

REVIEW

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A review of safety and immunogenicity of a novel measles, mumps, rubella (MMR) vaccine

Nitin Shaha, Apurba Ghoshb, Kishore Kumarc, Trayambak Duttad, and Manish Mahajand

^aDepartment of Peadiatrics, P.D Hinduja Hospital & Medical Research Centre, Mumbai, India; ^bDepartment of Peadiatrics, Institute of Child Health, Kolkata, India; ^cDepartment of Peadiatrics, CloudNine Group of Hospitals, Bengaluru, India; ^dMedical Affairs, Zydus Lifesciences Ltd., Zydus Corporate Park, Ahmedabad, India

ABSTRACT

Measles, mumps, and rubella (MMR) are highly infectious viral diseases affecting young children and have high secondary attack rates. Present MMR vaccines show consistent seroconversion rates for anti-measles and anti-rubella antibodies with variable responses for anti-mumps antibodies. Most common strains for MMR vaccines, currently available in India, are the Edmonston-Zagreb measles strain, Leningrad Zagreb (L-Z) mumps strain, and the RA 27/3 rubella strain. L-Z strain of mumps virus has been found to be associated with aseptic meningitis by different studies from different parts of the world including India. Recently, a novel freeze-dried MMR vaccine developed by Zydus Lifesciences (Zyvac MMR) contains Edmonston Zagreb measles strain, Hoshino mumps strain, and RA 27/3 rubella strain. The Hoshino strain is WHO approved and was found to induce interferon gamma production. This review article aims to provide a comprehensive appraisal of the data available on the safety and immunogenicity of the novel MMR vaccine.

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Introduction

Measles, mumps, and rubella are serious infectious diseases in children and associated with complications which can be severe and potentially life-threatening. 1 Measles is a highly infectious communicable disease of children characterized by fever with generalized body rash and complications such as pneumonia, ear infections, diarrhea, and subacute sclerosing pan-encephalitis, which can prove fatal.² According to the World Health Organization (WHO), the largest outbreak of measles was seen in India in 2022 with reported measles cases of 12,773 making India's goal to eliminate measles by 2023 to be impractical.^{3,4} There was a recent outbreak of measles in Maharashtra with 3075 cases and 13 deaths.⁵ Mumps mainly affects the salivary glands and is mild as compared to measles.⁶ In 2016, the Ministry of Health and Family Welfare Government of India and Integrated Disease Surveillance Program, reported 45 outbreaks of mumps from the different parts of the country. Rubella is highly contagious and it is estimated that in India about one-fifth of women in reproductive age group are susceptible for rubella infection.8 Rubella infection during pregnancy causes detrimental effects on the fetal growth including congenital rubella syndrome (CRS)⁹ and it is estimated that India has the largest burden of CRS, accounting for 40,000 cases annually. 10

Effective vaccination approaches combined with long-term high vaccination coverage can lower the risk of such highly contagious diseases, as well as the morbidity and complications that accompany them.¹¹ The MR (measles, rubella) vaccination campaign in India against measles and

rubella is the largest one in the world. In India, the coverage of measles vaccine is 89.1%, which is lesser than that of other vaccines like BCG (91.9%). This can leave a substantial number of children susceptible to the disease leading to disease outbreak. 12-14 Despite high vaccination coverage for individual vaccines, India's full immunization coverage has plateaued around 65% (Rapid Survey on Children (RSOC 2013-14) in the last few years with slow progress, thus contributing to continued high burden of morbidity and mortality in children from vaccine-preventable diseases (VPDs). 15 The elimination of measles and rubella (and in effect Congenital Rubella Syndrome) is a national health priority. To achieve the goal of providing full immunization coverage of more than 90% and to reach the goal of universal immunization program, India has launched an Intensified Mission Indradhanush (IMI) 4.0 in phases in 2022. Although the prevention of measles and rubella is a priority, according to the recommendations of FOGSI [Federation of Obstetric and Gynecological Societies of India (FOGSI)], the combination of MMR vaccine is preferred over rubella vaccine for the purpose of routine preconception vaccination. 4,16 Despite the availability of MMR vaccines, recent outbreaks of measles and a higher prevalence of mumps⁷ are alarming and warrant a broader MMR vaccination coverage in the country. The present review intends to evaluate the safety and immunogenicity of MMR vaccines, the AEFI (Adverse Events Following Immunization) associated with them (especially the incidence of aseptic meningitis) and highlight the availability of new MMR vaccines launched recently in India.

