

# **Determination of spectrum of symptoms observed followed by administration of 1<sup>st</sup> and 2<sup>nd</sup> doses of COVISHIELD™ vaccine in Datta Meghe Institute of Medical Sciences (deemed to be university) – A Study Protocol**

## **Abstract :**

**Background:** The 2019 novel coronavirus (2019-nCoV or SARS-CoV-2) was first detected in December 2019 in Wuhan City of Hubei, Province of China with population of 11 million, after outbreak of pneumonia. Present study deals with acceptability of newly manufactured vaccines against Covid 19 disease component of social misconceptions regarding the post vaccination symptoms and/or adverse events. Main rationale of this study is to list all post vaccination symptoms observed at multiple points of time to clear misconceptions resulting in possible increase in acceptability of newer vaccines.

**Aim :** To determine the spectrum of symptoms observed followed by administration of 1<sup>st</sup> and 2<sup>nd</sup> doses of COVISHIELD™ vaccine in Datta Meghe Institute of Medical Sciences (deemed to be university).

**Methods:** This will be a Prospective analytical cohort study conducted over a period of 5 years.

**Procedure:** Followed by letter of informed consent, pre validated questionnaire will be circulated amongst the healthcare professionals having been administered the 1<sup>st</sup> and 2<sup>nd</sup> doses of COVISHIELD™ vaccine filled and submitted to authorized email for further study and will be evaluated for enlisting post vaccination symptoms with time of onset and duration following 1<sup>st</sup> and 2<sup>nd</sup> doses of COVISHIELD™ vaccine. Follow up will maintained at regular intervals and questionnaire will be amongst participants at 6 months, 1 year, 2 years, 3 years, 4 years and 5 years after the 2<sup>nd</sup> dose of COVISHIELD™ vaccine.

**Expected outcome:** Post vaccination symptoms following 1<sup>st</sup> and 2<sup>nd</sup> doses of COVISHIELD™ vaccine with range of time of onset and duration of the same will enhance status of the COVISHIELD™ vaccine awareness, social acceptability and willingness.

**Conclusion:** All conclusions will be drawn after proper statistical analysis.

**Keywords:** COVID 19, Vaccination, symptoms, post vaccination symptoms

## Introduction:

The 2019 novel coronavirus (2019-nCoV) or the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) as it is now called was first detected in December 2019 in Wuhan City of Hubei, Province of China with a population of 11 million, after an outbreak of pneumonia without an obvious cause.

The virus has now spread to over 200 countries and territories across the globe. It was characterized as a 'pandemic' by the World Health Organization (WHO) on 11 March 2020(1,2). As of 15 February 2021, there were 109,390,539 [laboratory-confirmed cases](#) of coronavirus disease 2019 (COVID-19) infection globally, with 2,411,501 reported deaths. Total vaccination done till date 15 February 2021 is 8285295. A safe, efficient, preventive or prophylaxis vaccine is urgently needed to control recent COVID-19 pandemic or possible future coronavirus outbreak. Several efforts have been attempted in the last 17 years to design a successful vaccine against coronavirus. In view of the present COVID-19 pandemic, vaccination approach may be of high interest to avoid the further infection/transmission and future outbreak of coronavirus.

About the virus, Coronavirus genus can be further divided into 3 antigenic groups. The new strain of coronavirus ( SARS-CoV ) encountered recently and having been given the birth to this pandemic does not belong to any of the 3 antigenic groups. However, some reports point out that this new strain has certain similarities to the group 2 coronavirus. (2)

In this project we are going to find out various side effects as well as adverse effects of inactivated SARS-CoV vaccine named ChAdOx1 nCoV-19 Corona Virus Vaccines (Recombinant).

Government of India started the vaccine drive directing the administration of ChAdOx1 nCoV- 19 Corona Virus Vaccines (Recombinant) on 16<sup>th</sup> of January, 2021. Our institute Datta Meghe Institute of Medical Sciences (deemed to be university) was provided with COVISHIELD™ . The vaccine drive was scheduled to include all health workers in the initial phase of vaccine distribution highlighting the frontline warriors or the first contact with risk of contact with the virus.

As prescribed by Indian Council of Medical Research (ICMR), the undesirable effects are injection site pain, headache, fatigue, myalgia, pyrexia, chills and arthralgia, nausea in decreasing order of occurrence.

Our project has been designed in order to provide a bird's eye view about side-effects as well as adverse effects of the first as well as the consequent dose of newly developed ChAdOx1 nCoV- 19 Corona Virus Vaccine (Recombinant) in vaccinated individuals over a period upto 5 years. This study encompasses upon the side effects or adverse effects observed in the vaccinated population from immediate, 6 hourly, 12 hourly, 24 hourly, 48 hourly, 72 hourly, more than 72 hours, 1 month, 6 months, 1 year, 2 years, 3 years, 4 years and 5 years respectively – attempting to prepare an approachable repository studying the array of side/adverse effects followed by the administration of COVISHIELD™ vaccine in the sample population at Datta Meghe Institute of Medical Sciences (deemed to be university).

