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Safety and Immunogenicity of COVID-19 Vaccines in Patients Under Medical Conditions: A Systematic Review and Meta-Analysis

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Abstract

A comprehensive search was carried out in mainstream bibliographic databases or Medical Subject Headings, including ScienDirect, PubMed, Scopus, and ISI Web of Science. The search was applied to the articles that were published between January 2020 and early 2023 With strict literature search and screening processes, it yielded 14 articles from 373 articles of initial literature database. Among 14 study results, there was acceptable for immunogenicity (both humoral and cellular immune responses (a key response for the development of a vaccination-induced immunogenicity and safety in 11 studies (78.57 %), whereas acceptable potent immunogenicity was found in patients aged more than 40 years with chronic diseases, particularly, chronic respiratory diseases and coronary artery diseases, only potent T-cell response was identified in one study, and no significant difference in vaccine safety compared with healthy subjects and effective neutralizing antibodies (two doses completion) against SARS-CoV-2 (COVID-19) in patients older than 60 years with diabetes and/or hypertension were demonstrated after completion of COVID-19 vaccination. In conclusion, Immunogenicity (both humoral and cellular) and safety in aged people and individuals living with various chronic diseases (both infectious and non-infectious) is highlighted in this study and can decrease COVID-19 vaccination hesitancy in these persons.

Keywords: *Adverse reactions, COVID-19, immunogenicity, neutralizing antibody, safety, vaccine, titer.*

Abbreviations :

AEs : Adverse Events

BNT : Pfizer Vaccine (BNT162b1, BNT162b2)

ChAd : AstraZeneca vaccine (AZD1222 or ChAdOx-nCov19)

CI : Confidential Interval

COVID-19 : Coronavirus Disease 2019

ELISA : Enzyme-Linked Immunosorbent Assay

GMR : Geometric Mean Ratio

HIV : Human Immunodeficiency Virus

IMIDs : Immune-Mediated Inflammatory Diseases

GMT : Geometric Mean Titer

MNA : Microneedle Assay

PLWH : People Living with Human Immunodeficiency Virus,

VLA : Valneva (VLA2001) vaccine

Objective of the Study

To identify immunogenicity and safety profiles of COVID-19 vaccination (two or three doses) among patients with various medical conditions, such hypertension, diabetes, endocrine diseases/disorders, neurological diseases/disorders, malignancies, organ transplantation, solid-organ transplantation, etc.

Intruduction

Several COVID-19 vaccines were developed to limit its ability to spread **[**1**]**. Currently, several studies support immunogenicity and safety of a third-dose-COVID-19 vaccination in healthy persons, patients with hematological malignancies, and solid-organ-transplant recipients, but are still questionable in patients with immune-mediated inflammatory diseases (IMIDs) **[**2-18**]**.

