REVIEW ARTICLE

Global Resurgence of Mumps Outbreaks: Causes, Vaccine Challenges and Special Reference to India

Jayakrishnan Thayyil[1*], Jeeja Mathummal Cherumamnalil[2], Sruthikrishna Punathukandi[3]

[1,3]Department of Community Medicine, KMCT Medical College, Calicut, Kerala, India
[2]Postgraduate Studies and Research, KMCT Medical College, Calicut, Kerala, India

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ABSTRACT

Background: Traditionally mumps was perceived as mild childhood self-limiting disease. But it's resurgence with demographic shift, affecting increasing proportion of young adults irrespective of their vaccination status raised concerns among public health experts. In these contexts, with the aims to synthesize evidence on cause of mumps resurgence and evaluate policy options for India a review was done.

Methods: An online database search was performed which include PubMed, Embase, Scopus, World health organization (WHO) and governments portals during 1st July 2025 to 30th August 2025. Articles published in English from Jan 2000 to December 2024 were included. After selecting the articles, potential information related to epidemiology and vaccine effectiveness, waning of Immunity etc. were extracted and classified into categories and results were summarized.

Results: During recent years mumps outbreaks are known to occur periodically from several countries from east and west irrespective of the vaccination status was due to waning of immunity. It was understood that there is a mismatch between currently circulating wild strains and vaccine virus strains and studies and evidence are scarcely available about their cross protection. It was seen that in outbreak situation the VE lower than non-outbreak situation. To know the duration of protection offered by the third dose no study has yet been done.

Conclusion: There are evidence gaps in protective efficacy of MuCV to prevent current outbreaks among young adult population. In India MuCV should be introduced universally in phased manner after cost effective studies and intensifying mumps surveillance system in the country.

Keywords: Mumps, Waning immunity, Vaccine failure, Herd immunity, MMR vaccine

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***Correspondence:** Dr. Jayakrishnan Thayyil (Email: drjayakrishnanthayyil@gmail.com)

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Introduction

Mumps is a public health problem worldwide caused by mumps virus (MuV), which replicates in upper respiratory tract and spread by direct contact with respiratory secretions, saliva or through fomites.[1] The virus primarily infects the salivary glands, causing pain, tenderness and swelling in one or both parotid glands. Mostly children at the young age group are affected. It can involve older age groups also but as age advances, this disease becomes more severe.[2] Infection may be clinical or subclinical.[3] Most of the cases are self-limiting but complications such as orchitis, ovaritis, pancreatitis, meningoencephalitis, thyroiditis, neuritis, hepatitis, and myocarditis may develop in some cases and mortality was rare ,<0.01 in most settings.[4-6] Since due to high rate of transmission (Basic reproduction rate R0 estimate vary from 3-10 depending on setting)[5] and morbidity affecting children vaccination is recognized as the best way to prevent mumps.[5]

The mumps vaccine (MuCV) was first licensed in the United States (US) in 1967 and in 1971 it was included as a component of the trivalent measles, mumps, and rubella (MMR) vaccine as single dose.[7] Within ten years after the introduction of the single dose mumps vaccine (MuCV) more than 95% mumps cases were reported to be reduced.[8] Later due to out breaks among children in vaccinated communities' second dose was added in schedule from 1989.[9] By 1990s widespread use of two doses of MuCV markedly reduced mumps incidence among school children[4] and by 1996 Finland become the first country in world to eliminate indigenous mumps.[4,10] By 2024 around globe 124 countries have included this MuCV in their national immunization schedule as two doses.[11] In countries where MuCV was introduced and sustained high coverage the MuV circulation stopped and the incidence has dropped tremendously. In others where MuCV was not introduced universally the incidence of mumps remains high, mostly affecting children below 10 years.[12]

