International Journal of Medical Sciences And Clinical Research
(ISSN – 2771-2265)
VOLUME 03 ISSUE 03 PAGES: 05-19
SJIF IMPACT FACTOR (2021: 5. 694) (2022: 5. 893) (2023: 6. 184)
OCLC – 1121105677
Crossref doi Google Scholar WorldCat MENDELEY
Publisher: Oscar Publishing Services

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Journal Website: https://theusajournals.com/index.php/ijmscr

Research Article

STRATEGIES FOR VACCINE DEVELOPMENT OF COVID-19 IN THE WORLD

Submission Date: March 02, 2023, Accepted Date: March 07, 2023,
Published Date: March 11, 2023
Crossref doi: https://doi.org/10.37547/ijmscr/Volume03Issue03-02

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ABSTRACT

The purpose of this phase is to study the best doses to use, the most common side effects and how many doses are needed and protect individuals at highest risk from serious illness or death.

KEYWORDS

Antibody; antibody-dependent enhancement; mucosal immunization; vaccine..

INTRODUCTION

An epidemic of acute respiratory syndrome in humans, which appeared in Wuhan, China in December 2019, was caused by a novel coronavirus (SARS-CoV-2).This disease was named as "Coronavirus Disease 2019" (COVID-19). SARS-CoV-2 was first identified as an etiological pathogen of COVID-19, belonging to the species of severe acute respiratory syndrome-related coronaviruses (SARSr-CoV).The vaccine against COVID-

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19, regarded as an effective prophylactic strategy for control and prevention, is being developed in about 90 institutions worldwide. The experiences and lessons encountered in the previous SARS and MERS vaccine research can be used for reference in the development of COVID-19 vaccine. The present paper hopes to provide some insights for COVID-19 vaccines researchers.[1]With the constantly mutating of SARS-CoV-2 and the emergence of Variants of Concern (VOC), the implementation of vaccination is critically important. Existing SARS-CoV-2 vaccines mainly include inactivated, live attenuated, viral vector, protein subunit, RNA, DNA, and virus-like particle (VLP) vaccines. Viral vector vaccines, protein subunit vaccines, and mRNA vaccines may induce additional cellular or humoral immune regulations, including Th cell responses and germinal center responses, and form relevant memory cells, greatly improving their efficiency. However, some viral vector or mRNA vaccines may be associated with complications like thrombocytopenia and myocarditis, raising concerns about the safety of these COVID-19 vaccines. Here, we systemically assess the safety and efficacy of COVID-19 vaccines, including the possible complications and different effects on pregnant women, the elderly, people with immune diseases and acquired immunodeficiency syndrome (AIDS), transplant recipients, and cancer patients. Based on the current analysis, governments and relevant agencies are recommended to continue to advance the vaccine immunization process.[2]

Multiple COVID-19 vaccines, representing diverse vaccine platforms, successfully protect against symptomatic COVID-19 cases and deaths. Head-to-head comparisons of T cell, B cell, and antibody responses to diverse vaccines in humans are likely to be informative for understanding protective immunity against COVID-19, with particular interest in immune memory. Here, SARS-CoV-2-spike-specific immune responses to Moderna mRNA-1273, Pfizer/BioNTech BNT162b2, Janssen Ad26.COV2.S, and Novavax NVX-CoV2373 were examined longitudinally for 6 months 100% of individuals made memory CD4+ T cells, with cTfh and CD4-CTL highly represented after mRNA or NVX-CoV2373 vaccination. mRNA vaccines and Ad26.COV2.S induced comparable CD8+ T cell frequencies, though only detectable in 60-67% of subjects at 6 months. A differentiating feature of Ad26.COV2.S immunization was a high frequency of CXCR3+ memory B cells. mRNA vaccinees had substantial declines in antibodies, while memory T and B cells were comparatively stable. These results may also be relevant for insights against other pathogens.[3]

