Journal of Advances in Science and Technology

Vol. 10, Issue No. 21, February-2016, ISSN 2230-9659

AN ANALYSIS UPON ECONOMICS OF INTEGRATED MALARIA VECTOR CONTROL: A REVIEW

AN INTERNATIONALLY INDEXED PEER REVIEWED & REFEREED JOURNAL

www.ignited.in

Journal of Advances in Science and Technology
Vol. 10, Issue No. 21, February-2016, ISSN 2230-9659

An Analysis upon Economics of Integrated Malaria Vector Control: A Review

Parveen Kumar Rai[1]* Dr. Surendra Sarsiya[2]

[1]Research Scholar, SSSUTMS, Sehore

[2]UTD, SSSUTMS, Sehore

Abstract – Malaria is one of the most common vector-borne diseases widespread in the tropical and subtropical regions. Despite considerable success of malaria control programs in the past, malaria still continues as a major public health problem in several countries. Vector control is an essential part for reducing malaria transmission and became less effective in recent years, due to many technical and administrative reasons, including poor or no adoption of alternative tools. Of the different strategies available for vector control, the most successful are indoor residual spraying and insecticide-treated nets (ITNs), including long-lasting ITNs and materials. Earlier DDT spray has shown spectacular success in decimating disease vectors but resulted in development of insecticide resistance, and to control the resistant mosquitoes, organophosphates, carbamates, and synthetic pyrethroids were introduced in indoor residual spraying with needed success but subsequently resulted in the development of widespread multiple insecticide resistance in vectors. Vector control in many countries still use insecticides in the absence of viable alternatives.

The call for malaria control, over the last century, marked a new epoch in the history of this disease. Many control strategies targeting either the Plasmodium parasite or the Anopheles vector were shown to be effective. Yet, the emergence of drug resistant parasites and insecticide resistant mosquito strains, along with numerous health, environmental, and ecological side effects of many chemical agents, highlighted the need to develop alternative tools that either complement or substitute conventional malaria control approaches. The use of biological means is considered a fundamental part of the recently launched malaria eradication program and has so far shown promising results, although this approach is still in its infancy. This review presents an overview of the most promising biological control tools for malaria eradication, namely fungi, bacteria, carnivorous fish, parasites, viruses and nematodes.

---------------------------♦-----------------------------

INTRODUCTION

Malaria is one of the most common vector-borne diseases prevalent in tropical and subtropical areas of the world, including regions in Africa, Asia and America . In 2010, over 1.2 million global malaria deaths were reported in both children and adults . Malaria is caused by the protozoan parasites, belonging to the genus *Plasmodium*, residing in some female mosquitoes of the genus *Anopheles*. Among the 460 identified *Anopheles* species, 100 are reported as malaria vectors, and only 30–40 species of those reported vectors commonly transmit *Plasmodium* parasites . Of all *Plasmodia*, only *P. malariae*, *P. ovale*, *P. falciparum*, *P. vivax* and *P. knowlesi* infect humans. Despite the numerous established findings that explain the process of the parasite propagation within the *Anopheles*, this vector borne disease remains one of the major health threatening problems world-wide. Eradicating malaria by targeting the *Anopheles* vector using insecticide-treated nets (ITNs), long lasting insecticidal material (LMs), indoor residual spraying (IRS), and space spraying, along with proper preventive measures , was among the most important achieved strategies in the past years. For a period of two decades, the use of insecticides in controlling vector borne diseases, including malaria, was among the most reliable methods. Many compounds like mercuric chloride, Paris Green, phenols and cresols, naphthalene, Bordeaux mixture, rosin-fish oil soap, calcium arsenate, and nicotine sulfate, were used as conventional pesticides . In the twentieth century, dichlorodiphenyltrichloroethane (DDT), the first synthetic organic insecticide, introduced a new epoch of vector control . The use of IRS containing DDT and other chemicals in adult female *Anopheles* control showed great success. IRS resulted in a drastic decrease in the recorded annual parasite index (API) in various regions of the world, a fact that drove the World Health Assembly to implement this approach in the 1955 malaria control strategy . Also, there were many attempts to chemically control malaria by particularly targeting *Anopheles* at the larval stages. Paris Green (Copper Acetoarsenite) and petroleum oils were among the most successfully used chemicals in larval control. Although the widespread use of insecticide applications contributed to *Anopheles* control in various regions of the world, most of these applications, especially those relying on DDT usage, bypassed several important environmental and ecological considerations. As such, the environmental protection agency (EPA) prohibited the use of DDT in 1972 . In 2001, the Stockholm Convention on persistent organic pollutants (POPs) also listed DDT as one of the twelve identified POPs . Though epidemiological studies gave no evidence of the direct effect of DDT on inducing breast, liver, and pancreatic cancer, the ability of DDT to reside in many human tissues and cause various health related disorders, including problems in the liver, kidney, nervous, immune and reproductive systems, was another important reason to reconsider the use of such chemical compounds in malaria control. Likewise, apart from being highly potent and cheap, the presence of toxic arsenic compounds in the chemical makeup of Paris green was the major reason behind reassessing its role as a larvicide. Several other larvicides including synthetic pyrethroids and many organophosphates are also rarely used these days.