The present study deals with a very sensitive point regarding the acceptability of the newly manufactured vaccines against the CoViD 19 disease, specifically picturing the hearsay, rumours and component of social misconceptions regarding the post vaccination symptoms and / or adverse events. The main rationale of this study is to delve into these symptoms and come up with a list of all post vaccination symptoms observed at multiple points of time and to make an attempt to clear the rumour cloud rampant in the society, resulting in a possible increase in acceptability of these newer vaccines and eventually prevention of pandemics of such magnitudes.

## **Aim and objectives**

### **Aim**

To determine the spectrum of symptoms observed followed by administration of 1<sup>st</sup> and 2<sup>nd</sup> doses of COVISHIELD™ vaccine in Datta Meghe Institute of Medical Sciences (deemed to be university).

### **Objectives**

To enlist the post vaccination symptoms with time of onset and duration followed by administration of 1<sup>st</sup> and 2<sup>nd</sup> doses of COVISHIELD™ vaccine in Datta Meghe Institute of Medical Sciences (deemed to be university).

To compare the post vaccination symptoms with time of onset and duration followed by administration of 1<sup>st</sup> and 2<sup>nd</sup> doses of COVISHIELD™ vaccine in Datta Meghe Institute of Medical Sciences (deemed to be university).

## **Material and methods:**

**Period of Study :** 5 years

**Design :** Prospective analytical cohort study

### **Procedure:**

A letter of informed consent will be taken from all the participants of this study. A pre validated questionnaire will be circulated as a hard and soft copy amongst the healthcare professionals having been administered the 1<sup>st</sup> and 2<sup>nd</sup> doses of COVISHIELD™ vaccine on the day of vaccination.

The questionnaire will be filled by the healthcare professionals and submitted to the prescribed email for further study and compilation.

The questionnaire thus filled and collected will be evaluated for enlisting the post vaccination symptoms with time of onset and duration following 1<sup>st</sup> and 2<sup>nd</sup> doses of COVISHIELD™ vaccine.

Thereafter, the follow up of these patients will maintained at regular intervals and the questionnaire will be circulated in between the participants at the end of 6 months, 1 year, 3 years and 5 years after the 2<sup>nd</sup> dose of COVISHIELD™ vaccine in order to document any long term side effects or adverse events if any occur.

### **Data and collection Tools**

Pre validated questionnaire.

**Analysis Plan:**

After collection of required data, the total number of doses administered will be calculated. The total number of healthcare professionals having received 1<sup>st</sup> and 2<sup>nd</sup> doses will be calculated.

The total number of healthcare professionals not opting to take the 1<sup>st</sup> and 2<sup>nd</sup> doses of COVISHIELD™ vaccine will be calculated with reason thereto.

The total number of healthcare professionals previously affected by CoViD 19 and having been administered the 1<sup>st</sup> and 2<sup>nd</sup> doses of COVISHIELD™ vaccine will be calculated.

The post vaccination symptoms with time of onset and duration followed by 1<sup>st</sup> dose and 2<sup>nd</sup> dose will be enlisted separately and subjected to comparison with regards to severity taking into reference the time of onset and duration.

Follow up of these cases until a period of 5 years from the date of administration of the 2<sup>nd</sup> dose of COVISHIELD™ vaccine will be carried out using the questionnaire.

**Expected outcomes:**

A defined picture of post vaccination symptoms following the 1<sup>st</sup> and 2<sup>nd</sup> doses of COVISHIELD™ vaccine with range of time of onset and duration of the same will be cemented and enhance the status of the COVISHIELD™ vaccine and other vaccines also with regards to awareness, social acceptability and willingness.

**Discussion:**

Pondering about how the concept of vaccination came into being, it was Edward Jenner who tried to materialize it by using attenuated version of smallpox vaccine against smallpox viral disease, most probably the animal pox virus.

Then, it was more or less the same concept when the vaccine was prepared and named Baciilus Calmette Guerin.

Use of viruses from other classes to prepare a human variant was an idea behind these ventures. (7)

Pasteur contemplated the idea of attenuation to materialisation when he and his colleagues worked upon a diarrhoeal disease in chicken (3,4,5,6,8) and to all the more effect while working together against the rabies virus affecting both animals as well as humans.(9)

The same concept of attenuating the virulent causative organisms through an unusual host organism was utilised by Koprowski et al when they developed working vaccines against both rabies and polio by passing the causative organisms through unusual hosts like chicken embryo or mice. (10-15)

Then, it was shown by Enders, Weller and Robbins that the viruses causing a particular disease in a particular species could be grown in culture media outside the body of the host organism i.e. in vivo which emerged a ground breaker. (16)

Some examples of vaccines prepared using this principle of in vivo cell culture of causative organisms were the oral polio vaccine prepared by Sabin, measles, mumps and rubella vaccine.(17,18,19,20,21)

The era moved on further ahead with time as more and more complex virus and other causative organisms came to affect human species. Of which the most recent and perhaps the most feared is the SARS-CoV-2 virus.