The transmission of SARS-CoV-2 has caused serious health crises globally. So far, 7 vaccines that are already being assessed in Phase IV clinical trials are, Comirnaty/ Pfizer; Spikevax/Moderna (m RNA vaccine); Vaxzevria or Covishield; Ad26.COV2.S; Ad5-nCoV (adenoviral vector-based vaccine); CoronaVac and BBIBP-CorV (inactivated virus vaccine). Besides, there are about 280 vaccines that are undergoing preclinical and clinical trials including Sputnik-V, Covaxin or BBV152, and NVX-CoV2373. These vaccines are being studied for their immunological responses and efficiency against COVID-19, and have been reported to demonstrate effective T and B cell responses. However, the long-lasting immunity of these vaccine regimens still needs to be investigated. An in-depth understanding of the vaccine efficacy and immune control mechanism is imperative for the rational purposing and implementation of the vaccines. Hence, in this review, we have comprehensively discussed the immune response induced in COVID-19 patients, as well as in the convalescent individuals to avoid reinfection. Moreover, we have also summarized the

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immunological responses and prophylactic efficacy of various COVID-19 vaccine regimens. In this context, this review can give insights into the development of effective vaccines against SARS-CoV-2 and its variants in the future.[4] Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), is a threat to the health of the global population. As the result of a global effort in the determination of origin, structure, and pathogenesis of SARS-CoV-2 and its variants, particularly such the variant of concern as Delta Variant and Omicron Variant, the understanding of SARS-CoV-2 are deepening and the development of vaccines against SARS-CoV-2 are ongoing. Currently, AstraZeneca-Vaxzevria/SII-Covishield vaccine, Janssen-Ad26.COV2.S vaccine, Moderna-mRNA-1273 vaccine, Pfizer BioNTech-Comirnaty vaccine and Sinovac-CoronaVac vaccine have been listed as WHO Emergency Use Listing (EUL) Qualified Vaccines by WHO. Because of the antigen escape caused by the mutation in variants, the effectiveness of vaccines, which are currently the main means of prevention and treatment, has been affected by varying degrees. Herein, we review the current status of mutations of SARS-CoV-2 variants, the different approaches used in the development of COVID-19 vaccines, and COVID-19 vaccine effectiveness against SARS-CoV-2 variants.[5] Coronavirus disease 2019 (COVID-19), which broke out at the end of 2019, is a global pandemic and seriously threatens human health. Vaccination is the most effective way to prevent and control COVID-19. At present, more than 13 COVID-19 vaccines have been urgently authorized for use, but the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variants has brought unprecedented challenges to the protective efficiency of these COVID-19 vaccines. In particular, the recent emergence of Delta and Omicron variants, which are rapidly spreading worldwide, may bring many challenges to the medical systems. Interestingly, previous studies have shown that the Bacillus Calmette-Guerin (BCG) vaccine used to prevent tuberculosis can induce non-specific trained immunity, protecting against infectious diseases caused by respiratory viruses. Therefore, there is a hypothesis that BCG plays an essential role in reducing the incidence, severity, hospitalization, and mortality of COVID-19 and enhancing the protection efficiency of the COVID-19 vaccine. To confirm this hypothesis, 56 clinical trials have been conducted globally to assess BCG's protective effectiveness against COVID-19 infection. Herein, this review discussed the trained immunity induced by BCG and its underlying mechanisms and summarised BCG's latest research progress in preventing COVID-19, especially the ongoing clinical trials. We hope this review will provide new strategies for fighting against COVID-19.[6] Pregnant women were excluded from the initial phase 3 clinical trials of COVID-19 vaccines resulting in limited data on their efficacy and safety during pregnancy and postpartum. As a result, since December 2020, there has been conflicting advice from public health, governmental, and professional authorities on this matter. From the end of 2020 up to now, some consensus guidance has been published with a prevalent precautionary approach on the administration of vaccines in pregnant women, in breastfeeding ones, or for those who are planning a pregnancy (either spontaneously or with assisted technologies). After the first few months of vaccine administration in some countries, more permissiveness seems to prevail, although with inconsistencies. At the moment, the results obtained by preclinical experimental and observational clinical studies suggest that the risks of the maternal COVID-19 outweigh the undocumented and hypothetical risks of the COVID-19 vaccines in pregnancy. Also, until two viral vector COVID-19 vaccines were associated with very rare thromboembolic events, all guidance had