Status of MMR vaccines available in India

The recent outbreak of measles with a high prevalence of mumps and congenital rubella syndrome in India has raised the need for development of a better MMR vaccine with a favorable efficacy, and a good safety profile in order to protect against all the three infections. 17,18 According to the recommendations of the Indian Academy of Paediatrics (IAP) ACVIP (Advisory Committee on Vaccines and Immunization Practices) 2021 (which is also aligned with WHO recommendations), MMR should be administered after 9-months of age, and irrespective of the vaccination status, an additional dose of MMR can be administered to the children between 9-15 years of age. 18 As a part of catch-up vaccination, all school-going children and adolescents should receive 2 doses of MMR vaccine with 4 weeks as the minimum time interval between two doses. During an outbreak, either MMR or MR vaccine, based on availability, can be administered. 19 According to the recommendations of WHO, children should receive their first dose of the MMR vaccine between the age of 12 and 18 months. Due to programmatic factors aimed to optimize immunization coverage, the age at which the second dose gets administered can vary from the second year of life to the age at which a child starts to attend school. Although, the interval between the first and second doses must be at least one month.²⁰

Until 1992, in most parts of the world the most extensively used MMR vaccines were - (a) M-M-R II, containing the Enders Edmonston measles strain, the Jeryl Lynn mumps strain, the RA/27/3 rubella strain), and (b) the MMR vaccine containing the Schwarz measles strain, the Urabe Am 9 mumps strain, and the RA27/3 rubella strain. Both have been shown to be highly effective. However, higher risk of developing aseptic meningitis has been reported after immunization with Urabe strain than with the Jeryl Lynn strain, in fact, Jeryl Lynn strain had shown the least incidence of aseptic meningitis among all the different mumps strains used for different MMR vaccines (see Table 1)17,28,29 However, the two mostly used MMR vaccines in India contain - (i) the Edmonston Zagreb measles strain, Leningrad Zagreb (L-Z) mumps strain and RA 27/3 rubella strain – manufactured by Serum Institute of India Limited (SII) and (ii) GSK's (GlaxoSmithKline) MMR vaccine containing the Schwarz measles strain, RIT 4385 mumps strain (derived from Jeryll Lynn strain) and

Table 1. Currently distributed major mumps vaccine strains worldwide.

	Aseptic meningitis per	
Strain	administered	Distribution/Country
Jeryl Lynn	1/1,000,000 to 1/1,800,000	North America, Europe
Urabe AM9	1/28,400	Developing countries
	1/11,000	United Kingdom ²¹
Leningrad-3	1/1,000	Russia
	1.7/10,000	Brazil ²¹
	9/10,000	Croatia ²²
Leningrad-Zagreb	1/1,000	Croatia, Slovenia, India
	2.9/10,000	Brazil ²³
Hoshino	1/140,000	Japan ²⁴
	1/14,109	Iran ²⁵
	1/10,500	Korea ²⁶

Adapted from: Kitano T. Close the gap for routine mumps vaccination in Japan. Hum Vaccin Immunother. 2021 Jan 2;17(1):205–210.²⁷

the RA 27/3 rubella strain. Recently, a new MMR vaccine has been launched by Zydus Lifesciences (Zyvac MMR) which contains the Edmonston Zagreb measles strain, Hoshino mumps strain and RA 27/3 rubella strain.³⁰ Studies reported that the present MMR vaccines have shown consistent seroconversion rate for anti-measles and anti-rubella antibodies, with a variable response to antimumps antibodies and safety profile. 11,28,29 The development of antibodies against a virus depends, among other things, on the viral strain used in the vaccine. 23,31-35 All the MMR vaccines mentioned above have diverse strains of mumps virus in their formulations which could be the reason for the variable seroconversion seen for antimumps antibodies. Moreover, MMR vaccine with L-Z mumps strain was found to be associated with higher risk of aseptic meningitis when compared with non-vaccinated community. 23,32 Although the immunogenicity of GSK MMR vaccine was reported to be high and was associated with virtually no risk of aseptic meningitis, studies highlighting the usage of GSK MMR vaccines in Indian children are scarce.³⁶

