A Brief Report of the NASI Webinar on Building Confidence on COVID Vaccines

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Globally vaccination against COVID19 virus is being advocated and millions of people have been vaccinated. The COVID Task force constituted by the Government of India has recommended for rapid vaccination of all eligible persons. The both Central and State Governments have undertaken massive awareness programs through advertisements and multimedia including social media and have made adequate arrangements for free vaccination at government hospitals. But some persons have concerns and misconceptions and are not coming forward for vaccination. Therefore, the Lucknow Chapter of the National Academy of Sciences, India (NASI) organised a webinar on Building Confidence on COVID Vaccines on 29 April 2021. Ever since the outbreak of COVID19 in the country, NASI had launched a Jagrukta Abhiyan for mass awareness and has organised several programs through its Chapters all over the country, including remote Northeast regions.

Prof. Randeep Guleria, Director AIIMS, New Delhi started his inaugural address by giving a glimpse of the current status of COVID19 in the country. He pointed out that country is passing through a severe phase of pandemic as it has about 10–20% of world's COVID19 cases which is the second highest number of cases and third highest COVID19 related deaths as of 24 April 2021. He said the situation is grim, though the number of deaths is much less as compared to world figures. He drew the attention to Spanish Flu which occurred in 1918 and was the cause of deaths to the magnitude of millions.

There were 3 waves of Spanish Flu, after the 1st wave, when the number of cases subsided, people became care-less and happy, started mixing having parties and this led to 2nd wave that was much more severe and larger, leading to several deaths. The masks were still worn but there was hesitancy. It looks that history repeats itself and there are lessons to be learned. The present second wave is far more dramatic and rapid that burdened the health infrastructure of the country. He briefly talked about the Strategic Response by AIIMS, the topmost hospital and research institution in public sector of the country, to COVID19 ever since it hit India. This included reorganisation of infrastructure creating more wards, ICU beds, etc. During the peak on an average 800–900 patients/day were treated at AIIMS. An important aspect of the strategic response was supporting research and AIIMS was the 1st institute to announce funding for COVID19 related research projects including clinical, epidemiological and diagnostics. More than 200 papers were published in various national and international journals out of these 17% were research papers and 18% were patient management guidelines. He emphasized that data generated and new guidelines formulated at AIIMS will help in effective management of the disease.

Prof. Guleria speaking on the vaccine said it has been touted as the most effective public health measure to end pandemic. In last 3 months, COVID19 vaccines have been administered under emergency authorization to millions of people worldwide and this has led to widespread optimism about the “beginning of the end” of COVID19 pandemic. He mentioned that several questions such as, are vaccines really safe? will they prevent disease transmission? and how long will the benefit last? are being raised about the vaccines. Briefly mentioning the vaccine scenarios, he said

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that vaccines induce immune responses of host against a pathogen without exposing them to disease. At present there are 60 candidate vaccines in human trials and 180— are in preclinical trials. He explained that they may work by preventing infection, severe illness & death and prevent transmission. Subsequently, he talked about the design of the vaccine that include selection of antigen which could be S protein, W protein, M protein & E protein and only antibodies against S protein can neutralise & prevent infection. All vaccines in development include a portion of S protein. He also described the selection of vaccine platform and best are live attenuated virus vaccines. Recombinant viral vaccines and inactivated or killed virus vaccines and the vaccination routes and regimens are integral part of any strategy. Touching upon the Indian Landscape he said, it is very heartening that India which has been considered as manufacturing hub of vaccine, now have robust research and development activity and has developed Covaxin, a totally indigenous vaccine. The COVID19 strain was isolated by ICMR Institute NIV, Pune and based on that Covaxin is being manufactured by Bharat Biotech. Also, Covishield developed by AstraZeneca is being manufactured by—Serum Institute of India. ZyCoV-D is being manufactured by Zydus Cadila and Russian Vaccine Sputnik V is being manufactured by Reddy's laboratories. NVX-Co V2373 is being developed by Serum Institute of India, Recombinant Protein Antigen Based Vaccine is being developed by Biological Evans Ltd, mRNA based Vaccine HGC019 is being developed by Gennova Biopharmaceuticals, Pune and inactivated rabies platform vaccine is being developed by Bharat Biotech. Some of these are in various stages of clinical trials. This shows India will soon have several vaccines to deal with the COVID19 pandemic.