Though very effective, synthetic pyrethroids are extremely toxic to aquatic non-target organisms, mainly fish. The remarkable toxic and persistent effects of many chemical applied insecticides were not the only obstacles facing the chemical control of malaria. The emergence of insecticide resistant mosquito strains was another major impediment in such control strategies. These outgrowing strains drove the World Health Assembly resolution (WHA) to call for adopting and developing alternative approaches in controlling vector-borne diseases, thus decreasing the usage of insecticides. Integrated vector management (IVM) efforts are now oriented towards controlling *Anopheles* either at the larval stages and/or at the adult stages using means of biological control, where various concerns at the ecological, environmental, social, and economical levels are highly considered . The use of biological agents shows no environmental contamination or *Anopheles* resistance. Their side effects on living beings including humans, domestic animals and on wildlife are minimal, if not completely absent. The importance of biologically controlling the malaria vector also falls within the functional diversity of different biological control agents.

Besides, many currently employed approaches and future set plans are now focusing on the use of genetically engineered microorganisms to either block the development of the malaria parasite within the *Anopheles* vector, or target the vector itself. The biological control of the malaria vector is now considered a fundamental part of the recently launched malaria eradication program.

Malaria is one of the most persistent infectious diseases of humans, and by some measures the most deadly. The disease has had a dramatic impact on human economic systems for millennia, having been implicated in the decline of the Roman Empire (Sallares, Bouwman et al. 2004). In modern times, intensive malaria within a given country has been linked to a 1.3% penalty in economic growth rates, controlling for other factors (Gallup and Sachs 2001).

The twin discoveries in the late 1800s of the malaria-causing pathogen *Plasmodia* and the *Anopheles* mosquito responsible for its transmission inaugurated an era of large scale malaria control programs. The strategy of these programs was to eliminate malaria via reductions in *Anopheline* densities, reduction of human contact with these mosquitoes, and via the "sterilization" of infected patients' blood through the use of drug therapies.

For the most part, these programs were aimed at immediate disease reductions, with little concern for sustaining initial successes over the long-term. The quote at the top of the page suggests that this problem was recognized at the time. However, as I show below, the sustainability of malaria control programs remains an open—and looming—question. This dissertation is aimed at addressing specific aspects of sustaining the positive impacts of malaria control programs.

Economic factors implicated in contributing to the stalled progress of malaria control include the macro-level relationship between malaria control financing and reduction in global burden of disease (a relationship touched on above), as well as a number of micro-level factors. Such factors include the behavior of households in deciding whether or not to commit their own resources (e.g. time, money, or assets) to the public good of malaria prevention or to seek effective treatment. Analysis of such behavior constitutes an active area of research among development economists (Dupas 2009). Moreover, quantifying the economic value of reducing malaria, as perceived by exposed households, provides information for improving priority-setting in development assistance.

