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MEASLES: GLOBAL INDICATORS AND PROGRESS ON THE ROAD FOR ACHIEVING AND SUSTAINING VIRUS ERADICATION: A REVIEW

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Abstract

Measles morbillivirus is regarded as one of the most influential contagious viruses in the timeline of human history. Measles is usually known for its high infection potential and to date it remains a global killer, despite safe and effective vaccination. Unvaccinated young children, particularly from the developing states including regions from Asia and Africa, are among those who are at an acute risk of contracting measles. Industrious states and congested, overcrowded living situations have growing statistical rates, as 95% of fatalities due to measles are reported from these regions. Further, malnutrition in developing states are also main triggers of measles as those deficient in vitamins for instance vitamin A, are usually vulnerable. This is however an alarming rate and measles is to-date perceived as a worldwide concern of public healthiness. The study covers a review which cover world scenario on measles disease, the economic and potential condition, measles disease burden; effect of vaccine program, measles control programs, barriers in controlling the measles disease/ for the eradication of measles disease, and at the end major issues that have to be tackled for achieving a planet free from measles.

Keywords: Family medicine, Immunization coverage, Measles elimination; Measles eradication, Pediatrics, Retrospective Observational Study

INTRODUCTION

Measles is a feverish rash sickness that could result in severe medical conditions, mortality and one of the most infectious viral ailments, globally. Measles had previously triggered considerable human infection and mortality all over the globe, transmitting to almost every person reaching 15 years of age. This virus was commonly observed in every global region, causing an approximate 0.135 billion cases along with more than 6,000,000 annual fatality rate all over the globe (1). Only in the United States, around a quarter-half million individuals contracted the virus annually (possibly comparable to a birth cohort), out of which around 0.5 million diseased and about 500 fatalities were registered per year (1). The basic average or reproductive number of derived cases originated from an infectious individual in an entirely vulnerable population; for this disease is projected as 12–18 years of age, which is more than that of various other routine childhood sicknesses (e. g. pertussis, influenza).

Measles is a severely infectious ailment developed as a typical erythematous, maculopapular skin condition owing to the measles morbillivirus (MeV) (2). During 2000–2016, this ailment was significantly

dropped from 145 per million individuals to 18 per million individuals. Besides this, the current situation is that, this virus has re-surfaced, and its cases have been increased up to 25, 49, and 120 per million individuals, respectively from 2017 to 2019 (3). Additionally, the outbreaks of this virus have also monitored in the developed states with high acceptability of vaccination. The World Health Organization's pursued objective of eliminating measles is exigent, and it still prevails as a primary public healthiness challenge for mankind. The postponement caused in pediatric vaccines as a repercussion of the COVID-19 contagion, might intensify viral transportation of both; measles and additional vaccine-avertable ailments (1, 3-5). The eradication of measles eradication is achievable; however, serious commitment from all over the globe is necessary for sustaining long term developments to reduce measles mortality and morbidity trends along with achieving regional eradication objectives. The paper attempts to review the potential influence that the measles vaccine uptake has brought upon decreasing the burden of this disease on a global scale, the historical foundation of measles vaccination and their safeness and efficiency profiles, worldwide scenario of vaccination, the economic potential of investment in effective vaccines, the multiple impediments observed in control of measles in modern years, along with the major issues that have to be tackled for achieving a planet free from measles.

MEASLES VIRUS

Measles, additionally regarded as rubeola, is among the most transmissible contagious ailments, with at least a 90% derived infection ratio in vulnerable local contacts. Regardless of being viewed mainly as a childhood sickness; measles could be contracted by people of all age groups. It is an acute, monophasic illness categorized by fever, conjunctivitis and a maculopapular skin condition (6-8). Despite the vaccine being available for more than 30 years, measles remains a major cause of fatality in children in the developing regions and continues to cause outbreaks in developed countries (6, 9-12). The etiologic agent of measles is an *orbivirus* of the Paramyxovirus family. Other *Morbilliviridae* include Rinderpest virus, pest de petit ruminants, and canine, phocid and cetacean distemper. Although other primates bear a considerable chance of contracting measles, experimentally, humans are the only known reservoir for this organism (12-14).