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agreed that all approved COVID-19 vaccines could be administered in pregnancy.[7] The mRNA COVID-19 vaccine and COVID-19 infection caused by the SARS-CoV-2 virus may be immunologic triggers for the development of thrombotic thrombocytopenic purpura (TTP). There is not yet literature that discusses TTP induced by COVID-19 vaccination or infection in pediatric or adolescent patients. We describe three adolescents presenting with TTP (both de novo and relapsed disease) following administration of the Pfizer COVID-19 vaccine or after COVID-19 infection. Our observations demonstrate that the Pfizer-BioNTech mRNA vaccine and COVID-19 infection can act as triggers for the development/relapse of both congenital and acquired TTP.[8] The COVID-19 vaccination campaign is going on in Nepal through different phases of immunisation. It has been observed that people are misusing antipyretics and analgesics with the fear of adverse events following immunisation. The possibility of antipyretics and analgesics blunting the antibody response of the human body can be a potential cause for lower immune response and thus a reason for lower efficacy of the vaccine. Prophylactic use of over-the-counter analgesics and antipyretics is to be discouraged until the data for or against its use is available.[9] On April 13, 2021, the CDC announced that the administration of Johnson and Johnson's COVID-19 vaccine would be paused due to a rare blood clotting side effect in ~ 0.0001% of people given the vaccine. Most people who are hesitant to get a COVID-19 vaccine list potential side effects as their main concern (PEW, 2021); thus, it is likely that this announcement increased vaccine hesitancy among the American public. Two days after the CDC's announcement, we administered a survey to a group of 2,046 Americans to assess their changes in attitudes toward COVID-19 vaccines. The aim of this study was to investigate whether viewing icon arrays of side effect risk would prevent increases in COVID-19 vaccine hesitancy due to the announcement. We found that using icon arrays to illustrate the small chance of experiencing the blood clotting side effect significantly prevented increases in aversion toward the Johnson and Johnson vaccine as well as all other COVID-19 vaccines.[10] Of the various adverse reactions to COVID-19 vaccines, fever is a common systemic symptom that often resolves spontaneously without treatment. However, rare vaccine-induced conditions that present with fever and systemic inflammation have been reported. In this case, a 65-year-old man with BNT162b2 mRNA COVID-19 vaccination underwent 18F-FDG PET/CT to evaluate prolonged fever and elevated serum C-reactive protein. PET/CT showed hypermetabolic infiltration in the pericardium and peritoneum suggesting immune-mediated pericarditis and peritonitis. After administration of high-dose corticosteroids, the patient's symptom resolved. This case suggests that multisystem inflammatory syndrome and polyserositis can be induced by the COVID-19 vaccine.[11] BACKGROUND Guillain-Barre syndrome (GBS) is an autoimmune condition that presents as weakness, numbness, paresthesia, and areflexia. GBS may occur following infection or vaccination. The pathogenesis of GBS is characterized by inflammatory infiltrates and segmental demyelination. The mechanism of GBS following COVID-19 vaccination is hypothesized to arise from an autoimmune-mediated mechanism leading to an increase in inflammatory cytokines. While there were no reported cases of GBS during the mRNA COVID-19 vaccination clinical trials, there have been a few case reports of GBS following COVID-19 vaccination. CASE REPORT We report a case of symmetric weakness and paresthesia that began 3 days after the patient received his first dose of the Moderna COVID-19 vaccine. Cerebrospinal fluid (CSF) studies demonstrated albuminocytologic dissociation. The combination of the patient's CSF findings and clinical

