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COMMENTARY

Robust public health evidence should concede multifactorial causation

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Abstract

The recent controversy surrounding Covishield vaccine and its rare side effects reported by AstraZeneca raises an important ethical question in public health practice. Public health ethics has not been perceived as distinct from medical ethics and by default, evidence in medicine is at times interpreted as being the same as public health evidence, when the context of practice of the two disciplines is distinct. There is a tendency in public health practice to opt for those interventions with maximum benefit to the maximum number, guided by utilitarian ethics, whereas in medical ethics the focus is on benefits vs risks. It is important to examine whether the side effects of any public health intervention can be justified against the risk it can pose to even a single healthy individual.

Keywords: *public health evidence, multifactorial causation, social determinants of health, vaccine ethics.*

Public health decisions and policy making during crises and in normal situations need to be evidence based, and this is crucial for efficient public health practice. Recently, AstraZeneca acknowledged the side effects of Covishield vaccine and withdrew the vaccine when several cases were filed against the pharmaceutical company in courts in the United States (US) and United Kingdom (UK). This has revived the unresolved debate on the policy of national governments which implemented a Covid-19 vaccine drive during the pandemic [1]. The crux of the debate is the implications of "rare side effects" of Covishield vaccine, proven time and again across different groups of people and contexts. Uncertainty about the side effects of the vaccine existed even during the pandemic, as the small sample size in clinical research was insufficient to identify side effects which are rare. The scientific community now agrees about the "rare" side effects of Covishield, estimated to be around 1 to 2 per lakh population, which is posed as beneficial against the number of lives saved [2, 3]. A recent article mentioned that 35-40 deaths per lakh population were prevented due to vaccination [4]. This is apparently based on several studies on clinical trials of vaccines carried out in clinical settings [5, 6].

Contextualising public health evidence

To measure the effectiveness of clinical intervention systematically, based on scientific reviews and on best practices across the world, evidence-based medicine (EBM) became the gold standard for clinical practice. Public health evidence is often misconstrued as similar to EBM by those from the fields of medicine and biological sciences. Best public health evidences (PHE) in India are the Home-Based Neonatal Care (HBNC) trial to reduce neonatal mortality carried out by Society for Education, Action and Research in Community Health (SEARCH) in Gadchiroli, Maharashtra [7]; the Ekjut trial in Jharkhand on the effectiveness of Participatory Learning and Action (PLA) in reducing maternal and infant mortality [8], the deployment of Mitanin in Chattisgarh as a means to improve maternal and neonatal mortality, which was upscaled for the entire country as the flagship programme of Accredited Social Health Activist (ASHA) under National Health Mission (NHM) [9], with the latest being the RATIONS trial that has demonstrated the importance of nutrition in reducing the incidence of TB and treatment outcomes [10].

What is unique in public health evidence is that there must be a community trial demonstrated in a real-life setting, which then needs to be measured for its efficacy. This is based on the core understanding of public health that reminds us that even if a biological interaction exists as a possibility between human and other species, what ultimately decides the outcome — which could be the occurrence of a disease or improvement in treatment to the extent of preventing death — are the social, political, economic, cultural, and ecological contexts of an individual and the population to which they belong. This becomes obvious when one carefully examines the results of community trials of vaccines. For instance, a study on the effectiveness of rotavirus vaccine based on pre- and post-vaccination data, reveals that there has been a decline in the positivity rate [11]. Further, a systematic review of vaccine efficacy studies on Rotavirus raises the possibility of multiple

factors contributing to the lower efficacy in low-and middle-income countries (LMICs). They could also be "due to differences in rotavirus epidemiology with the high force of infection, co-infections with other enteric pathogens, malnutrition, environmental enteropathy, interference of vaccine uptake by maternal antibodies, and co-administration of other vaccines" [12: p 4]. Another study that compares the disease characteristics of rotavirus-infected children in hospitals and in the community highlights the factors in operation at the community level that reduce severity of the disease. The proportion of rotavirus infections among the total diarrhoeal episodes in the two settings were 27.4% and 7%, respectively. Further, the proportion of breastfed children was 34.8% and 73.4% in hospital and community samples respectively, an important factor in the severity of rotavirus infection in children [13]. What emerges from the community characteristics of disease is that there are multiple factors in operation at the community level that have the potential to reduce the intensity of biological factors affecting a population. It is this understanding in public health that is popularly known as the social determinants of health (SDH) approach [14, 15]. What it implies is that even if all humans are exposed to the same biological organism, not all of them will get the disease and in situations with better living conditions, economic status, and better access to health services, the probability of getting diseases and dying of them will vary. The official recognition of this idea came globally with the World Health Organisation (WHO) report of the commission on the social determinants of health in 2008. A corollary to this novel idea is the acknowledgement of multifactorial causation of disease/health that argues that even if biological susceptibility to a disease exists as a probability, the real outcome is determined by the socioeconomic, cultural and political contexts that mediate human lives. This is the core principle of public health that gets overlooked when clinical evidence alone is presented as public health evidence.

