



Comparative study of scientific articles on MMR vaccines published from India over the last few decades

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The MMR vaccine as we know is a vital vaccine to protect against three disease-causing microbes- measles, mumps, and rubella. To commemorate 75 years of Indian independence, the present study delves into the achievement of Indian research and lists out articles retrieved from the Web of Science Core Collection database on the domain of MMR vaccine research. The data has been restricted to the publication from India, thereby, has throwing some understanding into the MMR vaccine research in India over the last 28 years- 1994 to 2021. The data have been compared based on scientometric analysis. Qualitative and quantitative analysis have also been taken into account in order to give a comparative insight into the research. The comparison was done based on citation data, usage count data, year of publication, journals, publication media, domains focussed on the papers, and type of document. Astonishingly, in 2021, the most number of papers were published, most of them have related MMR vaccine as a potential immunity developer against COVID-19 infection. A total of 43 articles were retrieved from the search, the numbers are quite big, and the highest citation among them being 99 which was published in 2014, which is quite impressive for such a short duration of time. The comparative study suggests a positive growth of MMR vaccine research in India.

Keywords: Citation, Journals, MMR vaccine, Scientometrics, *Varicella*

The MMR vaccine is meant to give protection against measles, mumps, and rubella, also known as German measles¹. The first dose of this vaccine is generally given to children who are around 9 months to 15 months of age, the consecutive dose is given at 15 months to 6 years of age, with a gap of at least 4 weeks between the doses¹⁻³. Recent study showed that around 60% of the proportion of children aged 5-10 years lacked protective immunity against measles and about one-fourth (15-25%) were susceptible to the infection with mumps and rubella virus⁴.

MMR vaccination scheme in India is slightly different from the other developing countries, as India is not a part of the national immunization programme that consists of two dose scheduling of the vaccination programme, rather it mostly follows the state immunization programme of Delhi as a single dose between 15-18 months^{5,11}.

Commemorating 75 years of Indian independence, the Government of India has been launched an initiative - Azadi Ka Amrit Mahotsav. Through this year-long program, dedicated to the people of India, the glorious history of our people, achievements, and

culture is being portrayed. This celebration is categorised under five themes: Resolve@75, Ideas@75, Actions@75, Achievements@75, and Freedom Struggle.

India has achieved a significant foot in the field of science and technology during the last 75 years. "She" has become a world leader in certain sectors. Medicine and drug development is one such field. To achieve this global status, we had a significant advancement in basic science research, educational facilities, and infrastructure. With the aim of throwing some understanding towards the research on MMR vaccine from India, scholarly articles were retrieved from the Web of Science. Qualitative, quantitative, and scientometric analysis were taken into account to reach the conclusion.

Materials and Methods

The data were retrieved from the Web of Science (WoS) database. This database allows the users to access the data based on a subscription-mode process. Web of Science is considered to be the most impactful and reputed journal database because of its high standard of journal selection and indexing⁶. Presently, the web of science core collection has six online databases which provide citation data for many

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academy journals. WoS was created by the Institute for Scientific Information (ISI) and is maintained by Clarivate Analytics. It covers an index data from the year 1900 till the present and disciplines go across disciplines starting from the sciences, humanities, social sciences to arts⁷⁻⁹. The keywords used for this search was “MMR Vaccines” and restricted the country of search to only Indian articles. The data collected are over the years 1994 to 2021 (Fig. 1). The date of export of the current data (43 articles) is 28th February 2022. This data has been used to analyse and compare the research that has been published in and from India in the area of Mumps Measles and Rubella vaccine from 1994 to 2021.

