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Evaluation of Human IgM and IgG Titers in Iraq Following Vaccination with the mRNA and the Inactivated COVID-19 Vaccine at One Month and Six Months

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ABSTRACT

After the outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) in 2019, many types of vaccines have been designed and some are approved by the World Health Organization (WHO). This study conducted to measure the efficacy of tow type of vaccines, the mRNA vaccine and inactivated vaccine, by detecting the concentration of IgM and IgG in serum of human after one month and six months of vaccination with the two types of the vaccine mentioned above. Concentrations of IgM and IgG in serum of participants were measured using a VIDAS device (bioMérieux, France) and following the manufacturer's instructions. The results showed that IgM concentrations decreased to below the protective level in both types of vaccine after one or six months of vaccination, and there were no significant differences ($p > 0.05$) between the two types of vaccine. However, after one month of vaccination, there was a significant difference ($p \leq 0.05$) in the IgG concentration in the serum of the mRNA vaccine group (32.7898 BAU/mL), and the inactivated vaccine group (8.17 BAU/mL). Likewise, after six months there was a significant difference ($p \leq 0.05$) in the IgG concentration in the serum of the mRNA vaccine group (27.03 BAU/mL) and the inactivated vaccine group (6.91 BAU/mL). The mRNA vaccine is more efficient than the inactivated type as the IgG concentration

remain higher and it lasts more time.

1. Introduction

The first identification of SARS-COV-2 was in Wuhan, China in late 2019, causing COVID-19 disease. SARS-COV-2 spread throughout the world, and WHO announced it as a pandemic [1]. The SARS-COV-2 virus is a zoonotic virus, belonging to the family Coronaviridae that infects birds and mammals, including camels, bats, mice, dogs, cats, and humans. Human coronavirus (HCoV) is member of Betacoronavirus [2]. There is similarity between the previous types of HCoV (SARS-COV-1 and MERS-COV) and SARS-COV-2 [3].

The close genetic relationship of bat coronaviruses to HCoV suggests that bats are potential animal reservoirs of the majority of HCoVs [4]. SARS-CoV-2 belongs to bats of the family Rhinolophidae, 96.2% sequence of SARS-CoV-2 similar to an intermediate horseshoe bat (Rhinolophus affinis) [5]. Exotic animals that include a large group of species (Bats, Snakes, Pangolins, Insects, ...etc) can transmit coronaviruses to humans, especially in areas that used exotic animals as food [6]. COVID-19 can transmit from humans to companion animals (cats and dogs) by fecal-oral contact [6].

Despite their genomic and structural similarities, they differ significantly epidemiologically [7]. SARS-CoV-1 and MERS-CoV have higher fatality rates but lower transmissibility than SARS-CoV-2. SARS-CoV-2 is less pathogenic than SARS-CoV-1, and much less pathogenic than MERS-CoV [8].

SARS-COV-2 is enveloped virus, spherical with diameters of 125 nm, have abundant RNA viral genome, single stranded positive-sense RNA linked with a nucleoprotein [9]. The virus contains four structural proteins, spike (S) glycoprotein, envelope glycoprotein (E), membrane glycoprotein (M), and nucleocapsid protein (N), which are responsible for viral structural properties and replication [3]. The distinct feature is spike club-shaped projections on the surface of the virions. These spikes give them the look of a solar corona by inspiring the name coronaviruses [10].

The virus bind to human angiotensin-converting enzyme 2 (ACE2) by S protein [11]. S protein is formed by two subunits; S1, which contains the (RBD) and S2, responsible for the fusion of the virion with the host cell membrane (7]. ACE2 expression in the respiratory tract with high levels [8] and in different organs in humans, including the cardiovascular system, adipose tissues, the gastrointestinal tract, kidneys, the central nervous system, and the lungs [12].

Once the virus begins to replication in the host cell, the immune system is stimulated [13]. Innate immunity recognizes virus through the cell of the innate immune response, such as monocytes, macrophages, neutrophils, and some other cells [7]. TLR3 and TLR7

in these cells recognize the viral RNA (7), where they stimulate antiviral interferon (IFN) production and different cytokines and chemokines [14-16]. This response must be capable of inhibiting viral replication and eliminating the host's infected cells with minimal tissue damage and low inflammatory reaction [7]. Cytokine profile is associated with COVID-19 disease severity [17,18]. Adaptive immunity produces SARS-CoV-2-specific antibodies, $CD4^+$ T cells, and $CD8^+$ T cells in response to SARS-CoV-2 infection [19].

