



# POST-COVID VACCINATION HEARING DISORDER

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## ABSTRACT

**Introduction:** COVID-19 is an infectious disease caused by the SARS-CoV-2 virus, with vaccination as a preventive measures. Hearing loss is a side effect of the COVID-19 vaccination. Purpose: to understand side effects of the COVID-19 vaccination on hearing loss.

**Literature Review:** Post-vaccination hearing impairment may include hearing loss, ear pain, tinnitus, dizziness and vertigo. Exacerbations may occur in patients with Meniere's disease and AIED. These symptoms can be caused by hypersensitivity reactions, thrombosis, inflammation, patient anxiety or just coincidental events. There have been SSNHL events in patients vaccinated with Pfizer and Moderna.

**Conclusion:** Most of the AEFIs of COVID-19 are local, such as pain and edema at the area of injection. Hearing loss following vaccination is a rare AEFI. Impairment can be new onset or exacerbations of previously existing symptoms.

**Keywords:** COVID-19, hearing impairment, AEFI.

## INTRODUCTION

COVID-19, also referred to as Coronavirus Disease-2019, is a highly transmissible and infectious disease that has rapidly spread across the globe. It is caused by a specific type of virus called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which possesses a single-stranded RNA structure. In recognition of the significant impact and widespread nature of this disease, the World Health Organization (WHO) officially classified COVID-19 as a pandemic in March of 2020, highlighting the urgency and seriousness of the situation.<sup>1</sup>

The first cases of COVID-19 in Indonesia appeared on March 2, 2020. The cases quickly increased dramatically to 1,528 cases with 136 deaths on March 31 2020. The death rate in Indonesia at that time was 8.9% and had the highest mortality rate.<sup>2</sup> In Southeast Asia, Indonesia is ranked 13th with a total of 4.1 million cases and 139 thousand deaths.<sup>3</sup>

As stated by the Centers for Disease Control and Prevention (CDC), prevention feasible done by washing hands before touching the face, reducing contact with other people, using masks, and carrying out vaccinations.<sup>4</sup> In Indonesia, the first vaccine was carried out on January 13, 2021 with CoronaVac.<sup>5</sup>

Currently, there are four category of vaccines in circulation; inactivated virus, viral vector, nucleic acid, and protein subunit. Vaccines that are often used today in Indonesia are types of inactivated virus (CoronaVac), viral vector (AstraZeneca) and nucleic acids (Moderna and Pfizer-BioNTech).<sup>6</sup> Despite having greater advantages, Adverse Events Following Immunization (AEFI) can still occur and affect patient adherence in receiving vaccines.<sup>7</sup> AEFI is any unwanted medical event that occurs after immunization, a maximum of 42 days after vaccination.<sup>8,9,10</sup> 95.1% of the population reported non-serious AEFIs, while the remaining 4.9% reported serious AEFIs. Most of the AEFIs were in the form of allergic skin reactions (26.3%), pain, and erythema or edema at the injection site (21.6%).<sup>11</sup>

Post-vaccination hearing loss is a rare AEFI. Research conducted in the United States reported 147 cases of hearing loss from 86 million patients who received vaccines.<sup>12</sup> Another research conducted by Wichova et al. reported that hearing loss was the most common disorder found. Other complaints such as tinnitus, dizziness and vertigo are also found in a small proportion of patients. Exacerbations in patients with Meniere disease and Autoimmune Inner Ear Disease (AIED) were also reported in a minority of cases.<sup>13</sup> A study conducted in England reported otologic disorders in a subset of patients who received the

AstraZeneca vaccine. The most common complaints are tinnitus, vertigo, ear pain and hearing loss.<sup>14</sup> Formiester also reported the incidence of Sudden Sensorineural Hearing Loss (SSNHL) in post-vaccinated patients using Pfizer and Moderna.<sup>12</sup> This research aims to identify any negative impacts of the COVID-19 vaccine against hearing loss.

## Literature Review

### COVID-19

#### Definition

The etiologic agent responsible for the onset of the infectious disease known as Coronavirus Disease 2019 (COVID-19) is Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). This particular virus belongs to the family of positive single-stranded RNA viruses. It is characterized by its genetic material, which consists of a single-stranded RNA molecule. It is worth noting that SARS-CoV-2 is the specific strain responsible for the ongoing global pandemic that has affected millions of individuals worldwide. The identification of SARS-CoV-2 as the causative agent for COVID-19 has been crucial in understanding the nature and transmission of the disease, enabling scientists and healthcare professionals to develop effective strategies and measures to combat its spread and mitigate its impact on public health.<sup>1</sup>

