

## Review Article

# Measles, mumps, and rubella (MMR) vaccine and COVID-19: a systematic review

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**Abstract:** This study was performed to investigate published literature about the association between measles, mumps, and rubella (MMR) vaccine and COVID-19. This is a systematic review in which the databases of Chocrane, Pubmed, Scopus, Web of Science as well as reliable journals including Lancet, New England Journal of Medicine, Jama and also Centers for Disease Control and Prevention (CDC) publications were searched. Out of 169 documents discovered during the literature review, 56 ones were somehow related to the association between MMR vaccine and COVID-19, of which 11 ones mentioned the association between these two, and 8 of them contained a hypothesis about this relationship. A quasi-trial study reported the positive effect of the MMR vaccine on reducing the severity of COVID-19 symptoms among those who received it. Also, a cross-sectional study showed an association between the level of Immunoglobulin G (IgG) mumps and COVID-19. Moreover, a genomic data analysis study also reported the effect of Rubella Immunoglobulin G (IgG) level on COVID-19. It seems that due to the similarity of respiratory diseases including measles, rubella, and mumps to COVID-19, MMR vaccine should be investigated more deeply to see if it is effective in order to deal with this novel disease.

**Keywords:** MMR vaccine, SARS cov 2, immunization

## Introduction

With the emergence of COVID-19 disease in the world and its transformation into a severe pandemic, the World Health Organization entirely focused on controlling it. Although many strategies have been used to control this disease so far, no big change will happen until a safe and effective vaccine is discovered [1].

Since the beginning of the pandemic, many pharmaceutical companies in different countries have started looking for an effective vaccine to protect against COVID-19, but only a few of which could successfully entered the third stage. The Pfizer vaccine can be mentioned as one of the most important of these attempts [2]. Despite the remarkable success of this vaccine, there are still concerns about its long-term side effects [3, 4].

On the other hand, studies have shown that a very small percentage of children, compared to

other age groups, are infected with SARS-COV-2, and out of these few, they mostly do not get the severe form. These circumstances were also observed in SARS and Mers disease, and children were less likely to be infected with these two viruses [5]. These results have led to formation a hypothesis expressing that immunizing children may cause a protection against severe COVID-19.

Among all the vaccines that children receive, the MMR vaccine is a one that has been considered in their routine immunization programs and is used for prevention from three viral diseases: mumps, measles and rubella [5-7]. Investigating different dimensions of the MMR vaccine in several studies have led to creation of a hypothesis that states this vaccine is associated with mild COVID-19 in children [6, 8, 9]. If the immunogenicity of this vaccine against COVID-19 is proven, it will be a big step forward to control this disease. Since this vaccine has been used for immunization in children for

many years and to our knowledge, no major side effects have been reported so far, it can be tested alongside other ones being tested against this disease.

This study was performed to review various published documents in order to investigate the association between the MMR vaccine and COVID-19 disease. In the current study, a systematic search was conducted using different databases by means of extracting the relevant documents.

### Methods

#### *Search strategy*

Databases and e-journals including PubMed, Cochrane, Scopus, Web of Science, Google Scholar, Nature, Lancet, CDC, Nejm, JAMA, were searched using keywords derived from MeSH and accessed until November 28, 2020. The search strategy was as follows: (MMR immunization OR MMR vaccine) AND ("COVID-19" OR Coronavirus OR "Corona virus" OR "2019-nCoV" OR "SARS-CoV-2"). Searching of databases was performed independently by 2 of authors (KR and SMT) and the final articles were reviewed by one of the authors (MTS). Also, reference list of published studies was evaluated to increase sensitivity and to select more studies.

In order to avoid missing any suitable article which is related to the effect of MMR vaccination on prevention from COVID-19, along with digging the articles, the references of each were also investigated and related one were selected too. Finally, unrelated articles were removed. The articles obtained from the databases were imported into the reference manager (Endnote).

#### *Inclusion and exclusion criteria*

The original studies which reported the effect of MMR vaccination on preventing COVID-19, were included into this study. The exclusion criteria were: animal trials; theoretical research; and unregistered clinical trials. Also, review articles and the articles with incomplete data were excluded from this study.

#### *Data extraction*

The key data were extracted from the articles through a researcher-made checklist which

included the first author's last name, country and the place of research, year of publication, type of study, target population, and taken actions. Data were extracted by all of the authors.

