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Short communication

Covid-19 Vaccine Surveillance in Saudi Arabia: Opportunities for Real-time Assessment

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ABSTRACT

After months of confronting COVID-19 pandemic, several countries, including Saudi Arabia, have recently approved newly developed vaccines to prevent COVID-19 infection. With the new technology utilized to develop some vaccines, questions arise about their long-term safety. To provide rapid response to emerging safety issues, robust surveillance programs that provide near real-time analysis of vaccines effects are required. Saudi Arabia has a well-established passive pharmacovigilance system that monitors drugs and vaccines safety. However, recent development in health digitalization in Saudi Arabia may provide a unique opportunity to harvest existing resources to generate high-quality evidence. This commentary provides an overview of the available systems that can be utilized to monitor the COVID-19 vaccines' safety and discusses opportunities for data integration to improve data quality and generate real-world evidence on COVID-19 vaccine safety.

1. Introduction

Since the beginning of 2020, COVID-19, caused by the severe acute respiratory syndrome coronavirus 2, (Fauci et al., 2020, p. 19) has spread worldwide. The world health organization (WHO) declared COVID-19 a global pandemic (World Health Organization, 2020) to tackle the virus and slow down the spreading. In early December 2020, newly developed vaccines were conditionally approved by drug authorities in several countries that could halt the pandemic. The Saudi Food and Drug Authority (SFDA) reviewed the data presented by vaccine manufacturers and concluded that early results demonstrate that vaccines are safe and effective to be authorized for use in Saudi Arabia. ("Saudi Food and Drug Authority Approves Pfizer-Biontech COVID-19 Vaccine," 2020)

Given the unprecedented global effort to expedite the COVID-19 vaccine development coupling with incomplete safety and effectiveness information in specific populations such as pregnant women, new challenges emerge including short and long-term unwanted effects. Therefore, close monitoring is imperative to enable rapid responses to protect the public and ensure vaccines' benefits outweigh their risks. Besides, in a time when social media presents real-time news that permits for widespread dissemination of misinformation about vaccine safety, (Puri et al., 2020) it is essential for governments to utilize available resources for real-time analysis of any emerging safety issues to counter unproven news and maintain public trust.

In Saudi Arabia, health digitalization has been unprecedented during COVID-19 pandemic. The Saudi government launched digital applications to monitor COVID-19 cases, schedule screening tests, and notify residents if they were in the vicinity of a confirmed COVID-19 case (Hassounah et al., 2020). These efforts, coupled with precautionary interventions such as curfews, school closures, and border closures, were fundamentals to curb the COVID-19 spread (Alshammari et al., 2020). Saudi Arabia is also equipped with essential tools to monitor safety and effectiveness of approved vaccines including passive surveillance programs. However, potential opportunities are available for active surveillance that could generate near real-time analysis.

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2. Passive vaccine surveillance using spontaneous reporting

SFDA established the National Pharmacovigilance Center (NPC) in 2009 and shortly thereafter, the NPC joined the WHO International Drug Monitoring program (Aljadhey et al., 2015). The NPC receives safety reports from various stakeholders for comprehensive evaluations. Vaccine recipients, healthcare providers (HCPs) who administer the vaccine or treating patients who received the vaccine are encouraged to report suspected vaccine adverse events (AEs). The spontaneous reporting, in addition to reports submitted by pharmaceutical companies, are stored in an electronic database managed by the Saudi NPC (Alshammari et al., 2017). The main aim of AEs reporting is to provide early detection of potential safety issues empowering SFDA for interventions to minimize possible risks to ensure a favorable benefit-risk profile.

Passive surveillance systems possess limitations that inherent in spontaneous reporting restraining regulatory authorities from rapid response. AEs reported to passive surveillance systems are generally underreported (Hazell and Shakir, 2006). One of the main drivers for AEs underreporting in Saudi Arabia is uncertainty about the causal relationship between the drug and AEs. About 50% of the public do not report AEs to NPC because they are not certain whether AEs are linked to the consumed drug (Sales et al., 2017). HCPs also fail to report AEs if the causal relationship was unclear. About 45% of HCPs choose not to report AEs due to uncertainty in the causal relationship between an AE and drug use (AlShammari and Almoslem, 2018). Underreporting is likely exacerbated for delayed AEs. For instance, vaccines recipients and HCPs may not report delayed AEs because they might not believe the vaccine could have caused the AEs after a considerable time since vaccination. Furthermore, spontaneous reporting systems lack important information to assess causal relationship between a drug or vaccine and certain event, such as lack of exposure data, biases, and lack of control group (Goldman, 1998). Such challenges in passive reporting systems may limit the ability of SFDA and other regulatory authorities for early detection and proper assessment of possible risks. Therefore, alternative methods and data sources, such as routinely collected information, might be of a high relevance to mitigate the uncertainty and produce timely and high-quality evidence for emerging safety concerns.

3. Active surveillance using real-world data

An active surveillance program using real-world data (RWD) is not contingent upon voluntary reporting; thus, it may not be affected by limitations in spontaneous reporting systems. Researchers with specific safety questions could query existing RWD from routinely collected information to examine the association between certain exposure and potential risks. Active surveillance using RWD has an important potential of generating near real-time and high-quality evidence for suspected safety issues to support rapid regulatory response.