Results and Discussions

Qualitative Analysis

The 43 studied papers are discussed here. “Low vaccine efficacy of mumps component among MMR vaccine recipients in Chennai, India” by Malaiyan J *et al.*, 2014 aimed at investigating the mumps infection in MMR vaccinated and non-vaccinated populations in Chennai by analysing the IgM antibody against mumps, IgG antibody against measles, mumps and rubella viruses by ELISA test. The study observed that the MMR vaccine failed to generate anti-mumps IgG as a result of infection of mumps resulting in vaccinated individuals¹⁰. The article, Titled “Immune response to the second dose of MMR vaccine in Indian children” by Gomber Sunil *et al.*, 2011, also investigated the efficiency of the MMR vaccine in children in India. This study showed alarming low protection against infection in vaccinated individuals¹¹. “Immunogenicity and safety of a novel MMR vaccine (live, freeze-dried) containing the Edmonston-Zagreb measles strain, the Hoshino mumps strain, and the RA 27/3 rubella strain: Results of a randomized, comparative, active-

controlled phase III clinical trial” by Sood A *et al.*, 2017, was on Immunogenicity and safety of a novel MMR vaccine (live, freeze-dried) containing the Edmonston-Zagreb measles strain, the Hoshino mumps strain, and the RA 27/3 rubella strain: Results of a randomized, comparative, active controlled-phase III clinical trial. *Human Vaccines and Immunotherapeutics* 2017; 13(7):1523-1530. This is a phase III clinical trial study that was conducted to evaluate the immunogenicity and safety of the single-dose and multi-dose formulations of a novel MMR vaccine developed by Cadila Healthcare Limited, India. The novel vaccine contained the Hoshino mumps strain was compared to an already existing MMR vaccine developed by the Serum Institute of India Limited, India, named the Serum MMR vaccine. The study was funded by Cadila Healthcare Limited, India showed that the novel Cadile MMR vaccine was non-inferior to the serum MMR vaccine¹². Article “Vaccine repurposing approach for preventing COVID 19: can MMR vaccines reduce morbidity and mortality?” by Anbarasu A *et al.*, 2020, observed an increased immune response against COVID-19 in MMR vaccinated individuals, particularly children below 10 years of age¹³. “Repurposing of the childhood vaccines: could we train the immune system against the SARS-CoV-2” by Sharma D, 2021, also observed an increased immune response against COVID-19 in MMR, BCG and OPV vaccinated individuals²⁸. Article “Uptake of newer vaccines in Chandigarh” by Gujar Nilesh, 2021, suggests that Measles Containing Vaccines (MCVs provide a good immune response against COVID 19 infection in children³². Article by Bhatnagar N *et al.*, 2014 on “Introducing Combined Measles, Mumps and Rubella Vaccine in Chandigarh, India: Issues and Concerns!” suggests Chandigarh, a state of India to provide MMR vaccine to individuals¹⁴. Article on “Evaluation of Immune Response to Measles Component of MMR Vaccine in Children with HIV Infection Receiving Antiretroviral Therapy” by Seth A *et al.*, 2016 was aimed to study the prevalence of measles antibodies in CLHIV receiving ART before and after MMR vaccine immunization. The study observed an MMR vaccine leads to an excellent seroconversion to measles component in immune-reconstituted CLHIV¹⁵. Article “A Randomized Comparative Study of MIP and MMR Vaccine for the Treatment of Cutaneous Warts” by Kaur A *et al.*, 2021 MIP compare the efficacy of MMR vaccine and MIP vaccine in curing Cutaneous warts (Cw). The

