

Vaccines as the Medical Weapon for a Promised Healthy Generation

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Abstract: Vaccines are the health promise to the next generation. Immunization is the powerful tool that provides immense health benefits to the individuals by the eradication and protection from several diseases. The neonate health promise begins with the maternal immunization. This immunization strategy is an established strategy for the public health. For e.g., studies show immunization of pregnant mother with influenza vaccine decreased the infant infection up to the 6 months of age by 63%. Vaccine efficacy should consider the health and non-health benefits of the individuals of both vaccinated and unvaccinated population. This vigilance helps to know the efficacy of the vaccine in the individuals, effectiveness in the communities and further the impact in the society. The source from which vaccine develops also have impact on the society. For eg.; the administration of vaccine developed from Fetal cell line puts a negative impact to certain societies. Vaccination has significant role in the creation of a healthy population and hence a healthy and prosper nation.

Date of Submission: 30-01-2020

Date of Acceptance: 17-02-2020

I. Introduction

Immunization is a powerful tool that provides immense health benefits to the humanity by extended life expectancy with the eradication and protection from several diseases. Diseases like polio, small pox, diphtheria, measles, mumps, rubella etc are some among them that have been thrown out from the globe with the introduction of routine immunization programs [23, 25]. Vaccines are one of the medical interventions in the 20th century for the upliftment of public health [10]. Reports reveal that lack of awareness about the routine vaccination and safety measures among public leads to the re-emerge and out-break of defeated diseases. The recent outbreak of measles, H1N1 influenza etc link to the lack of safety concerns in the public [7]. Currently there are routine vaccinations for pregnant mother, infants, children at different age groups and even for adults. The CDC and American Academy of Pediatrics introduced a guideline for the wider awareness and monitoring the parent's concern in vaccination in association with National Immunization survey. The ratio of immunization and medical visits of teens and adults are very low compared to young children [23]. The complete benefits of all the medical interventions can be achieved by the sustained social and political support. However, the efficacy and safety of the vaccines are crucial during the regulatory decisions of the vaccine to be licensed [6].

The status of poor countries that unable to raise the fund for vaccine availability makes them vulnerable to various diseases [25]. Another reason that makes certain population or communities to disagree to administer the vaccines is the source of development of the vaccines. Certain vaccines are developed from cells derived out of human fetal cells obtained from elective abortions that are used in pharmaceutical industries and in medical research.

Vaccination in pregnant mother transfers the immunity to the fetus, hence both mother and the child are protected. Rubella, Hepatitis B, whooping cough, zika etc are some of the diseases that get transferred from mother to the fetus during pregnancy. The health promise to the neonates begins at immunization of pregnant mother. Hence vaccination during pregnancy has to be established wisely for the buildup of a healthy generation [30]. There are various routine immunizations programs conducted by the governments to look after the public health. This review tries to put light on some of the issues that sustains and hinders the vaccination and further a healthy generation.

Benefits of Immunization

Invention of vaccines is one of the great achievements in the medical field for the public health during the 20th century [11]. Immunization programs benefit by promising healthy immune system in a healthy body and hence an extended life with the eradication of several diseases. Smallpox, polio, diphtheria, measles, mumps, rubella, etc are some of the deadly diseases that have been thrown out with the introduction of routine immunization programs. Some vaccines are introduced specifically for travelling and occupational purposes also

[26]. By increasing the immunization coverage in young children, the elimination of diseases can be sustained. During the 21st century, the routine immunization recommendation expanded in the US. In 1980s the recommended list included vaccines against 6-7 diseases, but in the following decades the recommendations expanded to about 20 diseases, which include rotavirus, HepB, HepA etc. The NIS report, 2013 says high vaccine coverage could sustain the low proportion of unvaccinated children of age 19-35 months old, and the target named *Healthy People 2020* monitors the children to get vaccinated and hence to create a healthy nation. [21] The wide immunization programs increases the herd immunity of the population.