CLINICAL MEASLES

Clinical measles is characterized by fever, malaise, coryza, and conjunctivitis. These symptoms typically occur between the eighth and twelfth day after exposure and constitute the viral Prodromal, (15-17) measles-specific signs and symptoms appear: Koplik's spots (red spots on the buccal mucosa) and the typical maculopapular skin rash between day 3 - 6. In immunocompetent hosts, the virus is cleared within 5 - 7 days of the onset of the rash and immunity after natural infection is thought to be life-long (18, 19). Complications following infection are common. Secondary viral or bacterial pneumonias occur in 1 % - 7% of measles cases, and account for almost all of the mortality associated with this disease (20). Neurologic complications include post-infectious encephalomyelitis (an autoimmune disease) and subacute sclerosing panencephalomyelitis (a rare, progressive and fatal syndrome due to persistence of heavily mutated virus). Measles can be a progressive and fatal disease (giant cell encephalitis or pneumonitis) in children with T cell dysfunction.

Individuals that have contracted measles are infectious for many days after and before the inception of rash. In preliminary stage, clinical revival is just successive to rash appearance, along with resulting in viral clearance and lifelong immunity (2, 5, 21, 37, 40). As a consequence of the immunosuppression induced by measles infection, and the direct damage to the respiratory tract (loss of cilia), secondary bacterial, viral and parasitic infections may occur. In developed countries, complications such as otitis media, gastroenteritis, pneumonia, myocarditis and pericarditis occur in approximately 10% of measles cases, with encephalitis occurring in a very small subset of cases (21, 22). In developing countries, complication rates may reach 80%. Pneumonia and gastroenteritis due to secondary infections are the most common fatal complications, especially in malnourished and immunocompromised children. Up to 15% of

immunocompetent adults with measles may also experience pneumonia as a direct result of the measles virus (MV) infection, as opposed to a secondary infection (4, 23-25).

ORIGIN OF MEASLES VACCINATION

Edward Jenner discovered the measles vaccination development initially in 1796 when he observed that dairy maids infected with cowpox, exhibited immune behavior towards smallpox. Advances in vaccine development and discovery have been of additional importance with reference to measles virus control (7, 26, 27). In 1963, Dr. Maurice R. Hilleman patented the vaccine and since 1970, more than 500 million units of the vaccinations have been distributed globally.

MEASLES DISEASE BURDEN; EFFECT OF VACCINE PROGRAM

During the 1980s, the usage of vaccines of measles was widespread all over the globe. This resulted in decreased and lowered levels of recorded cases and mortality ratios due to measles in all global regions. Through 2000–2018, the yearly measles cases per million individuals reduced about 66%, to 49 records from 145, the yearly record of registered measles contractions reduced by 59%, to 353 236 from 853 479, and annually projected measles fatalities reduced about 73%, to 142 300 from 535 600, worldwide (9). Furthermore, in 2000, United States achieved measles riddance (i.e, non-existence of constant endemic measles morbillivirus spread for more than 12 months), (9, 28, 29) and during this time fresh measles cases initiated via introduction from foreign countries, primarily from unvaccinated individuals (1, 30).

MEASLES CONTROL PROGRAMS

It is important to note that, in 2019 the World Health Organization (WHO) described hesitancy in vaccination to be among the 10 crucial issues in worldwide public health. It is estimated that before the global use of measles vaccines, there were approximately 2.6 million measles-related deaths annually, and that more than 90% of children would have been exposed to measles by 15 years of age. A two-shot vaccine dose for measles enclosed vaccine is the most efficient way to reach the stage of population immunity (~95%) needed for interrupting measles transmission. Approximately 16% of children jabbed of 09-11 months of age, and about eight percent vaccinated at =12 months, fail to develop immunity to measles when given one dose of MCV. This primary vaccine failure is generally overcome through delivery of an additional shot of MCV (MCV2).