Because RWD exist for non-research purposes, careful considerations must be followed. A query must be developed as a research question with detailed protocols that comply with Good Pharmacoepidemiological Practices (GPP) to minimize the limitations of observational study designs ("Guidelines for good pharmacoepidemiology practice (GPP)," 2016). For instance, a thorough quality assessment of RWD such as measurement misclassifications and missingness evaluations should be carried out before conducting a study.

The U.S Food and Drug Administration (U.S. FDA) established the Sentinel Program to provide evidence on safety of medicines and vaccines. The program comprises various RWD sources including electronic health records (EHRs) and health insurance claims (Platt et al., 2018). In 2018, the Sentinel Program implemented rapid surveillance of the 2017–2018 flu vaccine by harvesting claims data on a monthly basis for specific safety issues (Catherine Panozzo et al., 2019). Likewise, the U.S. FDA plans to provide rapid surveillance of COVID-19 vaccine safety using RWD. The U.S. FDA identified specific safety issues, including birth outcomes and anaphylaxis, through manufacturer's documents, experience with previous vaccines and in coordination with international regulatory partners and academic experts for near real-time monitoring (Anderson, 2020). Moreover, Health Canada established the Drug Safety and Effectiveness Network (DSEN) to provide high-quality RWE of drug safety and effectiveness. DSEN utilizes RWD, including registries, EHRs and claims data, from eight Canadian provinces in addition to MarketScan claims data from the United States and Clinical Practice Research Datalink (CPRD) from the United Kingdom (Suissa et al., 2012). Furthermore, Data Analysis and Real World Interrogation Network (DARWIN) has recently been initiated to expedite drug safety and effectiveness evidence generation for European Medicine Agency (EMA) (Domergue and Candore, 2020). Regulatory agencies manage the aforementioned initiatives following the common data model (CDM) framework. CDM standardizes data inputs from various sources and facilitates data integration minimizing time and cost-related in conducting observational studies (Kent et al., 2021).

In Saudi Arabia, an active surveillance system that utilizes RWD is currently unavailable. However, the SFDA established a pilot database that receives EHRs from several hospitals using the CDM (Alnofal et al., 2020). The database is currently being developed and expected to undergo quality evaluation. Participating hospitals can collaborate with the SFDA to supply the database on a monthly basis with pre-specified information from vaccinated and unvaccinated patients. The SFDA then can establish specific queries based on experts' opinions to evaluate vaccines' safety according to approved protocols for each outcome of interest. However, the Saudi ministry of health (MOH) is currently managing the vaccine administration and data collection as a part of a national COVID-19 vaccination campaign. Consequently, hospitals' records currently lack COVID-19 immunization information limiting the SFDA central database from actively monitoring vaccine safety.

4. Importance of data integrations and governance

The Saudi MOH manages the Health Electronic Surveillance Network (HESN) which consists of all COVID-19 confirmed cases. Once a COVID-19 case is confirmed through laboratory tests, hospitals are mandated to report it to HESN. Moreover, the MOH launched a smartphone application, SEHATY, mainly for health promotion campaigns (Hassounah et al., 2020). However, the scope of the application has been expanded in 2020 to allow residents to schedule appointments for COVID-19 testing and vaccination. SEHATY also records information about COVID-19 positive individuals, and who received the vaccine and who is still scheduled to receive the vaccine (Ministry of Health, 2020). Data integrations between MOH, hospitals and SFDA will overcome the limitations of missing information such as immunization and allow for active monitoring of the safety and effectiveness of the COVID-19 vaccines. Moreover, data integration allows not only to monitor the vaccine safety and effectiveness but to build a future active surveillance program that is capable of evaluating safety and effectiveness of health interventions and provide real-time and high-quality evidence to inform decision-making.

The main challenges of data integration include data heterogeneity and data governance. The SFDA utilized the CDM framework to overcome the data heterogeneity between participating

hospitals in the central database. The CDM transforms various databases, including EHRs and health insurance claims, into a common format allowing researchers for performing standardized analysis. The SFDA may contribute to facilitating data integration between Saudi health institutions using their experience with the CDM framework. Furthermore, because health institutions store sensitive patients' data such as genomics information (Alfares, 2018), data sharing and integration have been debatable, and institutions might be reluctant to share their data. However, the Saudi Data and Artificial Intelligence Authority (SDAIA) may provide solutions to data governance. SDAIA was established in 2019 by a royal decree to lead the national data strategy (SDAIA, 2020). SDAIA, through the national information center, has established the national data bank that provides real-time data integration between government entities in addition to a cloud computing platform (DEEM cloud) ("National Information Center," 2020). DEEM, which currently hosts 153 data centers, permits data sharing between different government entities allowing for efficient digitalization of government services while ensuring high data security ("National Digital Transformation Annual Report," 2020) SDAIA initiatives may contribute to overcoming challenges of data governance between various health institutions. Overall, challenges for establishing active surveillance system using RWD in Saudi Arabia exist but recent developments in health digitalization may provide an opportunity to advance the Saudi public health.

5. Conclusion

Transforming large data to high-quality evidence requires not only data availability but also data integration, data governance, and well-designed research protocols. Recent health digitalization in Saudi Arabia brings a unique opportunity to expedite drug surveillance and retaining high-quality assessment to support decision-making. To encounter any emerging COVID-19 vaccine safety issues, data integration between government entities is encouraged to provide rapid response and maintain the benefit-risk balance

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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