Grappling Covishield fear in India: the urgent need for strong countermeasures to build vaccine confidence

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The Oxford/AstraZeneca COVID-19 vaccine (ChAdOx1 nCoV-19), a chimpanzee adenovirus-vectored non-replicating recombinant vaccine, has significantly managed COVID-19 globally. Of the 13 billion COVID-19 vaccine doses administered, ChAdOx1 nCoV-19 is the most widely used, reaching 180 countries and saving over six billion lives.[1] The Serum Institute of India (SII) was pivotal in producing and distributing this vaccine, branded as Covishield, which was crucial in India's contribution to the COVAX initiative, supplying vaccines to over 96 nations and UN agencies. Covishield made up over two-thirds of these contributions. In January 2021, Covishield received emergency use authorization in India, leading to a large-scale vaccination program with a national acceptance rate of 98.3%, surpassing the global average of 79.1%.[2]

Recently, however, the vaccine has been the subject of public debate and anxiety in India. This was sparked by reports of AstraZeneca's 'first time' acknowledgment of thrombosis with thrombocytopenia syndrome (TTS), also known as vaccine-induced thrombotic thrombocytopenia (VITT), as a very rare side effect in an April 2024 British High Court hearing.[3] This anxiety was further heightened by endorsements from prominent figures and the coincidental withdrawal of the vaccine from the global market due to unrelated factors.

VITT is not new! Instead, it presents an exceptionally low-risk profile (approximately 1 in 2.5 million) where the underlying mechanism remains poorly elucidated.[4] This favorable risk-benefit ratio justified the emergency use authorization granted by regulatory agencies. This decision was further supported by the findings of multiple global clinical trials, including a Phase 2/3 trial conducted within India that reported no VITT occurrences.[5] Furthermore, India's active pharmacovigilance program and the passive adverse effect reporting system integrated into the COWIN application have not documented any VITT cases to date.

Susceptibility to VITT appears to be influenced by a confluence of predisposing factors. Notably, thromboembolic events were common in the population even before the pandemic.[6] A landmark study by Hwang et al. (2021) identified specific individual risk factors associated with VITT severity, including fibrinogen levels, age, platelet count, and a history of intracranial hemorrhage (ICH) or cerebral venous thrombosis (CVT).[7] Further complicating the diagnosis of VITT is the potential overlap with long COVID, a condition characterized by similar disease manifestations.[8] With an estimated global prevalence of over 65 million individuals suffering from long COVID, definitively linking vaccination to VITT incidence becomes increasingly challenging.

Unfortunately, current news events have often overlooked these critical pieces of information. This trend risks eroding public confidence in India's robust biopharmaceutical regulatory mechanisms (Fig. 1). Such occurrences highlight the detrimental effects of misinformation on public health initiatives. Given India's prominent role as a scientific and manufacturing hub for vaccines, its public stance on vaccination significantly influences regional vaccine acceptance rates. The current focus on negative news events can potentially exacerbate vaccine hesitancy across the region, posing a challenge to implementing future vaccination campaigns.

India needs robust countermeasures to manage the spread of misinformation. Enhancing pharmacovigilance frameworks for localized risk assessment is crucial. Existing challenges such as the limited numbers of Adverse Drug Reporting (ADR) centres, technical difficulties with the ADR submission, insufficient public awareness, underreporting of ADRs, and funding constraints need to be addressed as a priority.[9] Strengthening pharmacovigilance through awareness and research can improve vaccine confidence. The exchange of best practices from other countries can significantly improve the program's effectiveness.

Effective science policy in India necessitates a robust foundation in three key areas: investment in science policy itself, rigorous regulatory studies, and fostering public engagement. However, current website-centric communication strategies, laden with technical jargon, fail to effectively engage the public, hindering capacity building in regulatory matters. Past attempts, such as UNEP-GEF-supported biosafety programs, lacked scalability, resulting in a disconnect between policy and practice.

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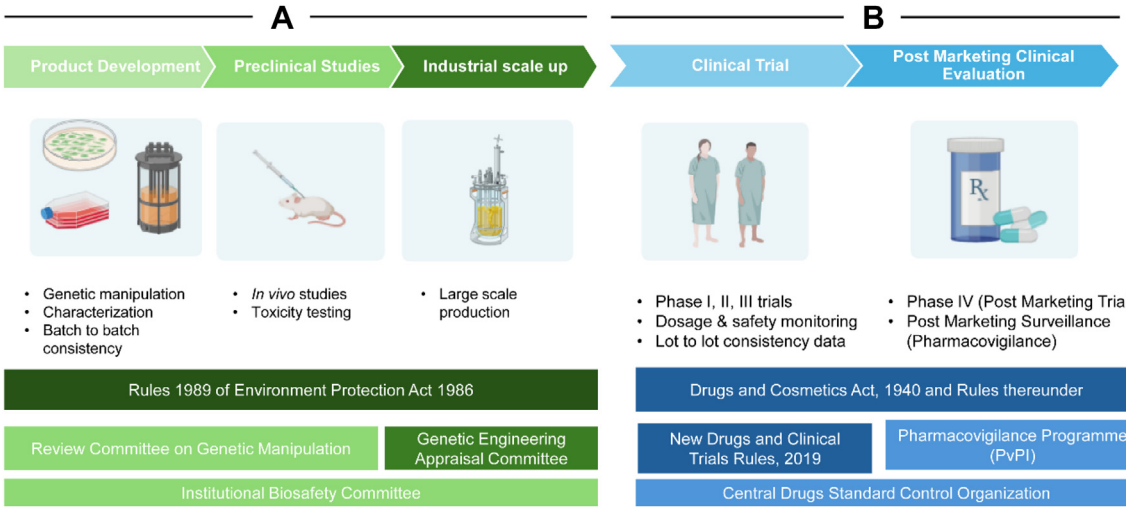

Fig. 1: **Two stage regulatory pathway for vaccine approval in India. (A)** The "Rules for the manufacture, use, import, export and storage of hazardous microorganisms, genetically engineered organisms or cells, 1989" (Rules, 1989), implement a Biosafety Risk Assessment and Risk Management (RARM) framework through three competent agencies to oversees the safety of genetic engineering employed in vaccine research and development process. **(B)** The Drugs and Cosmetics Act, 1940, and the Drugs and Cosmetics Rules, 1945, categorize vaccines as "new drugs." The New Drugs and Clinical Trials Rules, 2019 (and subsequent amendments), enacted under the 1940 Act, govern clinical trials involving human participants. Launched in 2010, India's Pharmacovigilance Programme (PvPI) is operated under CDSCO's oversight and the Indian Pharmacopoeia Commission (IPC) as the National Coordination Centre (NCC). It is operated through a network of approximately 250 ADR monitoring centers (AMCs) across states and by all vaccine marketing authorization holders (MAHs). India's pharmacovigilance system utilizes the WHO-based ADR reporting system with Vigiflow software for reporting and VigiBase as the central database for adverse events associated with medicines and vaccines. Notably, healthcare professionals are required to report adverse effects within 15 days of drug administration.

To address this, a dedicated regulatory and health information system designed for direct public engagement is crucial.[10] Furthermore, meticulously tailored communication strategies that acknowledge India's rich social, cultural, and linguistic diversity are essential. This can be achieved through multistakeholder collaboration and the promotion of responsible journalism. Establishing a specialized pool of legal professionals with expertise in scientific principles and regulatory processes would further safeguard the integrity of scientific information and mitigate public anxieties.

Contributors

AP: conceptualization, literature search, writing–original draft and revision. SRR: expert input, revision, and corrections. All authors read and approved the manuscript.

Declaration of interests

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