Infectious diseases such as small pox, whooping cough, diphtheria, tetanus etc that were devastating throughout the history until 20th century are now rarely seen or eradicated from the globe by the introduction of vaccines [25]. Another deadly disease called Hemophilus influenzae type b (Hib) that claimed about a lakh of deaths in children of under 5 years age worldwide in the recent past has been reduced drastically with the help of vaccines.

The CDC and American academy of pediatrics introduced a guide to expand the awareness and also monitor parent's concern with national immunization survey. The ratio of vaccination and medical visits among teens and adults are very low compared to young children. The complete benefits of all the medical interventions can be achieved by the sustained social and political support to immunization programs [23]. Wide range of vaccines for various diseases are in the developmental stage. Effective vaccines for malaria, tuberculosis, AIDS, cardiovascular disease, autoimmune diseases, various types of cancers may be anticipated in nearby future. [8]

Immunization during pregnancy – A health promise to next generation

The neonate health promise begins with the maternal immunization. This immunization strategy is an established strategy for the public health [30]. Vaccinated pregnant mother protects the baby from diseases by immunizing them during their first few months of life. The antibodies developed in the mother's body get transferred to the fetus during pregnancy [15]. Several diseases that may pass on to the fetus through placenta and to the new born through breast feeding from the mother include rubella, hepatitis, flue, whooping cough, zika, measles, mumps, chickenpox etc. Effective vaccines are available except zika virus infection. About 9% of pregnant mother infected with varicella virus are prone to develop pneumonia and the placental transmission of virus cause congenital varicella syndrome to the fetus that results neurological defects, skeletal abnormalities etc [29].

Vaccination against influenza during 2nd and 3rd trimester of pregnancy becomes necessary to reduce the risk of fetal complication [2]. Studies show immunization of pregnant mother with influenza vaccine decreased the infant infection up to the 6 months of age by 63%. Also vaccinating the pregnant mother against whooping cough, protect the babies from the severe complications of pneumonia and brain inflammation that may develop following the infection [19]. Tetanus claims the life of more than a lakh of neonates worldwide every year. Tetanus is caused by toxin produced by an aerobic bacterium called *Clostridium tetani*. Infection occurs environmental exposure of broken skin or wound to the spores of the bacteria that is present universally in the soil Tetanus vaccination to the pregnant mother is one of the successful proof of antibody transformation from mother to the fetus [30,17,28].

Recent evidences show maternal exposure to infection 'in utero' prime the infant immune system, not necessary the infant's exposure to the infection [15]. IgG transfer through placenta during pregnancy is responsible for the passive immunity of the new born. Vaccination during pregnancy boosts the mother's immunity against the vaccine specific antigen by increasing the antibody concentration, further increase in the transplacental antibody concentration.

Effectiveness and safety of vaccination

Vaccines are boon to the public health however, safety and effectiveness after the vaccine administration is an important concern to be investigated. The recent outbreak of vaccine preventable diseases such as measles, H1N1 influenza etc. can be linked to lack of safety concerns among the public [23]. The detailed clarification of risk and benefits of vaccines during pregnancy increases the confidence of pregnant mothers on vaccination [32]. Vaccine efficacy should consider the health and non-health benefits of the individuals of both vaccinated and unvaccinated population. This vigilance helps to know the efficacy of the vaccine in the individuals, effectiveness in the communities and further the impact in the society [6]. Efficacy is the performance of an intervention under controlled circumstances, effectiveness is the performance of the same intervention under real world or real condition. The effectiveness in a vaccinated population is high by decreasing the disease rate, whereas the effectiveness in the unvaccinated population will be low with a high rate of disease cases.

The evaluation of a vaccine efficacy by the traditional method i.e. against a placebo in an individual randomized clinical trial (iRCT) gives insufficient data. In certain circumstances cluster randomized clinical

trial (cRCT) is more reliable than iRCT in evaluating the vaccine. The impact of vaccination covers the health and non-health benefits of the public. The non-health benefits include income, employment, education etc. that emerge from the vaccine research, manufacturing and distribution and, another indirect impact is the cost of the vaccine. Cost effectiveness broadens the vaccinated population [17, 27, 22].