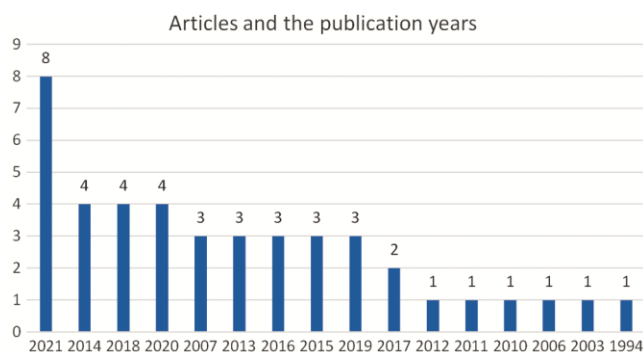


Fig. 1 — Article published on MMR vaccine from India over 1994 to 2021

results showed that intralesional injections are more effective in treating Cw compared to MMR vaccine¹⁶. Article “A comparative study of the efficacy and safety of intralesional measles, mumps, and rubella vaccine versus intralesional vitamin D3 for the treatment of warts in children” (Mohta, Alpna *et al.*, 2020) discusses intralesional injections of MMR vaccine to intralesional injections of vitamin D3 in children as a new effective treatment for cutaneous warts⁴². Article by Bavdekar A *et al.*, 2018 on “Immunogenicity and safety of measles-mumps-rubella vaccine delivered by disposable-syringe jet injector in India: A randomized, parallel-group, non-inferiority trial”, conducted a randomized, clinical, non-inferiority study of MMR vaccine administered subcutaneously by a disposable syringe jet injector in toddlers (15-18 months) in India rather than the conventional process. Bill & Melinda Gates Foundation and Serum Institute of India Pvt. Ltd. have funded the study¹⁷. “Effect of jet injection on infectivity of measles, mumps, and rubella vaccine in a bench model” by Coughlin Melissa M *et al.*, 2015 also showed that administration of MMR vaccine by the disposable-syringe jet injector is as efficient and safe as the conventional method²¹. Article “No demonstrable association between the Leningrad-Zagreb mumps vaccine strain and aseptic meningitis in a large clinical trial in Egypt” by Sharma HJ *et al.*, 2010 evaluated the claim whether Leningrad-Zagreb (L-Z) mumps vaccine strain is associated with aseptic meningitis. The study showed that Leningrad-Zagreb (L-Z) mumps vaccine is considerably cheaper than its Western competitors and had not developed any aseptic meningitis¹⁸. “A New Combined Vaccine Against Measles, Mumps, Rubella and Varicella in India” by Shah N *et al.*, 2017 on A New Combined Vaccine against Measles, Mumps, Rubella and Varicella in India tests the effectiveness of a newly launched quadrivalent MMRV (measles-mumps-rubella-varicella) combination vaccine in India- the vaccine is highly immunogenic. The study has shown results of higher fever and febrile convulsions compared to the conventional MMR+/-V when used as the first dose, but not when it is used as the second dose, irrespective of the age of the second dose. GlaxoSmithKline Biologicals had funded the study¹⁹. Article by Yadav S *et al.*, 2003, “Comparative evaluation of measles, mumps & rubella vaccine at 9 & 15 months of age” had carried out a study to evaluate the safety of the MMR vaccine in India. The result suggested the vaccine to be safe and effective

for children at 9 and 15 months of age²⁰. Article by Chauhan Payal *et al.*, 2021, on “Effect of jet injection on infectivity of measles, mumps, and rubella vaccine in a bench model” showed that MMR vaccine is effective and safe in treating mucocutaneous viral infection²². Article “Intralesional measles, mumps, and rubella vaccine immunotherapy in molluscum contagiosum: A retrospective observational study from a tertiary care centre in north India” published in 1994 by Singh R *et al.*, says that a single dose of MMR vaccine may be given in 12 months old children who are not previously Immunized with measles vaccine²³. “Long-term Seroprotection Rates Following Second Dose of Measles as MMR Vaccine at 15 months in Indian Children” by Hansashree P *et al.*, 2018 showed that a single dose of rubella vaccine may provide adequate long-term protection, but for measles, a single dose is inefficient²⁴. “Mumps Antibody Titer in MMR-Vaccinated and Vaccine Naive Children at a Public Hospital in Delhi” by Saxena B *et al.*, 2021, article “Persistence of antibodies induced by measles-mumps-rubella vaccine in children in India” by Kulkarni PS *et al.*, 2007, article “Measles Specific Immunoglobulin G Response in Children Aged 4-12 Year Who Received Two Doses of Measles Containing Vaccine in Infancy” by Kumari P *et al.*, 2021, and “Seroprevalence of measles, mumps and rubella among children in American Samoa, 2011, and progress towards West Pacific Region goals of elimination” by Mahamud Abdirahman *et al.*, 2013, also suggest a double dose of the MMR vaccine for efficient protection^{26,27,39,46}. Article by Vaidya SR and Hamde VS, 2016 on “Is it Right Time to Introduce Mumps Vaccine in India's Universal Immunization Program?” shows that according to the World Health Organization, mumps could be near-eliminated by maintaining high vaccine coverage through a two-dose strategy. The Government of India has not yet decided on the mumps vaccine. This article has reviewed the decision and so had studied the seroprevalence, virus isolation and virus genotyping research on mumps, and had investigated some outbreaks²⁵. “Indian Academy of Pediatrics (IAP) Recommended Immunization Schedule for Children Aged 0 through 18-years India, 2014 and Updates on Immunization” by Vashishtha Vipin M *et al.*, 2014 justifies that there is a need to revise recommendations about existing vaccines in regarding the recent developments in the field of vaccinology²⁹. The research article “Characterisation of mumps virus