The B cells (assisted by helper T cells) differentiate into plasma cells, to produce antibodies specific to a viral antigen. A neutralizing nature antibody is efficient in blocking the virus from entering into host cells to limit the infection [17]. The protective response is T cell-dependent, with $CD4^+$ helping B cells, geared toward the production of specific neutralizing antibodies, and cytotoxic $CD8^+$ cells capable of eliminating infected cells [7]. SARS-CoV-2-specific $CD4^+$ T cells have association with a reduced severity of COVID-19 disease [13]. Multiple COVID-19 vaccines have been approved for emergency use authorization, including inactivated vaccines, adenovirus-vectored vaccines, and mRNA vaccines [20].

In the current study a serological enzyme Linked Fluorescent Assay (ELFA) used to measure IgG and IgM levels after one and six months in individuals whose vaccinated with two doses of an mRNA or inactivated vaccine that authorized in Iraq.

2. Material and methods:

2.1 Sample and procedures

The study started on October 1st, 2021, and lasted until the end of May 2022, and was conducted in Tikrit, Iraq. All of the participants were consent obtained. The study was started after obtaining ethical and official approvals from the Salah-Elden Health Directorate. The participants received two doses of COVID-19 vaccines, mRNA vaccine or inactivated vaccine (0.3 ml and 0.5 ml respectively) 21 days apart given intramuscularly into the deltoid muscle. The number of participants was 135. The vaccinated with the mRNA vaccine (Pfizer–BioNTech COVID-19 vaccine, BNT162b2) was 107 (51 after one month and 56 after six months of vaccination, in two doses). As for those vaccinated with the inactivated vaccine (Sinopharm vaccine, BBIBP-CorV), their number was 28 (an equal number of participants, 14, after one and six months of vaccination, in two doses). Participant's ages ranged between 16 and over 60 years. We excluded participants with a probable or confirmed SARS-CoV-2 infection, had received one dose of the vaccines, and who non-vaccinated.

About 5 ml of venous blood was drawn from all subjects. The blood was lifted to clotted and then centrifuged to separate the serum. The separated serum kept in deep freezing (-20C°) until used in the *measuring* of IgM and IgG levels. Measurement was conducted by using a Vitek Immuno Diagnostic Assay System device (VIDAS, bioMérieux, France) and following the manufacturer's instructions.

For the estimation of SARS-CoV-2 IgM, IgG in vaccinated persons, 100 µl of

the serum were added to the sample well, standard, negative, and positive controls in the plate. The procedure of VIDAS was conducted according to the guidelines of kit manufacturer anti-SARS-CoV-2 IgM and IgG antibodies. Results were calculated automatically, the positive Results (index ≥ 1), and the negative results (index < 1), and the unit is a binding antibody unit per milliliter (BAU/mL) [21]. Graph Pad software (Chicago, v. 18) was used for statistical analysis by applying T-test to assess current study IgM and IgG parameters, in accordance with central tendency measures. *P*- value with ≤ 0.05 was considered statistically significant.

3. Results and Discussion:

The results in Table (1) showed the levels of IgM in serum of individuals vaccinated with mRNA vaccine and those with inactivated vaccine after one month of vaccination.

Table (1): Serum Levels of IgM among the mRNA Vaccine Group and Inactivated Vaccine Group after One Month.

Study group	Mean ± SD	*P* - value
IgM (BAU/mL) in mRNA vaccine group after one month (n=51)	0.32 ± 0.23	0.67
IgM (BAU/mL) in inactivated vaccine group after one month (n=14)	0.28 ± 0.34	
(BAU/mL): Binding Antibody Units per milliliter.		

The value of IgM in the group vaccinated with the mRNA vaccine (n = 51) after one month of vaccination was 0.32 (BAU/mL), and the value of IgM in the group vaccinated with the inactivated vaccine (n = 14) after one month of vaccination was 0.28 (BAU/mL). The level of the IgM decreased to less than 1 and there was no significant difference (P > 0.05) between the two types of vaccines. Also, the same result was found when comparing the IgM levels between the two groups after six months from vaccination and there was no significant difference between them (Table 2).

Table (2): Serum Levels of IgM among the mRNA Vaccine Group and Inactivated vaccine Group after Six Months.

Study group	Mean ± SD	*P* - value
IgM (BAU/mL) in mRNA vaccine group after six months (n=56)	0.29 ± 0.23	0.2948
IgM (BAU/mL) in inactivated vaccine group after six months (n=14)	0.22 ± 0.23	
(BAU/mL): Binding Antibody Units per milliliter		

In contrast, there were a significant difference ($p \leq 0.05$) in the concentration of IgG is serum of those vaccinated with the mRNA vaccine after one month 32.7898 (BAU/mL), and group vaccinated with the inactivated vaccine after one month 8.17 (BAU/mL) (Table 3). There was a significant difference ($p \leq 0.05$) in the IgG concentration after six months in the serum of the mRNA vaccine group 27.03 (BAU/mL) and the inactivated vaccine group 6.91 (BAU/mL) (Table 4).

