International Journal of Pharmacological Research
ISSN: 2277-3312 (Online)
Journal DOI: https://doi.org/10.7439/ijpr **Original Research Article**

Current status of clinical research in Covid-19 vaccines: A registry based audit

Jyoti Gadhade, Rajesh S. Hiray* and Mukthambika B

Department of Pharmacology, Byramjee Jeejeebhoy Government Medical College and Sassoon General Hospitals, Pune-411001, Maharashtra, India

Abstract

The COVID-19 or Coronavirus has impacted the world in an unprecedented way. More than 200 countries have been affected because of this novel corona virus. There is a surge for identifying vaccine or repurposing existing drugs for this virus. The rapid spread has globally become a serious issue. The objective of the study was to provide a comprehensive overview on clinical trials that are being conducted in India and globally on vaccines for COVID-19. This is an observational study. All the clinical studies conducted in the field of vaccines registered on the ClinicalTrials.gov website and Clinical Trial Registry of India (CTRI) up to March 2021 were reviewed and analysed. The variables such as types of trials, study design, status of study whether ongoing or completed, type of intervention tested, sample size of trials, phases of trials were recorded. The data were analysed using descriptive statistics using SPSS 16.0.Out of all the studies registered, 263 were related to vaccine clinical trials among which 201 were interventional and 62 were observational. Out of 201 interventional studies, 75.62% were randomised trials. Out of 62 observational studies, 53.22% were cohort studies, 20.96% were case control studies, 9.67% were cross sectional studies. Pure biologicals constituted 56.65% of the total interventions. Majority of the trials (23.88%) were in phase 1 and phase 3 respectively.3.8% trials have been completed, 44.48% trials are open for recruitment.2 trials have been suspended and withdrawn and 1 trial has been terminated. This study is helpful for researchers, policy makers, and general public for understanding COVID-19 clinical trials eco-system. It will also be useful for global scientific community to know what clinical trials are being conducted on COVID-19 vaccines and potential source of information for international collaborations.

Keywords: Covid 19, Vaccine, CTRI.

***Correspondence Info:**
Dr. Rajesh S. Hiray,
Professor and HOD,
Department of Pharmacology,
Byramjee Jeejeebhoy Government Medical College & Sassoon General Hospitals, Pune (MS) 411001, India

***Article History:**
Received: 04/07/2021
Revised: 26/07/2021
Accepted: 28/07/2021
DOI: https://doi.org/10.7439/ijpr.v11i7.5653

QR Code

How to cite: Gadhade J, Hiray R. S. and Mukthambika B. Current status of clinical research in Covid-19 vaccines: A registry based audit. *International Journal of Pharmacological Research* 2021; 11(07): e5653. Doi: 10.7439/ijpr.v11i7.5653 Available from: https://ssjournals.com/index.php/ijpr/article/view/5653

1. Introduction

The COVID-19 or Corona virus has impacted the world in an unprecedented way. More than 200 countries have been affected because of this novel corona virus. Global public health, economy and society have all faced near breakdown. There is a surge for identifying vaccines for this virus. The rapid spread of corona virus disease 2019 (COVID-19) has globally become a serious issue [1]. The disease, caused by a severe acute respiratory syndrome corona virus 2 (SARS-CoV-2, has been first reported in December 2019 (Wuhan, China) and declared by the World Health Organization (WHO) as a pandemic on March 11, 2020 [2]. To date, the COVID-19-associated deaths keep rising in most of the European countries. This phenomenon can be influenced by the pandemic precaution measures, such as mandatory face masks wearing; however, the end of the pandemic may not be seen until an effective anti-COVID-19 vaccine is developed [3, 4]. In India also this pandemic has been causing enormous medical, socio-economic problems. Given the nature of Indian public health system it is worrisome for Indians to see the large number of cases being reported in strong economic states such as Maharashtra, Karnataka and Tamil Nadu especially in second wave. India

is amongst the top 10 countries in terms of research publications generated for Covid-19 but no systemic analysis of the registered clinical trials is available.[5]