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symptoms was concerning for Guillain-Barre syndrome. Given the clinical findings 3 days following COVID-19 vaccination, there was a high concern for COVID-19 vaccine-induced GBS. The patient was treated with IVIG followed by plasmapheresis but failed to show significant improvement from either treatment. CONCLUSIONS Our case report demonstrates occurrence of GBS soon after the patient received the COVID-19 Moderna vaccine. Although rare, there is some evidence to support an association between COVID-19 vaccination and GBS, but this is generally limited to case reports and case series. Clinicians, however, should remain vigilant to mitigate potential risks, such as autonomic dysfunction, respiratory failure, permanent disability, and death in patients who develop GBS after vaccination.[13] mRNA COVID-19 vaccination was initiated worldwide in late 2020, and its efficacy has been well reported. However, studies about vaccine-related side effects are sparse. A total of 262 health care workers who received mRNA COVID-19 vaccine BNT162b2 were recruited, and their vaccine-related side effects were investigated. Impact of sex and age on the side effects was statistically analyzed. A higher number of vaccine-related side effects among females versus males was identified (median 3 versus 2, $P < 0.05$, after the first dose, and 5 versus 2.5, $P < 0.01$, after the second dose). General fatigue, headache, chills, and fever were the culprit adverse symptoms. In multivariate analysis, females had an increasing number of side effects after receiving their first (B = 0.7; 95% confidence interval [CI], 0.2 to 1.2) and second (B = 1.5; 95% CI, 0.7 to 2.2) vaccine doses compared to that of males. In age analysis, the older group (≥60 years old) had a lower number of side effects than the younger group (B = -0.5 with a 95% CI of -1.1 to -0.02 after the first vaccine dose, and B = -2.1 with a 95% CI of -2.9 to -1.2 after the second vaccine dose). Additionally, prolonged time to recovery was found among females ($P = 0.003$ after the first dose; $P = 0.008$ after the second dose). Specifically, symptoms of general fatigue, headache, itching, swelling at the injection site, and dizziness were the culprit symptoms affecting recovery time. Several cutaneous and membranous symptoms, including "COVID arm," were identified among females. These results highlight the impact of sex and age on side effects from mRNA COVID-19 vaccine and will aid in creating a safer vaccine.

IMPORTANCE We demonstrate sex- and age-related impact on mRNA COVID-19 vaccine-related side effects, with a higher number and frequency of side effects and prolonged time to recovery in females compared to males and negative correlation between age and vaccine-related side effects. Identification of unique age- and sex-specific adverse symptoms will provide the opportunity to better understand the nature of sex- and age-associated immunological differences and develop safer and more efficacious vaccines.[14] Vaccines are crucial to ending the COVID-19 pandemic. An mRNA-based COVID-19 vaccine can cause mild to moderate side effects. A number of cases of cardiac, gastrointestinal, and psychiatric side effects have been reported as rare side effects associated with the COVID-19 vaccine. This article presents a patient, who after the second injection of the mRNA-based COVID-19 vaccine, immediately developed anxiety, nonspecific fear, and insomnia as the prodromal phase of psychosis. Starting from the second week, the patient manifested delusions of persecution, delusions of influence, thoughts insertion, and delusional behaviour, culminating in the suicide attempt. The duration of psychosis was eight weeks, and symptom reduction was observed only after the gradual administration of antipsychotics over four weeks. The investigations of the patient did not support any structural changes of the brain, any severe medical conditions, a neurological abnormality, a confusion or

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a state of unconsciousness or alterations in laboratory tests. Psychosis due to the use of alcohol or psychoactive substances was excluded. The psychological assessment of the patient demonstrated the endogenous type of thinking, and the patient had schizoid and paranoid personality traits strongly associated with schizophrenia. This case indicates a strong causal relationship between the mRNA-based COVID-19 vaccine injection and the onset of psychosis. We intend to follow up this case for possible development of schizophrenia and understand that the COVID-19 vaccine could possible play a trigger role in the development of primary psychosis. Longer-term supporting evidence is needed to estimate the prevalence of psychosis following vaccination with the mRNA-based COVID-19 vaccine.[15] Thus far, the investigations on the efficacy of the COVID-19 vaccines in randomized trials [8,9] have been centered around reducing the risk of severe infection and mortality. We opine investigations on the efficacy of the COVID-19 vaccines to reduce the risk of cardiovascular outcomes should be performed to understand if COVID-19 vaccination has cardiovascular benefits. Such investigations could also develop more confidence toward the acceptance of COVID-19 vaccines by the public, especially when some of the COVID-19 vaccines (particularly the mRNA vaccines such as BNT162b2 and mRNA-1273 vaccines) have been associated with the rare occurrence of cardiovascular complications, including myocarditis and pericarditis [10,11]. While the infrequency and the mild nature of the myocarditis and pericarditis cases after vaccination greatly exceed the small increased risk, specious reports on social media are still fueling the COVID-19 vaccine hesitancy. Therefore, we urge the performance of prospective investigations to establish the relationship between COVID-19 vaccines and cardiovascular outcomes.