Supplementary immunization activities (SIAs) greatly enhance vaccination equity by reaching more unvaccinated children than routine vaccination alone but follow-up campaigns must be conducted every two to four years to prevent outbreaks until routine coverage reaches at least 90%. Implementation of this strategy allowed the Americas to eliminate measles in 2000. By 2008 all WHO member nations (193) offered one dose of MCV1 (measles vaccine) although the timing of schedules varied, 132 countries offered MCV2 as part of the routine schedule and 152 countries conducted SIAs with the result that 192 countries provided a 2nd shot of MCV either as a regular second jab, or SIAs or mutually. By 2010, all member countries offered MCV2, with 139 countries offering it as part of the routine schedule (CDC, 2012) (8, 31-34). The level of vaccine coverage varies greatly between countries and in 2009 the average global measles vaccination coverage was only 82%, and increased from 58% in 2000 to 78% in 2010 in the 47 priority countries (CDC, 2012). In the post-vaccine era, measles outbreaks occur in regions where there is suboptimal vaccination coverage. For example, in Africa, susceptible individuals are generally those who have not been offered vaccination, or are too young to be vaccinated (under 9 months of age) (14, 31, 35). In Europe, many susceptible individuals live in communities comprising immigrants originating from countries in which there is low vaccine coverage, or in communities that choose not to be vaccinated or have restricted access to healthcare due to religious convictions; they are generally surrounded by highly vaccinated populations and therefore benefit from the herd immunity of these populations. The objective of the MDG 4 (Millennium Development Goal 4) is the reduction of overall children fatalities by 66% by 2015 as compared with stats from 1990 (36, 37).

Global fatality rate associated with measles has reduced by 78% from 2000 to 2008, 92% reduction in the African Region in (2001-2009) which represents approximately a 23% of the total reduction in childhood deaths from 1990 as well as 24% from 2000, averting an estimated 4.3 million deaths. This progress, especially in the 47 high-measles burden countries, was made possible by the technical and financial assistance of the MI (Measles Initiative), commenced around the year 2001. The MI is an international organization founded and led by the World Health Organization (WHO), United Nations International Children's Emergency Fund (UNICEF), Centers for Disease Control and Prevention (CDC) and American Red Cross. However, due to global financial constraints, financial assistance to the Measles Initiative reduced from US\$ 150M in 2009 to US\$ 35M in 2010, (33, 37-39) and a number of prioritized states have been unable to generate the required 50% of the operating costs, resulting in the delay of scheduled SIAs and drops in the range of targeted age groups. It is estimated that the progress in measles fatality reduction will be lost unless the financial situation can be improved, and indeed, a reappearance of measles has been observed influencing 28 counties in sub-Saharan Africa from the latter part of 2009 resulting in more than 200, 000 recorded cases as well as more than 1400 recorded fatalities but as there is under-reporting of both cases and deaths, it is estimated that the figures are likely to be 10-20 fold higher. Despite decreases in measles case reporting in 2010 in three of the WHO regions (Western Pacific, Eastern Mediterranean, South East Asia), global incidence increased as a result of outbreaks in Africa and the European region.

STRATEGIC PLANS FOR MEASLES ELIMINATION

Measles prevails as a primary source of ailment and fatality, accounting for close to 970,000 records and more than 140,000 measles-connected mortalities in 2018. Rubella remains a priority contagion in a number of states and CRS (congenital rubella syndrome) continues to be reported with long-term consequences. As one of the most contagious diseases has given the need to maintain higher population immunity for prevention of viral outbreak, measles eruptions act as a hint (the “canary in the coal mine”) that highlights health system weaknesses and inequities (38, 40).