Methods of the Study

Search Strategy and Inclusion Criteria

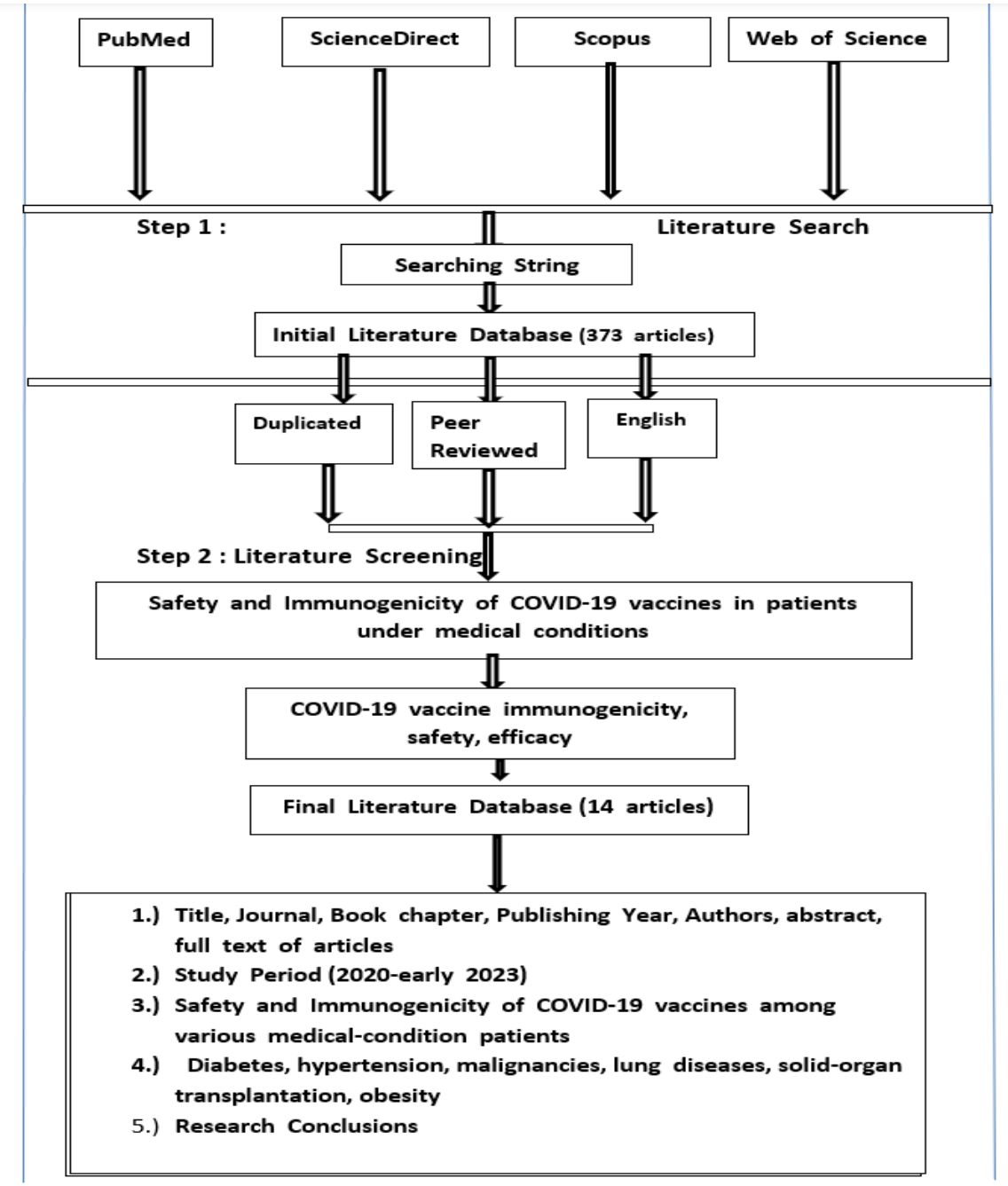
A comprehensive search was carried out in mainstream bibliographic databases or Medical Subject Headings, including ScienDirect, PubMed, Scopus, and ISI Web of Science, following the PRISMA guidelines. The search was applied to the articles that were published between January 2020 and early 2023 **[**Figure 1**]**. Our first involved performing searches of article abstract/keywords/title using strings of **[**("COVID-19" or "SARS-CoV-2", "severe-acute-respiratory-syndrome-coronavirus-2",

“coronavirus-disease 2019”, “nCoV 2019”, “SARS-CoV-2 vaccines”, “ COVID-19 vaccines”, SARS-CoV-2 vaccination”, “COVID-19 vaccination”, “efficacy”, “immunogenicity”, “safety”, “medical conditions ”, “metabolic”, “ immunocompromised ”, “ organ transplant “, “ solid-organ transplant ”, “ malignant or cancer”, “ pulmonary ” or “ lung ”, “ renal ” or “ nephrological ”, “ endocrinological .”, “ diabetic ”, “ hypertension ”, “ hypertensive ”, “ obese ”, “ obesity ” **]**. After a first approach of search, published articles focusing on medical conditions or diseases or disorders that related to SARS-CoV-2 or COVID-19 vaccine immunogenicity and safety were retained and the information on COVID-19-related medical conditions or diseases or disorders was extracted for having a crude knowledge involving their themes. Another round of publication search was conducted for adding the missing published articles that were not identified by the first round.