MATERIALS AND METHOD

This study used an online Google Form questionnaire as the instrument. Invitation to participate in this survey was sent through the email and social media such as Telegram . The questionnaire was distributed in this way.. Therefore, using online Google Form to reach each participant is a good choice.

The target respondents are the young people of Tashkent, Uzbekistan and India between the age of 18 to 30 because the young people ratio are more in these areas. The questions in the developed questionnaire were distributed for this pilot to test the awareness of public on COVID-19 Vaccine . The population of this survey was 130 members. . This work was done to create a awareness on the development of COVID-19 vaccine among the people . The search for literary sources was carried out using the bibliographic databases Web of Science, Scopus, DBLP, PubMed. When selecting sources, they paid attention to experimental articles, literary reviews, the number of their citations over the past year.

RESULTS

The seminars were conducted using information and communication technologies, booklets, brochures, presentations, etc. All were asked to answer using a specially designed public awareness on COVID-19 VACCINE questionnaire

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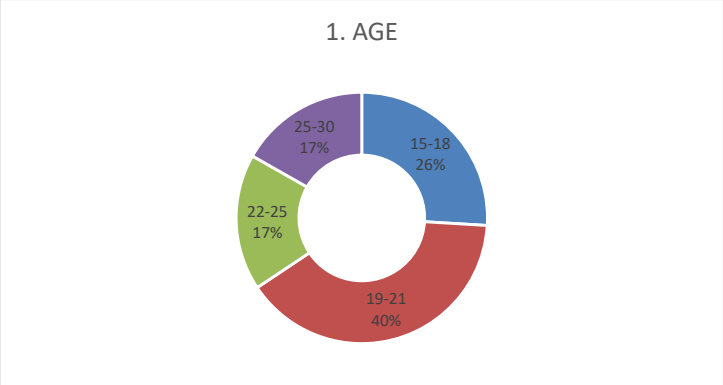

DIAGRAM 1: what is the age of the participants?

The age of the participants was from 15-18 years old (26%), from 19-21 years old (40%),from 22-25 years old (18) and from 25-30 years old (17).

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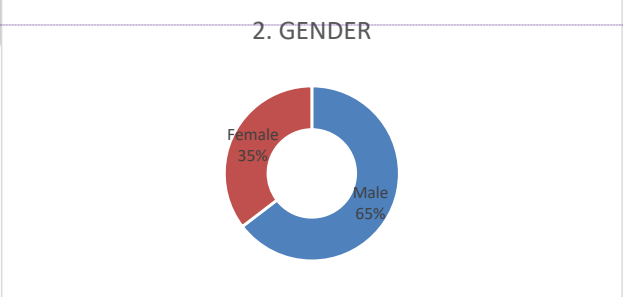

DIAGRAM 2:What is the Gender of the participants?

The gender of participants male(65%), female (35%).

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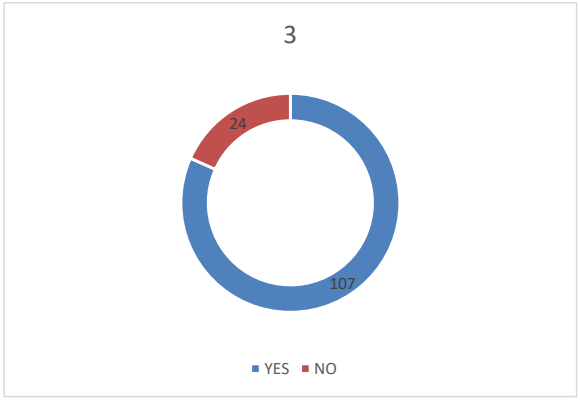

DIAGRAM 3:Are you fully vaccinated or not?