#### Epidemiology

The first case of COVID-19 showed up in Indonesia on March 2, 2020. The number of cases quickly increased dramatically to 1,528 cases with 136 deaths on March 31 2020. The death rate in Indonesia at that time was 8.9% and had the highest mortality rate in South East Asia.<sup>2</sup>

#### Virology

The coronavirus is a type of virus that possesses a positive single-stranded RNA genome, denoted as +ssRNA, with a size of approximately 29.9 kilobases (kb). This particular virus family is further classified into four distinct genera, namely alphacoronavirus, betacoronavirus, gammacoronavirus, and deltacoronavirus, each exhibiting unique characteristics and genetic variations. Within this expansive family, the coronavirus strain responsible for the current global health crisis is identified as SARS-CoV-2, which falls under the betacoronavirus genus. The classification and categorization of SARS-CoV-2 as a betacoronavirus provide crucial insights into its genetic lineage

and helps researchers and medical professionals better understand its behavior, transmission patterns, and potential treatments. By studying the distinctive features of betacoronaviruses, scientists can gain valuable knowledge to inform preventive measures, therapeutic interventions, and public health strategies aimed at combating the spread and impact of SARS-CoV-2 and related viral strains.<sup>15</sup>

SARS-CoV-2 is formed from a nucleocapsid protein (N) which forms a capsid on the outside of the genetic material. The membrane (M), spike (S) and envelope (E) proteins attach to the lipid layer that coats the nucleocapsid. Coronavirus is also formed from 16 non-structural proteins which play a part in maintaining the life virus cycle in the host, such as the process of forming and replicating RNA.<sup>15,16</sup>

Coronaviruses can be transmitted between animals and humans. SARS-CoV-2 is naturally found in bats. Spread to person can occur through droplets or indirect contact. Droplets that contain the virus can enter the body through contact with the mucous tissues of the nose, mouth, and eyes. Several studies have reported the spread of the virus via aerosols during medical procedures.<sup>17</sup>

**COVID-19 Vaccination**

Initiation of SARS-CoV-2 vaccine started from the first genetic chain isolated on January 10, 2020 in China.<sup>21</sup> The Ministry of Health of the Republic of Indonesia (Kemenkes RI) reported eight types of vaccines that may be used in Indonesia, namely Sinovac, Sinopharm, AstraZeneca, Novavax, Moderna, Pfizer, Cansino and Sputnik V. Vaccines are administered intramuscularly at different intervals.<sup>18,19</sup>

**Vaccine Classification**

- a. Inactivated virus  
An alum adjuvant-containing inactivated viral immunization is known as CoronaVac (previously PiCoVacc) made by Sinovac. The SARS-CoV-2 CN2 chain was excavated from the Bronchoalveolar Lavage (BAL) of inpatients in Wuhan, then harvested, deactivated with -propiolactone, purified, and finally absorbed into aluminum hydroxide after being cultured in vero cells.<sup>20</sup> CoronaVac has a higher immunogenicity low compared to other vaccines, this reflects one of the shortcomings of the inactivated virus.<sup>21</sup>
- b. Viral vectors  
Both replicating and non-replicating viral vectors can be used as a medium to introduce viral genes into cells, which are then transcribed into viral proteins and delivered via MHC I to the host immune system. <sup>22</sup> ChAdOx1 nCoV19 (or AZD1222) based on the adenovirus vector developed by the Oxford University in the UK and in partnership with the Swedish-based pharmaceutical company, AstraZeneca.<sup>13</sup>
- c. Nucleic acid  
Nucleic acid vaccines are based on the principle of conveying genetic information, in addition to antigens. In the host cell, transcription and translation processes will occur to build intracellular antigen before it is expressed through the presence of MHC I. The fact that all preparations for this vaccine can be carried out in vitro without the use of any living organisms is a benefit, and independently create the main antigen, so it is expected to have the highest immunogenicity. The nucleic acid type vaccines that are currently widely used are Pfizer-BioNTech and Moderna<sup>20</sup>
- d. Protein subunit  
Recombinant protein vaccines can be generated out of a variety of expression systems using insect, mammalian cells, or yeast, without requiring the actual microorganism. Subunit vaccines

can provide a strong humoral immune effect with the support of adjuvants and the cellular-mediated memory immune system is quite uncertain, so a booster dose is needed.<sup>6, 25</sup>

**Mechanism of Action**

SARS-CoV-2's entry into host cells is influenced by the attachment of S protein to cell receptors and modification of S protein by host proteases. This virus uses ACE2 as a receptor for internalization and Type-2 Transmembrane Serine Protease (TMPRSS2) to modify protein S. TMPRSS2 will cause breakdown of ACE2 which plays a role in virus internalization.<sup>15,17</sup>