The ClinicalTrials.gov of US National Library of Medicine has listed 4952 clinical trials on drugs as of March 2021 and 263 covid vaccine trials and Clinical Trial Registry of India (CTRI) has listed 864 clinical trials for drugs and 12 for covid vaccine. [6]

1.1 Objective:

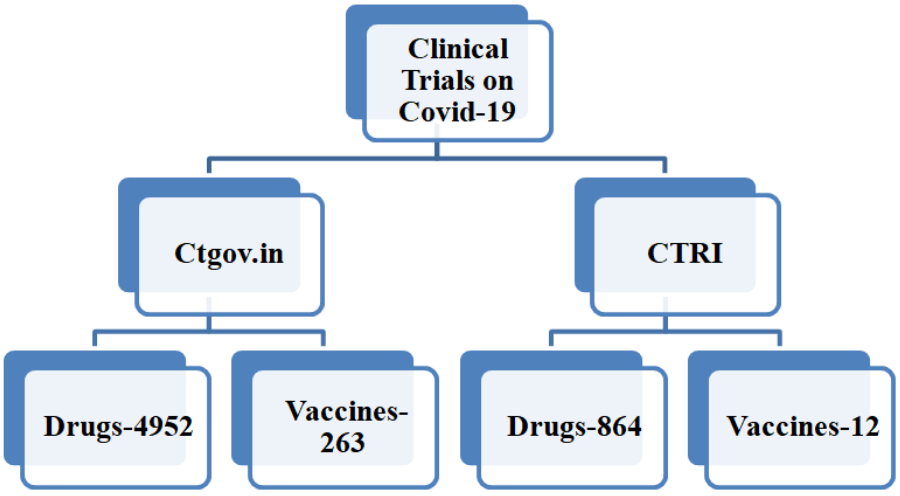
To provide a comprehensive overview on clinical trials that is being conducted in India and globally on vaccines for COVID-19.

2. Methodology

All the clinical studies conducted in the field of covid vaccines registered on the ClinicalTrials.gov website and Clinical Trial Registry of India (CTRI) up to March 2021 were reviewed and analysed. The variables such as types of trials, study design, status of study whether ongoing or completed, type of interventions tested, sample size of trials, phases of trials were recorded. The data were analysed using descriptive statistics using SPSS for Windows, Version 16.0.

3. Results

The following flowchart depicts the retrieval of the registered clinical trials on Covid-19 as of March 2021



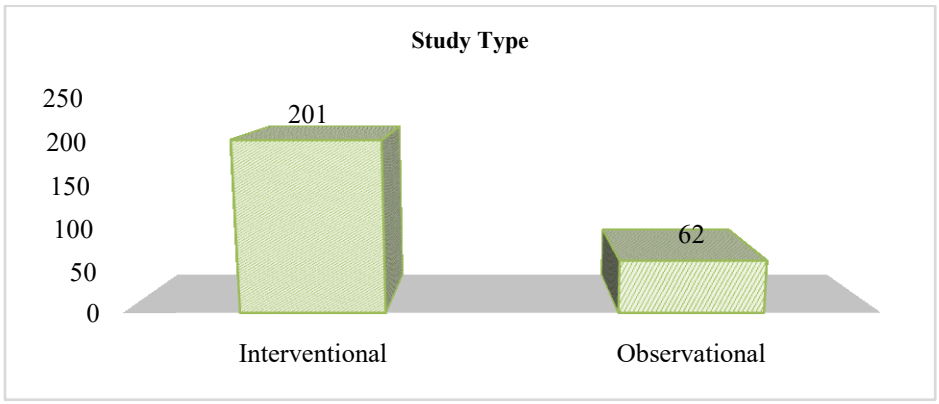


Figure 1: Shows types of studies in clinical trials on covid vaccine registered on ctgov.in

Out of all the studies registered, 263 were related to vaccine clinical trials. Of these 263 studies, 201 were interventional and 62 were observational.