Explaining the efficacy for COVID19 vaccine he said that US FDA and WHO have laid down the criteria that minimum efficacy should be > 50%. He described the efficacy of available vaccines like Pfizer, Moderna and others. Here briefly the efficacy of AstraZeneca Covishield and Covaxin is mentioned. Referring to a Lancet paper of 8 December 2020, Prof. Guleria said that Covishield had an efficacy of 71% and participants who received a low dose followed by the standard dose showed an efficacy of 90%. With respect to timing of the booster dose of Covishield, Dr Guleria, referring to Lancet study published on March 6–12, 2021 concluded that when second dose was administered after 12 weeks the efficacy was 81% and if administered in less than 6 weeks the efficacy was 55%. WHO has also recommended an interval of 8 to 12 weeks between the two doses. With respect to Covaxin developed by Bharat Biotech, he said that the clinical trial studies of Phase 2 reported in Lancet Infections, 8 March 2021 have shown significant efficacy and subsequently, Bharat

Biotech has announced an efficacy of 81% in the interim Phase III clinical trial results.

Dr. Guleria later drew attention to the challenges of vaccination that are emergence of new strains, duration of efficacy and vaccine hesitancy. He described the new strains such as B.1.1.7 lineage United Kingdom which contains > 12 mutations, several within the spike protein region. This strain has been of concern as it has been responsible for infection in Punjab and other northern states as revealed by genome sequencing data. The strain has increased transmissibility by 25–40%, slightly increases the mortality and there is no evidence that it impacts vaccine efficacy. The other strain B.1.351 lineage South Africa shares many mutations with B.1.1.7 Spike protein mutation E484K, which may impact immunity from prior infection or vaccination. It exhibited reduced neutralization with convalescent plasma and mRNA vaccine recipients carry antibodies which neutralize this variant at lesser titres. Therefore, this is a cause of concern and more data is needed. Hence the vaccines may still be effective but magnitude of protection will be lower. The third variant P.1 lineage Japan/Brazil, includes several mutations, including 3 in the spike protein, N501Y, E484K, and K417T. There is concern about increased transmissibility and an impact on immunity. He said that there is little evidence to suggest that the British and South African variants could escape the immune protection afforded by current vaccines. There is concern among immunologists about the possibility of further mutations of virus, which could render these vaccines less effective but the good news is that such vaccines could be “tweaked” to overcome this problem. The production of a new influenza vaccine each year demonstrates that it is possible to adapt existing vaccines to keep up with viral mutations. Dr Guleria described vaccine hesitancy, as one of the most important factors concerning the vaccination drives. He said that vaccine hesitancy has become more common worldwide and has been cited by the WHO as a top 10 global health threat in 2019. It presents a major obstacle to achieving vaccination coverage that is broad enough to result in herd immunity. There are unfounded public perceptions that corners are being cut with regard to safety assessments and there is misinformation about SARS-CoV-2 infection and the vaccines. Touching upon tackling of the vaccine hesitancy he said that health care providers can improve vaccine acceptance by making direct recommendations for vaccination, identifying concerns, educating patients on vaccine risks and benefits and dispelling misconceptions about the disease and the vaccine like Covishield causes blood clots. He said as far as India is concerned, as per a questionnaire-based study in a recent 2021 issue of Lancet, 91% of the population is ready for vaccination. He further said that the duration of protection from various COVID19 vaccines is an outstanding

concern of immense public health importance. For this ongoing follow-up of trial participants and additional observational studies are necessary and it is also important to identify rare effects like blood clotting and delayed adverse events of vaccines through efficient surveillance networks.