Zyvac MMR, an MMR vaccine with a novel combination of already available and tested live, attenuated freeze-dried viral strains, has been developed by Zydus Lifesciences with a compact packaging and tested safety and immunogenicity profiles. ¹¹ Each dose of the 0.5 ml Zydus MMR vaccine (Zyvac MMR) contains no less than 1000 CCID50 Live Attenuated Measles Virus (Edmonston Zagreb Strain) propagated on Human Diploid Cells, 5000 CCID50 Live Attenuated Mumps Virus (Hoshino Strain) Propagated on Chick Fibroblast Cells, and 1000 CCID50 Live Attenuated Rubella Virus (RA27/3 Strain) Propagated on Human Diploid Cells. ¹¹

Methodology

This review article was conceptualized to provide a comprehensive appraisal of the data available on "safety and immunogenicity of MMR Vaccines." A Medline search updated on 09 January 2023, with search terms "MMR vaccines in aseptic meningitis" (70 hits), "MMR vaccines L-Z strain" (2 hits), "vaccines horizontal transmission" (3 hits), was conducted. Publications with relevance to safety and immunogenicity of MMR vaccine with a context to incidence of aseptic meningitis were considered of prime importance in writing this review. Articles with incomplete data and non-English articles were excluded from this review.

Ethical approval and informed consent

Ethical Approval and informed consent were not required for this review.

Safety of MMR vaccines

The MMR vaccines introduced during the 1970s contain the Edmonston Zagreb strain as the measles component, L-Z as the mumps component, and the RA 27/3 as the rubella strain. Although L-Z strain is an immunogenic and efficacous strain, adverse event following immunization such as aseptic

meningitis (which is ususally mild and self limiting) have been reported.^{23,32} Though effective vaccination programs with the optimum vaccine coverage has been implemented in various countries, a complete elimination of MMR is still not acheived. The reasons for the same include societal factors, poor surveillance systems, lack of vaccine supply, primary and secondary vaccination failure, mismatch of viral strain between which is available in vaccine and which is present as wild type, and waning immunity, apart from the existence of adverse effects associated with the vaccine. We discuss safety and immunogenicity of MMR vaccine containing the L-Z strain which was used in observational studies and large scale vaccination campaigns. Introduction of MMR vaccine was believed to have resulted in a decline in the incidence of measles, mumps, and rubella infections. However, studies suggest the reemergence of mumps infection worldwide in the vaccinated populations. It was proposed that the reason for this reemergence was poor efficacy of MMR vaccine. Malaiyan et al. 31 aimed to investigate mumps infection in MMR vaccinated and non-vaccinated populations in Chennai, India, in 2014. A total of 74 serum samples from suspected mumps cases were collected over a period of 16 months (July 2011 to November 2012) from Sri Ramachandra Medical College and Research Institute and V. K. Nursing Home, Chennai, India. Out of these 74 subjects, 42 were pediatric patients, aged less than 12 years of age. Sixtyseven (91%) patients had received one dose of MMR vaccine with L-Z strain while the others were not vaccinated. All these subjects were investigated for IgM and IgG antibodies for mumps. Results for mumps IgM in vaccinated cases indicated that all samples (100%) tested were positive, whereas 57 of 67 (85%) samples were negative for mumps IgG. These facts narrated that one dose of MMR vaccine failed to offer sustained active immune protection in vaccinated individuals against breakthrough mumps infection and also ascertains need of 2nd or even 3rd dose of MMR vaccine as is recommended by the Indian Academy of Pediatrics^{18,19} and certain parts of USA during outbreaks (3rd dose given to adolescents and young adults).7 It is already mentioned that Aseptic meningitis is one of the most challenging post vaccination adverse effects that was identified successively in three Brazilian studies. 21,23,32 In a large public immunization campaign in Brazil²¹ involving 590,609 people, 1.7 cases of Aseptic meningitis per 10,000 doses was observed. The vaccine utilized was Leningrad-3-Zagreb mumps strain, Edmonston-Zagreb measles strain, and RA 27/3 rubella strain and the most common clinical findings that were reported include severe headache with meningismus (92.5%), fever (87.5%), nausea/vomiting (82.5%). Also, three cases developed mild mumps. The journal "Vaccine" reported that the risk of vaccine-related mumps and meningitis was also seen in two mass immunization campaigns in two states in Brazil,32 in which L-Z mumps strain was used. Increase in the incidence of the vaccine-related meningitis and mumps were observed in both the states three weeks after the vaccination campaign.²⁹ Wild mumps meningitis cases for 3 years following vaccination were nil compared to 16 in previous 2.5 years. Annual incidence of mumps reduced from 115/100,000 to 8/100,000 [93% (86–96)].²⁹

