Review Article

Indian Journal of Preventive Medicine
Volume 1 Number 2, July - December 2013

In Era of MMR, Measles and its Factors Still Exist Round the Globe: Searching for Solution?

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Abstract:

Many single as well as mixed outbreaks of measles, german measles, varicella and herpes joster were investigated. In outbreak settings, it is usually observed that more than one viruses are concurrently infecting the population, e.g., measles and german measles can go simultaneously; Likewise laboratory confirmed measles with chickenpox outbreaks had also been investigated in Himachal Pradesh. The presenting complaints are quite confusing in the beginning. Mild febrile rashes are present both in german measles and measles and symptomatogy is so similar and fleeting. Nowadays there is distinct change in the measles and mumps disease pattern due to measles and MMR vaccination. More and more case patients of measles and rubella are being examined in higher age group adolescent children. Crowding, intense exposure and lack of vitamin A supplementation were the some of the factors responsible for its spread. Is MMR is the vaccination of choice or something more?

Keywords: Measles-rubella and varicella; Triple outbreak; Atypical rash; MMR Vaccination; Kangra.

Introduction

Before active immunization was available, epidemics of measles/german measles in outbreak settings used to occur in the cyclical trend of two to three years during spring months and before the age of fifteen years 95% of the population used to suffer from the disease. Typically, a disease of children, it may occur at any age in the remotest isolated communities if the disease is introduced for the first time. These epidemics in the virgin population are accompanied by high mortality

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(Received on 20.06.2013, Accepted on 01.07.2013)

rate. Outbreaks in Faroe Islands in 1846 and in Fizi Island in 1875 are examples of this type of transmission. There are a number of other examples of such type of virgin epidemics and the highest mortality rate, as Greenland had its first exposure in 1951 and the epidemics affected as high as 99.9% of the indigenous population (Christensen *et al*, 1952). According to WHO report, in the absence of immunization, 90% of the persons can be expected to develop clinical measles sometimes in their life time as noted in Greenland in 1951 epidemic[1] and german measles in 2012 in Kangra.[2]

Review of Literature

Historical Background

Rubeola or Measles, one of the earliest recognized diseases, probably was not the significant problem before the building of the large cities. The name Rubeola is derived from Arabic, meaning thereby Red Spots.[3] The name Morbilli was derived from Italian word Morbillo[4] diminutive of morbus, meaning disease, bubonic plague, morbilli being a minor disease. There is some doubt about the origin of the name measles. Most probably it comes from the Latin term miselus or misella, itself a diminutive of the Latin miser meaning miserable which was given to the inmate of the medieval leper house.

In Ayurveda measles has been mentioned as Romontika. But it has not been given any special importance. Charak (1800 B.C.) has described it under small pox which was named as Masurika. Madhava in 7th century described it as derangement of Pitta and Kapha.[5] The earliest medical description was given by Rhazes in 9th century in Bagdad (Black *et al*; 1977). It was Sydenham's published work in 1675 which differentiated measles from other exanthemas. Home established measles as an infectious disease in 18th century. Another worker Withering in 1792 reasserted that the difference of measles with small pox existed. Recognition of the *measles* as a separate entity from *German measles* dates back to early 19th century. Panum was the first worker who did classical studies on the epidemiology of measles in Faroe Island in 1847. Measles virus was isolated from eleven years old boy named David Edmonston in USA in 1954 (Enders *et al;* 1954). The Kopliks spots which are absolutely pathognomic of the invasion of the measles were described by Koplik in 1896.[6]

Epidemiology of Measles

Global Scenario: Measles is a cosmopolitan disease of great antiquity, yet its history and origin are both obscure. However, the provisions of the ancient remedies and divinities specific for this affection prove the devastation of childhood population in China, Japan, India and other eastern nations by measles epidemic in ancient time.[7] Measles remains an important cause of childhood mortality, especially in developing countries. In 2000, measles killed 770,000 children worldwide, accounting for nearly half of vaccine preventable deaths.[8] Failure to deliver at least one dose of measles vaccine to all infants remains the primary reason for high measles mortality and morbidity in developing countries like India, Pakistan and African countries.[9]

Although global immunization coverage increased from less than 20% in 1983 to 80% in 1990 and the number of reported cases of measles declined from over 4 million per year to 0.7 million in 1997, but still the case fatality ratio ranges (from 0.1 to 30 % in outbreaks among high-risk population in various countries.[9,10,11] The largest percentage reduction in estimated measles mortality during 1999-2005 was in the Western Pacific region (81%), followed by Africa (75%) and the eastern Mediterranean region (62%). Africa achieved the largest total reduction, contributing 72% of the global reduction in measles mortality.[12]