The safety of pregnant mother is a key consideration after the vaccine administration. Despite the vaccine recommendation and awareness on the benefits of immunization during pregnancy, there is reluctance to accept the vaccine [1]. However the adverse effect after vaccination during pregnancy has been studied and still in progress, in low and middle income countries (LMIC) the vaccine safety study is hindered by lack of standards for post vaccine outcome measurements and harmonized methods. This drawback affects the pharmacovigilance program and other observational studies. Hence there is recommendation for need of globally harmonized method to monitor the safety and efficacy of vaccines and immunization by Food and Drug administration (FDA), European Medicine Agency (EMA) and International Conference for Harmonization (ICH) [31, 4].

The FDA issued the pregnancy and lactation labeling rule (PLLR) that summarizes the information of risk of administration of different ingredients in vaccines and drugs during pregnancy [18]. The global alignment of immunization and safety assessment in pregnancy (GAIA) project that funded by the Bill and Milinda gates foundation in response to WHO call is for the active monitoring of the safety of immunization in pregnancy program and with LMICs needs and requirements as a specific focus. In GAIA 13 organizations were collaborated globally along with 200 volunteers to achieve the goal [14]. Lack of base line guidelines for vaccination during pregnancy may lead to challenges like unpredictable epidemiology, receiving and retaining of pregnant mothers in the clinical trial etc. These challenges can be overcome by tying up with Maternal, Neonatal and Child Health (MNCH) and Antenatal care (ANC) providers. MNCH and ANC are involved in the welfare of pregnant mothers by identifying and monitoring them. This helps the clinical trial flexibility and conducting the research in low resources [4].

Different measures such as Vaccine Preventable Disease Incidence (VPDI), Number Need to Vaccinate (NNV) etc for the vaccine evaluation need to be used more systematically to get a complete evaluation. Even though VPDI and NNV have limitations that their metrics depends on local epidemiological study, but advantage is that it focus not only on degree of vaccination but also on disease prevention capacity of vaccine [25].

Vaccine development from Fetal cell line and its impact on society

Vaccines were developed using various cell lines that were extracted from different animal sources (such as chicken eggs, monkey cells, rabbit cells etc.) as well as human cells from aborted fetuses. The cell culture technique to grow vaccine viruses in human cell lines rather than animal's is a significant step in the development of vaccine. Human pathogens grow well in human cells compared to animal origin. Cell culture technique involves growing the cells in a cultured vessel. Cells extracted from a living tissue and never sub cultured is primary culture. Primary culture contains many types of cells. The single type of cells that developed from the sub culturing is called *cell strain*. Different methods to isolate single type cell from the mixture include centrifugation, colony isolation etc. This cell strains can be used for growing human pathogens like viruses. These viruses grow using the nutrients of the host cell, but with the attenuation of the viruses. The attenuated viruses are able to grow and replicate, but unable to cause disease.

The real issue is that most of the current vaccines are developed using electively aborted human babies' cell lines. Even though the vaccines itself do not contain the baby's cells, they contain biological residues of fetal cells including cell protein and DNA. The 2 fetal cell lines that have been used in the development of vaccines are WI-38 and MRC-5. WI-38 developed in Wistar Institute in Philadelphia was isolated from lung cells of an aborted female baby in the year 1962 and MRC-5 developed in Medical Research Council in England was also from lung cells of an aborted fetus in the year 1966 [13]. Apart from these two fetal cell lines, another was developed in the year 1985 and that is being used in the vaccine developmental research to treat several infections like Ebola, HIV etc. The importance of using induced aborted fetal cell lines in the study of variety of diseases and medical conditions is because of it is not completely developed into adult tissue and hence able adapt to any environments. The U.S. Department of Health and Human Services reports that fetal tissue research study is going to be the critical platform for studying down syndrome, autism, schizophrenia, other degenerative diseases etc. [9]

