent and treat COVID-19. Interferons contain antiviral factors that produce fibroblasts after viral infections in which interferon-inducible PKR kinase catalyzes RNA degradation. Therefore, COVID-19 being a newly emerging virus, with no approved effective drug or vaccine, an intimate understanding of the role of interferons in prevention is essential to implement novel therapeutic strategies (13)

Table (3-1) Anti –Sars–Cov 2 (IgM and IgG) Antibodies level among. S tudied groups

Antibodies	Studied Groups		N	Mean	SD	LSD
Anti Sars - Coc2 IgM	Test	Vaccinated	85	0.06	0.04	.012
		Control				
		Curd (+ve) Healthy (-ve)	35 30	0.14 0.13	0.11 0.10	
Anti Sars - Coc2 IgM	Test	Vaccinated	85	33.21	16.06	.001>
		Control				
		Curd (+ve) Healthy (-ve)	35 30	20.36 21.47	14.00 13.77	

Table (3-2) level of cytokines (IL-12, IL-15, and INF- γ) in the studied groups.

Cytokines	Studied Groups		N	Mean	SD	P.Vale
IL - 12	Test	Vaccinated	85	26.24	4.78	.001>
		Control				
		Curd (+ve) Healthy (-ve)	35 30	6.00 6.04	0.92 0.95	
IL - 15	Test	Vaccinated	85	596.84	60.62	.001>
		Control				
		Curd (+ve) Healthy (-ve)	35 30	294.53 292.80	37.06 39.11	
INF- γ	Test	Vaccinated	85	143.29	50.92	.001>
		Control				
		Curd (+ve) Healthy (-ve)	35 30	54.92 54.72	12.81 11.92	

1. The Covid -19 infection and Ant-Sars –Cov 2 antibodies (IgM and IgG) level of studied population.

The result of table (3-3) show that the Non infected Vaccinated population have high level of Anti Sars – Cov 2 IgG antibody in comparison with infected population, This result might be refer to that the using of vaccine revealed IgG level more than infected vaccinated population, this might be due to the random viral dose doesn't give complete protection against virus, while the constant vaccine doses do that by increased the memory B-Cells and enhancement of specific IgG production.

2. The Covid -19 infection and (IL-12, IL-15 and INF - γ) level of studied population.

The cytokines (IL-12 , IL-15 and INF - γ) level among infected population after receiving vaccine have higher level than non-infected person and repeated more than one infection , as like as the control groups curried and healthy population, at P Value < 0.05 . The table (3-4) show these results. This result might be refer to that the Sars-Cov2 virus might be induce reactive immunity after exposure to first infection after receiving the vaccination doses , at cellular types by increased level of certain cytokines such as IL-12 , IL-15 and INF - γ . Recurrent infection does not provide the optimum immunity against such infection in regarding to the present study .

Table (3-3) The Covid -19 infection and Ant-Sars – Cov 2 antibodies (IgM and IgG) level of studied population

Antibodies	Studied Groups	Covid - infection	N	Mean	SD	LSD
Anti Sars - Coc2 IgM	(Vaccinated)	Infected	41	0.04	0.05	.001>
		Non Infected	44	0.07	0.14	
	Control (+ve & -ve)	Cured	35	0.56	0.05	.001>
		Healthy	30	0.02	0.01	
Anti Sars - Coc2 IgG	(Vaccinated)	Infected	41	31.65	17.32	.001>
		Non-Infected	44	34.66	14.85	
	Control (+ve & -ve)	Cured	35	30.53	4.47	.001>
		Healthy	30	18.22	14.33	

Table (3-4) The Covid -19 infection and (IL-12, IL- 15 and INF- γ) level of studied population.

Cytokines	Studied Groups	Covid - infection	N	Mean	SD	LSD
Interleukin -12	(Vaccinated)	Infected	41	26.66	5.99	.001>
		Non-Infected	44	25.86	3.90	
	Control (+ve & -ve)	Cured	35	6.04	0.84	
		Healthy	30	6.01	0.95	
Interleukin -15	(Vaccinated)	Infected	41	639.76	93.78	.001>
		Non-Infected	44	556.84	53.61	
	Control (+ve & -ve)	Cured	35	296.04	22.20	
		Healthy	30	293.10	41.13	
Interferon - γ	(Vaccinated)	Infected	41	149.88	53.51	.000
		Non-Infected	44	137.14	49.97	
	Control (+ve & -ve)	Cured	35	62.96	14.21	
		Healthy	30	52.60	10.86	