As early as in 18th century A.D. pyrethrum (Persian insect powder) and during 19th century A.D. many compounds were discovered as conventional pesticides viz.,mercuric chloride (1860) paris green (1865), phenol and cresols (1867), naphthalene (1882), Bordeaux mixture (1883), rosin-fish oil soap (1886), calcium arsenate (1907) and nicotine sulphate (1909). The remarkable discovery of the utility of DDT as insecticide in 1942 by Paul Mueller revolutionized the field of pest control and the control of insect vectors of medical importance like mosquito. In mosquito control, insecticides are used against both larvae (larvicides) and adults (adulticides). The present review gives a brief account of various aspects related to the use of chemical insecticides against malaria vectors.

Most of the successful attempts at malaria eradication or control have exploited the 'weak link' in the life cycle of *Plasmodium,* represented by the fact that most *Anopheles,* which have picked up an infecting dose of gametocytes, die of natural causes before the process of sporozoite production has been completed. Increasing this mosquito mortality rate, for example with residual insecticides, reduces the number of sporozoite infective mosquitoes almost to zero. Through such means, malaria has been successfully controlled or eradicated from many regions of the world but, in others, it has proved refractory to such efforts. However, improvements in methods for reducing these relatively small numbers of dangerous mosquitoes have recently been made or are now in prospect.

Furthermore, molecular and recombinant DNA technology offers new possibilities for malaria vector control and for evaluating the role of mosquitoes in malaria epidemiology. In this article, we review the successes and difficulties with currently available control methods and examine ways in which molecular entomology may contribute to more effective control.

VECTORS OF MALARIA

In India malaria is transmitted by nine vector species. Of these, six are of primary importance. These are Anopheles culicifacies (transmits malaria in rural and peri-urban areas), An. stephensi (in urban areas),
An. fluviatilis (in hills and foot-hills), An. minimus and An. dirus (in north-eastern states) and An. sundaicus (in Andaman and Nicobar islands)[1] (Fig. 1). Of these, An. culicifacies is responsible for the transmission of 60-70% and An. fluviatilis, 15% of new cases of malaria in India. Control of malaria in India is actually control of An. culicifacies as each year 60-70% of the allotted budget
for malaria is spent for control of this species. The understanding of the transmission of malaria is further complicated by the existence of species complexes of cryptic species or sibling species or isomorphic species in this taxon and also in other malaria vectors. Except for An. stephensi all other malaria vectors exist as species complexes comprising several cryptic species. Studies have clearly indicated differences among sibling species that result in considerable impact on the transmission of malaria including susceptibility to commonly used insecticides in public health programmes.

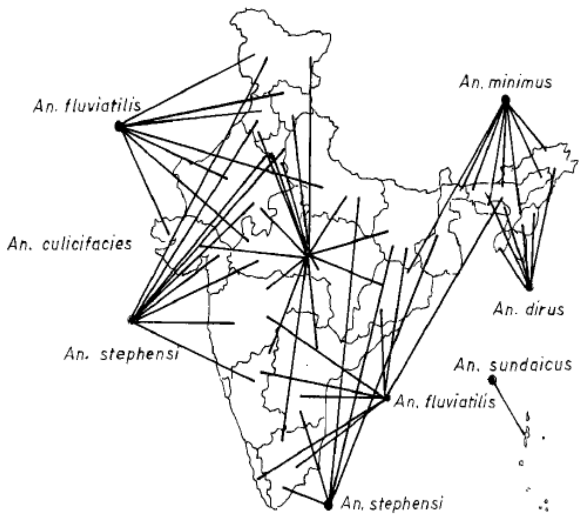

Fig. 1. Distribution of primary malaria vectors in India.

VECTOR CONTROL

Intervention measures to restrict the transmission of malaria by controlling the vector population forms the main part of the vector control. Effective vector control strategies are based on four facets viz. incrimination of vector species, knowledge and understanding of vector biology and ecology, surveillance, public education and implementation of effective control measures.

