Editorial

Real life vaccine effectiveness against COVID-19: Proof of the pudding!

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In the current COVID-19 pandemic, where most anti-viral and anti-inflammatory drugs have fallen short of passing the stringent test of Randomized Controlled Trials, therapeutic options are unfortunately limited.[1] With variable (and often sub-optimal) acceptance of public health interventions and strained/limited health infrastructure, vaccines against SARS-COV2 virus seem to be our shining hope in controlling the pandemic. Over 200 vaccine candidates are in various stages of development, with Emergency Use Authorization (EUA) having been granted to nine of them worldwide. In India, COVISHIELD® (Astra Zeneca) and COVAXIN (Bharat Biotech) were granted EUA in January 2021.[2] While the former is a viral vector vaccine (adenovirus) carrying the genetic material of spike protein of SARS-COV-2 the latter is an inactivated SARS-COV-2 vaccine with intact proteins.[1,3] Other vaccines are expected to follow.

How does one assess if a vaccine is effective? This is determined by vaccine efficacy and effectiveness studies. Both types of study calculate the risk of infection and disease among vaccinated and unvaccinated persons, and determine the reduction in risk.[4] While vaccine *efficacy* is studied in an ideal setting, as a prospective randomized control trial (where effect of vaccination in prevention of infection or disease can be proven), vaccine *effectiveness* studies are done in real world settings in prospective cohort or retrospective case–control studies. While the cohort studies compare the incidence

rates of various outcomes like infections or deaths between those vaccinated and unvaccinated; retrospective studies infer them by comparing the odds of antecedent vaccination among cases (individuals with disease) and controls (individuals who did not develop the disease).[5]

The current issue of MJAFI is rich with four articles that assessed vaccine effectiveness in different ways. The VIN-WIN cohort study by Ghosh et al analysed surveillance data of 1.59 million Health Care Workers and Frontline Workers from Indian Armed Forces. They were followed from 16 Jan to 30 May 21 as they were progressively vaccinated.[6] In this predominantly male cohort, with a mean age of 27.6 years, 95.4% were at least partially vaccinated with COVISHIELD® while 82.2% were fully vaccinated. The daily incidence rate (per million) of COVID infections and deaths due to COVID among the three groups was assessed and the average incidence rate calculated. The Incidence Rate Ratio (IRR) between groups estimated vaccine effectiveness to be over 93% in reducing infection among both partially and fully vaccinated individuals. Due to the very small numbers of deaths in the vaccinated groups and wide confidence intervals, no valid statistical inference could be drawn.

In a cross sectional analysis by Agrawal et al on 1.79 lakh Air warriors given COVISHIELD® (87% fully vaccinated) there was a 87.1% absolute risk reduction (ARR) of contracting infection.[7] Hospitalization was significantly lower with complete vaccination. Among the 57 with moderate to severe disease requiring hospitalization, just 03 belonged to the fully vaccinated group while 35 were unvaccinated.

The study by Muthukrishnan et al retrospectively analysed moderate to severe COVID-19 disease, hospitalized during the peak of the second wave at one hospital, and studied the association of vaccination status with mortality (adjusted for age, sex and co-morbidities).[8] The 1168 patients included in

the study had a male preponderance with a mean age of 54.6 (±17.5) years. A total of 266 (23%) patients were partially vaccinated with COVISHIELD® and 184 (16%) were fully vaccinated. Overall, 518 (44.3%) patients had comorbidities and 332 (28.4%) died. While the unvaccinated group had a 31.5% mortality, the fully vaccinated had 70% lower odds of death with 12.5% mortality. In a logistic regression model, complete vaccination status and younger age were found to be associated with survival.

The study by Bobdey et al looked at breakthrough infections among 3196 employees at one institution as they were progressively vaccinated over time and documented 113 events.[9] The overall vaccine effectiveness was 88.6% in completely vaccinated and 44.1% in partially vaccinated individuals. The Hazard Ratio for likelihood of infection dropped significantly after 28 days of the second dose. They also found that the secondary attack rate (SAR) to be 4.25%, which was lower than the SAR (20.6%) of pre-vaccination period, suggesting a reduction in transmission of infection.

Vaccine effectiveness can be assessed in multiple dimensions, like – occurrence of subsequent infections (both asymptomatic and symptomatic disease), transmission, hospitalization and mortality. These four studies in this issue of MJAFI show the effect of vaccine on various dimensions of the COVID epidemic. While the VIN-WIN Cohort study has shown a 93% reduction in COVID infections, the study by Agrawal et al showed reduced hospitalization due to severe disease.[6,7] The study of Bobdey et al showed a reduced community transmission after vaccination while the study of Muthukrishnan et al showed that among moderate to severe hospitalized COVID-19 patients, complete vaccination lowered the odds of death.[8,9]

Earlier studies and real world data has shown that vaccinated individuals are less likely to have asymptomatic or symptomatic disease (by 60–90%) and lesser hospitalization (by 96%) due to severe disease.[3,10] The VIN-WIN Cohort study and the study by Bobdey et al suggest similar benefits.[6,9] The study by Muthukrishnan et al suggests that vaccination further lowers the odds of death among those hospitalized with moderate or severe COVID.[3,8,11]

The second wave of pandemic in India had numerous variants of concern (VOC) including the B.1.617 variant. COVISHIELD® vaccine, while developed using the strains involved in the first wave, has possibly shown real life effectiveness against the novel VOCs too.[12,13] The duration of protection with vaccination however remains uncertain and further studies are needed to address this issue.

The current studies from Indian Armed Forces have looked at the effectiveness of COVISHIELD® vaccine from different perspectives and tell a promising story. Vaccination is effective in real life reducing the risk of acquiring infection, hospitalization, mortality and transmission. These studies will help add to evidence regarding vaccine effectiveness from India and promote the immunization drive, especially since future waves are expected.

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