genotype C among patients with mumps in India” by Jeevan M *et al.*, 2013 reports that genotype C may be responsible for the then increase in mumps infection³⁰. “Changes in Cytokine Profile with Immunotherapy in Viral Warts using Purified Protein Derivative, Mumps Measles Rubella Vaccine, and Mycobacterium w Vaccine” by Sil Amrita *et al.*, 2021 administered MMR vaccine to study the IL-1, TNF- α upregulation and IL-10 downregulation that confirm that cytokine milieu plays an important role in wart immunotherapy³¹. Article “Uptake of newer vaccines in Chandigarh” by Puri S *et al.*, 2007 reports that the newer vaccines in India, including MMR vaccine, are increasingly used by people in India³². This study in “Seroprevalence of measles, mumps & rubella antibodies among 5-10 years old children in north India” by Gupta M *et al.*, 2019, on “Seroprevalence of measles, mumps & rubella antibodies among 5-10 years old children in north India” was conducted in Chandigarh among 196 randomly selected healthy children (5-10 years) in order to estimate the seroprevalence of measles, mumps and rubella (MMR) antibodies among children of age 5-10 years to get an idea of prevalent immunity levels. The result of the study showed that around 60% of the proportion of children aged 5-10 years lacked protective immunity against measles and about one-fourth (15-25%) were susceptible to the infection with mumps and rubella virus. The concluded with the note that mumps vaccination may be considered to be included in the National Immunization Schedule for children. This study was funded by the Department of Science and Technology, Chandigarh and the Department of Science & Technology, India⁴. Article “Seroprevalence of Measles, Mumps, and Rubella Antibodies in College Students in Mumbai, India” by Gohil DJ *et al.*, 2016 on “Seroprevalence of Measles, Mumps, and Rubella Antibodies in College Students in Mumbai, India”, financially supported by the Serum Institute of India Research Foundation, Pune, aimed to determine the prevalence of IgG antibodies against MMR among young adults- this involved 192 healthy college students from Maharshi Dayanand College, Mumbai³⁴. “IAP position paper on the burden of mumps in India and vaccination strategies” by Vashishtha Vipin M *et al.*, 2015, reports a low rate of vaccinated individuals in India and calls for the inclusion of mumps vaccine in the National immunization program³⁵. Article “IAP perspectives on measles and rubella elimination strategies” by Vashishtha Vipin M *et al.*, 2014 showed that the first

dose of MMR/MR vaccine can be given safely at different ages of children including at 9 months of age. The second dose should also be given along with 1st DPT booster at 16-24 months of age⁴⁰. “Vaccines-safety in pregnancy” by Arora Mala, 2021 suggests that pregnant women who are not immunized earlier vaccinated should be offered MMR vaccination³⁶. Article “Serosurvey of rubella in five blocks of Tamil Nadu” by Ramamurthy N *et al.*, 2006, discusses the need of implementing a routine MMR immunization programme for under-five children and adolescent girls³⁷. The study in the article “Immunogenicity and safety of early vaccination with two doses of a combined measles-mumps-rubella-varicella vaccine in healthy Indian children from 9 months of age: a phase III, randomised, non-inferiority trial” by Lalwani Sanjay *et al.*, 2015, compared the safety and efficiency of measles-mumps-rubella (MMR) followed by MMR+varicella (V) vaccines to (1) 2 doses of combined MMRV and (2) MMR followed by MMRV, in Indian children which showed an acceptable safety profile of the vaccine in Indian scenario³⁸.

