

#### **Review Article**

# Vaccine Hesitancy: An Old Phenomenon Still Alive in the COVID Vaccine Era

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# A B S T R A C T

With the introduction of vaccines, mortality and morbidity among children have significantly reduced. While a good proportion of the population accepts the vaccine, still a gap remains in the immunisation coverage in India. A growing number of people are delaying or refusing the vaccines. This phenomenon is called "vaccine hesitancy." In spite of the tremendous effort to develop an effective COVID 19 vaccine, a major deterrent for coverage of the same is vaccine hesitancy towards the approved and future COVID-19 vaccination. Consideration and addressing the determinants for such hesitancy is the need of the hour to surge the vaccine coverage. The databases were searched for English- language articles. The data were extracted from PubMed, Web of Science, Google Scholar databases and websites including WHO, UNICEF etc. Keywords such as vaccine hesitancy, vaccine acceptance, parents, confidence, counselling etc were used. This review was done to explore the history and factors responsible for vaccine hesitancy.

**Keywords:** Vaccination, Hesitancy, Acceptance, Parents, Immunisation

## Introduction

Vaccine hesitancy refers to the delay to accept or refuse the process of vaccination in spite of its availability.<sup>1</sup>Addressing the determinants of vaccine hesitancy is crucial for improving the vaccination coverage and thereby for the prevention of infectious disease mortality and morbidity. Immunisation and Vaccination is considered one of the greatest triumphs of public health. The mortality from vaccine-preventable diseases has shown a dramatic decline in Asia, Africa and Latin America as a result of the expansion and acceleration of the global Vaccination programme at the end of the 20th century.<sup>2</sup> The success of vaccines in the control of many diseases has been well documented in the literature. Eradication of smallpox and elimination of polio is a tell-tale victory of vaccination discovery. World Health Organization

has reported a nearly 73% drop in measles deaths from an estimated 5.36 lakhs to 1.4 lakhs between the year 2000 and 2018 globally.<sup>3</sup> UNICEF has reported that nearly 1.5 million mortality can be alleviated globally with proper vaccination.<sup>4</sup>

India has made tremendous process in the last decades in terms of control of infectious diseases. Mission Indradhanush has also been launched to amplify the vaccination coverage in the country.<sup>5</sup> It has been certified as polio-free in the year 2014 and maternal/ neonatal tetanus has been eliminated in 2015. In spite of the progress the country has made, a significant percentage of children less than 5 years of age have mortality and morbidity because of infectious diseases. UNICEF<sup>4</sup> has reported that only 65% of Indian Children get their full immunisation. According to NFHS-4<sup>6</sup>, only 63.9% and 61.3% of children aged 12 to 23 months had

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full immunisation coverage in urban and rural populations respectively. In spite of the steady progress, there is still a gap in immunisation coverage in the country which varies between the states.

#### Source of Information

The databases were searched for English-language articles. The data were extracted from PubMed, Web of Science, Google Scholar databases with the keywords like vaccine hesitancy, vaccine acceptance, parents, confidence, counselling etc. and websites including WHO, UNICEF, National Health Portal, National Family Health Survey and National Institute of Health. References from the recognised articles were also assessed for gathering relevant articles. The extracted information included statistics, definitions, policies, and recommendations.

#### **Historical Perspective**

The era of vaccination began in the year 1800 when Edward Jenner developed the smallpox vaccine. Anti-vaccine emerged alongside the emergence of the first vaccine. In spite of the deadly consequence of smallpox, reluctance for the vaccine was present.<sup>7</sup> Vaccination acts were passed in the year 1853 in the United Kingdom to make the vaccination compulsory which was also revoked because of the resistance the public showed against it.<sup>8</sup> Leagues such as Leicester Anti-Vaccination was formed and many journals and books were published on anti-vaccination in the 18th century.<sup>9</sup> Many such activities were seen in Europe, North America etc in the 18th century.