In recent years, a number of countries have had notable success in eliminating measles using a variety of vaccination strategies. Three WHO regions – the Americas, the Eastern Mediterranean and Europe – now have measles elimination goals. In the Americas a strategy based on supplementing high routine coverage with an initial catch-up and periodic follow-up campaigns has achieved a dramatic reduction in measles incidence and interrupted

transmission in many areas. Other countries have eliminated indigenous measles transmission with a routine two-dose schedule by reaching coverage of over 95% (e.g. Finland, Hungary and United States). A similar result has been achieved in Canada, Oman and the United Kingdom by following a catch-up campaign with a routine two-dose schedule.[13]

In addition, the awareness and political commitment towards measles elimination remains at an all-time high with the recent success of poliomyelitis control, and is clearly evident in many countries (e.g. Malaysia, the Philippines and Viet Nam) setting up national elimination goals. In 2003, the Regional Committee, at its fifty-fourth session, resolved to adopt measles elimination as a regional goal and to set a target date to achieve that goal at the earliest opportunity.[14] A total of 91,765 cases were reported in the Region through the Joint WHO/UNICEF Reporting Forms 2004, with 99% of all cases being reported from eight countries. These eight countries are China, Japan, Malaysia, the Philippines, the Lao People's Democratic Republic, Papua New Guinea, Cambodia, and Viet Nam in the order of number of cases reported.[15]

South East Asian Region (SEAR) Scenario: All countries in the WHO South East Asia Region joined the global measles elimination initiative. Between 1997 and 2001, South East Asia region countries reported an overall of 42 outbreaks for a total of 781 cases. Most of these outbreaks have been reported from India, Bangladesh, Myanmar and Nepal. In addition, the number of reported cases in the South-East Asia Region increased from 78,574 in 2000 to 94,562 in 2006, primarily because of improved measles surveillance in India and Indonesia.[16]

Measles vaccination coverage among infants in Southeast Asia and Africa is still low, ranging between 54–55% in 1999 to 65–67% in 2003.[17] However, Sri Lanka, Latin America[18], Romania[19] and South Korea[20] experienced outbreaks of measles inspite of sustained high coverage with single-dose vaccination strategy. Thus, the 2001–2005 WHO/UNICEF strategic plan for measles mortality reduction and regional elimination recommended achieving high routine vaccination coverage (>90%) in every district and ensuring that all children receive a second opportunity for measles immunization.[21]

India profile: In developing countries like India, measles infection has devastating effects due to the severity of primary diseases as well as the secondary infections. The age at which measles is contracted depends on duration of maternally derived protection, propensity to associate in large crowd and vaccination coverage in the area.[22] Cyclic increase in incidence of measles has been recorded every third year till the launch of Universal Immunization Programme (UIP).[23] During 1987 about 250,000 cases were reported, whereas after implementation of universal immunization programme, the number of reported cases came down sharply to 39,000 during the year 1999.[24] The progress made under the UIP was impressive (Minimum 80% coverage of infants). Nearly 22 million infants[25] are reported to be receiving full courses of immunization annually since then. But the evaluated coverage for the fully immunized children revealed a complete different picture. The coverage decreased from 68% in 1996-97 to 38% in1999-2000.

The Indian scenario of vaccine preventable diseases has improved much after the launching of UIP. In India immunization showed steady increase in coverage from 1980-1989. But from 1996-99 the coverage declined even to 50% in case of Measles. Diseases reappear when immunization coverage drops.[26] National Polio Surveillance Project (NPSP), India has estimated that around 2-3 million measles cases and 100,000 – 200,000 measles deaths occur every year in India.[27] But in the country, Delhi state has higher vaccine coverage since it has taken the lead and initiative of the two dose schedule of measles and measles, mumps, rubella (MMR) at 9 months and at 15 months respectively. Goa, Maharashtra, and Tamil Nadu reached 84-88 per cent coverage. Six states, Andhra Pradesh, Chhatisgarh, Delhi, Gujarat, Punjab and Madhya Pradesh achieved coverage of more than 70 per cent.[28]