The MRSP 2012-2020 (Global Measles & Rubella Strategic Plan 2012-2020) gathered struggles to guard and recuperate the lifestyle of youngsters all over the globe through monitoring the spread of rubella and measles. By the end of 2019, all Member Countries of the World Health Organization initiated MCV2, a 2nd shot of measles-enclosed vaccine and 173 initiated rubella vaccine coverage program (41). In 2019, worldwide coverage with both rubella and MCV2 vaccines increased to 71%. Surveillance capacity and quality to detect and respond to outbreaks improved in Strategic Plan 2012-2020. While significant attainments were made, numerous circumstantial variations and operation challenges obstructed improvement and added to a growing number of occurrences and reappearance in measles records such as a transition in the measles epidemiology with an increased ratio of infection in young infants and elderly people, highlighting unattended immunity loopholes. Augmented recognition of immunity gaps in immigrants and emigrants other than cross-border inhabitants who are often not involved in the national vaccination strategies. The postponement of scheduled SIAs and distraction in amenities owing to the COVID-19, further aggravated the immunity breaches.

The MRSF 2021-2030 (Measles & Rubella Strategic Framework 2021-2030) established to outline the national and regional strategic frameworks as well as operational planning using a comprehensive participatory cycle to get systematic responses on the attainments and main shortfalls of the previous decade, as well as the pivotal strategies, priority areas and focal points needed for the upcoming decade. The goal of MRSF 2021-2030 is the provision of guidelines to every immunization stakeholder at all levels; Global, National and Regional, with respect to planning and implementation of much more efficient eradication programs for rubella and measles whilst raising the ambition efforts towards realizing a planet free from rubella and measles.

Measles and rubella eradication tactics might not accomplish the similar in all states, and practices of the GPEI (Global Polio Eradication Initiative) divulge the significance of recognizing, predicting and handling obstructions to operational execution of contagion monitoring strategies.

BARRIERS IN CONTROLLING MEASLES VIRUS



A number of challenges are prevalent in the way forward for accomplishment and upholding the herd immunity limit required for elimination of measles, which is usually projected to be more than 92%–94%. The achievement of this immunity level needs extensive political strategy as well as eradication of physical and financial access impediments in measles vaccination cycle;

- Modification of public health facilities (e. g. inconvenient hours and clinic location).
- Fighting Spread of misinformation causing mistrust and hesitancy in vaccination.
- No nonhuman reservoirs (i.e. unimmunized human body is necessary for the life cycle of the measles morbillivirus).
- Presence of hands-on and systematic indicative equipment, e. g. Molecular tests for identification of individuals with acute measles and Immunoglobulin M (IgM) serologic assays.
- Highly effective measles vaccines.
- Maintenance of review records for the elimination status in 2019.
- Inadequate monitoring system.
- Insufficient surveillance and monitoring capacity and quality for confirmation of removal.
- Lack of effective management, communication and coordination at the national and international levels.

DISCUSSION

Measles is usually known for its high infection potential and to date it remains a global killer, despite safe and effective vaccination. Unvaccinated young children, particularly from the developing states including regions from Asia and Africa, are among those who are at an acute risk of contracting measles. In 2002, the Global fatalities owing to measles virus totaled 611,000 deaths. But, in 2008 this toll has considerably dropped to 164,000. This is however an alarming rate and measles is to-date perceived as a worldwide concern of public healthiness. In the United Kingdom, 10% of infected individuals are clinical admissions and the statistical trend is 1 in 5000. Moreover, industrious states and with congested, overcrowded living situation have growing statistical rates, as 95% of fatalities due to measles are reported from these regions. This is additionally recognized from evidence stating that malnutrition in developing states are main triggers of measles as those deficient in vitamins for instance vitamin A, are usually vulnerable. The measles is from the family of paramyxoviridae which also include the respiratory syncytial virus and mumps.

The infectious transmission of measles is a primary concern for the 'Global Health Response' and disease control; as their objective was to bring reduction in fatality trends through 1990 to 2015. Due to its single stranded RNA and gram negative viral nature, measles is a severely contagious ailment. It enters the human body through throat and nose via air-borne spreads. This is usually due to the close proximity sneezing or coughing of an infected individual. Inside the atmosphere, its survival life cycle is about 120 minutes in water droplets. As only the humans could be infected, they are the only carrier or host of this virus. Hence, direct transmission takes place as it impacts the upper respiratory system, at first. As the virus could survive externally for 120 minutes, it could be eradicated through Ultraviolet radiation / High temperatures. This describes why measles is perceived as a worldwide concern and why the eradication of this virus is challenging. The RNA of measles virus is helical with proteins contained in a nucleocapsid. These proteins are fusion proteins along with hemagglutinin contained inside a lipid bilayer.