These anti-vaccination campaigns and movements begin to decline slowly in the twentieth century in the United Kingdom. With the introduction of the National Immunization Schedule in the 1950s, the acceptance of vaccination was increased.<sup>10</sup> After the 27th World Health Assembly, Expanded Programme on Immunization (EPI) was launched globally in May 1974.<sup>11</sup> In India, the Minister of Health and Family Welfare adapted the EPI against 6 tuberculosis, pertussis, diphtheria, tetanus, polio and measles. It was later modified to Universal Immunization Programme in 1985.<sup>12</sup> Although the acceptance of the vaccines has increased, the opposition for the same still existed.

#### **Determinants Contributing to Vaccine Hesitancy**

Decision-making for acceptance of vaccination depends upon a complex integration of psychosocial, cultural, cognitive and political factors. These factors can be divided into three categories.<sup>21</sup>

- 1. Lack of Confidence
- Safety, Effectiveness, Policy etc
- 2. Complacency
- Perception of low risk of Vaccine-preventable diseases
- 3. Lack of Convenience
- Accessibility, Availability etc.

#### Media

At present, internet is the main backbone for the antivaccination movement, which makes the general population believe in misinformation without questioning their legitimacy.<sup>22</sup> Group of vaccine-hesitant people set their frightening footprint since the early 2000s. Studies have shown that an alarming amount of misinformation about the vaccines were anti-vaccination messages.<sup>23</sup> Nevertheless, certain compounding factors also have an impact on social media which include spreading the disinformation intentionally. Broniatowski DA et al. have stated that Twitter bots and Russian trolls along with its foreign broadcast network, have posted several large-scale anti-vaccination messages on Western social media.<sup>24</sup> Deliberate posting of these messages may be a fragment of a wider effort to tactically challenge the public health system in both the developing and developed countries. A similar incidence has been reported in the year 2014 and 2019 in the Democratic Republic of Congo.<sup>25</sup> Deception campaigns arguing that the spread of Ebola was done by foreign medical workers, resulting in the incidence of attacks on several medical workers.

S. No.	Report	Allegation	Evidence
1.	Kulenkampff M et al. <sup>13</sup>	36 children who have been inoculated with DTP vaccine developed neurological complications.	UK Joint Commission reassured about the vaccine safety later in the year 1974 based on a large sample study. <sup>14</sup>
2.	Wakefield AJ et al. <sup>15</sup>	Temporal association between MMR and Autistic spectrum disorder	Further studies failed to find any association between MMR and autism leading to the retraction of the former study <sup>16</sup>
3.	Bernard S et al. <sup>17</sup>	Thimerosal in vaccine causes mercury toxicity expressed as autism	Further studies found that ethyl mercury in Thimerosal does not accumulate in the body <sup>18</sup>
4.	Gatto M et al. <sup>19</sup>	6 women with HPV vaccination developed autoimmune diseases	Large population studies did not find any correlation <sup>20</sup>

#### Table I.Major Vaccine Controversies leading to Anti-vaccination Campaigns recorded in Literature

#### **Religious Influences**

In 1988 an article titled "Well, You Will Think, That It Is Only a Prick?" stated that vaccination may be more than just an injection, but can result in hazardous health effects. One of the main weapons used is religious beliefs. Religion plays an important role among certain communities in decisions on vaccination. A study conducted in the Netherlands has shown that mumps outbreak happened in a specific orthodox group as most of them were unvaccinated because of their religious restrictions.<sup>26</sup> An Indian study has shown that religion is a predictive factor for vaccination hesitancy.