This virus belongs to the group Coronaviruses and is well known to affect human and cause respiratory pathology and even multisystemic disruption at the same time which is quite unclear at the moment(22). Of the 7 genera, four cause mild symptoms but the remaining three namely the Severe Acute Respiratory Syndrome Coronavirus, Middle East Respiratory Syndrome Coronavirus and Severe Acute Respiratory Syndrome Coronavirus 2 are known to cause severe symptoms being relatively highly pathogenic and may lead to a fatal outcome. (15).

The latest affliction by SARS CoV 2 arose in Wuhan in Guangdong province of People's Republic of China and due to its rampant mode of spread and severity of virulence, the globe underwent severe ergonomic as well as economic disruption other than health as its primary target. (15).

Coming to the structure of the SARS CoV 2, the main role in its binding to the host cell is played by S protein present on its many arms, chiefly due to presence of the Receptor Binding Domain on it which assists the virus to enter the targetted host cell with ease and for this same reason if this protein can be targetted for production of a vaccine, it can yield a very productive outcome.(23)Some other studies have concluded that antibodies produced in response to such a vaccine prepared by targeting S protein are relatively effective and last longer yielding protection against viral infection.(23,24)

One of the studies published in Lancet in 2021(19) evaluated safety and efficacy of the ChAdOx1 nCoV-19 vaccine by analysing four ongoing blinded, randomised, controlled trials which were done across the UK, Brazil, and South Africa. In their study, participants aged 18 years and above were randomly assigned to the vaccine and control group. The participants in the vaccine group received two doses of ChAdOx1 nCoV-19 vaccine (standard dose; SD/SD) and a subset in the UK received the first dose as low dose and a standard second dose (LD/SD). 23848 participants were enrolled for the study out of which 11636 were included in the primary efficacy analysis (symptomatic COVID-19 participants who were seronegative with NAAT-positive swab more than 14 days after second dose. The results of the study was that the ChAdOx1 nCoV-19 has a good safety profile and is effective against symptomatic COVID-19.

Another study published recently in The Lancet Infect Dis 2021; 21: 181–92 (20)investigated CoronaVac (Sinovac Life Sciences, Beijing, China) which was an inactivated vaccine candidate against COVID-19 and contained inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). They tested its safety, tolerability and immunogenicity. In their randomised, double-blind, placebo-controlled study that underwent phase 1/2 clinical trial healthy adults aged 18–59 years were recruited. They were divided into two vaccination schedule cohorts, the days 0 and 14 vaccination cohort and the days 0 and 28 vaccination cohort by block

randomisation and administered either low dose or high dose of vaccine/placebo. The result suggested that CoronaVac is an inactivated vaccine candidate against COVID-19 as it has a good immunogenicity in mice, rats, and non-human primates with vaccine-induced neutralising antibodies to SARS-CoV-2. The vaccine provided partial or complete protection in macaques from severe interstitial pneumonia after a SARS-CoV-2 challenge with no identifiable antibody-dependent accentuation of infection and hence can be taken into consideration for progression to clinical trials in humans.

Dong et al (2020) (21) In their systematic review of SARS-CoV-2 vaccine candidates enlisted, evaluated and analysed various vaccines such as inactivated vaccines, nucleic acid based vaccines and vector vaccines. They gave an overview of the experimental and clinical data which was obtained from the recent trials conducted for SARS-CoV-2 vaccines and highlighted the safety concerns. They also summarized the strategies which were used in development of vaccines. Moreover they also wrote about the factors like delivery system which was important for the vaccine efficacy and the adjuvant added which would increase its immunogenicity.

Shibo Jiang et al (2005)(22) in their review article in 2005 said that if a vaccine for severe acute respiratory syndrome (SARS) associated coronavirus (SARS-Cov) is needed to prevent this condition which can be a major health problem in coming years. An inactivated vaccine may be one of the first one that can be made available for clinical use as it's easy to generate. But the major problem with this vaccine would be the safety. The spike (S) protein is the major inducer of neutralizing antibodies and the receptor-binding domain (RBD) in the S1 subunit of S protein contains multiple conformational neutralizing epitopes suggesting that recombinant proteins containing RBD and vectors encoding for the RBD can be used to develop safe and effective SARS vaccines.

The present study is designed to take into account the symptoms observed and experienced by the sample population after the 1st and 2nd dose respectively at different points of time. This study aims to enlist the side effects, adverse drug reactions arising out of vaccine administration and/or any cases of reinfection of CoViD 19 disease after the 1st or 2nd dose of the vaccine.

## **Conclusion:**

All conclusions in conformity with the aim and objectives of the present study will be drawn after proper statistical analysis. Taking into consideration the present pandemic scenario, the present study will help and try to resolve the hearsay and rumours regarding the vaccine for CoViD 19 disease amongst the concerned population and will result in an increase in awareness and readiness to undergo the process of vaccination against the dreaded pandemic.

## **COMPETING INTERESTS DISCLAIMER:**

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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