Alongside considerable achievement in reduction of measles cases and fatality trends on a global scale since 2000, the eradication plans have faced major setbacks recently. The projected MCV1 covering globally has peaked around 84%-85% for about 10 years and the recorded worldwide measles diagnosis amplified to 869770 in 2019, from a record low of 132 490 in 2016; about 556% increased rate. Moreover, among individuals with confirmed diagnosis of measles registered in World Health Organization through 2013-2018, 30% had an unconfirmed vaccine history and 45% had never received MCV prior to their diagnosis. Committed attempts and intensified resource allocation by international associates and states are required for getting progress towards measles eradication. The World Health Organization (WHO) as well as Center for Disease Control and Prevention (CDC) have framed thorough guidelines to tackle vaccine

hesitancy. In this connection a detailed document outlining immunizations guidance, known as the Immunization Agenda 2030 (IA 2030), was co-created by World Health Organization (WHO) and associates and will be recommended by the World Health Assembly (WHA). The IA 2030 focuses on the lessons absorbed and achievements of Global Vaccine Action Plan (GVAP). The IA 2030 has attempted to utilize measles, an efficient tracer or indicator for evaluation of Expanded Program on Immunization (EPI), for driving commitment to reinforce immunization and primary healthcare facilities.

Concentrating on elimination strategies for measles could possibly increase conveyance of regular immunization for secondary vaccine-preventable ailments, assist in the identification of under vaccinated or non-vaccinated populations and close immunity lags, direct modifications in expansion and surveillance of cold-chain capacity, generate opportunities for provision of refresher trainings on vaccination system to public health employees, and forward the utility of tactics utilized for measles eradication in an attempt to guarantee elevated covering trends for vaccination of other sicknesses (eg, college-entry requisites). IA 2030 hence creates a prospect to reinforce vaccination systems, focus on public healthiness associations, as well as promote data-oriented strategies which utilize disease monitoring for growth in vaccine covering trends and parity in every population.

In a nutshell, measles is perceived as a potential killer sickness specifically if it is left uncontrolled. It prevails as an extremely infectious ailment alongside having supplementary and secondary medical concerns for instance blindness and SSPE. It has constantly proven itself to be a challenge for the Global Health Response and with additional research it could hopefully be eliminated globally.

CONCLUSION

The infectious transmission of measles is a primary concern for the 'Global Health Response' and disease control; as their objective was to bring reduction in fatality trends. Measles is one of the harmful disease that remain a leading threat for infantile at global level. Its effects become much higher during the humanitarian catastrophes. Despite decrease in measles case worldwide as noticed in last decade, global incidence in measles cases increased as a result of outbreaks in Africa and the European regions. In controlling the measles disease several challenging barriers were identified, these include lack of highly effective measles vaccines, non-accessible of vaccination centers, deficiency in distribution of vaccine services, low knowledge about measles disease, low presence of hands-on and systematic indicative equipment, Inadequate monitoring system, lack of effective management, communication and coordination at the national and international levels etc. due to these hurdles which increase the risk of spread of measles disease especially in outbreaks of measles in catastrophic conditions. Global commitments to increase community access to and demand for immunizations need reinforcement of local and international partnerships for the development of public health infrastructure, and implement research based innovations that can overcome access barriers and developed vaccine confidence, necessary for eradication measles disease. A notable success in measles control by vaccinations have been recorded worldwide by development and testing of dissolving microneedle patches for the delivery of measles vaccine that shows intradermal vaccination method is a promising way to improve the efficiency of delivery of vaccination for eradication of measles disease.

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