All keywords combinations from medical conditions or disease types and SARS-CoV-2 (COVID-19) vaccine efficacy (immunogenicity and safety) variables to bind the population of cases under consideration. Search string for disease groups include **[** “ SARS-CoV-2 vaccines (vaccination)” or “ COVID-19 vaccines (vaccination) ” or “ medical conditions ” or “ medical diseases ” or “ immunocompromised ” or “ organ transplant “ or “ solid-organ transplant ” or “ malignant or cancer ” or “ pulmonary ” or “ lung ” or “ endocrinological ” or “ diabetic ” or “ renal ” or “ nephrological ” or “ hypertension ” or “ hypertensive ” or “ obese ” or “ obesity ” **]**. The initial literature databases were further manually screened with the following rules : 1) non-SARS-CoV-2 (COVID-19)-related articles were excluded; 2) articles that did not report immunogenicity and safety related to SARS-CoV-2 (COVID-19) vaccines (vaccination) were not considered, such as commentary articles, or editorial; 3) non-peer reviewed articles were not considered to be of a scholarly trustworthy validity; and 4) duplicated and non-English articles were removed. The articles were carefully selected to guarantee the literature quality, which is a trade-off for quantity **[**Figure 1**]**.

With strict literature search and screening processes, it yielded 14 articles (Table 1) from 373 articles of initial literature database. Needed article information was extracted from each article by : 1) direct information including journal, title, authors, abstract, full text documents of candidate studies, publishing year; 2) place name of the study area; 3) study period; 4) research method used; 5) type of variables studied; 6) types of SARS-CoV-2 (COVID-19)-immunogenicity- and-safety-efficacy-related medical conditions or diseases or disorders studied; and 7) the conclusions made about the impacts of

SARS-CoV-2 (COVID-19)-immunogenicity-and-safety-efficacy-related medical conditions or medical diseases or medical disorders on human health.



Step 3 : Literature Information Extraction

Figure 1 Literature Search and Screening Flow

Results

Published Year	Results	Reference
2023	Supporting the safety and immunogenicity of a third COVID-19 vaccination in IMIDs patients	[19]
2023	Acceptable safety profile of SII-NVX-CoV2373 vaccine compared to NVX-CoV2373 vaccine	[20]
2022	Acceptable safety and immunogenicity of COVID-19 vaccines in people living with AIDS	[21]
2022	Acceptable safety of COVID-19 vaccines in lung-cancer patients receiving immune checkpoint inhibitors	[22]
2022	At day 146, all three dose levels of all three age cohorts reached 100 % of seroconversion, and at day 236, were maintained at 100 % of seroconversion.	[23]
2022	The positive seroconversion rates of serum neutralizing antibody in the four groups (diabetes, hypertension, combined diabetes and hypertension, and healthy controls) were 97.3 %, 97.3 %, 100.0 %, 98.7 %, respectively at 28 days after the second vaccination.	[24]
2022	Induced SARS-CoV-2-specific neutralizing antibody and T-cell response had reasonable protection level (vaccine efficacy > 50 %, etc.) against ancestral SARS-CoV-2 strains and up to Omicron variant with dose fractionation of mRNA and protein subunit vaccines, whereas safety profiles were non-inferior to the standard fractional dose.	[25]
2022	At day 14-28 post-first-dose vaccination, there was no significant different neutralizing antibody between the group of chronic diseases with aged > 40 years and healthy controls, except for persons with chronic respiratory diseases (p = 0.0416) and persons with coronary artery disease (p = 0.0287). Immunogenicity, safety, and T-cell immunity in persons with chronic diseases and aged people were comparable.	[26]
2022	Immunocompromised patients treated with anti-CD20 medication demonstrated potent T-cell-response preservation, but severely impaired humoral immunity after COVID-19 vaccination. Whether a COVID-19-vaccine-induced-cell response facilitate protective-SARS-CoV-2-infection-effects is still unclear in the case of absence of humoral response.	[27]
2021	COVID-19 vaccine (QazCOvid-in®) was well tolerated and safe in both clinical phase 1 clinical trial (randomized, single-blind, placebo-controlled) and phase 2 clinical trial (open-label). Seroconversion reached 59 % after one dose of vaccine and 100 % after two doses (MNA and ELISA methods). (ClinicalTrials.gov NCT04530357).	[28]
	The geometric mean ratio (GMR) of SARS-CoV-2 50 % neutralizing antibody titers after two doses of vaccination (BNT162b2) in the group of 12-15 years old related to the	