Though progress have been made in the use of vaccine up take, after late 1990s mumps out breaks has been on the rise. Regardless of long existence of vaccine use US, Canada, Australia, and few European countries, have reported large outbreaks of mumps.[4] As reported in several high income countries the peak of age specific attack rates shifted from young children (5 to 15 years) to young adults (18-24 years) and the cyclic trend occur in 5-10 years intervals.[5,12] In others including India where MuCV were not universalized, it occur in 3 to 4 years intervals in various levels according to their herd structure, population immunity, density and force of infection.[13] Most outbreaks were reported among young adults at close settings in schools and colleges. Following these resurgence first group of countries had switch over to an extra third dose to their older children and in countries like India where MuCV is not introduced in routine immunization program, the health professionals are demanding to the governments to include MuCV in routine child immunization program.[5,13,14] The Indian Association of Pediatrics (IAP),[15] Kerala state government have demanded ministry of health government of India to include MuCV in universal program of immunization (UIP).[16]

Contrary to the old perception of mumps as mild disease affecting children the sudden resurgence showing an unexpected demographic shift, affecting increasing proportion of young adults irrespective of their Vaccination status. These raised concerns among public health experts, health care professionals, government agencies and policy makers.[14] Public health experts recognize the existing substantial knowledge gaps in the generation and long-term maintenance of immune responses to MuCV. In these contexts, with the aims to synthesize evidence on cause of mumps resurgence and evaluate policy options for India a review was done.

Methodology

This narrative review was done by an online database search which include PubMed, EMBASE, Scopus, World health organization (WHO) and Government portals during first July 2025 to 30th August 2025. Articles published from Jan 2000 to December 2024 were included. We prioritized good quality original research, review articles (Narrative reviews, Systematic reviews, Meta-analysis) published in peer reviewed journals and Surveillance reports. The search strategy using in combination Key terms "Mumps Epidemiology", "Mumps Vaccine", "Vaccine Efficacy", "Resurgence" was used. Additional sources were identified from the references of relevant literature. The articles for review were restricted to articles published in the English language. Articles without abstracts and animal studies were excluded from the review. Articles were screened by first author (JKT) and quality assessment was done by all three authors. Of the 1603 articles retrieved after removing unrelated and duplicate papers it was reduced to 72 papers. After selecting the articles, potential information related to epidemiology and vaccine effectiveness, waning of Immunity, Failure of mumps were extracted and classified according to the categories. The results were summarized and discussed.

Results and Discussion

Global epidemiology: During the last few years mumps outbreaks are known to occur periodically from several countries from east and west, with widely varying incidence by country.[12,13] During the years 2022, 2023 WHO reported an increasing incidence rate of mumps cases as 0.6 to 1.9 per lakh population in South East Asian and 67.2 to 76.2 per lakh population African Region.[17] In 2024 the incidence in African region was highest with 36.2 per lakh and south Asian region and western Pacific

countries were similar (6.8 and 6.4 per lakh population).[17] In 2022 European union (EU) with 27 member countries where average 90% children received MuCV, reported 2,593 mumps cases (0.7 per lakh population) which was higher than previous year (0.4 per lakh population).[18] During the year 2016-17 United states reported 150 outbreaks involving 9,000 people of which 78% are vaccinated.[19] Since most of the mumps cases are subclinical these numbers are under reported figures.

India Epidemiology: Although mumps is endemic in India it is not included in the routine national Integrated Disease surveillance program (IDSP) or integration Health information portal and it is not notifiable.[14,20] So the disease burden is not accurately documented and a reliable nationally represented data were not available.[13,15] However IDSP only documented mumps out breaks in its weekly reports.[12] As per the available information from the country the cyclical trend of mumps occurring every 3 to 4 years with its high communicability, among non-immunized children with poor social and environmental conditions.[19] Mainly out breaks occur in areas where there is over crowding or there is increase social contacts like class rooms in schools.[12,19] There were inconsistency on the recent information about mumps burden in India the data extracted from different sources are as follows. From India during 2021-22 Global Health Observatory (GHO) data repository reported 764 mumps cases.[21] As mentioned above the IDSP weekly out breaks reports during the year 2024 in India 144 out breaks were reported (each affecting 5 to 200 people) with maximum in southern states.[22] The state Kerala with 34 out breaks and 1,387 cases and Tamil Nadu with 40 out breaks 1,058 cases.[23] During first six months of the year 2025 these states keep the same trends with reported 17 and 25 outbreaks affecting 321 and 275 cases respectively.[22] [Table 1]