Vector control programme in India, as is the case with many anti-malaria programmes elsewhere in the world mostly rely on usage of natural and synthetic chemical molecules, which have potential to kill the target insects. During the years 1901-1903, a concept had
emerged known as naturalistic control which was implemented in Malaya based on the knowledge of breeding habitats of anopheline species. The other concept that was prevalent during the early thirties in South Africa was to attack the adult mosquitoes with pyrethrum extract space spray within the houses.

Presently different formulations of synthetic chemical insecticides are in use for vector control. Wettable powder (WP) formulation of different insecticides are used for adult vector control for indoor residual sprays (IRS) while emulsion concentrate (EC) formulations are used for larval control. For IRS insecticides in use are DDT 50% WP, malathion 25% WP as well as synthetic pyrethroids (SP). SP insecticides include deltamethrin 2.5% WP, cyfluthrin 10% WP, lambda cyhalothrin 10% WP and alpha cypermethrin 5% WP. Synthetic pyrethroid insecticides are also used for impregnation of bednets. For larvicidal control temephos EC 50% and fenthion EC 82.5% are in use, in addition to the application of a distillate of crude oil, and malaria larvicidal oil (MLO). For space sprays technical malathion and pyrethrum extract (2% WP) are used.

The historic successful eradication of malaria in various parts of the world is achieved mainly by vector control. In addition, the Global Malaria Control Strategy emphasizes the need for selective and sustainable preventive measures for reducing malaria transmission. The options available for present day vector control efforts mainly include chemical, biological, natural plant products, and environmental management. Immense literature is available for malaria vector control, and a WHO manual on vector control prepared by Rozendaal (1997) is highly informative, in which various methods are given on use of insecticides, insecticide-treated materials, biological control agents, insect growth regulators (IGRs), environmental management, and personal protection methods against mosquito vectors. World Health Organization Pesticide Evaluation Scheme (WHOPES) is involved in the development of new tools and methods for malaria vector control, regular updation of knowledge, and in the support in selection of safe and judicious use of public health pesticides by member states and other stakeholders.

Adult control - Control of adult mosquitoes is the most important facet of controlling vector-borne diseases. It is accomplished by application of chemical pesticides against adult-stage mosquitoes.

BIOLOGICAL CONTROL

Entomopathogenic Fungi - The use of entomopathogenic fungus, as an alternative method for malaria vector control, seems to be very promising. Fungal species belonging to the genera *Coelomomyces*, *Culicinomyces*, *Beauveria*, *Metarhizium*, *Lagenidium*, and *Entomophthora* were mostly considered when studying the role of fungus in vector disease control . Unlike other infectious agents, fungus does not require host ingestion; external contact with the insect's cuticle is all that is needed to promote an infection. This way of launching an infection is not only practical and easily applied in the field, but also resembles many currently used chemical insecticide delivering strategies. Fungal spores can be applied in outdoor attracting odor traps, on indoor house surfaces, on cotton pieces hanging from ceilings, bed nets, and curtains, and can persist for a couple of months on many of these surfaces. The fact that fungal infections can either act alone or in synergy with various insecticides, including DDT, and is equally effective against both insecticide resistant and insecticide susceptible mosquitoes was another major reason behind incorporating fungus in integrated vector management or in insecticide-resistant management approaches. Many studies showed that insecticide resistant *Anopheles gambiae* are significantly more susceptible to fungal infections than insecticide susceptible strains, and that fungal infections kill mosquitoes at slower rates as compared to the insecticide killing rates. Suppressing insecticide resistant mosquitoes at faster rates compared to susceptible ones and within prolonged durations compared to insecticide treated ones will eventually remove all insecticide resistant genes from the mosquito population, allow insecticide susceptible strains to breed, keep the fungus "evolution proof", and collectively result in insecticide resistance management, without further insecticide usage. This approach is highly effective for two major reasons.