“Anti-mumps virus activity by extracts of *Mimosa pudica*, a unique Indian medicinal plant” by Malayan Jeevan *et al.*, 2013, showed the efficacy of *M. pudica* in inhibiting mumps virus genotype C⁴¹. “Indian Academy of Pediatrics (IAP) Advisory Committee on Vaccines and Immunization Practices (ACVIP) Recommended Immunization Schedule (2018-19) and Update on Immunization for Children Aged 0 Through 18 Years” Balasubramanian S *et al.*, 2018) discusses the need to revise/review recommendations regarding existing vaccines in view of current developments in vaccinology⁴³. Article “Immunization in urbanized villages of Delhi” (Chhabra Pragti *et al.*, 2007) assessed the immunization coverage of BCG, DPT, OPV, Measles, MMR and Hepatitis B vaccines in two urbanized villages of East Delhi⁴⁴. There is no standard unified global Immunization procedure to vaccinate children against Measles, Mumps, Rubella, and Varicella (MMRV), thus, in India, the measles vaccine is administered alone or as MMR at 9 months age. Varicella vaccine has not been seen to be routinely used. In view of the measles-WHO initiative, this article by Malshe N *et al.*, 2019 on “Early disappearance of maternal anti-measles, mumps, rubella, and varicella antibodies in Indian infants.” aimed to assess the validity of the current immunization age for measles as immunization age is

an important function to determine the disappearance of maternal antibodies and naturally expose the children to the pathogens. In addition, the kinetics of IgG and IgM antibodies against rubella, mumps and varicella viruses was also examined by the study accompanied by this article. The study was carried out in a tertiary care hospital care in Pune among 600 children of age ranging from 6 months to 15 months. The research was funded by GlaxoSmithKline Biologicals⁴⁵. Article by Saeedan AS *et al.*, 2018, “Effect of early natal supplementation of paracetamol on attenuation of exotoxin/endotoxin induced pyrexia and precipitation of autistic-like features in albino rats” discusses the claim of whether paracetamol (PCM) can precipitate autistic-like features when used to counteract vaccine-induced fever. Measles mumps rubella (MMR) vaccine, diphtheria tetanus and pertussis (DPT) vaccines and lipopolysaccharide (LPS) were used to induce the fever⁴⁷. The study in “Congenital B-cell Acute Lymphoblastic Leukemia with Congenital Rubella Infection” by Bagri DR *et al.*, 2019 says that congenital leukemia may be rarely associated with congenital rubella infection⁴⁸. As known, Malaria is one of the most important and prevalent infectious diseases in India. *P. falciparum* genome contains homologues to most of the components of the mismatch repair (MMR) complex. The study “Plasmodium falciparum MLH is schizont stage-specific endonuclease”, Tarique M *et al.*, 2012 reported the detailed biochemical characterization of one of the main components of MMR complex, MLH, from *P. falciparum*⁴⁹. Another study, “Single cell immune profiling of dengue virus patients reveals intact immune responses to Zika virus with enrichment of innate immune signatures” (Zhao YJ *et al.*, 2020) tested functional responses to Zika virus in the context of pre-existing dengue infection using samples from dengue patients and healthy controls from India⁵¹. Studies showed that pediatric measles vaccine which expresses dengue antigen might induce durable serotype-specific neutralizing antibodies to dengue virus⁵². Fifty to hundred million people in tropical and subtropical countries, including India are infected with dengue virus per year. Dengue infection results in approximately 25,000 deaths around the world⁵³. The article by Ajay M *et al.*, 2021, on “Seroprotection for Diphtheria, Pertussis, Tetanus and Measles in Children with Nephrotic Syndrome” concludes that children with nephrotic syndrome especially have lower seroprotective titers for diphtheria, tetanus, pertussis, and measles. The

protection can be increased by a booster dose of DPT/DT/Td and MR/MMR⁵⁰.

Quantitative analysis

Out of forty-three papers retrieved from the Web of Science Core Collection about 8 articles have been published in 2021. Years 2014, 2018, and 2020 – got 4 articles each. 3 articles were published in 2007, 2013, 2015, and 2016. Finally, in 2017, only 2 articles were published in the journals listed in the Web of Science Core Collection. The years 1994, 2003, 2006, 2010, 2011, and 2012 saw one publication each from India on the MMR vaccine.