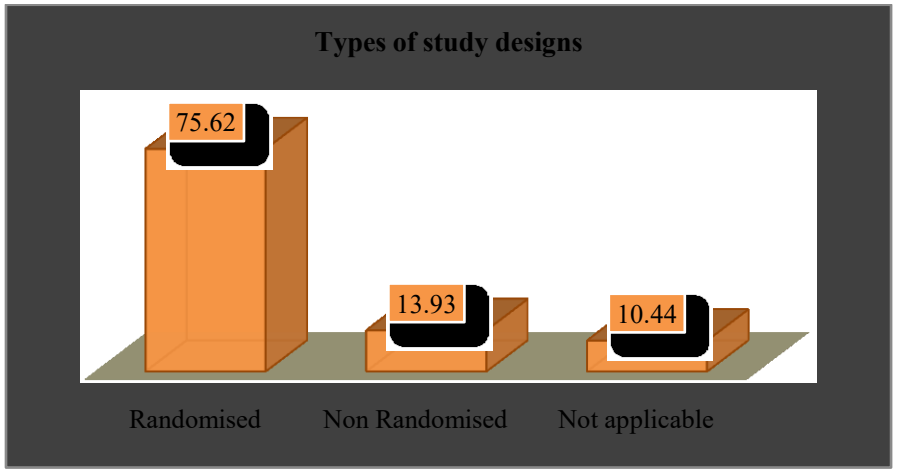


Figure 2: Shows types of study designs in clinical trials on covid vaccine registered on ctgov.in

Out of 201 interventional studies, 75.62% were randomised controlled trials. Out of 62 observational studies, 53.22% were cohort studies, 20.96% were case control studies, 9.67% were cross sectional studies.

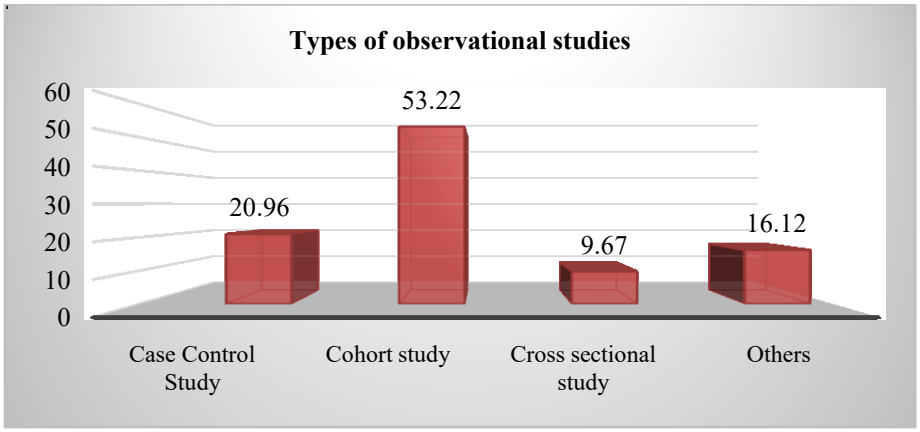


Figure 3: Shows types of observational studies conducted in vaccine for covid registered on ctgov.in

Out of 62 observational studies, 53.22% were cohort studies, 20.96% were case control studies, 9.67% were cross sectional studies.