The Catholic Church's Magisterium debates in 2 documents, the bioethical issues regarding the outlawed sources of human biological materials. Dignitas personae expresses the dishonest origin of human biological material, establishing its opinions on the person's dignity was stressed in the documents Evangelium Vitae and Donum vitae.<sup>27</sup> The Islamic tradition prohibits the usage of certain foods (haram). Some animals are legitimate (halal) depending upon their way of death.<sup>27</sup> These issues became a problem in the usage of gelatin among medical products. The use of gelatin from halal animals is permissible. The first of the Ten Buddhist Precepts is "not taking life." According to Buddhism's essential teaching, the usage of vaccines from other life forms is debatable. It thus fundamentally forbids any act that will cause destruction to any potential life. Appropriate communication regarding the essence of theological perspectives of vaccination can avert such religious perspectives of vaccine hesitancy.

#### **Role of Public Health and Health Care Providers**

Public health system should ensure proper education of the community regarding vaccines and vaccine-preventable diseases. Proper Adverse Effects Following Immunization surveillance; Monitoring of the guidelines of storage of vaccines; Financial compensation among those who have experienced the adverse effects can gain the confidence of immunisation among the general public. The 3 main ways where the primary health care system can influence the acceptance of vaccines are:<sup>28</sup>

- Proper drafting and implementation of immunisation/ vaccination recommendations
- Vaccine policy such as mandatory school admission
- Monitoring of vaccine safety

Paediatricians and other health care providers who have frequent and direct contact with the parents play a major role in vaccine acceptance and confidence. In a study done by Berry NJ et al.<sup>29</sup> in an area with higher rates of vaccination hesitancy, the practitioners had a conflicting and challenging relationship with the patients. With the increased availability of newer vaccines and schedules, they should have upto-date knowledge regarding the same. Having abreast knowledge will help them to provide health education and clarify the vaccine concerns among the parents. Paterson P et al.<sup>30</sup> did a review of 185 articles related to vaccine hesitancy. It showed that the knowledge about the vaccine efficacy and safety will increase the confidence and prescription of the vaccines by the professionals.

#### Sociodemographic Characteristics

Certain socio-economic determinants such as education, socio-economic status, age of the mother, composition of the family have an effect on the vaccine hesitancy. Schoeps A et al.<sup>31</sup> on assessing the socio-demographic determinants' influence on the adherence to vaccination, found that poverty, education of the mother, residing area and seasonality have a greater influence on vaccine acceptance. Rahman M and Obaida- Nasrin S<sup>32</sup> in their study stated that age and education of the mother, spacing, parity, wealth and access to the vaccination site have an impact on the acceptance of the vaccines. Similarly, determinants such as race, ethnicity and immunisation card possession also have an influence. Literature has shown that mother's formal education is related to increased child survival as they possess knowledge about the immunisation's protective function and its schedule.<sup>33</sup> Immunisation program implementers should understand the prevailing socio-economic status of the region and make better efforts to address the issue.

## **Access to Vaccination Services**

Even though we have vaccines for more than nearly 20 diseases, it has been estimated that nearly 20 million infants are not properly immunised because of insufficient access to vaccines. The World Health Organisation is integrating with its partner countries to improve the vaccination coverage through "Immunization Agenda 2030". It is working to increase the fund for a reliable and safe supply system.<sup>34</sup>

# Information and Past Experiences with the Vaccination

The level of association between the awareness about vaccination and acceptance of the vaccination is not forthright. Literature has shown that parents without proper knowledge tend to deny vaccines to their children.<sup>35</sup> These pieces of literature have shown that their acceptance of vaccination was based on the recommended guidelines and conformity rather than knowledge. Nevertheless, studies have shown that parents who refuse vaccination have a lot more information.<sup>36</sup> Apart from the convenience and accessibility, past experiences with the vaccine also plays a crucial role in determining vaccine acceptance. Any undesirable encounters in the past can influence the parent's decision making related to vaccination. Fear of needles, pain and encountered adverse reactions to vaccination are considered as the barrier to vaccination acceptance. In a study done by Taddio A et al.,<sup>37</sup> it was shown that nearly

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one-quarter of the parents had needle fear making them refuse vaccination for their children as well.