3. Study the effect of vaccine duration on the immunological parameters

Follow-up time after full vaccination of only 2–3 months

or more. Estimates of vaccine effectiveness among people vaccinated as part of national vaccine rollouts were similar to the efficacy results in the first few months after vaccine taking. Assessing the duration of protection for COVID-19 vaccines over longer time periods. The results in tables (3-5 and 3-6) showed that there were statistically significant differences between the time of doses at (P –value = 0.009). It was showed that the decline in vaccine efficacy or effectiveness against severe COVID-19 disease with timelines vaccination was less than that for SARS-CoV-2 infection and symptomatic COVID-19 disease and the average change in vaccine efficacy or effectiveness over time was estimated using a linear mixed-effects model for the repeated measures within each study vaccine Because the immune system forms memory cells that can be activated upon exposure to a virus and includes cellular immunity, it is not clear, whether this observed antibody decay results in diminished vaccine efficacy or effectiveness, and if so, over what timeframe and against which outcomes. Immunity comes from evidence showing that after giving a booster dose the vaccine efficacy or effectiveness increases compared with people who had only received the primary vaccine series (11; 15).

Because the immune system forms memory cells that can be activated upon exposure to a virus and includes cellular immunity, it is not clear, whether this observed antibody decay results in diminished

vaccine efficacy or effectiveness, and if so, over what timeframe and against which outcomes. Immunity comes from evidence showing that after giving a booster dose the vaccine efficacy or effectiveness increases compared with people who had only received the primary vaccine series (11; 14). The two-dose COVID-19 vaccination campaign substantially reduced hospitalisations and deaths despite high infection rates, However, the effectiveness against infection, as happens also for other vaccines, wanes within months of the second dose (15). Only two studies found minimal vaccine effectiveness against SARS-CoV-2 infection by six months, and none found decreases in vaccine effectiveness against positive SARS-CoV-2 test as large as those reported in our study (16; 17)

Table (3-5) Percentage of time duration after vaccination

Time after vaccination		Frequency	Valid Percent	P -value
Valid	2 Weak - 1 Month	12	14.1	0.009
	2 -3 Month	44	51.8	
	4 - 5 Month	26	30.6	
	> 5 Month	3	3.5	
	Total	85	100.0	

Table (3-6) the cytokines and antibody in relation to time after vaccination

Descriptive		N	Mean	Std. D	P. Value
IL- 12	2Weak-1 Month	12	53.2592	18.44050	.001>
	2 - 3 Month	44	25.8255	23.27407	
	4 -5 Month	26	14.3023	11.18821	
	> 5 Month	3	27.9300	23.92808	
	Total	85	26.2480	24.78393	
IL- 15	2Weak-1 Month	12	1086.09	646.057	.001>
	2 - 3 Month	44	489.37	480.402	
	4-5 Month	26	531.36	514.326	
	> 5 Month	3	783.50	769.056	
	Total	85	596.84	560.628	
INF – γ	2Weak-1 Month	12	270.7583	134.50875	.011
	2 - 3 Month	44	126.0161	124.66123	
	4-5 Month	26	108.7608	106.51379	
	> 5 Month	3	186.0333	127.94500	
	Total	85	143.2905	140.92096	
IgM –Ab	2Weak-1 Month	12	0.0842	0.08140	.826
	2 - 3 Month	44	.0607	0.13952	
	4-5 Month	26	.0508	0.05238	
	> 5 Month	3	.0367	0.03215	
	Total	85	.0601	0.10864	
IgG- Ab	2Weak-1 Month	12	31.9825	20.28090	.938
	2 - 3 Month	44	33.5477	16.17758	
	4-5 Month	26	32.6381	14.73486	
	> 5 Month	3	38.2900	13.63823	
	Total	85	33.2159	16.06797	

4. Correlation of IL- 12 and anti-Sars - Cov 2 –IgG antibody among studied groups.

The figure (3-1) show that direct or positive

correlation between IL-12 and Anti –IgG antibody level , this result might be show that increased IL-12 production enhancement of antibody production ,

especially in late infection because the IgG was produced later than cytokines and other antibodies such IgM