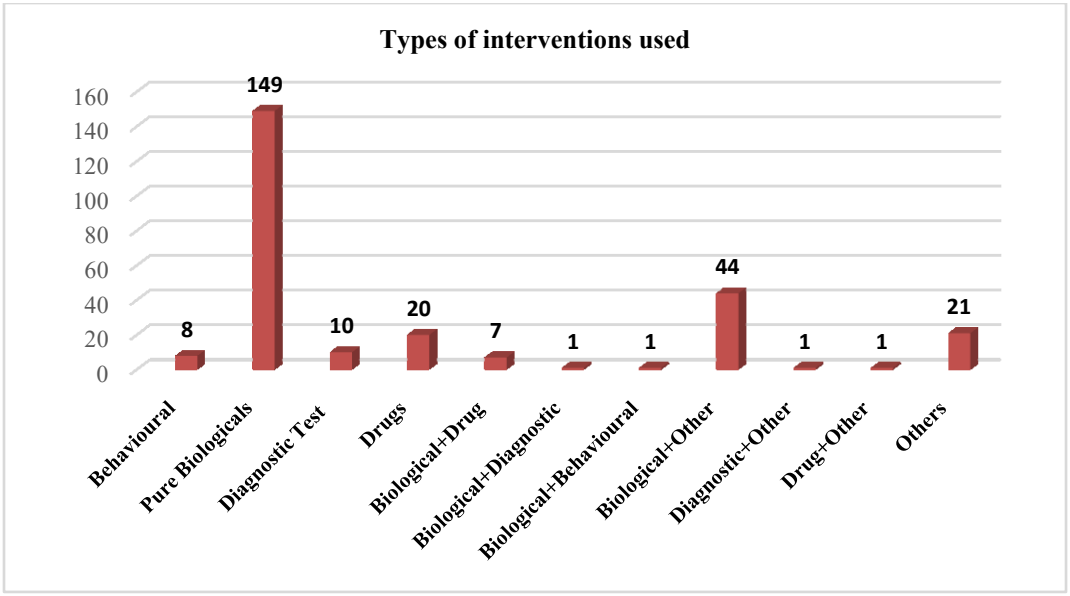


Figure 4: Shows types of observational studies conducted in the field of vaccines for covid registered on ctgov.in

Pure biologicals constituted 56.65% (149 of 201) of the total interventions. Among these, repurposing of vaccines that is pure biologicals showed the following observations: (Table No 1)

Name of the vaccine	Number (n)
BCG	19
Adenovector	7
Polio	3
Influenza	3
MMR	2
Zoster	1

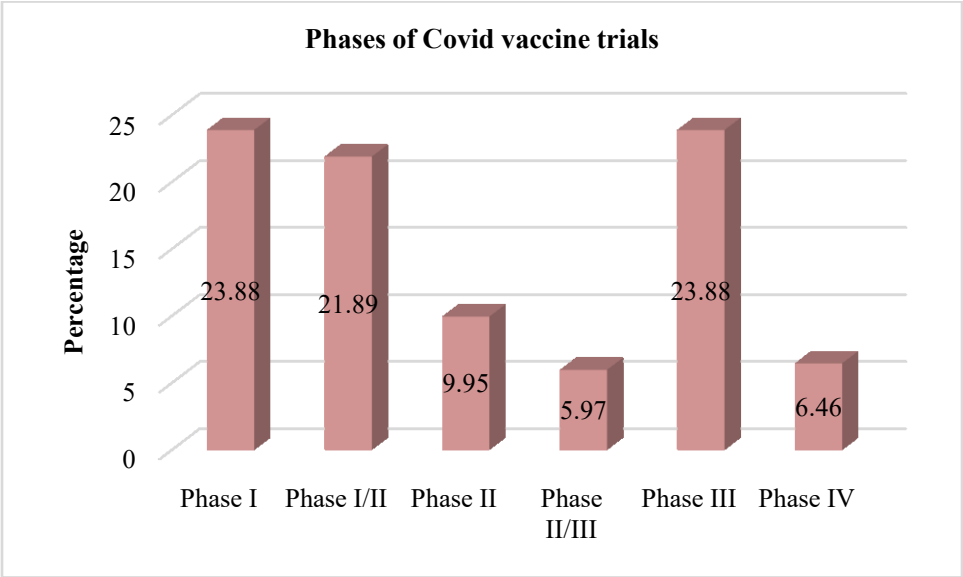


Figure 5: The bar diagram shows majority of the trials (23.88%) were in phase 1 and phase 3 respectively registered on ctgov.in

Out of these 44% of the trials were sponsored by the pharmaceutical industry.