The papers are usually categorized by Web of Science based on the research area. The categories that have been obtained by retrieving the papers are Immunology, Pediatrics, Medicine Research Experimental, Medicine General Internal, Dermatology, Infectious Diseases, Biotechnology/Applied Microbiology, Microbiology, Parasitology, Virology, Biochemistry/Molecular Biology, obstetrics-gynaecology, Pharmacology Pharmacy, Toxicology, and Tropical Medicine. The top three categories in which the most number of articles belong are- Immunology with 19 articles, Pediatrics with 16 articles, and Medicine Research Experimental with 10 articles (Fig. 2).

14 out of the 43 articles were published in open access journals and one was published in a hybrid journal. Out of the 14 papers, which were published as open access articles, six were published as Bronze articles by Green Open access journals. The others out of 14 articles were published as Gold and Green open access articles. In Gold open access journals, literature can be published in an online open-access journal⁵⁴. Whereas, in the case of Green open access journals, firstly an article is being published in any journal and later with the permission of the journal, the author(s) may self-archive a copy (pre-print) in a



Fig. 2 — Research Area of the Articles

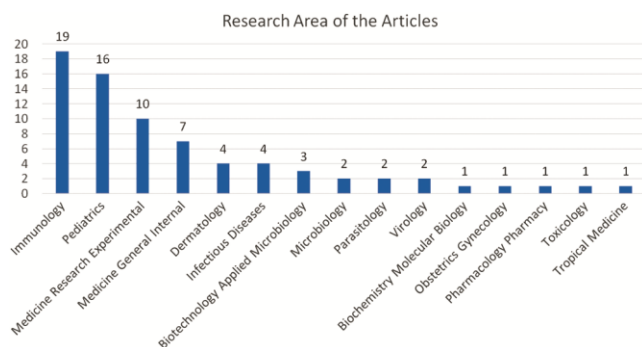


Fig. 3 — Articles published in journals and their publishers

freely accessible repository⁵⁵. Bronze open access literature are freely available, but only on the publisher page, the journal articles are free to read, but cannot be redistributed or reused⁵⁶.

One paper was published each in Human Vaccines and Immunotherapeutics, *Indian Journal of Medical Research*, and *Viral Immunology*.

Human Vaccines & Immunotherapeutics is a monthly journal covering medical research from areas in vaccines and immunotherapeutics, particularly in humans. The *Indian Journal of Medical Research* is an online open-access medical journal, which is published by the Medknow Publications on behalf of the Indian Council of Medical Research (ICMR). *Viral Immunology* focuses on research on rare, emerging, and under-studied viruses, the publisher is Mary Ann Liebert. *Indian Pediatrics* is a monthly journal published by Springer India. It focuses on the complete spectrum of contemporary clinical and basic science-related issues in the field of pediatric. It is the topmost ranking speciality journal of South East Asia, as this region is currently the focus of attention for most child health programs in the world. Over 12 articles were published in this journal. After *Indian Pediatrics* comes the journal published by Medknow Publications called *Indian Journal of Medical Research* with 6 articles. Four papers were published in Elsevier publication, the *Vaccine*. As the name suggests, the journal focuses on research articles interested in vaccines and vaccination. The journals - *Human Vaccines Immunotherapeutics* & *Indian Journal of Dermatology* from the publishers Taylor & Francis & Medknow Publications |have published 3 and 2 articles, respectively. All other journals as shown in (Fig. 3) have published one research paper each.

All the above-mentioned journals are peer-reviewed journals.