The measles vaccine used now in India is a

live attenuated strain of measles virus, the immunity of which is life long.[29] However, these vaccines are not 100% effective. In countries where immunization is undertaken at 12-15 months of age, measles vaccine efficacy ranges between 90% and 95%. In India, where the first dose is given at 9-12 months of age, the vaccine efficacy is approximately 85%. Although measles immunization is an effective strategy to prevent the cases, outbreaks can continue to occur especially in densely populated areas such as urban slums, even with the good coverage. The effective vaccination has reduced the incidence in children and the adolescent groups are affected. Though major age group involved is 1 to 14 years, infant measles is also reported.[30,31,32] Measles mortality is the highest in the malnourished populations.[33] Priority immunization of children of remote isolated populations may prevent such epidemics.[34] The lack of reliable surveillance data and understanding of local measles epidemiology makes it difficult to fully appreciate the public health burden in India and to organize targeted measles morbidity and mortality reduction strategy.[35]

Himachal Pradesh and Kangra district: Measles immunization coverage in India ranging from 42.2%[36] to 50.7%[37] to 58.8%[38] suggests that there is gradual rise over the years while it satisfactorily rises from 71.8%[39] to 89.1%[40] to 86.3%.[41] As the coverage increases, inter epidemic interval increases as well as focus shifts towards older age groups as observed as in Thailand and Kangra.[42,43] This is on account of high measles immunization (>95%) in Himachal Pradesh the incidence of the measles cases have gone down from 19 to 11 to 8/lac[44] from 2001-2003 while in district Kangra the incidence have turned out to be 1.5/ lac in 2003. on the basis of remarkable observations derived from laboratory confirmed measles/rubella outbreaks followed by analytical retrospective cohort studies in district Kangra and elsewhere of Himachal Pradesh, the recommendations was approved by government of India for MR vaccination[45,46] at the age of 16-24 months for those states in India which are well performing like Himachal Pradesh. Secondly, the circulating measles strains in the district have been detected to be genotyped as D4 by Laboratory of National Institute of Virology, Pune. Their findings have been officially documented for the first time in Himachal Pradesh in India.

Morbidity and Mortality round the world

Global Scenario

In the study related to unacceptably high mortality related to measles epidemics in Niger, Nigeria, and Chad (West Africa), R. F. Grais *et al* in 2006 noticed that measles attack rates (AR) were the highest in children under 5 years old; 17.1% in Boukoki; 17.2% in Moursal and 24.3% in Dong District. Case Fatality Ratios in under 5-year olds were 4.6%, 4.0%, and 10.8% in Boukoki, Moursal and Dong District respectively.[48]

In assessment of routine surveillance data as a tool to investigate measles outbreaks in Mozambique (West Africa) Jagrati V Jani *et al* in 2006 observed that in three cities of Mozambique; the attack rate and case fatality rate (CFR in Maputa province in 1998 was 20/ lac and 4.4%; being highest, followed by Manica city-10/lac & CFR-0.0% and finally, Gondola city-9/lac & CFR-0.0% respectively.[49]

Yeung LF, Lurie P (2005) in a limited measles outbreak in a highly vaccinated US boarding school students recorded who received both doses outside the United States had a higher attack rate 0.96% (3 of 75) than those who received both doses in the United States 0.59% (3 of 509). Vaccine effectiveness among students who had received 2 doses of measles containing virus (MCV) was 98.6%.[50]

Amy A. Parker *et al* in 2005 analysing the implications of a 2005 measles outbreak in Indiana for sustained elimination of measles in the United States noted that the overall attack rate was 0.07% and complication rate was 0.006%. Religious belief barrier for unvaccination was the reason for this outbreak in the highly immunized community.[51]

In the outbreak of measles in a highly vaccinated secondary school population,

Sutcliffe PA, Rea E in 1997 recorded that overall attack rate was 7.7%. The measles vaccination rate was 94.2%.[52]

Susan van den *et al* ,(2001) studied measles outbreak in a community with very low vaccine coverage, in the Netherland noticed that overall attack rate was 37% (0% for the oldest groups of pupils to 88% for the youngest) with complication rate 25%. Religious belief barrier for unvaccination was the reason for this outbreak in 2% of the Dutch community.[53]

Asia

In a case-control study conducted on the factors associated with a measles outbreak in children admitted at Mahosot Hospital, Vientiane, Laos, Mayfong Mayxay *et al* (2007) observed that the overall AR was 6.7%. Immunization coverage was only 36% in 0-23 months of children.[54]

During the morbidity and mortality study in Turkey in 2004 on measles epidemics in Turkey, Ismail Hamdi Kara1 Ali Ceylan *et al* recorded that the morbidity and mortality rate from 1998-2001 in Turkey are 4186; 2481; 2395; 4497 (per lac) and 0.32; 0.27; 0.01 & 0.13 (per lac) respectively.[55]