It was realized that the current resurgence started in south India in October 2023 with outbreaks in few districts of Kerala and Tamil Nadu and later spreads to other states. This was followed by out breaks in other south Indian states Telangana and Andhra Pradesh in 2024.[23] From 2021 to 2024 a rise in incidence from 0.07 per lakh to 1.30 cases were recorded from Tamil Nadu.[24] In north India at Kashmir a special surveillance drive conducted in seven districts in 2017 by a state health officials for six months reported 15 outbreaks with 260 cases with average affecting 17 persons.[19] All out breaks occur in educational institutions and there was no case fatality except few complications which need hospitalization.[19] Though there is rare chance of mortality mumps, it needs weeks of isolation which leads to increased absenteeism in school children with lose of working days. In Odisha an economic analysis done found that the average treatment cost of one mumps case was Indian rupees 1,030 as direct expenditure.[25] Adding to large number of affected children and youths the cost of indirect expenditure along with opportunistic cost of adult care takers the economic burden is high.

Use of MuCV in India: MuCV is not yet included in the Universal immunization program (UIP) of India. This vaccine which is indigenously manufactured in India with two doses given to children at 9 months and 15-18 months of age and is only available in the private sector as optional vaccines. Since from 2012 bivalent Measles and Rubella (MR vaccine) is being given in 2 doses in UIP excluding mumps component. Since more than 80% of children in India are receiving vaccination in the public sector most of the children are being deprived of MuCV.[14]

Table 1: MUMPS IDSP -weekly outbreak report: 2025[23]

Month	State	District	Cases
January	Kerala	Palakkad	36
	Tamil Nadu	Thiruchirappali	6
	Chhattisgarh	Baloda Bazar	15
	Kerala	Kottayam	6
	Kerala	Thrissur	9
	Tamil Nadu	Dindigul	13
	Tamil Nadu	Tuticorin	13
	Kerala	Ernakulam	22
	Kerala	Idukki	20
	Kerala	Pathanamthitta	13
	Kerala	Wayanad	7
	Tamil Nadu	Pudukkottai	12
	Tamil Nadu	Sivaganga	8
	Tamil Nadu	Sivaganga	12
	Kerala	Ernakulam	11
	Tamil Nadu	Coimbatore	12
	Tamil Nadu	Namakkal	15
	Tamil Nadu	Sivaganga	10
	Tamil Nadu	Tirupathur	29
	Tamil Nadu	Villupuram	8
February	Kerala	Thrissur	30
	Tamil Nadu	Tuticorin	11
	Kerala	Ernakulam	5
	Tamil Nadu	Dindigul	6
	Kerala	Idukki	9
	Kerala	Idukki	20
	Kerala	Kottayam	13
	Kerala	Wayanad	24
	Andhra Pradesh	Konaseema	30
	Kerala	Palakkad	38
	Tamil Nadu	Namakkal	9
March	Kerala	Pathanamthitta	17
	Tamil Nadu	Coimbatore	21
	Tamil Nadu	Mayiladuthurai	6
	Tamil Nadu	Pudukkottai	6
	Tamil Nadu	Ramanathapura	9
	Assam	Charaideo	4
	Tamil Nadu	Mayiladuthurai	20
	Kerala	Kottayam	17
	Madhya Pradesh	Narsinghpur	4
	Tamil Nadu	Salem	10
April	Tamil Nadu	Erode	5
	Tamil Nadu	Sivaganga	12
	Tamil Nadu	Erode	13
May	Tamil Nadu	Villupuram	7
	Kerala	Pathanamthitta	24
	Assam	Darrang	14
June	No outbreaks		