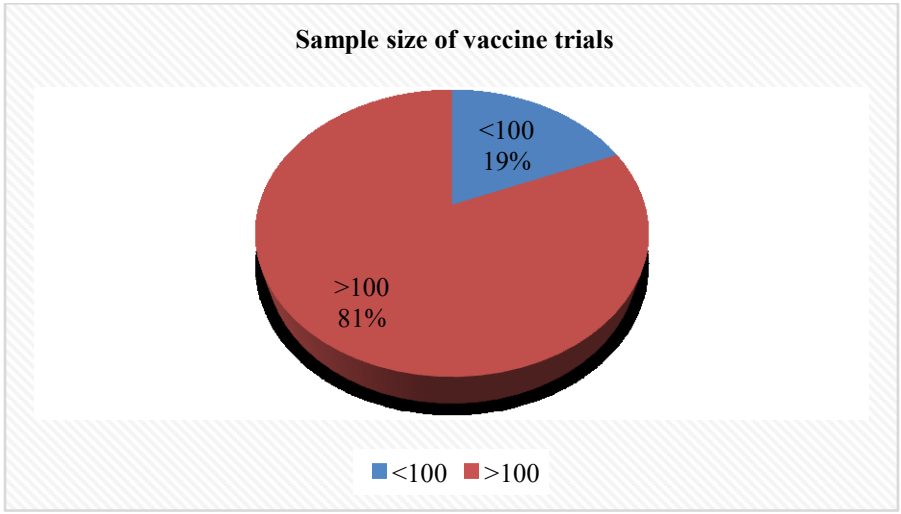


Figure 6: Pie chart showing the sample size of the interventional trials on covid vaccine registered on ctgov.in

81.36% trials had sample size above 100.

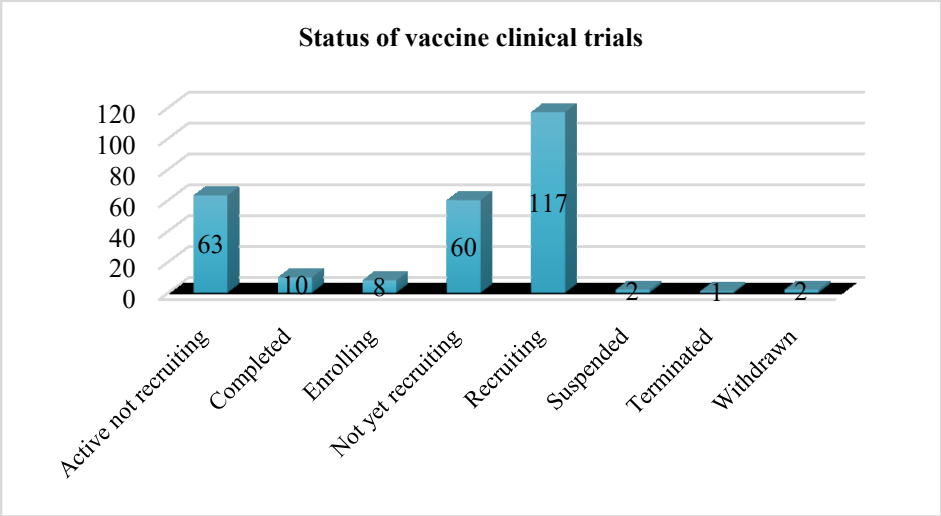


Figure 7: This diagram shows the recruitment status of the trials on covid 19 vaccine registered on ctgov.in

Out of total 263 trials registered, 63 are active; 10 are completed; 60 are not yet recruiting while 117 are open to recruitment. On the other hand, 2 trials have been suspended due to occurrence of SUSAR (Suspected Unexpected Serious Adverse Reaction) and other due to failure of subject recruitment; 2 withdrawn due to lack of funding and sponsorship and 1 trial had been terminated after interim assessment of immunogenicity.