According to Megan Murray and Zeba Rasmussen,who studied measles outbreak in a northern Pakistani village: epidemiology and vaccine effectiveness; 2000, the age specific attack rate were noticed as 0-5 months-0.0%; 6-8 months-22%; 9-11 months-38% and 12-14 months-31% with CFR as 3% in less privileged Sunni Muslim community; with vaccine efficacy as 73-90%.[56]

Puvimanasinghe JP *et al* noted measles outbreak in Sri Lanka in 1999–2000 that maxmimum age specific morbidity rate was 114/lac for infants and 81/lac for 15-19 years of age. 54% of the cases belonged to ≤ 15 years of age with the case fatality rate 0.1%. Male to female ratio was 1.1:1. There was age shift to higher age group in this outbreak.[57]

India

SN Gupta and Naveen Gupta in 2009 recorded that overall attack rates ranged between 4.2% and 6%. All case patients were between 6 years to 11 years of age. Age-specific attack rate in double outbreaks ranged in between 1.7% and 21.6%, the highest being in the age range 11-17 years. No deaths or complications were reported. The first outbreak imported virus after an interschool game competition (relative risk, 6.44%; 95% confidence interval, 3.81-10.91); followed by the second outbreak, in which people exchanged foods in the festival in one infected village of the first outbreak (relative risk, 5.3; 95% confidence interval, 1.90-14.77; P <.001). The vaccine efficacies were estimated to be 85% and 81% in the first and second outbreaks respectively.[44]

Arumugam Mohan and Manoj V. Murhekar *et al* who studied measles transmission following the tsunami in a population with a high one-dose vaccination coverage, Tamil Nadu, India, 2004–2005 recorded attack rates of 1.3 and 1.7 per 1000, respectively in Tsunami-affected (n = 71) and unaffected villages (n = 30). The median ages of case-patients in tsunami-affected and un-affected areas were 54 months and 60 months respectively (p = 0.471). 36% of cases from tsunami-affected areas were above 60 months of age.[58]

According to Sharma Munesh K *et al* 2004 who conducted the study on outbreak of measles amongst vaccinated children in a slum of Chandigarh noted an overall attack rate of 5.13% (Peak incidence 6% in 1-4 years age group). Among measles cases, one-fifth had post measles complications. No fatality was there. 32.76% children with measles had received measles vaccination in the past.[59]

B.P. Gupta *et al* (2004) during the study of the remote hill in Himachal Pradesh, in a rural area near Shimla,in measles outbreak noticed the high attack rates amongst boys and girls as 15.6% and 17.1% respectively. The overall attack rate was 16.2%. The youngest was 4 years of age and the oldest being 14 years of age and no case of infant was detected and no death was reported. Remarkably, all the 69 cases were unvaccinated.[60]

In a study conducted by VK Desai *et al* (2003)

on measles incidence and vaccination coverage in slums of Surat city recorded the high overall incidence rate as 7.7%. The incidence rates among boys and girls were 7.5 and 7.7% respectively. The peak incidence of measles was in 9-11 month age group (11.5%). The 12-35 month age group contributed to about 50% of all measles cases.[61]

Thakur JS, Ratho RK *et al* (2002)noted in measles outbreak in a periurban area of Chandigarh that the overall attack rate of 4.5% and male to female ratio of (M : F) 5.3%: 3.6%. High complications were reported in 31.1% cases.[62]

During the study on measles outbreak in slum area of Kolkata in 2000, Ray Sandip Kumar *et al* observed that incidence of measles was found as 5.76%. Incidence was 5.84% in males and 5.66% in females. But only in case of 0-11 months of age, higher incidence of measles was observed in male children (10.59%) compared to female (6.64%).[63]

Jagvir Singh *et al* 1996, during the morbidity and mortality study caused by epidemics, in wide spread of measles outbreaks in rural Uttar Pradesh, India, high risk area and groups,] recorded that the case fatality rates from 1992-1996 are 4.1%, 2.4%, 2.4%, 3.7%, 4.1% respectively. Overall cases fatality ratio (CFR) was 4.1%. CFRs were significantly higher in females and young children. The median age of cases was found to be below 5 years. There was heavy clustering of cases and deaths in rural areas. About 85% of the cases and virtually all the measles associated deaths occurred in unvaccinated children.[64]

(A) Factors associated with outbreaks of measles

(i) Factors associated with high coverage

SN Gupta *et al* 2001 noted that there were factors associated with (a) Program-related issues such as erratic charting of temperature log book leading to chances of failure of cold chain and (b) healthcare provider related issues like gaps in the knowledge of workers may be associated with measles outbreak in Shahpur block. (c) Beneficiary related issues may also be related with outbreaks such as socio-cultural, economic factors; traditional help seeking behavior such as treatment seeking and follow-up practices of mothers and distant and difficult access to healthcare facility in geographically tough areas.[47]

Manoj V. Murhekar *et al*, 2005 reported where one-dose measles coverage exceeded 95%, 36% of cases were above 60 months of age. There was no fatality. Population movement and high population densities; refugees and displaced populations; poor nutritional status in such settings are the factors responsible for such outbreaks. The World Health Organization recommends vaccinating children aged six months to 14 years in refugee and internally displaced persons camps.[65] However, vaccinating children only up to five years of age might have left some children susceptible to measles, as more than 36% of the cases were older than five years of age.