It was not possible to conduct a meta-analysis given the heterogeneity of the included trials and poor data availability. The heterogeneities that made it impossible to perform quantitative analysis were: study design, study protocol, diversity in experimental intervention groups, variety in control intervention groups, and differing primary outcomes. Consequently, the results are presented as an integrated qualitative review.

### Results

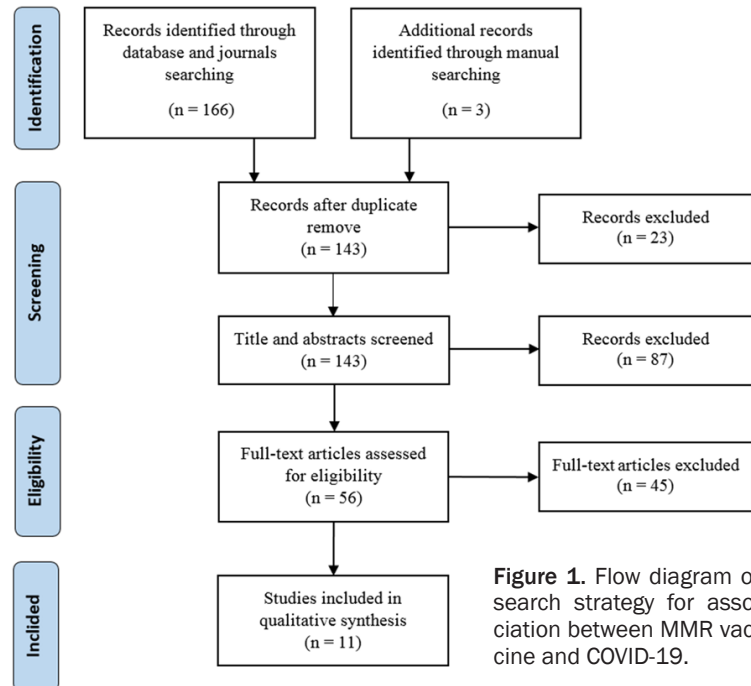
After reviewing 169 studies, 11 studies were identified that directly mentioned the effect of MMR vaccine on COVID-19, out of which 8 were Hypothesis (**Figure 1**). The study population in 7 of these literature was the whole community and for the rest, was children and people aged lower than 18 years old.

Among all of these studies, the MMR vaccine was discussed as a vaccine that can affect the normal course of COVID-19 disease. Some of them have hypothesized that the MMR vaccine may not be effective in preventing COVID-19 but may reduce its severity.

Some of these studies have also investigated Immunoglobulin G (IgG) level changes caused by MMR vaccine and its association with the severity of COVID-19. Mumps Immunoglobulin G (IgG) and rubella Immunoglobulin G (IgG) were identified as two influential factors on reducing COVID-19 severity. Also, a quasi-experimental study showed that out of the 225 people who received the MMR vaccine, only 36 got infected with SARS-COV-2 virus, all of whom had a mild form of the disease. **Table 1** shows more details about each study.

### Discussion

According to the literature, in most of published documents about the association between the MMR vaccine and COVID-19, it was discussed as a hypothesis. A quasi-trial study also found that a small proportion of people who received the MMR vaccine got COVID-19, all of which were mild. The results of these studies might



indicate a possible association between this vaccine and COVID-19, on the other hand, global reports from different countries show that children are accounted for only a small proportion of COVID-19 confirmed cases [5]. But the question is can these evidences show a causal association between the MMR vaccine and COVID-19?

Some researchers believe that if this claim about the association between the MMR vaccine and COVID-19 was true, lower prevalence and mortality rate of COVID-19 were observed in the countries with high MMR vaccine coverage, but it is still high in a country like Iran, with over 90% coverage of the MMR vaccine [10]. On the other hand, studies have shown that even in Iran with a relatively high mortality rate, the prevalence of COVID-19 infection in children aged under 16 is very low [11].

It seems that one of the reasons which may explain the low prevalence of COVID-19 in children is their high level of immunity due to receiving routine vaccines at that age. On the other hand, considering the similarity of COVID-19 to some other respiratory diseases such as measles, rubella and mumps, and the immunity followed by receiving MMR vaccine, it possibly had led to reducing the severity of COVID-19 in children [12].