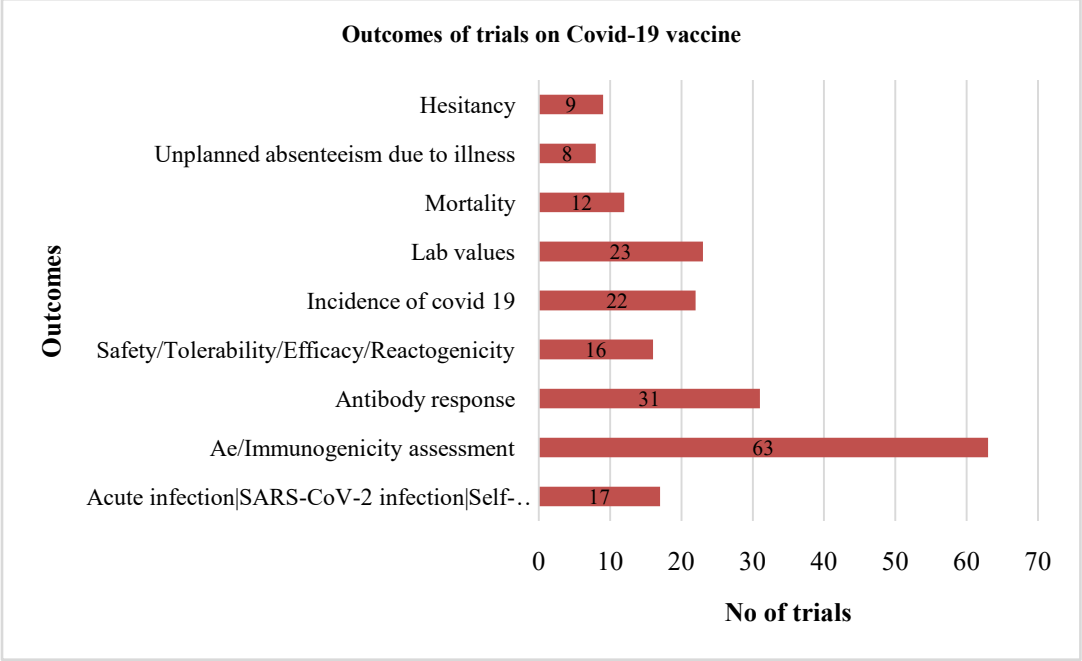


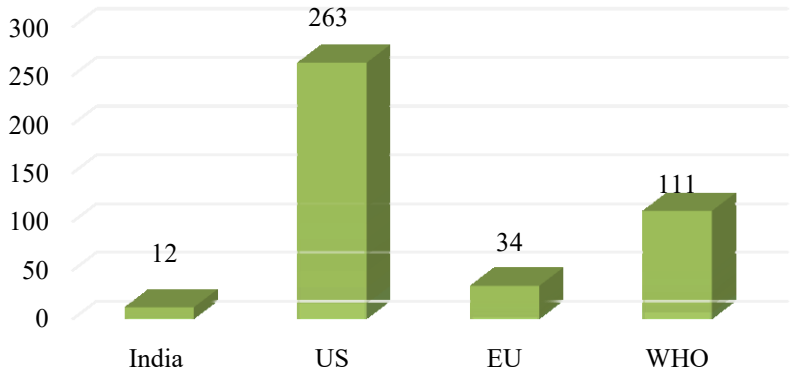
Figure 8: The bar diagram shows various outcomes of the trials on covid 19 vaccine.