Whereas parents seek service from private sector getting their children vaccinated with MuCV through MMR vaccine with out-of-pocket expenditure (OOPE)**.** Thus, the population immunity may invariably be below herd immunity threshold level in all states. Previously through selective initiatives some State governments implemented the MMR vaccine. Delhi introduced a single dose of MMR at 15-18 months in 1999[12] and Kerala briefly replaced the second dose of MR booster with MMR (during 2012 to 2017) both later discontinued.[12,24]

The decision of not including MuCV in UIP by the Government of India was influenced by several factors like perception of mumps as a not a significant public health concern, lack of published data on the exact burden of mumps and economic considerations related to MuCV costs. The points were summarized below.[12-14,19] a) Mumps is not considered a serious public health issue due to low mortality b) lack of published data on the actual burden of disease and c) lastly compared to MR vaccine the cost of the MMR vaccine is high." The lifelong immunity provided by natural infection, along with this low efficacy of mumps component of MMR vaccine are also pointed out by some authors.[10,13] At the same time in the context of recent out breaks in the country some experts suggest the use of the MR vaccine by substituting MMR vaccine is considered a 'missed opportunity' to address a significant vaccine preventable disease (VPD) which has a marked impact on child health.[12] They also argue that even though there is insufficient evidence to support the cost-effectiveness of the MMR vaccine in India, from the public health point of view, the incremental cost of adding a mumps component to the MR vaccine would be minimal and could be cost-effective.[12,14] In the current situation**,** considering the urgent need for MuCV, studies addressing this issue must be undertaken.

Circulating Wild virus strains: MuV is an RNA virus belonging to the Rubulavirus genus of the Paramyxoviridae family which are serologically monotypic and genotypically classified into 12 types from A to N (with exception of E and M) with varied geographic and temporal distribution. Till 1990 genotype A was prominent in circulation causing morbidity and no mumps out breaks due to wild B was reported after 1990s [5,6] Phylogenetic analysis revealed that the currently circulating new strains are different from those previous strains in circulation. Currently C, D, E, G and H genotypes are prevalent in EU.[5] In US Mumps genetic sequences available since 2015 in Gen Bank show that, 98.5% as genotype G.[26] In Germany it was type G and rarely with type H and K[6] in Russia C and H.[27] In Asian countries like India genotypes are C and G and in China it is F.[4,6,27,28] As per available reports C and G genotypes are in circulation in Indian states Karnataka, Maharashtra, Tamil Nadu, Assam and Punjab.[29,30]

Vaccine strains: Since the first MuCV were licensed in 1960s and the strains were of genotype A or B. The currently licensed vaccines are originated from the same strains that circulated in the pre vaccination era and the most widely used vaccine strain Jerry - Line JL belonging to genotype A[4]. The strains of Urabe AM 9 are B and L-Zagreb is N.[4,5] In India most of MuCV vaccine manufacturers use the Leningrad-Zagreb strain of genotype N.[31] Though MuCVs are used worldwide the currently used virus strains included in its formulation differ across countries.[4,31]

It was understood that there is a mismatch between currently circulating wild strains and vaccine virus strains and studies or evidences are scarcely available about their cross protection.[4,5,19] Some scientists opined that since the binding site of antibodies are similar for strains the diversity of MuV strains may not reflected in human antibody response.[32] Due to the perceived low priority for mumps among VPD s, only minor progress has been made to improve MuCV. The immunity provided by mumps vaccines were not fully understood, so still there are many unresolved challenges facing by researchers in these issues.[4,5]