Sharma Munesh K *et al*, 2004 have studied measles outbreak in the big slum of Chandigarh in Feb., 2003 which had outbreak twice in a span of three years where malnutrition, poverty, overcrowding, poor hygiene, vitamin A deficiency, improper immunization and decreased immunity are the factors associated with this disease. 32.76% had measles twice despite vaccination for measles. 80% of the cases belonged to 10-14 years of age, thereby indicating the waning immunity with passage of time.[59]

Yeung LF, Lurie P in 2005 studied the outbreak in US Boarding school, Pennsylvania, individuals who were vaccinated with 2 doses of measles containing virus outside the United States had a greater risk for developing measles. Reasons for this may include failure to maintain the cold chain mishandling of vaccine with respect to reconstitution, less accurate vaccination histories, or greater intensity of exposure during this outbreak.[50]

Puvimanasinghe JP *et al* studied the outbreak in Sri Lanka in 1999-2000 from the slum area of Colombo to the rest of country where over 90% of the primary vaccination was there. 54% of the cases belonged to ≤ 15 years of age with the case fatality rate 0.1%; a shift towards the higher age group. Crowding, intense exposure and lack

of vitamin A supplementation were the factors responsible for its spread.[57]

During August 10-November 23, 1998, transmission of measles among a highly vaccinated school population—Anchorage, Alaska, 33 confirmed measles cases were reported to the Anchorage Department of Health and Human Services and the Alaska Department of Health and Social Services (ADHSS). Accumulation of the susceptible children was the factor for the outbreak. This report underscores the importance of second-dose requirements for measles vaccine.[66] Sutcliffe PA, Rea E. *et al* examined in 1996 the factors associated with measles vaccine effectiveness and the effect of two doses of vaccine on measles susceptibility during an outbreak by retrospective cohort study in a highly vaccinated secondary school in the City of Toronto.[52] The findings support a population-based two-dose measles vaccination strategy for optimal measles control and eventual disease elimination.

Furesz J. 1996 studied that of the 5551 confirmed measles cases reported in 1995 in the Americas. Their findings support the use of a two-dose measles vaccination strategy. Two-dose programs in Finland, Sweden and the United States have dramatically reduced the incidence rates of measles in those countries. Many developed countries like Hungry, Canada, Oman, United Kingdom had eliminated measles by 2 doses schedule[67]. Measles was declared eliminated from the United States in 2000 but remains endemic worldwide.

In 2005, a 17-year-old unvaccinated girl who was incubating measles returned from Romania created the largest documented outbreak of measles in the United States since 1996.

Similar studies by other authors for the importance of second-dose requirements for measles vaccine have been done by Chen RT, Goldbaum GM in 1989[68]; Nkowane BM, Bart SW, 1987[69] and Shasby DM, Shope, 1977.[70]

(ii) Factors associated with low coverage

B.P. Gupta *et al* examined the measles outbreak in the remote village of Shimla in 2004 with the population of 1360 in which 425 children were surveyed; 31.3% were the children below the age of 15 years. The youngest was 4 years of age and the oldest being 14 years of age and no case of infant was detected and no death was reported. All the 69 cases were unvaccinated. 95.7% of the cases belonged to the age group of 5-15 years. It was the accumulation of unvaccinated susceptible children in this remote isolated area, due to non availability of health services 5 years back, which probably the determinants are contributing to this outbreak.