Limits of clinical evidence in public health practice

In a linear uni-causal interpretation of evidence, it is assumed that all persons (in a population) have an equal probability of getting the disease in the context of a pandemic, as long as they are humans and exposed to the prevalent viruses. It is assumed that all those who get the disease are likely to die without any treatment (in the case of Covid-19, it was assumed that all those who are elderly will have complications). While all those who have taken vaccination, will be protected from complications and death. This assumption is premised on biological determinism, wherein human beings are only treated as one passive entity in the chain of networks of living beings [16]. When "rare side effects" of Covishield vaccine are posed as being less severe and are weighed against number of deaths prevented due to the vaccine, what is missed is the very acknowledgement of the social context of disease occurrences, its distribution and vulnerability. Here, *multifactorial causation* of diseases gets sidelined against *biological determinism.* One of the reasons why community trials of Covishield or any Covid-19 vaccine are missing in India, till date.

Clinical evidence of a vaccine or drug trial is relevant only to the point of contemplating whether it can be considered as a potential public health intervention alongside several other non-pharmaceutical interventions. What really matters in public health evidence is not the clinical evidence that shows whether the intervention is effective or not (there are hardly any interventions that are 100% effective with no side effects); but the presence of sufficient conditions (contextual factors) that are favourable to translate the clinical interventions in a real-life setting, be it a vaccine or a drug. Having clinical evidence of higher degree does not really signify that the same intervention may become the best possible public health evidence [17], as in the case of Covishield vaccine for Covid-19. Several other non-pharmaceutical interventions have worked effectively like strengthened healthcare services and community engagement, which offered effective treatment for those affected, as demonstrated in the state of Kerala and Dharavi in Mumbai, in the early phase of the epidemic [18]. Further, there were a range of health behaviours for people to adopt, from the least coercive measures to highly coercive laws and policies. These included wearing masks, hand washing, and precautions following sanitary measures and so on, which were all found effective in specific contexts in controlling Covid-19 [19, 20]. A systematic review of the social determinants of Covid-19 reveal that racial and ethnic differences, health insurance status, and neighbourhood level socioeconomic deprivation had a significant impact on Covid-19 positive status and hospital admissions, among US and UK populations. Despite having limited evidence on diverse occupations, in China, labourers, retail staff, agricultural workers, and health care workers were most represented among those infected [21].

Public health evidence for vaccines

While evaluating public health evidence, it is less significant whether the side effects of Covishield vaccine are 1 in a lakh, or in a million. The critical question is — in what way Covid-19 vaccination was different from the vaccinations that were deemed successful as a public health intervention in the past. Whether it can ensure herd immunity to people as was the case with smallpox, measles, diphtheria and so on, thus protecting a population cohort from the disease for at least 30-50 years? Second, whether every person who is vaccinated will be free from the occurrence of that disease throughout their lifetime? The answers to both these questions were in the negative for Covid-19 vaccine when it was recommended as a public health intervention [22]. Instead, the rationale was that, as we do not have an adequate health services system to cater to the treatment needs of Covid-19 patients, and to create and strengthen the health services system in a short period was impossible, here is a vaccine which promises that those who take it will have

less chances of dying. In other words, it was the fear factor triggered by the sense of "individual protection" that was the major reason for adopting Covid-19 vaccine during the crisis, with hardly any public health evidence to support it. The possibility of side effects was not highlighted by the manufacturers (conveniently), and the policy makers for want of an alternative during a crisis. Now that the evidence on side effects has become more concrete, and the fear of Covid-19 also has subsided, there are different ways of revisiting the evidence. Any form of evidence that overlooks SDH is far from qualifying as public health evidence.

Finally, from an ethical point of view, in medical practice, it might be justified to prescribe a drug with side effects to an individual patient, believing that the benefit of the drug surpasses the risk due to the disease [23]. On the contrary, when the same logic is applied to public health interventions which have "rare side effects", it is highly possible that several healthy individuals will fall victim to the side effects when applied in large population. Can any intervention be treated as a public health intervention if its application can result in side effects for healthy individuals? That is why public health evidence needs to be validated only after community trials and hence must be people centric [24]. From an ethics perspective, the utilitarian logic of accepting "side effects", in the face of serious consequences projected due to the problem, cannot be applied in public health.

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