#### **Perceptions and Trust**

Perceptions about the role of vaccination in maintaining health is an important factor for vaccine acceptance. Smith PJ et al.<sup>38</sup> conducted a study among the parents to assess the factors determining the delay of vaccine or its refusal. It has shown that parents who accept the vaccination were likely to agree upon the fact that vaccines are very much necessary to protect their children from diseases and that their children are vulnerable to such diseases otherwise not. Parents who are hesitant to vaccination are of the perceptions that such incidence of diseases is necessary for the children to build up their immune system, good hygiene make their children not susceptible to diseases and preferences for natural immunity. A theory, "lay theory of immunity was proposed",36 stated that vaccines when taken instead of enhancing the immune system can lead to disruption of the immune system, leading to adverse effects. Perhaps, "Too many too soon" theory is also based on these perceptions.

Perception about the vaccination is often associated with the trust in the government and public health institutions and health professionals. A qualitative study done by Benin AL et al.<sup>39</sup> stated that lack of trust was crucial for new mothers in decision making about vaccination. It should be viewed that trust is not just based on awareness/ knowledge but also based on the leap of faith and familiarity of the system.

## **COVID** Vaccine Era

As of the end of last year, mortality due to COVID-19 has reached nearly 4 million globally with nearly 200 million cases.<sup>40</sup> The flux in the COVID-19 cases can be attributed to the personal determinants like attitude and practice of relevant protective measures and viral determinants like mutations.<sup>41</sup> Reduction in the economic and health impact due to the pandemic depend mostly on the preventive measures. Hence, globally, the Government supported the scientific and pharmaceutical industry to develop safe and effective vaccines for SARS-CoV-2. Literature has shown that approximately 36% stated hesitancy towards COVID-19 vaccination in South Africa.<sup>42</sup> However, the prevalence of vaccine hesitancy varies even within Africa. A study has shown that the prevalence of vaccine hesitancy was 6% and 41% in Ethiopia and the Democratic Republic of Congo respectively.<sup>43</sup> Thus the prevalence of vaccine hesitancy not just varies between the country but also within the country, worldwide.

COVID-19 vaccination reluctance is predicted to be exacerbated by a conjunction of perilous qualms and social inclinations.<sup>44,45</sup> The COVID-19 vaccine is being supplied to the public affected due to the pandemic weariness, whereas fabrication and intrigue theories regarding the COVID pandemic and immunisation continue to circulate in popular and social media. Research was done to determine the willingness for COVID vaccine acceptance and to measure complacency and confidence of the vaccines. The results show an overall drop in vaccine acceptance as well as an increase in vaccine hesitation.<sup>46</sup> COVID-19 vaccine hesitation is linked to many of the same factors that impact vaccination hesitancy for other vaccines. Vaccine-associated characteristics, political variables, and vaccine-associated attitudes and opinions are among these factors.

The major reason for vaccine hesitancy towards the COVID-19 vaccine was lack of confidence in the effectiveness and safety of the prevailing COVID-19 vaccines. Complacency on the hazard of getting infected, busy schedule was also considered to be a factor for vaccine hesitancy<sup>42</sup> Vaccination features such as immunogenicity and period of immunity and immunogenicity are slowly gathering and will differ by the makers or demographic. This new consideration of COVID virulence and immunology, along with the remarkable pace at which vaccines are being developed, threatens to erode public trust.<sup>47</sup>

Social Media is playing a major role in global information exchange, thereby resulting in increased sharing of disinformation and far-flung opinions making it difficult to differentiate truth from false information.<sup>48</sup> Dr Tedros Adhanom Ghebreyesus, Director-General of WHO has shown his concern towards the infodemic threatening the prevailing epidemic.<sup>48</sup> Infodemic refers to "extensive information including misleading and false information in digital and physical environments during a disease outbreak." Such infodemic can result in confusion, distrust in health care authorities and challenges the public health response. It may lead to intensification or lengthening of an outbreak, as people will be uncertain about the proper preventive measures.