Since the *Plasmodium* parasite requires 10–14 days to complete its life cycle within the mosquito, then there is no need for rapid killing of the vector. Besides, these slow killing rates would only result in minimal fungal resistance-selective pressure, even if any resistance would eventually develop. Many laboratory-based bioassays also showed that the mortality rates of adult *Anopheles* infected with the malaria parasite is considerably higher when exposed to fungal spores, and reaches 100% in some cases, compared to those of *Anopheles*, either infected with fungus or parasites alone. This killing effect was shown to be exerted within 7–14 days post-exposure, depending on the fungal strain used, the mode of infection, and the dose applied For practical application purposes, a small scale field study done in village houses in Tanzania showed that even relatively low doses of fungal application on small surface areas result in 34% mosquito infection and in 75% reduction in the entomological inoculation rates of infected mosquitoes. Such studies show that even with the currently available technologies, entomopathogenic fungus can be feasibly and effectively used as a vector control biopesticide.

Bacterial Agents - The use of bacterial agents in controlling vector borne diseases has raised several concerns as to whether these microorganisms are highly effective, environmentally safe, non-toxic, and exert selective effects. Among the many tested bacteria, *Bacillus thuringiensis* (*Bti*) and *Bacillus sphaericus* (*Bs*) are the most promising bacterial larvicidal strains in malaria vector control. *Bacillus* strains are cheap, can be locally manufactured, easily handled, and practically applied.

Compared to chemical insecticides, *Bti* and *Bs* showed faster spreading abilities. Within five years of their discovery, these bacterial strains rapidly colonized Europe and Africa, and methodically participated in routinely applied large-scale mosquito control operations in these regions. *Bti* is now thought of as an alternative approach to synthetic chemical insecticides, since its association with resistant mosquito strains and environmental crisis is comparably insignificant.

Other Biological Control Agents - Other biological control agents include the use of parasites, viruses and nematodes in controlling the malaria vector. Evaluating the effectiveness of these approaches is based on two major criteria. It is how efficient the control agent can be in substantially decreasing the rate of vector transmission and to what extent can this tool be evolutionary sustainable. Relying on certain parasites like *Vavraia culicis* and *Edhazardia aedis* to abort the development of other parasite species like *Plasmodium*, or to target the mosquito vector itself, might seem somehow peculiar. Recent studies have shown promising roles of microsporidian parasites in malaria control. The effectiveness of these parasites falls within their ability to exert combinatorial effects on several important epidemiological traits of the mosquito.

Microsporidians moderately decrease the larval survival rates, thereby decreasing the number of adult mosquitoes. They also, moderately, affect the adult longevity, the development of the malaria parasites in the mosquito, and the biting rates of the mosquito vector. Although only moderate, when combined, these affected traits result in a considerable reduction in the intensity of malaria transmission. If the 25% recorded increase in the larval mortality rates post microsporidian parasitic infection were added to the 20% increase in the adult mortality rates and to the 25% reduction in mosquito infectivity, along with a significant reduction in the biting rates of infected mosquitoes, then the overall malaria transmission process would be lowered by 80%.

INSECTICIDE RESISTANCE IN MALARIA VECTORS

Presently insecticides belonging to different groups viz., organochlorine, organophosphate and synthetic pyrethroid are used for public health sprays. Insecticides belonging to the carbamate group have yet not been introduced for public health sprays in India. Strategy for the change of insecticides has always been reactive.
Successive changes in insecticide were made after the failure of the control by the ongoing insecticide intervention. A subsequent change in the insecticides has led to sequential selection pressure of insecticides resulting in multiple insecticide resistant malaria vectors. Malaria vectors in India are resistant to DDT alone or double resistant to DDT and HCH or triple-resistant to DDT, HCH, malathion and quadruple resistant to DDT, HCH, malathion and deltamethrin (synthetic pyrethroid). HCH has been phased out of the programme in 1997. Of the six principal vector species, two viz. An. Culicifacies and An. stephensi (table 1) have shown wide spread resistance. Other vector species are mostly susceptible to these insecticides.