To assess the risk of aseptic meningitis following immunization with mumps vaccine in the United Kingdom, where both Urabe and Jeryl Lynn strains have been used, pediatricians were asked to report to the British Paediatric Surveillance Unit about all confirmed and suspected cases of aseptic meningitis.³⁷ Miller et al.³⁷ 1993, reported in Lancet about the incidence of Aseptic Meningitis to be 4-fold higher with Urabe strain of mumps vaccine compared to Jeryl Lynn strain. The study confirmed that the true risk with the Urabe strain was substantially higher than suggested by case reports from pediatricians, probably about 1 in 11,000 doses as compared to Jeryl Lynn which was relatively much safer. However, the possibility that the aseptic meningitis induced by vaccination was largely asymptomatic and a chance laboratory finding in children investigated for other clinical conditions, particularly febrile convulsions, could not be excluded.³⁷

As reported by Tesovic et al. 22 from the University Hospital of Infectious Diseases, Zagreb, Croatia, the incidence of vaccine-associated meningitis was found to be 9 per 10,000 doses in subjects vaccinated with the Leningrad-3-Zagreb mumps strain. Out of a total of 50 cases of aseptic meningitis reported, the median age of the patients were 14.1 months (10 months to 6 years). 36 (72%) were males; all were febrile, although the median duration of fever was only 4 days (2-9); 46 (92%) vomited; 4 had bilateral parotitis; and 7 (14%) had convulsions. Cerebrospinal fluid samples were obtained from all patients and showed a median leucocyte count of $642 \times 10^6/L$ with predominantly mononuclear cells. 22 In contrast to all the studies mentioned so far, a prospective, post marketing surveillance study that was conducted on 453,119 Egyptian children to address the causal relationship of L-Z mumps strain with occurrence of aseptic meningitis. Upon vaccination with L-Z strain, not a single case of adverse event following immunization was noted, although, the study had many limitations like it was not a double blind but an open label trial, the control groups were with slightly dissimilar ages, adverse events were not checked daily but on a pre-set time point.³⁸

This should be interesting to mention here that different studies reported horizontal transmission of the L-Z mumps vaccine virus. Atrasheuskaya et al.³⁹ reported that children from Belarus who were the source of transmission had been vaccinated with MMR vaccine that contained L-Z mumps virus. The etiology of all seven contact cases was confirmed by epidemiological linking, serology and by F, SH, NP and HN mumps virus genes sequencing. In a prospective, observational study conducted in Croatia, 16 patients with clinically evident parotitis were seen, of whom four were suspected of becoming infected by a horizontal transmission of mumps vaccine strain. 40 Similarly, Vukić et al. 41 reported that in Croatia, a 14-month boy vaccinated with MMR vaccine containing L-Z strain developed unilateral parotitis. It was found that six weeks later his 32-year-old mother developed unilateral parotitis and meningismus.

Santos et al.⁴² compared the incidence of adverse events following the administration of three commercially available MMR combination vaccines. In this, randomized double blind controlled trial, MMR vaccine containing Edmonston-Zagreb, L-Z, and the RA 27/3 strain was administered to 2,226 students aged between 6 and 12 years. It was identified that compared to other two commercial vaccines, MMR vaccine containing the L-Z strain had a higher risk of causing parotitis and

lymphadenopathy and vaccine related aseptic meningitis was identified in one child receiving this vaccine.