The protection provided by the vaccine works through a mechanism of virus-neutralizing antibodies. These antibodies work by blocking the interaction of the virus with its cellular receptors or by preventing conformational changes when cell membrane and the virus fuse. Most COVID-19 vaccine candidates target RBD with the aim of preventing infection by inhibiting viral attachment to ACE2. The second most frequent target is the intact S1 subunit.<sup>17</sup>

**Adverse Events Following Immunization Definition**

Based on the Regulation of the Minister of Health of the Republic of Indonesia (PMK) Number 12 of 2017 concerning the implementation of immunization, AEFI is defined as a medical event that is suspected to be related to immunization. According to WHO, Any unwanted medical event that occurs following vaccination is referred to as an AEFI, and it does not always have a direct correlation with vaccination.<sup>8,9,10</sup>

**Table 1. AEFI Symptoms**

AEFIs	Symptoms
Local reaction	<b>Mild local reaction</b> Pain, erythema and edema at the injection site measuring <1cm which appears <48 hours after immunization
	<b>Severe local reaction</b> Erythema/induration >8cm with systemic symptoms
Systemic reaction	Fever, myalgia, arthralgia, malaise and headache
Other reaction	Allergies (urticaria, edema), anaphylaxis, shortness of breath, enlarged lymph nodes, vomiting, diarrhea, seizures, muscle weakness, collapse, and syncope

**Epidemiology**

A study in Ontario in 2021 reported an incidence of AEFI of 47.9 cases per 100,000 cases with a prevalence of 0.05% of all doses administered.<sup>11</sup> Based on clinical trials conducted in China, local AEFIs were found more in inactivated vaccines such as CoronaVac while systemic AEFIs is more commonly found in mRNA vaccines such as Moderna and Pfizer.<sup>12</sup>

Post-vaccination hearing loss is rare. Research in the United States reported 147 cases of hearing loss from 86 million patients who received the vaccine. The symptoms caused vary, can be a new symptom or an exacerbation of an existing disease. Post-vaccination hearing symptoms were more common in women (63%) with an average age of 56 who were vaccinated with Pfizer (70%).<sup>12</sup>

**Diagnosis**

Diagnosis of post-vaccination hearing loss begins with anamnesis. Symptoms can appear on day zero to 21 with an average of four days after vaccination. Characteristics of the

disease such as duration, causative mechanism, presence or absence of hearing loss, type of hearing loss, vaccinations received and co-morbidities must also be asked.<sup>12</sup>

The physical examination includes inspection of the external ear for signs of inflammation, scarring and deformity. Otoloscopic examination can be done to determine the status of the external acoustic canal and tympanic membrane. Check for signs of infection, discharge, impacted ear canal, and perforation and retraction of the tympanic membrane. A tuning fork examination can be done to identify the hearing loss classification.<sup>12</sup> Pure tone audiometry aims to determine the threshold of hearing and the type of hearing loss. A study in Italy reported the importance of MRI examination to rule out possible abnormalities of the internal acoustic canal and cerebellopontine angle due to the many possible causes of post-vaccination ear disorders.<sup>7</sup>

### AEFIs Management

In serious AEFI cases, case tracking is carried out through four stages, namely tracking patients, incidents, vaccines and other people. Patient tracking begins by searching for vaccine history, previous comorbidities, and family history of similar events. Event tracking is carried out by searching for clinical descriptions, laboratory results related to AEFI, diagnosis of events, actions taken and the output of these actions. Vaccine tracking is carried out by seeking information regarding the condition of the vaccine sent, storage conditions, condition of the vaccine vial monitor, and vaccine storage temperature. The last stage is carried out by looking for other targets with vaccines and the same symptoms and investigation of immunization services. These results are then summed up to determine the link between AEFI and the vaccine given.<sup>14</sup>

In conclusion, the relationship between AEFI and vaccine administration was classified into four categories, namely consistent, intermediate, inconsistent, and unclassifiable. If the information submitted is insufficient to establish a causal relationship, AEFI is included in the non-classifiable category. Consistent categories are enforced if the causality relationship is clear. This category is subdivided into AEFIs related to vaccine products, defects in vaccine manufacturing, procedural errors, and anxiety. The intermediate category is enforced if there is a consistent relationship but evidence of vaccine causality is insufficient epidemiologically or the symptoms conflict with evidence of a causal relationship. The inconsistent category is enforced if there is a coincidental reaction or other condition due to exposure other than the vaccine.<sup>20</sup>