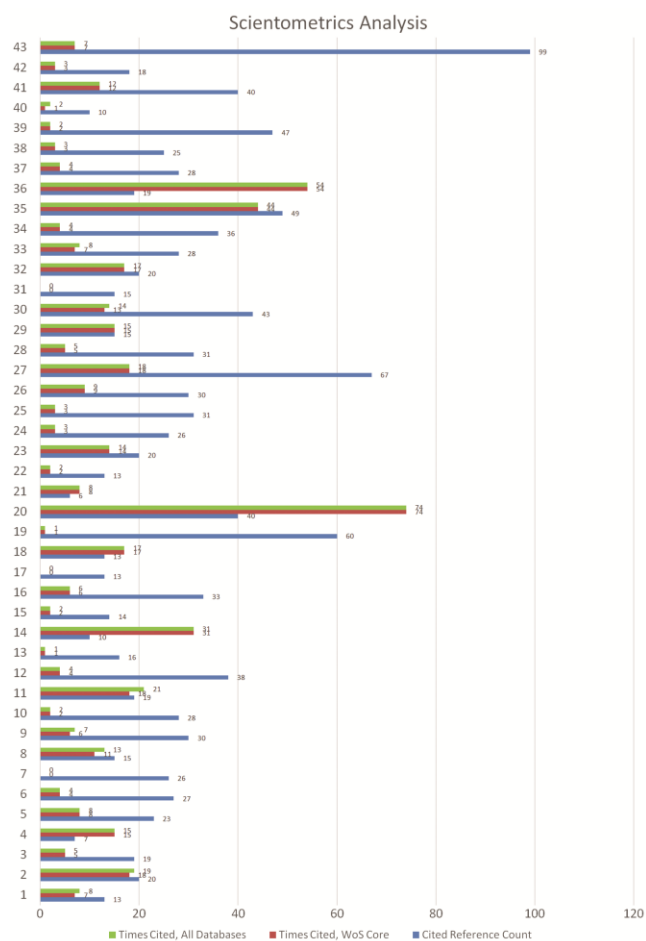


Fig. 4 — Scientometrics Analysis of the retrieved papers

Scientometric analysis

As we can see from Fig. 4, the retrieved articles have a similar pattern of the cited reference count. Article 20 have the highest times cited reference count, with a total of 74 counts as dated 28th February 2022, followed by article 36 with 54 citations and article 35 with 44 citations.

Times Cited, WoS refers to the number of times a particular article has been cited by other items from within the core Web of Science database and Times Cited, All Databases refers to the number of times a particular article has been cited by other items from within the “All Database” product of Web of Science⁵⁷.

Cited reference means the number of articles, books, works or publications that have been listed or cited by a particular publication.

180 days usage count mentions the number of times the full record has been accessed by a user in the last 180 days⁵⁷. Article 28 has been accessed 8

times during the last 6 months, followed by article 19 which has been accessed 4 times, article 24 accessed twice, and articles 4,7, and 43 were accessed 1 time during the last 6 months.

Conclusion

The present study has focused only on a very specific domain of MMR vaccine published from India, giving a comparative study in the Indian context, but there remain many specific areas that would need to be looked at closely, such as comparing the Indian data with the worldwide information. The citation indexes of the studied 43 papers ranged from 0 to 99, where gaining 9 citations over such a short period of time is quite significant. The one which got 9 citations in the WoS Core Database was published in 2014, and the three articles which yet still got none was published in 2021. Apart from the positive scientometrics results of the research articles published from India, recent studies showed an increase in the acceptance of the vaccine among Indians. The COVID-19 pandemic had opened another new dimension, researches published in 2021 showed that individuals, particularly children who were vaccinated with the child vaccines (like BCG, MMR, OPV), including MMR vaccine showed an increased immune response against the COVID-19 infections compared with non-vaccinated individuals. Researchers also showed the potential of MMR vaccine in treating cutaneous warts. The research articles studied here have accessed the efficiency of the MMR vaccine, surveyed the acceptance of the vaccine among Indians, and showed the growth percentage of Indians getting vaccinated. Some articles also suggested to include MMRV vaccine in the National Immunization Programme, which consists of two doses of the vaccine, since many study results suggest an increased immune response against mumps, measles, rubella, and varicella when vaccinated with two doses. The studies from India show an increased growth in academic research in India, particularly in the fields of immunology, pediatrics, and medicinal. In conclusion, the analytical study indicates a positive growth of vaccination-related to Mumps Measles and Rubella research in India. It is hoped that this comparative study may provide a helpful understanding of the Indian research scenario and this might be a helpful insight in a similar futuristic study.

Conflict of interest

All authors declare no conflict of interest.

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