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Opinion

Need for vaccination for VL elimination

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Opinion

To realize the targets of sustainable health goals and well-being it is necessary to realize that the health targets are set and are realized in time. One of the main SDG goals is the elimination of neglected tropical diseases(NTD). *Leishmaniasis* is one of the major diseases, where the endemic nations have committed to give impetus to their respective public health programs to eliminate the disease by the year 2020. WHO http://www.who.int/leishmaniasis/en/ estimates that 900000-1.3million new cases and 20000 to 30000 deaths occur annually due to *Leishmaniasis.* There are three main forms of *Leishmaniasis*, *Cutaneous, Mucocutaneous* and *Visceral Leishmaniasis* (VL). VL causes the most severe disease affecting visceral organs, can be fatal if untreated. VL begins with skin ulcers which are followed later with presentation of fever, low red blood cells, and enlarged spleen and liver. Sometimes in treated patients of VL, Post-Kala-Azar Dermal Leishmaniasis (PKDL) syndrome occurs characterized by macular, maculopapular, and nodular rash which is on the rise. Clinical symptoms of VL disease in the initial infective stages overlap with symptoms of other diseases that make it difficult to diagnose. The VL disease is still a major health challenge in parts of the developing world having people in the most impoverished conditions where the disease is endemic. VL is caused by parasite *Leishmania donovani* and is spread by female *Phlebotomine Sand fly (Phlebotomus argentipes)* which is the vector transmitting the disease to humans. In VL the parasite infects the mononuclear phagocytic system affecting spleen, liver and bone marrow. Chemotherapy and vector control are the main stay of management and control respectively for VL in the current existing programs. No effective vaccine for VL is available as yet. The efforts for Kala Azar management have increased and the major strategies included the following.

1. Early diagnosis & complete case management.
2. Integrated Vector Management and Vector Surveillance.
3. Supervision, monitoring, surveillance and evaluation.
4. Strengthening capacity of human resource in health .
5. Advocacy, communication and social mobilization for behavioural impact and inter-sectoral convergence
6. Programme management.

In South Asia, the spread of VL disease is Anthrophonotic in nature spreading from human to human. While in some other parts of world like in Europe the Leishmaniasis is Zoonotic in origin, which spreads from animals to humans, like from the canine population. Elimination programs focuses on breaking the transmission of the disease. Environmental factors in endemic areas like suitable breeding habitats of the Sand Fly vector are a major hindrance for VL elimination. This leads to rapid vector mediated transmissions of the Leishmanial parasite from the human to humans/animals. Sanitation also plays a major role in the disease spread. The vector control programs faced challenges due to toxicological issues of pesticides /insecticides like Dithiothreitol (DTT).

Thus after banning or curtailing its use in several parts of the world, synthetic pyrethroids, that are nature derived products, are now being used in larger scale. Sporadic cases of resistance to pyrethroids seems to be developing in vectors is being reported and in future large scale resistance is a possibility, Gomes et al.,[1] Karunamoorthi et al.,[2]

The main treatment regimens for VL are chemotherapy. Drugs have varying degree of successes against VL. The treatment with pentavelent anyimomonials like Sodium stibogluconate (SSG) during twentieth century have led to development of resistance in the parasite and have largely been discontinued. Treatment is moving towards use of Amphotericin B, Ambisome, Paromomycin and Miltefosine. New drug dosages regimens are being clinically tested to treat VL and PKDL, both singly and in combination. Majority of drugs have to be administered as infusions in the in hospitals under medical supervision which is a major drawback to bring treatment to the far flung endemic areas. Further the drug regimens have major drawbacks with adverse reaction, toxicity due to treatment over many weeks and varying dosage tolerance among patients. The treatment regimens cannot be tolerated with individuals affected with kidney, and liver disease. The prolonged treatment also has tendencies to give rise to resistance in parasite making them redundant for future treatment Yesinia et al.,[3] Kamhawi.[4]

The efficacy of interventions depends upon other factors like individual's genetic makeup and immune status. Protection of the individual from VL infection strongly depends upon the host immune response. In many healthy individuals self-healing or spontaneous healing of *Leishmania* infection occurs. Thus people can be naturally immunized from the *Leishmania* infection and many such cases have been reported. Leishmanization or deliberate introduction of *leishmania* into healthy individuals has been used a crude method of immunization in many countries from historical times. This used to provide protection to individual in endemic areas. The inherent dangers of the method leading to disease spread have curbed its use in modern times. So we can explain the prevalence of *Leishmania* infection among the economically improvised communities owing to lack of

nutrition and sanitation. This necessitates the need for prevention and treatment through new immunotherapy regimes which are one major of the research gaps for VL. Preventive measures are always better, so there is a need for successful vaccine for VL disease in the elimination program. Further vaccine research has to aim at both being preventive and therapeutic. The development of new vaccine candidates using latest technologies to prepare protein, DNA and live attenuated vaccines is now looking feasible Kumar et al.,[5] An introduction of successful vaccine candidate will reduce the drug dosage thus saving the cost of treatment as well as incidence of adverse effect of drugs. What is required is a comprehensive and uniform regulatory framework in South Asia and for the parts of world if possible where the VL disease is most prevalent. This will ensure that robust and speedy clinical trials of vaccine candidates takes place which will further ensure the choosing of the most effective candidate for introduction in the elimination program. This will coupled by data repository and information collation and dissemination system for surveillance and monitoring of program. The databases have to be accessible to all stakeholders both in public and private sector across endemic countries. This can be built along the lines of Global Health Observatory of WHO http://www.who.int/gho/ en/. There is also a need for integrating the welfare program for nutrition and development program along with the VL elimination program. So it is imperative that introduction VL vaccine in the elimination program is need of the hour and our efforts should in that direction. Thrust should be given for formulation proper policy impetus towards parasitic vaccines with focus on VL.

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Referencess

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