VK Desai *et al* in 2003 recorded in the study of measles incidence and vaccination coverage in slums of Surat city that the factors responsible for the repeated outbreaks in the city are poor urban population groups; vitamin A deficiency; low vaccination coverage-the commonest reason for non-vaccination was ignorance of parents about the seriousness of the disease and the need of vaccination.[61]

Thakur JS, Ratho RK *et al* in 2002 have examined measles outbreak in a periurban area of Chandigarh where mainly the children below 15 years of age were affected. Two hundred and eighty three cases of measles were reported with an attack rate of 4.5% and male to female ratio of (M: F) 5.3%:3.6%. Among the measles cases, 48.8% had received measles vaccination. The factors were poor socio economic strata and poor surveillance system in place.[62]

Ray Sandip Kumar *et al* studied measles outbreak in slum area in Kolkata in 2000. 290 measles cases out of total of under five 5038 children were taken by 20 cluster technique. The key findings related to low immunization coverage (19.7%); low vitamin A solution supplementation (16.7%) and 50% complications with no death. 21% of the cases were immunized for measles in over five 34.7% children. Large families, crowded homes and urban slums were the factors for the outbreaks.[63]

Jagvir Singh *et al* in 1996 in the study of wide spread of measles outbreaks in rural Uttar Pradesh, India, 1996, high risk area and groups noted poor vaccine coverage levels, inefficient

surveillance system, illiteracy, poor socio economic strata, and ignorance are the factors for the outbreaks.[64]

Mayfong Mayxay *et al*, 2007 in factors associated with a measles outbreak in children admitted at Mahosot Hospital, Vientiane, Laos observed the contributing factors as low to medium vaccination coverage; vitamin deficiency A (40%) and belief barriers like food and fruit avoidance during the outbreaks which further enhanced vitamin A deficiency.[54]

Ismail Hamdi Kara1 Ali Ceylan *et al* in 2004; noticed measles epidemics in Turkey and recorded low to middle income group; closed communities like refugees camp; low vitamin A intake as the predisposing factors for the outbreaks.[55]

Megan Murray and Zeba Rasmussen in 2000 noted in study of measles outbreak in a northern Pakistani village: epidemiology and vaccine effectiveness recorded neglected and less privileged minority Sunni Muslim community as one of the factors for the outbreaks.[56]

In the study of unacceptably high mortality related to measles epidemics in Niger, Nigeria, and Chad (West Africa), R. F. Grais *et al* in 2006 observed the contributing factors as low to medium vaccination coverage; poor socio economic strata and belief barriers.[48]

In assessment of routine surveillance data as a tool to investigate measles outbreaks in Mozambique (West Africa) Jagrati V Jani *et al* in 2006 noticed low socio economic strata, overcrowding in the huts as the predisposing factors.[49]

Susan van den *et al* in 2001 noted in the study of measles outbreak in a community with very low vaccine coverage, the Netherlands that low to medium vaccination coverage; socio-demographically clustered large families, mainly unvaccinated communities on religious grounds are the factors behind the outbreaks.[53]

Waning Immunity as the factors for outbreaks

Active immunity against measles was first attempted in Scotland during 18th century with a procedure similar to the variolization and named as morbilization (Ikic *et al*; 1970). There were other documented attempts to induce immunity cultured measles virus but the active immunity against measles became a reality since the cultivation and attenuation of the virus in the cell culture by Enders and Pebbles in the middle of this century (Enders *et al*; 1960). The new attenuated strain was named as Edmonton B and was used for mass prophylaxis with immune serum.

Cox MJ *et al* conducted an epidemiological study of measles-specific immunoglobulin G antibody levels using a representative sample of a vaccinated suburban population in Sao Paulo State, Brazil in 1998. It suggested that within highly vaccinated populations, a proportion of individuals had measles antibody level which may be insufficient to protect against reinfection or clinical disease. This has particular relevance in Sao Paulo following the recent measles outbreak. A number of recent reports suggest that vaccinated individuals with low levels of immunity may be at risk of subclinical measles infection.

In recent years, vaccination levels in England have dropped from above 90% in the 1990s to 84% in 2001/2002. The impact of declining vaccination levels on clinical and subclinical infections result into the sporadic outbreaks.[71] In their studies Sharma Munesh *et al* and Manoj Murhekar *et al* also recorded the waning immunity as one of the factors for the outbreaks in the higher age groups.[59]

Socio economic status

According to Thakur JS, Ratho RK *et al* in 2002 and Jagvir Singh *et al* in 1996, the most probable factors to complications seemed to be the socio-economic status of the families resulting into under nourished children, overcrowding, low immunization and superstitions regarding measles.[62] In a retrospective study by VK Desai *et al* in 2003, Surat, the complications rate was the highest (38%) in the lowest income group and the illiterates.[61]

Role of Vitamin A and its deficiency in measles

An association between vitamin A deficiency and measles occurrence has been observed by Shears *et al*[72] and Zak-ur-Rab.[73] In the study of Sharma Munesh K *et al*, 2004 at Chandigarh, only 29.47% of the study children had received Vitamin A supplementation. A highly significant relationship *(P<0.001)* was observed between Vitamin A supplementation and measles cases.[59]