If a local reaction appears, both mild and severe, suggest warm compresses and paracetamol according to the recommended dose. If there is a systemic reaction, the patient may be advised to consume warm drinks, use comfortable clothes and blankets, and administer paracetamol. Management of hearing loss is carried out according to the symptoms and causes of the symptoms. An Italian study reported the consumption of corticosteroids in patients with tinnitus.<sup>12</sup>

### Post-COVID-19 Vaccination Hearing Loss

Hearing loss has been reported in several cases following hepatitis B, rabies, measles and H1N1 vaccinations. The research conducted by Wichova et al. reported that thirty out of 1325 patients who received the COVID-19 vaccination experienced new audiologic symptoms as well as worsening of existing symptoms which were experienced approximately ten days post-vaccination. Twelve patients received the Pfizer vaccine, while eighteen patients received the Moderna vaccine. The majority of patients with ear disorders (25 patients) experienced hearing loss, fifteen patients (50%) experienced tinnitus, eight patients (26.7%) experienced dizziness and five patients (16.7%)

experienced vertigo. Eleven patients had a history of ear disease, six had Meniere disease, two had Autoimmune Inner Ear Disease (AIED), and three had both of them.<sup>13</sup>

An analysis conducted on all AstraZeneca vaccine recipients until September 1 2021 reported 9752 cases of ear problems after vaccination. The most common complaints were tinnitus (3970 cases), vertigo (2135 cases), ear pain (2024 cases) and hearing loss (367 cases).<sup>14</sup> Formeister et al. reported sudden hearing loss that occurred more in women (63%) with a median age of 56 years vaccinated with Pfizer (70%). Avci et al. reported a significantly greater amount of hearing loss in patients who had previously been infected with COVID-19.<sup>12</sup>

The mechanisms underlying hearing loss after vaccination are still being questioned. Some studies report the existence of coincidental factors that occur. The research by Parrino et al. reported the possibility of a hypersensitivity reaction causing an altered autoimmune response. This response is mediated by immune complexes and antibodies against the vestibulocochlear organs that cause cell death. Local damage can then lead to vasculitis. Dysregulation of the autoimmune response can increase and cause symptoms in patients with a history of atrophy and previous autoimmune disease.<sup>7</sup>

Case reports in Greece reported Sudden Sensorineural Hearing Loss (SSHL) in 0.3% of patients vaccinated with AstraZeneca. Oldenburg et al reported a high incidence of thrombosis after administration of this vaccine. The cochlea is an organ that is supplied by only one terminal artery, the labyrinth artery, which is sensitive to thrombosis and vasospasm. Changes in the labyrinth artery and the internal auditory artery can cause circulatory disturbances and ischemia which leads to SSHL. The role of ischemia in this case was demonstrated by significant improvement in the patient's audiogram after administration of 100 mg daily aspirin after 11 days of treatment.<sup>12</sup>

Although the mechanism by which vertigo develops after vaccination remains unclear, Picciotti et al. reported the possibility of inflammation leading to decalcification and destruction of otoconia. In addition, inflammation can also cause endothelial dysfunction in brain veins which function in maintaining the body's hemodynamics. This mechanism has also been found in patients with SSHL.<sup>20</sup>

A hearing loss of at least 30 dB at three frequencies consecutively is known as sudden sensorineural hearing loss (SSNHL), based on pure tone audiometry for less than 72 hours which is usually unilateral. Most SSNHL are idiopathic. However, this disease can also be influenced by many factors such as damage to the labyrinth, viral infections such as Cytomegalovirus (CMV) and rubella, use of ototoxic drugs, genetic mutations, chronic inflammation, immune disorders, microcirculation damage and neoplasms.<sup>21</sup>

### Conclusion

Coronavirus Disease 2019 (COVID-19) is an infectious disease caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and has been declared a pandemic by WHO since March 2020. According to the CDC, prevention can be done by washing your hands before touching your face, reduce contact with other people, use masks and vaccinate. One of the primary strategies for preventing the spread of COVID-19 is vaccination. The vaccine was first carried out in Indonesia on January 13 2021 with CoronaVac, a type of inactivated virus.

Most of the AEFIs that occur are local, such as pain, erythema and edema at the area of injection. Hearing loss after vaccination is a rare AEFI. Disturbances can be in the form of new symptoms or exacerbations of previously existing symptoms. New symptoms can include hearing loss, tinnitus, dizziness and vertigo. Exacerbations may occur in patients with Meniere disease and AIED. These symptoms can be caused by

hypersensitivity reactions, thrombosis, patient anxiety or just coincidental events.

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