The details of different mumps vaccine strains that are available worldwide is described in Table 1.

Advent of new MMR vaccines

Zydus Lifesciences limited developed a freeze-dried novel MMR vaccine (Zyvac MMR) that contains the Edmonston Zagreb measles strain, the Hoshino mumps strain, and the RA 27/3 rubella strain. In this MMR vaccine, for the first time the mumps Hoshino strain was combined with the Edmonston Zagreb measles strain and RA 27/3 rubella strain, making it a novel combination. The Hoshino strain of mumps is WHO approved and is a part of monovalent mumps vaccine in Japan and used in MMR formulations in Iran and Japan for more than 25 years. 25 Hoshino mumps strain has been used in 700,000 doses in pediatric immunization program of Japan and no cases of aseptic meningitis has been reported. 43 Both the single dose and the multi-dose formulations of the Zyvac MMR vaccine were found to be safe and immunogenic in the preclinical, phase 1 studies in adult subjects, and non-comparative phase 2 studies in the pediatric group. 11,43 Zyvac MMR finds its mention of purple book of latest IAP ACVIP guidelines, 2022.

Safety and immunogenicity of MMR vaccines with Hoshino as mumps strain

Nakayama et al.44 analyzed the MMR vaccine with Hoshino strain for mumps in 229 children (1-5 years) containing measles AIK-C strain, mumps Hoshino strain, and rubella Takahashi strain. It was identified that the vaccine induced a high seroconversion rate and induced a cellular immunity against each of the viruses in 90% of the subjects via production of virus specific Interferon Gamma (IFN-y). It was observed that mumps Hoshino specific IFN-γ was produced 14 days post-vaccination and significant correlation was found between serum antibody and IFN-y production six weeks post vaccination for both AIK-C measles strain and Hoshino mumps strain. Similarly, in a two-year stratified random sampling study conducted in Iran⁴⁵ involving 338 children aged 3-18 years, the immunogenicity and efficacy of Hoshino strain of mumps (in the MMR vaccine) was evaluated. It was identified that 86.1%, 77.7% and 75% of seroconversion rates were observed at 3, 12, and 24 months after vaccination, respectively. Makino et al. 46 conducted a study involving 1369 healthy Japanese children (8 months to 18 years) to evaluate the safety and immunogenic responses of trivalent virus vaccine (measles AIK-C strain, mumps Hoshino strain, and rubella Takahashi strain). Interestingly, 96.3% seroconversion rate was also observed for Hoshino strain of mumps virus, along with reporting of no significant adverse event. This study also establishes both the immunogenicity and safety of Hoshino strain in children of 8 months onwards till 18 years of age. However, in Iranian studies published, risk of Parotitis with Hoshino MMR was 8/139 (0.8%) in Makino study and 1.7-5% in Iran studies. Risk of aseptic meningitis in Korea in Moran cross-over study was 1:10,500 doses with Hoshino and Urabe vaccines.

Safety and immunogenicity of the novel MMR vaccine in the Indian settings

In a phase 2 clinical trial, 43 the immunogenicity and safety of a single dose and multi dose formulations of MMR vaccine containing the Hoshino mumps strain were evaluated in 123 healthy Indian children (15-18 months of age). It was observed that the seroconversion rates for anti-measles and anti-mumps antibodies were 100% and for anti-rubella antibodies, it was 98.9% following MMR vaccination.