More recently misleading information regarding the coronavirus vaccine has been abundantly posted on social media platforms. It has been stated that<sup>49</sup> to achieve herd immunity at least 55% of the population should have been vaccinated with the novel COVID-19 vaccine. Achieving this required vaccination will be difficult with the fuelled misinformation about the new vaccines on social media.<sup>50</sup> There is false information that the virus is linked to 5G networks and the prevailing pandemic is a bioweapon or a conspiracy.<sup>27</sup> Information like these can seed cynicism and doubts about the newer vaccines making it difficult to achieve the vaccination coverage rate. A study was done<sup>22</sup> to search for misinformation in a single social media platform. This showed that nearly 24.8% of the tweets were information and nearly 17.4% had unverifiable information about the epidemic.

Efforts to develop vaccines quickly with substantial funds and distribution of vaccines with emergency usage authorisation

from the US FDA may exacerbate safety and effectiveness problems. Findings from public surveys in the United States also demonstrate the impact of political considerations on reluctance, with public suspicion heightened by a lack of faith in individuals promoting vaccination, the country of origin of the vaccine, and fears about commercial or political objectives.<sup>51</sup>

A general aversion to vaccination, misunderstandings on the lethality of COVID infection, and a desire for naturally acquiring protection have all been linked to increased hesitation. Higher levels of apprehension were also seen in the individuals with less education, the unwaged, younger populations, and particular non-dominant groups, with varying race and ethnicity who are being adversely impacted by COVID-19.<sup>52</sup>

## 5 C model

5C model was proposed which includes Confidence, Complacency, Constraints, risk Calculation and Collective responsibility as the drivers of vaccine hesitancy.53 Confidence is defined as "trust in the safety and effectiveness of vaccines, vaccination administration system and people's motivation and needs."54 Complacency means when the perception of risks for vaccine-preventable diseases are less, and hence vaccination is not considered essential.<sup>1</sup> Constraint refers to that even though people desire to get vaccinated, structural or psychological barriers prevent them from the uptake of vaccination.<sup>55</sup> Risk calculation specifies a cautious assessment of the risks of both infection and vaccination, and form a decision.<sup>47</sup> Collective responsibility means "the willingness to protect others by their vaccination, through population herd immunity". Hence when these psychological constructs are met and addressed, the vaccination coverage can be increased.

## **Recommendation and Future Directions**

Tailored approaches are essential to moving the parents towards vaccine acceptance. The involvement of trustworthy and likeable influential figures can have an impact on vaccine acceptance. Along with the usage of tailored educational materials, storytelling can result in more motivation than just providing scientific communication.

Health care providers should be confident about the updates and facts about vaccines. Proper training of the Health care workers discussing the risks and benefits of the vaccines, critical trust and support relationship between the policymakers and health care workers could bring about the increase in the capacity and confidence among them. Nevertheless, concentration should be focussed on public health policies along with the provider-patient relationship. Healthcare providers must poise a wish to preserve their relationship with the family, and their wish to deliver what they contemplate the standard of care and prevent other families in their practice. Policies that mandate immunisation for school entry can contribute to significantly increasing the vaccination rates.<sup>28</sup>

A multifaceted approach and research are needed to develop the most effective strategy for vaccine acceptance. Sadaf A et al.<sup>55</sup> in their systematic review has shown that 3 key areas to be concentrated on for effective interventions are parent-centred education, state laws and school laws. Focusing efforts on determining factors contributing to vaccine acceptance; health care visits and communities at risk of increased hesitancy rate will increase the vaccine acceptance rate.

### Conclusion

Safety assurance for vaccination is the main concern of Immunization Programme. Appropriate Surveillance, monitoring and studies concentration on the adverse events following Immunization (AEFIs) and proper dissemination of the data to the general population is highly recommended. By this means proper health education regarding the safety, expected adverse events and recommended treatment can be given to the general population.

### Conflict of Interest: None

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