82% people are vaccinated

And 18 people are not vaccinated

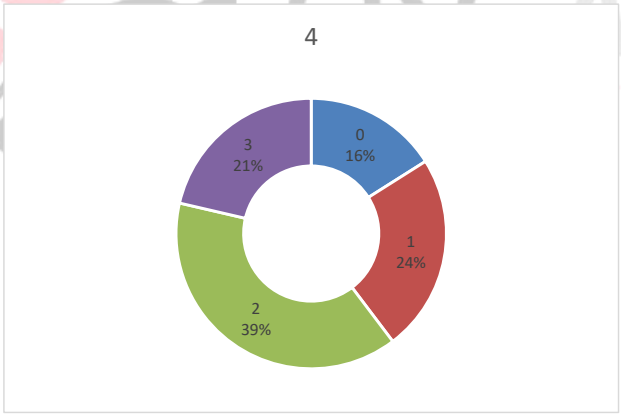

DIAGRAM 4: How many doses of vaccine you have taken?

0 Dose: 16%

1Dose: 24%

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2Doses:39%

3Doses:21%

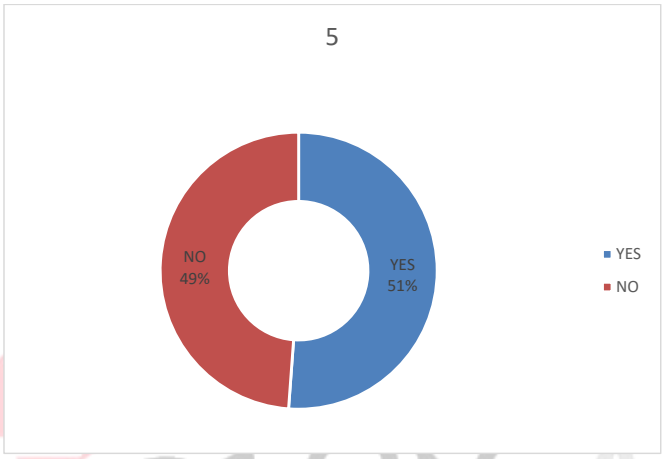

DIAGRAM 5: During COVID-19 infection can you take vaccine?

49% people choosed correct answer

51%people choose wrong answer

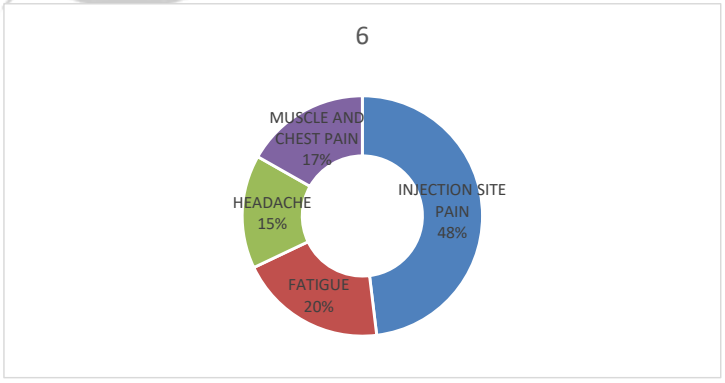

DIAGRAM 6: which side effects appears after vaccine?

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48% people have chosen Injection site pain

20%people have chosen Fatigue

15%people have chosen Headache

17%people have chosen Muscle and Chest pain

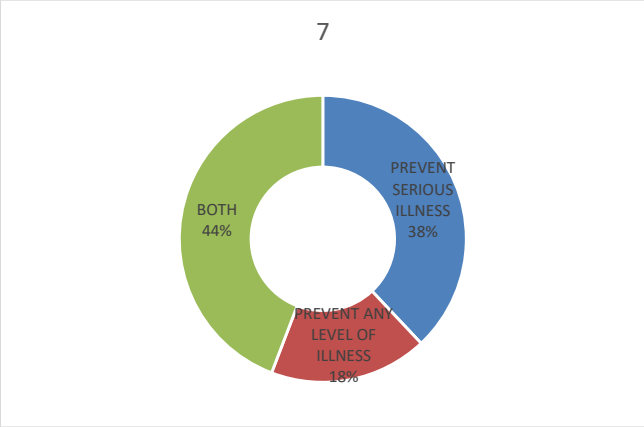

DIAGRAM 7: why are Booster doses recommended?