Vaccine efficacy (VE): VE studies mostly evaluate the efficacy either by estimating antibodies or clinical mumps in different settings, so they may vary .The VE of MuCV vary depends upon the strains used in vaccine and all have safety and efficacy limitations.[31] In an earlier study it was reported that VE of the JL strain was 72.8-91% and the Urabe strain was 54.4-93% and that of the Rubini strain was 0-33%.[33] Due to low efficacy Rubini strain vaccine were withdrawn from many countries and due to safety issues and Urabe strain was withdrawn from Japan in 1993.[32] The VE results of post licensure trials of vaccines were less than pre licensure trails.[3] Since 2005 across 13 studies with varying methodology, settings the VE of 2 doses of JL strains against clinical mumps disease has been estimated to be ranged from 32-95% (Median 88%).[3,34] Since the study was done in different settings among different population samples the median value to be interpreted with caution**.** Similarly VE of Urabe strain based on 5 five studies were 54-88%.[3] Compared to latest methods with measurement of protective antibody, all the efficacy studies previously are based comparison on classical "Bilateral presentation of parotiditis, hence chances of over estimation was high.[5] WHO experts opined that because MuV is ubiquitous in nature people are previously exposed to sub clinical mumps infection before vaccination, till date there is no reliable correlates of protection measurement after MuCV was established.[3] A modelling study concluded that a vaccination strategy to reduce transmission of MuV among young adult must achieve at least 73.1- 85.9% VE.[34]

According to a recent review, for mumps infection the thresh hold level of neutralizing antibodies or cell mediated immunity level for protection is not yet established.[4] Till date IgG measurement was used as serological surrogate of humoral immunity and now it was proved that it was not sufficient to evaluate the actual humoral response.[35] It was now proved

that the quality of the antibody present could be a more important correlation than its quantity. It was also proved that many of who lack detectable anti body levels against mumps after getting infection, were protected from significant illness due the protection by cell-mediated immune memory.[4,36] It was also mentioned that vaccination may not produce long lasting T-cell mediated immunity.[35,36] The recent out breaks among vaccinate population have questioned the effectiveness of MuCV.[5] But it was demonstrated that among them clinical symptoms, complications, viral shedding, transmissions have shown to be reduced as benefits.[37,38] Along with that it was reported that those received 2 doses of MuCV are found to have less bilateral parotitis, orchitis and virus excretion in their urine compared to unvaccinated.[39]

In a recently conducted meta-analysis which included 17 studies from 2002 to 2017 summarized the Effectiveness and safety of a MuCV in preventing Laboratory confirmed mumps cases by polymerase chain reaction (PCR) was included the following results were reported.[40] The credibility was ensured by sensitivity analysis and funnel plot with non-significant asymmetry (Begg's test P >0.05) by authors.[40]

In case-control studies, (n=3) a MuCV demonstrated vaccine effectiveness of 68% (95% CI 30-86%). (OR: 0.32; 95% CI, 0.14-0.70).[40]

In cohort studies and randomized control trials (n=14), the vaccine efficacy was 58%. (95% CI 31-74%). (RR: 0.42; 95% CI, 0.26-0.69).[40]

In the same meta-analysis during the outbreak period, the VE of MuCV was 49%, (95% CI 0-27-79%). (RR: 0.51; 95% CI, 0.21-1.27), whereas the VE during the non-outbreak period was 66% (95% CI 32-82), (RR: 0.34; 95% CI, 0.18-0.68). It was seen that in outbreak situation the VE lower than non-outbreak situation.[40]

In the multiple dose studies (n=10) reported one dose of MuCV, three studies that reported two doses, and one study that reported three doses. They reported the VE of one dose of MuCV was 58% (95% CI 12- 80), (RR 0.42; 95% CI, 0.20-0.88), whereas two and three doses were 65% (95% CI 39- 80) (RR 0.35; 95% CI, 0.20-0.61).[40] Since the 95% CIs of the two subgroups are overlapping , which points that there was no statistically significant difference between the two subgroups.[40] To know the duration of protection offered by the third dose no study was yet done.[3] All the values of VEs of recent time were less than the prior RCT s which may be attributed due to loss of boosting effect of sub clinical natural infection due to cohort effect.[34]