The ethical quandary of using the vaccine developed from aborted baby's cell line, otherwise beneficial to the humanity is vexing. However there are justification that these vaccines protect the children from life threatening diseases, the morality of developmental path cannot be justified. Hence the uncertainties of administration of these vaccines exist. Currently there are alternative vaccines for most of the human cell line vaccines (refer Table 3 and Table 4). [10, 5]

Vaccines such as VARIVAX, MMR-II, HAVRIX etc manufactured by giant Pharma companies are developed from human fetal cell lines. The catholic church abstains the use of human cell line developed vaccines, but they permit the temporary use until an alternative vaccine is available for the life threatening disease. [7]

Global economy and vaccination

Healthy individuals build up a healthy society and can contribute to the economic growth of the country (Fig-1). Vaccination has significant role in the creation of a healthy population. Childhood vaccination programmes offer individual child protection from dangerous diseases, hence preventing fatality as well as temporary and permanent sequelae rate. Thus transformation of healthy childhood into a healthy adulthood [16]. The poor countries that are in the claws of poverty, under nutrition and epidemiology may struggle to raise the fund for the health industry and hence the potential of youth diminishes due to health complications. Jeffrey Sachs, who is an economist at Harvard University, noted that impoverishment is the culprit of illness and mortality other than poverty. Immunization is at the forefront to face these challenges. This may be achieved through proactive information exchange, education, communication, sustained vigilance on public health. [11, 10]

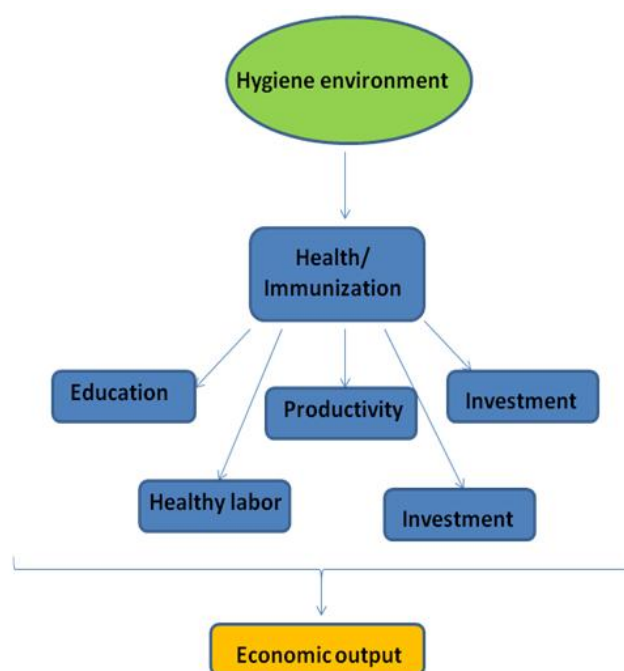


Fig:1- Interconnection of healthy individuals and economic growth of the country that is related to immunization

According to a recent report, about 1200 death cases among which most of them are children, due to measles epidemic in Madagascar. The main culprit was the cost of the vaccine. The families with small income and having several children were not able to afford the expense on vaccines [10]. The government should aware that an immunized population creates a healthy and economically improved nation. The study on cost benefits of vaccines' expanded immunization on disease cases, treatment and fatality rate found that the immunization could save about \$7.4 billion in acute care cost, about \$6.2 billion in treatment costs. Long term immunization program saved an estimated cost of \$151 billion and this economic benefit followed saving the lives of 6.4 millions, 426 million cases of illness and 63,000 children from being disabled due to meningitis. This analysis also adds the benefits of investing in immunizations over Decade of Vaccine by estimating the tangible monetary benefits. [33]

II. Conclusion And Future Perspective

Benefits of vaccination or immunization do not limit on prevention towards various diseases, but healthy individuals followed by a healthy society leads to economic growth. Immunization may starts at the fetal stage i.e. maternal vaccination and post natal vaccination. Maternal vaccination to prime the infant immunity is an emerging and exciting field to be investigated further. None of the scientific study reports the risk factors of fetus after the vaccination of pregnant mother with any of the vaccine type such as, toxoid, inactivated etc.

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