Emphasising the importance of vaccination, Dr. Guleira said that having vaccines alone will not end the pandemic, but vaccination of most of our population will. It is important to make the general public aware about the benefits of vaccination so that immunity can be developed. The WHO also states that at least 70% of the population should be infected so as to achieve “Herd immunity”. To illustrate his point, he took the example of Israel where Pfizer BioNTech has been used for vaccination. About 3.1 million people received the first doses and 1.8 million have received the second dose of vaccine. New cases and illnesses decreased significantly following two weeks of first dose as per their Health Ministry data and recently it became the first COVID19 mask free country. As Israel is a small country, it was possible to vaccinate almost the entire population, this unfortunately is difficult at present as ours is a large population.

Dr. Guleria said that developing vaccine is an only half of the work done, delivering equitably is the most important task. If only the high-income countries were to be vaccinated there would have been only 33% protection of the lives, while if it was given to countries with high population, the protection would have been 61%. He said that equitable global vaccine supply and its administration is our best bet to end the pandemic. In conclusion, he said that—(1) Vaccine is an important health measure, to end the pandemic. (2) A large number of vaccines are available, (3) Measures are required to ensure quick, efficient and equitable delivery of vaccines, (4) Current vaccines retain their efficacies against new variants. However, vaccines may need to be tweaked if newer strains show immune escape, (5) Studies are needed to explore their duration of protection and long-term adverse effects, and (6) Public health measures like social distancing and masks must be continued till the population coverage of vaccination is achieved and case load to community has declined.

The inaugural talk by Prof. Guleria, was followed by a lively panel discussion. It was chaired by Prof. G Padmanaban, Past President NASI and Ex-Director Indian Institute of Science Bangalore, and moderated by Dr. V.P. Kamboj, Chairman BCIL and Ex-Director CSIR-CDRI Lucknow and Dr. P.K. Seth, NASI Senior Scientist and Ex-Director CSIR-IITR Lucknow. Prof. Padmanaban expressed concern about the availability of the vaccine. He said that considering the present capacities of the two companies the Bharat Biotech and Serum Institute of India manufacturing Covaxin and Covishield, respectively, and

the availability of other vaccines in pipe line, it looks difficult to meet the demand for vaccination of large population. He stressed for urgent steps for making available the vaccine if large-scale vaccination is to be achieved.

Dr. Kamboj in his opening remarks stated that it is important to get the general public vaccinated, as it is only the vaccination that can end the pandemic or eradicate a disease as we saw in case of polio and small pox.

Dr. Anurag Agrawal Director, CSIR- IGIB discussed about the mutations in virus and pointed out the importance of D614G protein and how it is responsible for causing mutations. This perhaps helped COVID19 to bind better to the ACE-2 receptor and became more infective. He further mentioned that new strain called P1, severely prevented the binding of the antibodies. He expressed concern that the B.1.1.7 UK strain has spread ferociously so much that the 90% cases in Punjab are of B.1.1.7. He also mentioned about B.1.617 mutant strain that has emerged from Maharashtra, Dr Agrawal emphasized the need for continuous monitoring of mutations in virus and understand its behaviour related to transmission and infectivity.

Prof. Amita Jain, Head - Department of Microbiology and Pathology, K.G. Medical University, who has set up an ICMR funded virology lab and during current Pandemic trained a large number of people for undertaking RT-PCR tests, discussed about the sensitivity and issues associated with RT-PCR tests. She mentioned that vaccination for COVID19 does not result in false positive RT-PCR or antigen test results for SARS CoV-2. Further the Antigen detection test has lower sensitivity than RT-PCR. It should be used in symptomatic patients as per algorithm suggested by ICMR. In case result is negative then only RT PCR should be tried. Further the mutant strains of SARS-CoV-2 are easily detectable by most of the commercial reagents available for RT-PCR based diagnosis of COVID19. She added that RT-PCR for SARS CoV-2 is negative in some COVID19 patients who are symptomatic and have chest CT findings. It is possibly because these patients come to hospital late and by that time viral load in upper respiratory system has gone undetectable. Or else because of severe symptoms patients were non-cooperative and sample could not be collected properly.