Mechanism of vaccine failure

The re-emergence of mumps outbreak among fully vaccinated child population were due to nonrandom distribution of protective immunity or can be due to vaccine failure, which can be primary or secondary. Primary vaccine failure was due to lack of sufficient antibody response to vaccine recipients. Primary vaccine failure was reported from Ireland in young children with cyclical out breaks so the age of second dose was reduced to 4-5 years from 10-14 years.[41] Similarly from Russia[27] and Belgium primary vaccine failure was reported among vaccinees following break through infections with low neutralizing antibodies in early this century.[27,42] A paper published from India including 56 mumps cases of which 30 had been vaccinated and among them 93.4% were IgM positive for MuV, they concluded as a sign of vaccine failure.[43] A five year data (2008 to 2013) reported from Germany among the serologically proven and vaccination status known cases 69% were vaccinated.[35]

Many studies reported that compared to measles and rubella components (>90%) the protective efficacy of mumps was less, thus making the MuCV the less effective component of MMR. The efficacies of mumps antibodies following the first and second doses of the MMR vaccine are 78% (95% CI 49-91%) and 88% (95% CI 66-95%) respectively.[4] In an outbreak in South India among 67 mumps cases diagnosed by IgM and all were (100%) vaccinated among them 57 (85%) were tested negative for mumps IgG. Whereas 100% samples tested positive for rubella specific IgG and 97% samples tested positive for measles specific IgG, showing that the mumps component in the MMR vaccine failed to offer protection.[44] Kansas university US the vaccine policy insists mumps vaccination booster dose for admission. In 2006 the largest outbreak within the history of 20 years were reported with 453 cases among 18-19 year old students where 78% of students are vaccinated with 2 doses was a sign of vaccine failure.[39] Among them secondary attack rate (SAR) among primary contacts were found to be 2.2 to 7.7%.[39] In 2013 out breaks at Jews community school in UK among students of age 10-19 years among the reported 28 clinical cases 84% are vaccinated.[45] To correctly explain the current resurgence there exists a knowledge gaps in mumps immunity and vaccine failure.[46] Theoretically it is unlikely that the recent out breaks reporting from other western countries affecting older children and adults after long years of gap after vaccination were due to primary vaccine failure, but secondary vaccine failure due to gradual loss of immunity. Under Secondary Vaccine failure many causes are suspected, which are described below.

Waning of Immunity over time: Many of the recently reported out breaks reported from these countries were among young adults rather than children and have received their last dose of vaccine before ten years.[4,5,6] longitudinal follow up studies conducted in India by doing antibody titre have shown waning of immunity among mumps vaccinate individuals leading to age shift.[47] Another study from west compared those received two doses of vaccination within 2 years and more than 13 years and

found that the mumps infection rate was increased more than seven fold from 1.6 cases per thousands to 11.3 cases[46] and a follow up study in US revealed that 13 years after vaccination risk of contracting mumps was increased.[48] In France it was reported among those received 2 doses of vaccine that the risks for mumps infection was increased 10% for every year after vaccination (aOR 1.10; 95% CI: 1.02-1.19).[49] Similar in Spain after 3 years the odds was 10.2 (95% CI: 1.5-70.7)[50] and the immunity declined 20% in every decade[51]. In US out break it was proved among vaccinated population the risk of mumps infection increased with OR 2.46 (95% CI 1.25-4.82) in a gap of ten years of vaccination[35] and from another study reported that within 7.9 years (CI 4.7- 14.7 years) 25% lose protection, within 19 years (CI: 11.2-35.4 years) it was 50%.[37]