In a phase 3 clinical trial¹¹ involving 328 subjects aged 15-18 months, the immunogenicity of single dose and multidose formulations of the novel freeze-dried MMR vaccine was evaluated. The patients were randomized to receive either the Zydus or SII MMR vaccine. The proportion of subjects seropositive for anti-measles antibodies was 100% (in both groups), anti-mumps antibodies (94.5% vs 94%), and antirubella antibodies (95.5% vs 91%). The post immunization geometric mean titers obtained for Zydus MMR vaccine was mIU/ml (CI: 2066.9-2684.3), 41.4 EU/ml 2355.5 (CI: 35.4–48.4), and 73 IU/ml (CI: 57.0–93.5) for anti-measles, anti-mumps, and anti-rubella antibodies respectively. The post immunization geometric mean titers for the SII MMR vaccine in the comparator arm were 1448.1 mIU/ml (CI: 1223.4-1714.0), 52.6 EU/ml (CI: 41.0-67.6) and 53.6 IU/ml (CI: 34.7-82.8), respectively for measles, mumps and rubella. The titer levels were significantly higher for measles in the Zydus MMR as compared to Serum's MMR vaccine, p < .05(Figure 1). It was observed that the MMR vaccine with Hoshino strain was non-inferior to Serum MMR in terms of immunogenicity and both the vaccines were well tolerated (Figure 2).

Discussion

Measles, mumps, and rubella contribute to significant morbidity and mortality. The present review intended to evaluate the safety and immunogenicity of MMR vaccines in which different strains of viruses have been used.

The MMR vaccine offers excellent protection against measles, mumps, and rubella viruses, as well as against the complications brought on by these illnesses. A combined measles-mumps-rubella vaccine is tested to check the safety, immunogenicity, effectiveness and has the clear practical benefits of streamlining the pediatric immunization schedule, lowering costs, and reducing the number of physician-patient encounters.²⁰ In a systematic review conducted by Pietrantonj et al.¹⁷ it was identified that MMR vaccines are effective in preventing the infection of children by measles, mumps, rubella, with no evidence of an increased risk of autism or encephalitis and a small risk of febrile seizure. In countries with well-established effective childhood vaccination programs and high levels of vaccination coverage, routine mumps vaccination is advised.

Gidengil et al.47 conducted a systematic review to understand the safety of vaccines recommended for children, adults, and pregnant women in the United States where

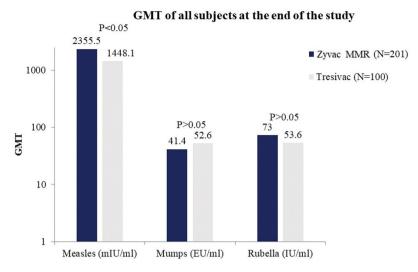


Figure 1. Post immunization geometric mean titers (GMT) of anti-measles, anti-mumps, and anti-rubella IgG antibodies (adapted from: Sood A, Mitra M, Joshi HA, et al. Immunogenicity and safety of a novel MMR vaccine (live, freeze-dried) containing the Edmonston-Zagreb measles strain, the Hoshino mumps strain, and the RA 27/3 rubella strain: results of a randomized, comparative, active controlled phase III clinical trial. Human vaccines & immunotherapeutics. 2017;13(7):1523–1530)¹¹.

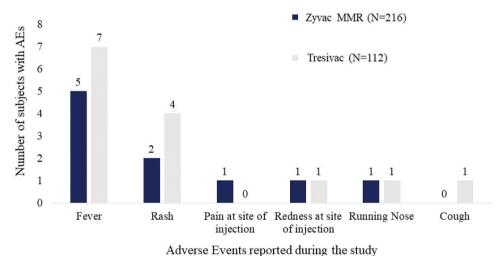


Figure 2. Adverse events reported post MMR vaccination in the Zydus and Serum Institute of India group. (adapted from: Sood A, Mitra M, Joshi HA, et al. Immunogenicity and safety of a novel MMR vaccine (live, freeze-dried) containing the Edmonston-Zagreb measles strain, the Hoshino mumps strain, and the RA 27/3 rubella strain: results of a randomized, comparative, active controlled phase III clinical trial. Human vaccines & immunotherapeutics. 2017;13(7):1523–1530)¹¹.

high strength of evidence was found for no increased risk of autism following MMR vaccination in case of children. The study also concluded that adverse events following vaccination should always be weighed against the protective benefits that a vaccine provides. A variety of combinations of strains of Measles, mumps and rubella viruses has been used to develop the trivalent MMR vaccine, worldwide. Most commonly, the Edmonston-Zagreb measles strain and the RA 27/3 rubella strain are combined with the L-Zagreb mumps strain. At the same time, Hoshino strain of mumps has also found to induce interferon gamma production, which is corelated with antibody production against mumps. 48 According to the WHO position paper 2007, the Hoshino strain of mumps was reported to possess immunogenic properties similar to the Urabe Am9 strain. 49 Over time, it has been clear that the monovalent and trivalent MMR vaccines containing the Hoshino mumps strain are both immunogenic and safe comparative to the L-Zagreb

stain.46 Although, since more than 25 years ago, the Hoshino strain of the mumps has been included in a number of monovalent and trivalent MMR vaccine formulations sold in Japan, and Iran, this has not been used in the Indian population.