Dr Sanjay Singh, CEO Gennova Biopharmaceuticals, said that as they had been working on vaccines for past 3 years for personalized cancer, the company decided to work on mRNA vaccines and the company used mRNA on the surface instead of inside the cell approach. The mRNA vaccine is self-amplifying and slowly induces the immune system and hits the germ cells, so it is the germ cells which give the memory. It has been tested against the Brazilian, UK and the South African strains as well. He pointed out that mRNA vaccine on which they are working will be stable at 2–8 °C. He also stated that it is important to

decipher the sequences of the new strains so as to tweak and develop further vaccines.

Dr. Santasabuj Das Scientist F at NICED, Kolkata, expressed concern regarding the hesitancy in taking vaccine shots and indifferent attitude of the people. He said that many people who took the first dose did not take the second dose. He said that steps are needed to create awareness among general public about the benefits from vaccination. It is important to address the concerns of the general public that vaccination will decrease the severity of infection, if not the incidence. Further priority should be defined on scientific basis about people who need to be given their 2nd dose or people who have to receive their first dose. People should be convinced to continue to follow appropriate COVID safety measures.

He also stated that it is important to vaccinate as many people as we can, as even in the people with first dose of vaccine, it is protecting against various sorts of antigens and thus the possibility of escaping mutations seems less likely to occur, i.e. people are less likely to develop mutant strain. He said, we have seen this in case of hepatitis and rabies vaccine where chances of developing mutant strain was very rare.

Dr. Kamboj raised a question to the panel that as seen in the Spanish flu and other pandemics such as SARS the pandemic, with the 1st and 2nd wave almost vanished with the third wave, so is it possible that the current pandemic, instead of the vaccines, the 3rd wave would lead to the end of the pandemic.

Responding to the question. Dr. Anurag Agrawal said that vaccinating the whole world might not be practically possible, yet in terms of vaccine development technology since those times, has advanced a lot especially with mRNA platform. It is possible to create the vaccines as soon as the sequences are procured. Thus, it is a process of continuous evaluation and we have to keep comparing our strategies so as to put the technology to save lives. So today it is possible to save lives with vaccination. Adding to this Dr. Sanjay Singh, said as witnessed by him during the SARS pandemic in the early 2000s the size of the virus was

only 30 nanomicros as compared to the COVID-19 virus which is about 100 nanomicros, which leads to its high infectivity and thus virus has improved itself regardless of the immune responses. Hence, we have to keep up with it and that is possible with continuous improvement of vaccine technology and vaccination.

The vaccine and mutant strains should be critically evaluated keeping in mind the time taken to develop the immunity against the various strains which might escape and cause further infection. Although the available vaccines have efficacy between 70 and 85% and offer protection against various mutants, it is believed that a vaccine with an efficacy of 95 or 96% will be effective against upcoming strains.

The questions and comments by the participants which included Prof. Narendra Mehra, Former Head, Department of Transplants Immunology & Immunogenetics All India Institute of Medical Sciences, New Delhi were adequately addressed.

Earlier, Dr. Mrs Manju Sharma, Chairperson NASI New Initiatives, giving a recap of Jagrukta Abhiyan, said that this is the 16th webinar on COVID19, and these have created awareness for more than 20,000 students and large number of public. The webinar also highlighted the applications of plant extracts for their anti-viral activity against SARS-CoV2. NASI has always promoted the intervention of Science and Technology for the benefit of the people reaching to poorest of the poor, as emphasized by Gandhiji. Prof Ajoy Ghatak, President of NASI, welcoming the participants emphasized the importance of vaccination and said it is important to follow the COVID appropriate behaviour till mass scale vaccination.

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