Increased rate of waning of MuV Abs in combined vaccine MMR is also another concern. After 8 and 12 years of MMR vaccination, comparison to Measles (7.1%) and rubella (8.2%) antibody titer waning rate for MuCV was high; 9.9 and 9.2% respectively.[38] Similarly a 20-year prospective cohort study found that, compared with decline for measles (58%) and rubella (65%), mumps antibody titres decreased by 75%.[52]

Lack of cross neutralization due to strain difference: Limited studies were done regarding MuCV induced immunity and the cross protection between MuV genotypes and strains. An earlier laboratory study from US reported that Jeryl Lynn vaccine derived from A strain have neutralization capacity against type G strains.[53] But later studies suggested the re-emergence was due to antigenic escapes caused by antigenic variations of new strains evading neutralizing immunity elicited by vaccination.[4,28,53] The antigenic mismatch with wild virus with genotype G and vaccine virus with A have already discussed.[26-31,34,53] This was first reported in Russia in 2002.[27] The neutralizing capacity of the antibodies produced by different vaccine strains are low to comparing the high virus load challenges during out breaks.[54] In India wild virus in circulation causing resurgence of mumps was C, G have raised queries regarding the effectiveness of currently administered MuCVs because the vaccines are from different strains. (Jeryl Lynn and L Zagreb from genotype A, N respectively).[31,42] Newer studies have demonstrated that the structural diversity of anti-bodies against JL epitopes may not interact with that produced by outbreak strain heterologous epitopes.[55] The genotype mismatch between JL vaccine and circulating strains may potentially result in immune escape leading to susceptibility.[56] It may be due to this reason in many out breaks the vaccinated children were also affected adding concerns about their ability to prevent outbreaks.[35,43] Reviewing the literature the WHO experts opined that with the low neutralizing antibody levels and high force of infection the cross neutralization capacity of vaccine strains will be reduced.[3] They also warrant a polyvalent MuCV in future to control out breaks.[3,55]

Lack of natural boosting: The prominent vaccines trials of currently used MuCVs were conducted during the time when there where high circulating wild virus (same or other strains) was in circulation. That may mask vaccine immunity and overestimate the VE in early years. So, the immunity measured during that period may not be solely due to vaccine virus but also partially contributed by natural infection.[56,57] During that time immunity may be subsequently boosted by sub clinical infections, leading to herd immunity thresh hold. Now since the endemicity state was controlled in many parts of world, there are less opportunities for sub clinical boosting and herd immunity, this may be one reason in re-emergence of infection.[57] A comparative pre-post immunity study with primary and revaccination conducted among 2,000 persons reported that among those groups not received primary vaccines hence had low antibody because of natural infection had high post immunity response (100%) after vaccination than the others with revaccination (68.4%).[58]

A recent study in India among school children compared with vaccinated (40%), 9.1% of unimmunized children were found to be seropositive for antibodies due to natural infection.[47] It was also seen that comparison of antibody estimation among post MuCV vaccinees and wild type infection the later was five folds higher.[5] It was also proved that the natural immunity is more durable with greater anti bodies and have a half-life of more than 50 years.[3,59] In a large outbreak among fully childhood vaccinated youths at UK (2004-05) investigators concluded that the outbreak was due to "lost cohort effect' among those missed the chance of natural infections.[60] In Sweden where the second dose was introduced for the first time in world (1982) for children at the age of 12, it was found that compared to earlier vaccinated sero positive children naturally immune had a higher mean titre both before and after vaccination.[61] All over the world the circulating wild virus are reduced, hence sub clinical infection, which may invariably reduce leading to natural boosting of vaccine generated immunity.