Vitamin A has two protective features to support immune defense system of humans. Vitamin A apparently has important immunomodulating properties, notably in patients with measles.[74] It helps in maintaining the integrity of epithelium of lungs and intestine.[75,76] Vitamin A therapy has been shown to reduce significantly the risk of complications (Hussey, 1990) and death (Fawzi, 1993) during measles disease. Clinical trials published to date have shown that vitamin A therapy resulted in a 65% reduction in the measles case fatality rate.[77] The two dose schedule has been advised but there were no trials that directly compared a single dose with two doses.[78]

(B) Factors associated with help seeking behavior of mothers of children with measles

Health care access

SN Gupta and Gupta Naveen observed in 2011 that For treatment (help) seeking behavior of mothers, 68% from case block go for faith healers followed by 12% by village elders/ neighbors/friends/relatives while 59% from comparative block opt for doctors. Nutritional care is given in the form of restricted diet in case area. As follow up practices in the post recovery phase from illness, 58% respondents from Shahpur block invoke the blessings of the goddess Sheetla while 68% of mothers from Nagrota Bagwan block attend the medical clinic.[31]

According to Sharma Munesh K *et al*, 2004 in Chandigarh and B.P. Gupta, S. Sharma *et al* in Shimla the communities which were provided with medical care and education over several years due to the vicinity of the medical college, the rate of complication and mortality was considerably less and mild (Complication rate 20% and nil mortality in both outbreaks)[59] as compared to Jagvir Singh *et al* in 1996 in U.P. where the case fatality rate was as high as 4.1% and the timely seeking of the medical help was also absent due to barrier beliefs.[64]

Megan Murray and Zeba Rasmussen in 2000 recorded that due to better awareness and availability of health services for majority Hassis Muslim community, their vaccination coverage was 37.6% and nil fatality vis a vis less privileged Sunni muslim community where vaccination coverage was 4.9% and 3% CFR.[56] According to Arumugam Mohan *et al* in 2005, there were lower attack rates and nil fatality in affected and unaffected Tsunami villages (1.3% & 1.7 per thousand) due to better awareness and availability of health services.[58] Puvimanasinghe *et al* 2000 studied in Sri Lanka, the maximum age specific morbidity rate were 114/lac for infants and 81/lac for 15-19 years of age. 54% of the cases belonged to≤15 years of age with the case fatality rate 0.1% on account of better health care.[57]

Prevention and Control

Jagrati V Jani *et al* (2006), in Mozambique recorded that the attack rates and case fatality rates in both of the cities of Manica and Gondola were 10/lac and 0.0%; 9/lac and 0.0% due to the traditions of their community to keep the ailing child separate till recovery and no treatment is sought except in complications.[49] The protective efficacy of the vaccination was proved due to the less severity of the symptoms and no case fatality in the study conducted by Sharma Munesh K *et al*, 2004 at Chandigarh.[59] B.P. Gupta *et al*,recorded zero mortality in Shimla despite 68% complications in the outbreak was due to timely supplemental immunization activities and vitamin A doses to all from 9 months to 5 years.[60] Compared to Susan van den *et al* in 2001, the Netherlands, where the overall vaccination coverage was 7-10%, the high attack rate turned out to be 37%, with complication rate 25% and the case fatality rate read as 1.4% signifying thereby that vaccination protection was not there.[53]

Complimentary Alternative Medicine Vs Modern Medicine

According to VK Desai *et al*, out of 233 suspect measles cases, 103 (44.2%) did not receive any treatment, 76(90%) were treated at public/ private center and 8 cases were taken to faith healers while as per study conducted by R. F. Grais *et al*, it was reported that 85.7% (979/ 1,142) of patients visited a health-care facility within 30 days after rash onset in Boukoki, 73.5% (519/706) in Moursal, and 52.8% (603/ 1,142) in Dong District. In Boukoki, the principal reasons provided for not visiting a medical facility were, lack of money (62%), traditional medicine was used (27% in Moursal and 19% in Dong District); and the patient did not have the money to pay for the visit (11% in Moursal and 16% in Dong District).[61]

Tabi MM, Powell M, Hodnicki D (2006) observed that traditional and modern medicines will always be part of Ghanaian healthcare delivery and efforts should be made to integrate traditional practitioners into the national healthcare delivery system. [79]In another study by Shaikh BT, Hatcher J,the health-seeking behavior of the people especially in developing countries calls for bringing all CAM healers into the mainstream by providing them with proper training, facilities and back-up for referral.[80] A positive interaction between the two systems has to be harnessed to work for the common goal of improving health of the people.