2021	group of 16-25 years old was 1.76 (95 % CI : 1.47-2.10), met the noninferiority criterion of a lower boundary of the two-sided 95 % CI > 0.67 (greater response in the group of 12-15 years old). (ClinicalTrials.gov-NCT04368728).	[29]
2021	COV-BOOST trial : Acceptable immunogenicity (homologous or heterologous) third dose boost (BNT or ChAd vaccine), except VLA vaccine	[30]
2020	After three doses of inactivated COVID-19 vaccines, no serious adverse reactions were demonstrated. (ChiCTR200034780). The geometric mean titer (GMT) of the neutralizing antibody at 14 day after third dose was acceptable, except the alum-only vaccination group.	[31]
2020	No severe adverse reactions were noted after three doses of mRNA-based COVID-19 vaccines (BNT162b1 and BNT162b2 vaccines). Acceptable immunogenicity (GMT) after three doses of mRNA-based vaccines were demonstrated.	[32]

Table 1 : Demonstrating the 14 study results

Discussion

Among 14 study results [19-32], there was acceptable for immunogenicity (both humoral and cellular immune responses (a key response for the development of a vaccination-induced immunogenicity [19]) and safety in 11 studies (78.57 %), whereas acceptable potent immunogenicity was found in patients aged more than 40 years with chronic diseases, particularly, chronic respiratory diseases and coronary artery diseases [26], only potent T-cell response was identified in one study [27], and no significant difference in vaccine safety compared with healthy subjects [24] and effective neutralizing antibodies (two doses completion) against SARS-CoV-2 (COVID-19) in patients older than 60 years with diabetes and/or hypertension [24] were demonstrated after completion of COVID-19 vaccination. After completion of COVID-19 vaccination, females revealed higher immune response than males [24]. All 14 studies demonstrated strong acceptable immunogenicity after completion of COVID-19 vaccination (2/3 doses) [19-32]. SII-NVX-CoV2373-vaccine-related-adverse-events (AEs) incidence was higher, compared to the healthy controls [20]. In India, among adults, SII-NVX-CoV2373 vaccine revealed well tolerated, safe, and immunogenic [20]. Pooled seroconversion rate in people living with HIV (PLWH) after the first and second doses were 67.51 and 96.65 %, respectively [21]. Number of doses (third dose, etc.) and intervals of mRNA-COVID-19 vaccination are suggested to maintain effective immunity in lung-cancer patients [22]. After full vaccination with WIBP-CorV, antibody response in young children was characterized up to 180 days [23]. To our knowledge, age, an important

factor that has been documented in other COVID-19 vaccines (Corona Vac, BNT162b2 and an adenovirus-vectored COVID-19 vaccine) in influencing vaccine responses and inducing higher antibody response in children and adolescent than in adults and aged people **[**23**]**.

Conclusion

Immunogenicity (both humoral and cellular) and safety in aged people and individuals living with various chronic diseases (both infectious and non-infectious) is highlighted in this study and can decrease COVID-19 vaccination hesitancy in these persons.

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