An. culicifacies has developed resistance to all groups of insecticides used so far in the public health programme. This species is reported to be resistant to organochlorine insecticides-DDT and HCH, organophosphate insecticide malathion and recently to synthetic pyrethroid also. Development of resistance to synthetic pyrethroid
warrants a caution of the impending possibility of widespread resistance to other compounds of this group that are introduced in public health programme for indoor residual spray as well as insecticide treated mosquito nets.

Vector	Type of resistance	No. of states	No. of territories	Total districts
An. Culicifacies	DDT	18	2	286
	Double	16	2	233
	Triple	8	1	71
	Quadruple	2	-	2
An. stephensi	DDT	7	1	84
	Double	6	1	27
	Triple	3	1	8

Table 1. Status of insecticide-resistance in two important vectors of malaria and its geographical distribution in India.

CONCLUSION

To date, many strategies have been used in malaria control. These strategies either abort the development of the *Plasmodium* parasite within the mosquito, or suppress the mosquito vector itself. Nevertheless, many factors such as relying on ineffective conventional vector control approaches, shortage of epidemiological control basis, scarce availability of resources and infrastructure, and poor management plans lead to a decline in the effectiveness of controlling malaria at the level of its vector.

It may be emphasized that the use of insecticides in vector control is limited due to non-availability of new insecticide molecules in near future. The strategy of replacement of insecticides being followed till now also has limitations due to the non-availability of new insecticides. It is not even cost effective and results in cost escalation for the vector control. The need of the hour is intensive research on management tactics and integration of such tested strategies in the ongoing vector control programmes.

REFERENCES

Alphey L, Beard CB, Billingsley P, Coetzee M, Crisanti A, Curtis C, Eggleston P, Godfray C, Hemingway J, Jacobs-Lorena M (2002). Malaria control with genetically manipulated insect vectors. Science 298: pp. 119–121

Bronner, U.; Divis, P.C.; Farnert, A., Singh, B. (2009). Swedish Traveller with *Plasmodium Knowlesi*

Malaria After Visiting Malaysian Borneo. *Malar. J.*, *8*, p. 15.

Dupas, P. (2009). "What Matters (and What Does Not) in Households' Decision to Invest in Malaria Prevention." American Economic Review 99(2): pp. 224-230.

Gallup, J. L. and J. D. Sachs (2001). "The economic burden of malaria." American Journal of Tropical Medicine & Hygiene 64(sup 1): pp. 85-96.

Mitchel, C.J. (1996). Environmental management for vector control. In: The Biology of Disease Vectors. Eds. B.J. Beaty and W.C. Marquardt. University of Colorado, Colorado, p. 492.

Murray, C.J.L.; Rosenfeld, L.C.; Lim, S.S.; Andrews, K.G.; Foreman, K.J.; Haring, D.; Fullman, N.; Mohsen, N.; Rafael, L.; Lopez, A.D. (2012). Global malaria mortality between 1980 and 2010: A systematic analysis. *Lancet*, *379*, pp. 413–431.

Raghavendra, K. and Subbarao, S.K. (2002). Case studies on insecticide resistance and its management. In: Proceedings of Mekong Malaria Symposium. Siem Reap Angkor Wat p. 17.

Raghavendra, K.; Barik, T.K.; Niranjan Reddy, B.P.; Sharma, P.; Dash, A.P. (2011). Malaria vector control: From past to future. *Parasitol. Res.*, *108*, pp. 757–779.

Sallares, R., A. Bouwman, et al. (2004). "The Spread of Malaria to Southern Europe in Antiquity: New Approaches to Old Problems." Medical History 48 (3): pp. 311-328.

Shiff, C. (2002). Integrated approach to malaria control. *Clin. Microbiol. Rev.*, *15*, pp. 278–293.

Corresponding Author

Parveen Kumar Rai*

Research Scholar, SSSUTMS, Sehore

E-Mail – **chairman.iab@gmail.com**