The various outcomes of the studies were acute infection of SARS-CoV2, various adverse events, immunogenicity assessment, antibody levels, safety, tolerability, efficacy, incidence of covid 19, various lab values like d-dimer, interleukins, ferritin, mortality, unplanned absenteeism due to illness and hesitancy to take the vaccine.

Where do we stand globally?

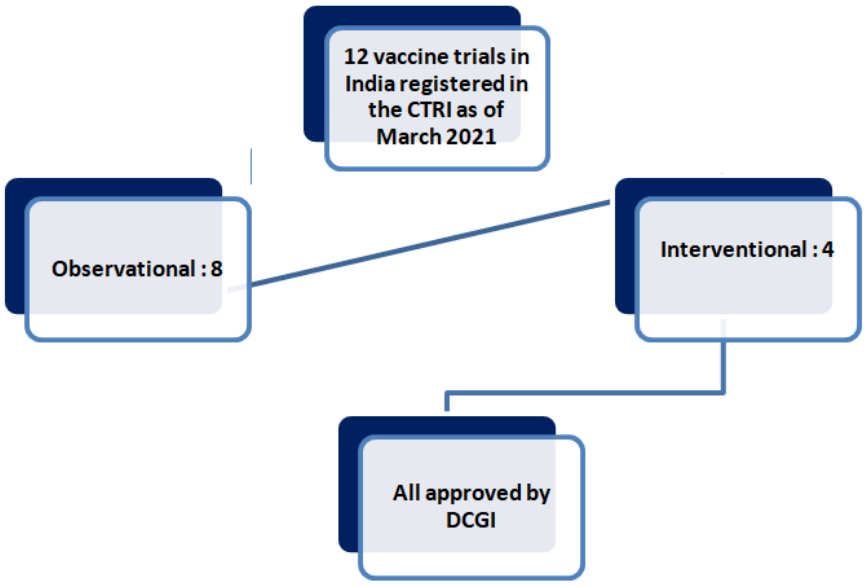
As this is a newer pandemic after 100 years, in a country like India, there exists a particular need for a keen understanding of the disease condition and its epidemiological aspects & this is reflected in the CTRI.

Global Covid VACCINE TRIALS in different registries



[India- CTRI; US- ctgov.in ; EU-European Union Registry; WHO-World Health Organization]

There were twelve vaccine trials in India registered in the CTRI. Out of the 12 trials, 4 are interventional and 8 observational. All the 4 trials have been approved by the DCGI and are sponsored by pharmaceutical industries. Randomized, parallel group trials and single arm trial were most preferred study designs. All the trials had sample size above 100.



Out of these, 2 vaccine candidates Covishield and Covaxin are already in post marketing and have been given Emergency Use Authorisation (EUA). Recently, Sputnik V was given emergency approval by Drug Controller General India (DCGI) and will be available from second week of June. This paves the way for India to rollout its third vaccine against corona infections.[7]

One of the vaccine candidate (adenoviral vector vaccine BBV154) is a double blinded, multi centric study with intranasal route of administration open for recruitment. Inspite of having 1/22nd of covid vaccine trials in India compared to that of US, India rolled out the world's largest vaccination drive on Jan 16th and vaccinated more than 200,000 health care workers and was the highest first day total of any country.[8]

With 1.26 million doses of vaccines administered on an average everyday, India's inoculation drive is now the world's second largest and is now behind only the US which is administering 2.5 million doses a day.[9]

4. Discussion

Asia contributing to nearly 60% of the world population started venturing into clinical research arena following globalization of clinical trials.[10] As of March

2021,there are 263 clinical trials for covid vaccine registered in US, 34 in EU and 111 registered in Australia, Canada, China, and Japan were obtained from WHO's international clinical trial registry platform for the same period. India has 12 trials for covid 19 vaccine registered in CTRI as of March 2021. This study showcases the efforts in finding pharmaceutical interventions to COVID-19 through the extensive analysis of COVID-19 vaccine clinical trials globally and in India. This is the first study in documenting and providing an extensive overview of vaccine clinical trials on COVID-19.