Beliefs and Barriers

SN Gupta and Gupta Naveen noted in 2012 that twenty three percent (27/116) of the cases went for the traditional treatment of *Vannan bushes* (medicinal herbal plant) which included repeated movements of the bushes upon the chest and face of the patients from nearby local *chelas/faith healers* (Traditional healers Vs modern medicine, $P<0.049$) and diet rich in *seul* (a herbal plant with small granules, more so in Bengali slum area, Sperrah and Gargoon villages and [restricted diet Vs Nutritious diet,$P<0.005$].[2]

Kalla AK Mahapatro M in 2000 studied health seeking behaviour in a tribal setting of a total of 621 Bhattara women from 473 households of six revenue villages in Madhya Pradesh. For any kind of illness, Bhattara women used home remedy on priority basis. It was observed that tribal women were not against the use of modern allopathic treatment in spite of the prevalence of the extensive use of traditional treatment. Interestingly, though their work output reduced significantly during their illness, they were not used to take bed rest, unless they were seriously ill. Since they believe that measles (gundi) and chickenpox (maa) occur due to the wrath of the Goddess (thakurani) on the patient, they visit the 'desari' rather than a medical practitioner.[81]

Similarly, in another study by Siddiqui N. Ghosh *et al* they noted that once upon the life time, *khasra* has to come out in life, it is goddess wrath, so worship is the only way.[82]

Coelho G in 1956 observed that the community believes that measles *(Khasra)* occurs due to the wrath of the Goddess-Sheetla, there is no need for medicines.[83]

Namuigi P, Phuanukoonnon S (2005) studied barriers to measles immunization and the beliefs and attitudes of caregivers in Goroka, New Guinea. They reported that funerals beliefs or election-related events in the area also affected the attendance at the clinic. It is important for all health workers to recognize that their performance and attitude can greatly improve the overall vaccine coverage in Papua New Guinea.[84]

Rosenstock I.M after studying poliomyelitis campaign in the United States for 27 years recorded that it is easier to make an extra visit than to change the beliefs of the people.[85]

BJ Selwyn (1978) found out that amongst all the adverse factors, there is some evidence that when economic and belief barriers are overcome, the distance and the like factors become less important.[86]

Amy A. Parker *et al*, 2005 observed that low vaccination was due to the fear of the adverse effects of immunization in which case Church intervened to help the two families for vaccination but rest of the families did not

agree.[51]

Padam Singh and R.J.Yadav (2000) conducted a Cluster Survey in 90 districts of India giving due representation to all the states and union territories. They found that 63% of the children are fully immunized, 27% are partially immunized and 10% are non-immunized. They recommended further improvements are possible by targeting illiterate mothers, inaccessible and tribal areas and low performing states.[87]

Latest changing trends in measles epidemiology and immunization

In order to lower the incidence of measles, a second dose of measles vaccine at either primary or secondary school entrance is effective, with a greater reduction occurring in states where the second dose/MMR is required for both age groups.[88] In U.S.A. and other European developed countries where this disease was once experienced by virtually all, have been reduced in incidence by more than 99% from pre vaccine era.[89] Nowadays there is distinct change in the measles and mumps disease pattern due to measles and MMR vaccination More and more case patients of measles and rubella are being examined in higher age group adolescent children[90,91] and multiple concurrent outbreaks of measles, rubella, varicella and herpes zoster have been observed in the higher age groups; 6-25 years; with attack rate more in 10-25 years group. MMR vaccines are given to the children according to our IAP schedule (1) immunity against measles and mumps lasts up to 12 to 15 years of age. Mumps was the disease of school going children, but now we see mumps patients in much older age group children. So introduction of MMR is very useful. Therefore, why not give booster dose of MMR say by 10 years of age?[92] There is a strong recommendation of rubella vaccine in adolescent girls. But why only rubella? Measles, mumps are also troubling our adolescents. If we start repeating booster dose of MMR vaccine, say by 10 years of age, then there is no need of rubella vaccination as well. The immunity from MMR lasts for 10-15 yrs of age. Then a booster dose at 10 years of age will give a life long immunity or should we go for third booster at what age? It is again a one million dollar puzzling research question for the medical scientists.

Acknowledgements

We extend our extreme thanks to the patients, their families and several individuals from Shahpur, Nagrota Bagwan, Jwali, Samote blocks; Health department Kangra at Dharamshala and Directorate of Health, Shimla, Himachal Pradesh. We also convey our thanks to laboratory support from National Institute of Virology, Pune and guidry support from National Institute of Epidemiology, Chennai.

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