Zyvac MMR vaccine is an indigenously developed MMR vaccine that offers protection with triple advantage like comprising a novel combination of already available and tested strains, efficacy, and safety and compact packaging. The Edmonston-Zagreb measles strain was found to be non-inferior to schwarz⁵⁰ and AIK-C strain⁵¹ and the Hoshino strain of mumps has a history of 25 years of global usage and has been checked for its safety in 700,000 children in Japanese community health vaccination records. 46 The RA 27/3 strain for rubella is the most accepted strain in terms of immunogenicity, safety, and tolerability.⁵²

A phase III clinical trial conducted to evaluate the immunogenicity and safety of the Zydus MMR vaccine and compared it to the MMR vaccine of SII, in healthy pediatric subjects aged 15-18 months, found that the MMR vaccine with Hoshino mumps strain was non-inferior to the Serum MMR vaccine with respect to the proportion of subjects seropositive at the end of the study and the seroconversion rates for all three viral strains. 11 In this study, the safety profiles of the two vaccines were comparable. However, past research has indicated that infants who received the MMR vaccine may develop aseptic meningitis, the occurrence of which has been linked to the L-Z mumps strain as well as other strains for mumps such as Urabe and Hoshino and to some extent even JL strain. 44 In spite of administering a standalone mumps vaccine containing Hoshino strain to children in a real-world pediatric immunization programme in excess of 700,000 doses, no cases of aseptic meningitis were detected, according to a prior report from Japan. 46 More than 14,000 children aged 12 months and 29,000 children aged 4–6 years were tested in Iran²⁵ and for the safety of the MMR vaccine with the Hoshino mumps strain, and it was identified that the incidence rates of adverse events following immunization (AEFI), especially the incidence of aseptic meningitis, were similar to the rates of AEFI reported in other studies. This is to be noted here that the incidence rates of aseptic meningitis found in Japan, ²⁴ Iran²⁵ and Korea²⁶ are 1 in 140,000 doses, 1 in 14,109 doses and 1 in 10,500 doses of MMR vaccine containing Hoshino or Urabe strain of mumps virus.

Conclusion

Routine vaccination is recommended by IAP against Measles, mumps and Rubella with effective childhood vaccination programme as lack of same may result in an epidemiological shift in the incidence of these diseases to older age groups leading to serious disease burden. A novel MMR vaccine that contains the Edmonston Zagreb measles strain, the Hoshino mumps strain, and the RA 27/3 rubella strain has been recently launched in India with Phase 3 non-inferiority to a standard reference WHO PQ MMR vaccine and finds its mention in the MMR vaccine section in the latest "Purple book of Immunisation Guidelines," published by IAP ACVIP, 2022. The Hoshino strain is WHO approved, finds its mention in the latest "WHO position paper of Mumps vaccines" and is a part of voluntary monovalent mumps government vaccination program in Japan. 700,000 doses containing Hoshino mumps strain were used in pediatric immunization program of Japan and no cases of aseptic meningitis were noted, providing evidence for its safety. Although MMR vaccines with Hoshino mumps strain seem to provide promising results, the efficacy and safety of these need to be validated in larger immunization programs, thus, Zydus Lifesciences is planning for a post-marketing surveillance study in India in near future.

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Disclosure statement

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Author contributions

NS: Contributed to conception and design; drafted manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

AG: Contributed to conception and design.

KK: Contributed to the acquisition and drafting.

TD: Contributed to conception and design; drafted manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

MM: Conception, critically reviewed the manuscript and provided final approval.

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