All of these hypotheses have been raised at the ecological and community level, which can be influenced by Ecological Fallacy. So, these findings are based on researches on a whole community and may not be generalized individually to every member of it. On the other hand, it should be noted that other health factors in countries with a relatively high national level of childhood vaccination coverage seems to be good, too; factors such as proper nutrition, health infrastructure and primary health care that every single of them may affect the prevalence and the severity of COVID-19 [13].

To investigate the effect of the MMR vaccine on protection against COVID-19, ecological

studies just give us a clue, and individual-based studies are needed in order to evaluate this association; studies such as cohorts, case-controls, and even controlled clinical trials can be used to do so.

Several vaccines against COVID-19 have been currently approved by FDA and are being distributed over many countries. Although the effectiveness of these vaccines has shown to be very high and no serious side effects have been reported so far [6], their side effects are not limited to a few months after receiving the vaccine and they may have some delayed side effects. Given that the MMR vaccine has been using for many years in different countries around the world and it's safety is fully approved, if the hypotheses about the effectiveness of this vaccine get confirmed, it can be a turning point for preventing and controlling COVID-19.

## Conclusion

Although most of the studies which discussed the association between MMR vaccine and COVID-19 were hypothetical and ecological, due to the biological evidences and the safety of this vaccine, it seems worth examining it through clinical trial studies in terms of effectiveness, since it will not cost more than the vaccines currently proposed for COVID-19.

## MMR vaccine and COVID-19

**Table 1.** Characteristics and key results of included studies

Authors	Country of origin of study	Title	Type of Study	Study population	Key Results
Anbarasu et al. [6]	India	Vaccine repurposing approach for preventing COVID-19: can MMR vaccines reduce morbidity and mortality?	Hypothesis	Children	MMR vaccine-induced induction of interferons (IFNs) and NK cells that could prevent or ameliorate SARS-CoV-2 infection.
Saad et al. [14]	Egypt	Measles vaccines may provide partial protection against COVID-19	Hypothesis	All population	due to shared structural similarities between measles and coronavirus the cross-reactivity and immunity between the measles vaccine and coronavirus leads to partial protection against COVID-19.
Young et al. [15]	UK	Homologous protein domains in SARS-CoV-2 and measles, mumps and rubella viruses: preliminary evidence that MMR vaccine might provide protection against COVID-19	Genomic data Analysis	All population	Patients with high illness severity had high levels of rubella IgG compared to patients with a moderate severity of disease.
Fidel et al. [16]	USA	Could an Unrelated Live Attenuated Vaccine Serve as a Preventive Measure To Dampen Septic Inflammation Associated with COVID-19 Infection?	Hypothesis	All population	“trained innate immunity” delivered by leukocyte precursors in the bone marrow more effectively functioning against broader infectious attacks.
Deshpande. [17]	India	MMR Vaccine and COVID-19: A Myth or a Low Risk-High Reward Preventive Measure?	Hypothesis	All population	MMR will not prevent COVID-19 infection but could Potentially reduce poor outcome.
Shanker [12]	India	Measles Immunization: Worth Considering Containment Strategy for SARS-CoV-2 Global Outbreak	Hypothesis	Under 18 Years	A few cases was reported in children. These similarities in structural construct may play a role in eliciting immune response against coronavirus in a child previously immunized against measles.
Islam et al. [18]	UK	COVID-19, seasonal influenza and measles: potential triple burden and the role of flu and MMR vaccines	Hypothesis	Children	MMR vaccination may reduce COVID-19 Severity.
Linnemann. [19]	Mexico	Thirty-six COVID-19 cases preventively vaccinated with mumps-measles-rubella vaccine: All mild course	Quasi-trial	All population	Out of 225 subject who were received MMR vaccine, 36 people have presented COVID-19, all with a remarkably mild course.
Jeffrey et al. [20]	USA	Analysis of Measles-Mumps-Rubella (MMR) Titers of Recovered COVID-19 Patients	Cross-sectional	All population	Mumps IgG titers were inversely correlated with severity and symptom scores.
Sidiq et al. [21]	Iraq	Does Early Childhood Vaccination Protect Against COVID-19?	Hypothesis	Children	humoral immunity, created through the MMR vaccination, provides children with Advantageous protection against COVID-19.
Ashford et al. [8]	USA	MMR Vaccination: A Potential Strategy to Reduce Severity and Mortality of COVID-19 Illness	Hypothesis	All population	MMR vaccine may provide strong protection from COVID-19 spread and mortality.

**Disclosure of conflict of interest**

None.

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