COVID-19 has made an unprecedented impact on economy and public health system across the world.[11] The study results found that compared to observational studies, more interventional studies or trials (76.42% of the total studies) were being conducted. It is in a way shows the speed in which countries across the world including India trying to develop vaccines. The clinical trials that were under way in India signifies similar pattern across globe.EUA of vaccine candidates in India gives us hope that vaccination maybe the only way to fight the pandemic.[12]

Pfizer, Moderna and Oxford Astrazeneca have been given EUA in UK and US has access to Pfizer, Moderna and Johnson and Johnson.

5. Limitations of the study

The major limitation of our study is that we could just give a snapshot of the trials registered in the trial registries over the study period across the few nations. We were not able to estimate the real status of the clinical trials conducted in these countries as there is a possibility of under reporting of clinical trials in the registries.

6. Conclusion

In this study we have tried to document the existing or ongoing clinical trials in India on COVID-19 vaccines. This study will be helpful for researchers, policy makers, and general public for understanding COVID-19 clinical trials eco-system. This study will also be useful for global scientific community to know what clinical trials are being conducted on COVID-19 vaccines in the world and potential source of information for international collaborations. Different countries have started vaccination and country like Israel has completed vaccination of majority of its population and has become 'COMPLETELY MASK FREE' Currently the entire world is in dire need of vaccines which seems to be the only solution in combatting the upcoming wave of infection and herd immunity.

Conflict of interest: None
Funding: Not required

References:

[1]. Weston S, Frieman MB. COVID-19: knowns, unknowns, and questions. *mSphere*. 2020; 5(2): e00203–20.

[2]. Hiscott J, Alexandridi M, Muscolini M, Tassone E, Palermo E, Soultsioti M, et al. The global impact of the coronavirus pandemic. *Cytokine Growth Factor Review* 2020; 53: 1–9.

[3]. Kaur SP, Gupta V. COVID-19 vaccine: a comprehensive status report. *Virus Research*. 2020; 288: 198114.

[4]. Strizova Z, Bartunkova J, Smrz D. Can wearing face masks in public affect transmission route and viral load in COVID-19? *Central European Journal of Public Health*. 2020; 28(2): 161–2.

[5]. Charan J, Kaur R, Bhardwaj P, Kanchan T, Mitra P, Yadav D, Sharma P, Misra S. Snapshot of COVID-19 related clinical trials in India. *Indian Journal of Clinical Biochemistry*. 2020; 35(4):418-22.

[6]. Prompetchara E, Ketloy C, Palaga T. Immune responses in COVID-19 and potential vaccines: lessons learned from SARS and MERS epidemic. *Asian Pacific Journal of Allergy and Immunology.* 2020; 38(1): 1–9.

[7]. https://cdsco.gov.in/opencms/opencms/en/Home/ Accessed on 15th April 2021

[8]. https://www.theguardian.com/world/2021/jan/20/indian-hesitancy-sets-back-worlds-biggest-covid-vaccination-drive Accessed on 30th March 2021

[9]. https://www.hindustantimes.com/india-news/indias-inoculation-drive-now-second-largest-in-world-101615745738512-amp.html accessed on 30th march 2021

[10]. Selvarajan S, George M, Kumar SS, Dkhar SA. Clinical trials in India: Where do we stand globally?. *Perspectives in Clinical Research*. 2013; 4(3):160-164. doi:10.4103/2229-3485.115373

[11]. MoHFW. (2020, July 31). Ministry of Health & Family Welfare, Government of India, Covid-19 India dashboard. Retrieved from https://www.mohfw.gov.in/

[12]. Mehta, H. B., Ehrhardt, S., Moore, T. J., Segal, J. B., & Alexander, G. C. Characteristics of registered clinical trials assessing treatments for COVID-19: a cross-sectional analysis. *British Medical Journal Open*, 2020; 10(6): e039978.