Table (3): Serum Levels of IgG among the mRNA Vaccine Group and Inactivated Vaccine Group after One Month.

Study group	Mean ± SD	*P* - value

IgG (BAU/mL) in mRNA vaccine group after one month (n=51)	32.79 ± 12.92	< 0.0001*
IgG (BAU/mL) in inactivated vaccine group after one month (n=14)	8.17 ± 11.01	
(BAU/mL): Binding Antibody Units per milliliter. * Highly Significant		

Table (4): Serum Levels of IgG among the mRNA Vaccine Group and Inactivated Vaccine Group after Six Months

Study group	Mean ± SD	*P* - value
IgG (BAU/mL) in mRNA vaccine group after six months (n=56)	27.03 ± 13.49	< 0.0001*
IgG (BAU/mL) in inactivated vaccine group after six months (n=14)	6.91 ± 10.95	
(BAU/mL): Binding Antibody Units per milliliter. * Highly Significant		

From the previous results it is clear that the level of IgM decreased to less than protective value after 1 moth of vaccination with both type of vaccine. The absence of IgM antibodies may correspond to the expected decay of a previous primary immune response against the virus [22]. Jiang *et al.*, [2022] found within a four-week observation period, IgM levels were elevated on day 14 after vaccination, followed by a decrease on the following weeks. However, the level of IgG antibody in the current study remains higher after six months of vaccination with both type of vaccine.

IgM antibodies are produced early in the humoral immune response against viral infections and provide fast protective immunity. Next, following maturation and isotype class-switching, memory IgG antibodies with increased affinity are produced [22]. COVID-19 vaccine induced a humoral immune response lasting at least six months [23].

Serum IgG levels were four times higher in individuals vaccinated with mRNA vaccine than those vaccinated with inactivated vaccine. mRNA vaccines are efficient preventive measures to combat the SARS-CoV-2 pandemic [24]. High levels of neutralizing SARS-CoV-2 antibodies are an essential component of vaccine-induced immunity.

Conclusion:

Both type of vaccine lead to production of protective antibodies which last more than six months, and mRNA vaccine is more efficient, as it produces high levels of IgG that are four times more than what the inactivated vaccine produces.

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تقييم عيار IgM و IgG في الانسان بعد التطعيم بلقاح mRNA واللقاح المعطل ضد COVID-19 بعد شهر وستة أشهر من التطعيم في العراق

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الملخص

بعد انتشار مرض فيروس كورونا ، ظهرت العديد من انواع اللقاحات التي تم اعتماد بعض منها من قبل منظمة الصحة العالمية. أجريت هذه الدراسة لقياس فعالية نوعين من اللقاحين (النوع الجيني mRNA والنوع الكلاسيكي المعطل) من خلال الكشف عن تركيز IgM و IgG في مصول الاشخاص بعد شهر وستة أشهر من التطعيم بنوعي اللقاح المذكورين أعلاه. تم قياس تراكيز IgM و IgG في مصول المشاركين باستخدام جهاز VIDAS (bioMérieux, France) واتباع تعليمات الشركة المصنعة، وأظهرت النتائج أن تراكيز IgM انخفضت إلى ما دون المستوى الوقائي في كلا النوعين من اللقاح بعد شهر أو ستة أشهر من التطعيم ، ولم تكن هناك فروق معنوية ($p > 0.05$) بين نوعي اللقاح. في المقابل، كان هناك فرق معنوي ($P \leq 0.05$) في تركيز IgG في مصول الاشخاص المحصنين باللقاح الجيني mRNA بعد شهر واحد (32.7898 BAU/mL) والمجموعة المحصنة باللقاح المعطل بعد شهر واحد (8.17 BAU/mL) ، كما كان هناك فرق معنوي ($P \leq 0.05$) في تركيز IgG في مصول الاشخاص المحصنين باللقاح الجيني mRNA بعد ستة أشهر (27.03 BAU/mL) والمجموعة المحصنة باللقاح المعطل بعد ستة أشهر (BAU/mL6.91). كان لقاح النوع الجيني mRNA أفضل من النوع التقليدي المعطل لبقاءه لفترة اطول مع تركيز عالي للأجسام المضادة IgG.