38% people have chosen prevent serious illness

18% people have chosen prevent Aray level of illness

44%people have chosen Both

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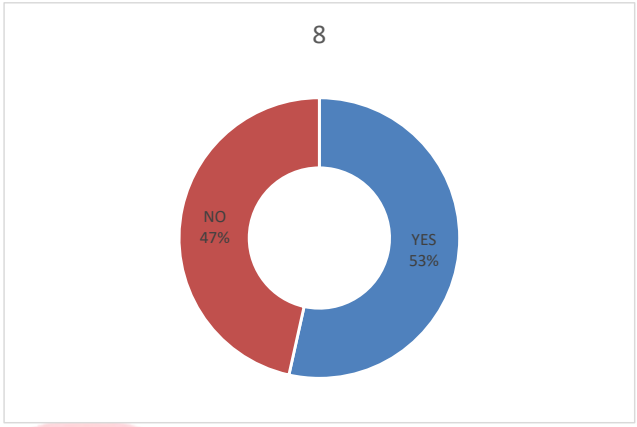

DIAGRAM 8: Do the COVID-19 VACCINE contain live virus?

47% people choose correct answer

53%people choose wrong answer

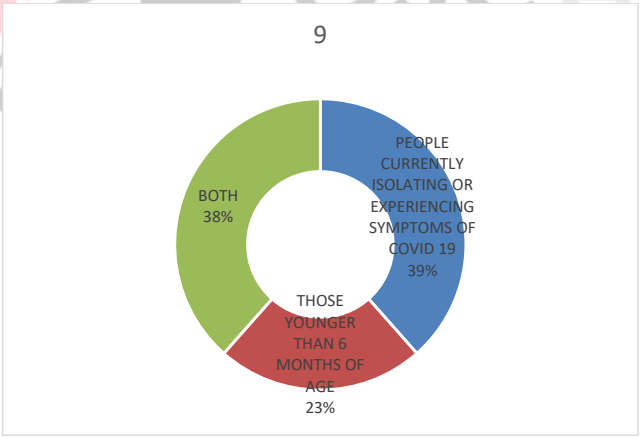

DIAGRAM 9: Who should not get the COVID-19 VACCINE?

38% people choose people currently isolating or experiencing symptoms of COVID-19

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23%people choose Those younger than 6 months of age

38% people choose Both

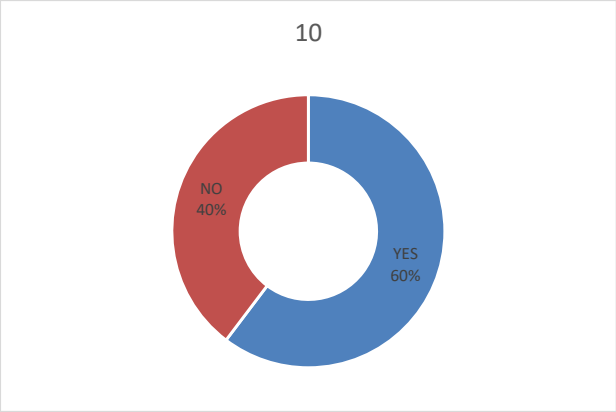

DIAGRAM 10: Do COVID-19 VACCINE Contain Antibiotics?

40% people choosed correct answer

In this survey we can see most of the people knew about the COVID-19 VACCINE, about 82% people are vaccinated till now.

The coronavirus disease 2019 (COVID-19) is a communicable respiratory disease caused by a new strain of coronavirus that causes illness in humans.

Most people infected with the virus will experience mild to moderate respiratory illness and recover without requiring special treatment. However, some will become seriously ill and require medical attention. Older people and those with underlying medical conditions like cardiovascular disease, diabetes, chronic respiratory disease, or cancer are more likely to develop serious illness. Anyone can get sick with COVID-19 and become seriously ill or die at any age.

The best way to prevent and slow down transmission is to be well informed about the disease and how the virus spreads. Protect yourself and others from infection by staying at least 1 metre apart from others, wearing a properly fitted mask, and washing your hands or using an alcohol-based rub frequently. Get vaccinated when it's your turn and follow local guidance.