Sterilizing Immunity: The Existing mumps virus vaccines were given by intra muscular injections which is different from the natural route of transmission i.e. respiratory route, so it will not produce mucosal immunity (IgA) to prevent natural infection hence could not able to produce sterilizing immunity.[5,62] This was similarly reported about newly discovered types of Covid19 vaccines which are not able to prevent transmission or infections and only severity.[63] Thus even vaccinated people can get infection (Clinical or subclinical), thus they can also excrete virus and facilitate transmission. So, when the force of infection is high, they may not control outbreaks.[63]

Potency of vaccine: Internationally the minimal level of neutralizing antibodies to neutralize MuV is not yet determined.[3,53] The international reference standard for MuCV is based on monovalent vaccine biological assay and currently MuCVs are given as combined form with other vaccines (MMR). Also, the minimum potency of vaccine may differ from various brands.[62] The degradation products in different MuCVs are neither identified nor quantified and the potency measurement may vary with different MuCV vaccine strains.[5,64] Vaccination may not produce B cell memory which is necessary for protection.[64] This may be another reason for the cause of failure.

Herd immunity and Immunity Gap: Many parts of world the proportion of uptake of MuCV is far lower than the WHO estimated herd immunity thresh hold of 95%.[5,65] WHO considers vaccine hesitancy as one of the ten threats to global health and in US due to vaccine hesitancy of parents about 1/8 children are not getting vaccine.[65] Heterogeneity of immunization coverage and susceptibility of infection in different populations/ geographic locations is also becoming an important epidemiological issue. In vaccinated community itself due to low efficacy and waning will result to sub threshold level of herd immunity. Thus, subpopulation immunity is also a cause for periodical outbreaks.

In areas with migration and population mobility there will be mixing of population with different immunity may also flare up further breaks with cyclic trends depending upon buildup of susceptible. The disease trends in the following areas can be considered as examples. Many cyclical trend related out breaks reported in UK documented that among the cases those natives vaccination status was known 72% in their childhood had received two doses of MMR.[46,66] Netherlands, where 96 and 93% received first and second doses still reported mumps outbreaks.[67] In EU countries the vaccination coverage was 92% for first dose and 90% for second dose and among the reported cases 47% were vaccinated.[17,68] In Indiana, US out breaks were reported from universities and communities among them documented evidences of mumps vaccination of 85% and 52% respectively.[32]

Effectiveness of 3rd dose of MuCV: To tidy over the recent upsurge, waning of immunity most countries have introduced third dose of MuCV. Introduction of a third dose MuCV resulted in a marked rise of antibody titters against MuV. During follow up it was found that one year later titers were similar to those prevalent before the third dose.[3,40] In lowa university among vaccinated community during an outbreak 3rd dose was given and it reduces the risk up to 78% or 6.7 Vs. 14.5 cases per 1,000[50] but within three months the antibodies return to previous levels.[51] In another study also it was found that those having low antibody titers prior to the third MuCV were increased transiently but returned to pre vaccination level soon.[69] The consensus reached among scientists was that a third dose of MuCV can be used only a stop gap measure to help to limit the outbreak but not generally recommended as a long term measure to prevent it.[6,69] In a meta-analysis the CI of vaccine efficacy of 2 and 3 doses overlap each other showing no statistically proven difference in efficacy[40] and in many VE studies soon after the third dose titre value return to low original base value.[6,70-72] The short duration of protection offered by third dose raised questions about its general applicability for long term solution in future.[51,69,73] To understand the potential of the third booster dose to prevent mumps epidemic the WHO experts also suggested further research.[3]

Conclusion

In India childhood MuCV should be introduced universally in phased manner after cost effective studies and implementing mumps surveillance system in the country. There are evidence gaps in protective efficacy of early childhood MuCV to prevent current outbreaks of mumps among young adult population after a gap of long years. The age and number of booster doses given can be fixed only after conducting cohort studies of waning immunity, sero-surveys and clinical severity assessment. Along with these strategies to improve the duration and quality of immune response to the current MuCV may also be needed. Research for new polyvalent vaccines, adjuvant platforms, recombinant immunogens or a booster with antigens contains circulating wild strains may be considered.

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