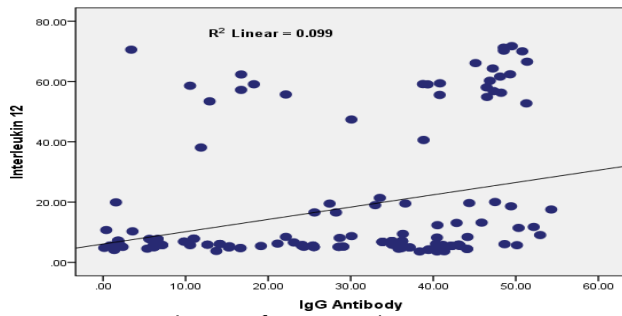


Fig (3-1) Correlation of IL- 12 and anti Sars - Cov 2–IgG antibody among studied groups.

5. Correlation of IL- 15 and anti Sars-Cov 2 –IgG antibody among studied groups.

The figure (3-2) show that direct or positive correlation between IL-15 and Anti –IgG antibody level , this result might be show that increased IL-15 production may enhancement of antibody production , especially in late infection because the IgG was produced later than cytokines and other antibodies such IgM

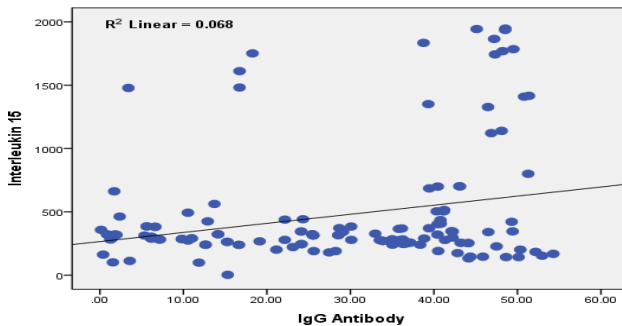


Figure (3-2) Correlation of IL- 15 and anti-Sars - Cov 2- IgG antibody among studied groups.

6. Correlation of INF – γ and Anti- Sars – Cov 2 IgG among studied groups.

In the result of figure (3-3) the correlation was show that direct relationship between INF – γ and anti Sras-Cov2 IgG antibody , this result might be indicted that increased of interferon level lead to enhancement of antibody production especially IgG against Sars-Cov 2 virus.

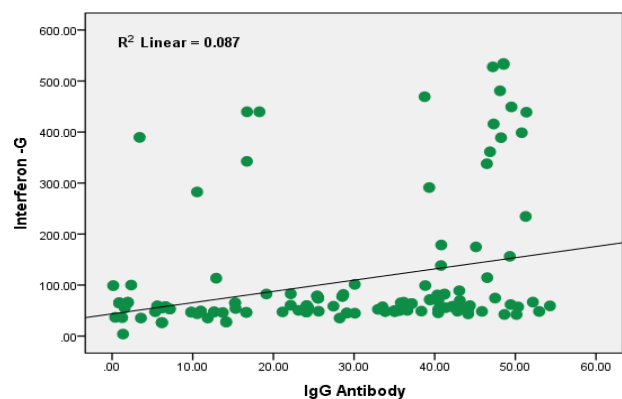


Figure (3-3) Correlation of INF – γ and Anti- Sars –Cov 2 IgG among studied groups.

7. The Correlation between anti-Sars-Cov2 IgM and IgG antibodies among studied groups.

Although the IgG more than IgM, there was a direct correlation between IgM and IgG antibodies against Sars-Cov 2 virus among the Vaccinated, curried and healthy population.

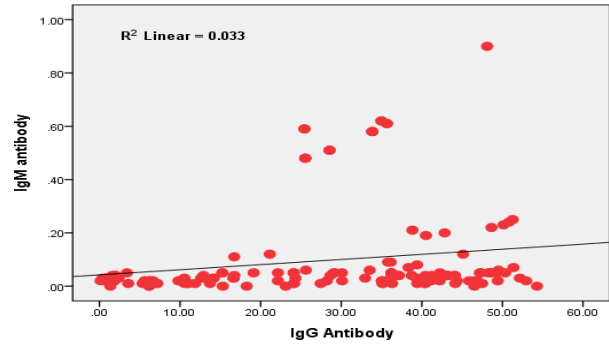


Figure (3-4) The Correlation between anti-Sars-Cov2 IgM and IgG antibodies among studied groups.

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