The virus can spread from an infected person's mouth or nose in small liquid particles when they cough, sneeze, speak, sing or breathe. These particles range from larger respiratory droplets to smaller aerosols. It is important to practice respiratory etiquette, for example by coughing into a flexed elbow, and to stay home and self-isolate until you recover if you feel unwell.

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How vaccines help

Vaccines contain weakened or inactive parts of a particular organism (antigen) that triggers an immune response within the body. Newer vaccines contain the blueprint for producing antigens rather than the antigen itself. Regardless of whether the vaccine is made up of the antigen itself or the blueprint so that the body will produce the antigen, this weakened version will not cause the disease in the person receiving the vaccine, but it will prompt their immune system to respond much as it would have on its first reaction to the actual pathogen.Some vaccines require multiple doses, given weeks or months apart. This is sometimes needed to allow for the production of long-lived antibodies and development of memory cells. In this way, the body is trained to fight the specific disease-causing organism, building up memory of the pathogen so as to rapidly fight it if and when exposed in the future.

DISCUSSION

When analyzing the efficiency of knowledge assimilation, the compared options, in contrast to the analysis of minimizing costs are characterized by greater or lesser, but not equivalent, efficiency.

In this regard, it is important to assess the degree of feasibility of the analysis, depending on the level of reliability of the data. The test results were expressed in points Participants' results were calculated using Microsoft Excel software.The assessment of the effectiveness of the assimilation of knowledge was calculated based on the application of the proposed methodological recommendation in practice Thus, each participant of the survey, on average. Increased his theoretical and practical level of knowledge in the field of COVID-19 VACCINE and its prevention by almost half.

CONCLUSION

There are hundreds of coronaviruses, most of which circulate in animals. Only seven of these viruses infect humans and four of them cause symptoms of the common cold. But, three times in the last 20 years, a coronavirus has jumped from animals to humans to cause severe disease. The current international situation for the Sars-Cov-2pandemic remains grossly uncertain. Yet it is clear that inoculant/vaccine efficacy wanes after 6 months, and that the treatment does not meaningfully prevent transmission of Sars-Cov- ,most the mRNA vaccines can do, is reduce symptoms. In submitting for approval for boosters, even the manufacturer acknowledges that alleviation of symptoms is the signature benefit of this new technology. Current policy appears structured around increasing controls, including mandates that are based on hypothetical sterile vaccine. Public health measures can shift towards more evidence-based measures that reflect the increasing rate of natural immunity in the population.

The statement noted that 'considering the risks vs. benefits of major policy decisions, I have reached consensus on three foundational principles:

1) Healthy children should not be subject to forced vaccination
2) Naturally immune persons recovered from Sars-Cov-2 shall not be subject to any restrictions or vaccine mandates;
3) All health agencies shall cease interfering with physicians treating individual patients.
4) "The successful development of the COVID-19 vaccine concerns almost all countries and people in the world. We must do an excellent job of researching the immunogenicity and immune reactivity of the vaccines. We hope

International Journal of Medical Sciences And Clinical Research (ISSN – 2771-2265)
VOLUME 03 ISSUE 03 PAGES: 05-19
SJIF IMPACT FACTOR (2021: 5. 694) (2022: 5. 893) (2023: 6. 184)
OCLC – 1121105677
Publisher: Oscar Publishing Services

this review can help colleagues at home and abroad."

RECOMMENDATION

1. Everyone stay up to date with COVID-19 vaccines for their age group:

2. Children and teens aged 6 months–17 years Adults aged 18 years and older

3. Getting a COVID-19 vaccine after you have recovered from COVID-19 infection provides added protection against COVID-19.

4. People who are moderately or severely immunocompromised have different recommendations for COVID-19 vaccines. COVID-19 vaccine and booster recommendations may be updated .

5. Develop and launch a COVID-19 vaccine promotion campaign.

6. Build an evidence base for effective strategies for COVID-19 vaccine promotion and acceptance

7. Support equitable allocation of COVID-19 vaccine globally.

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