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The Role of Larval Source Management (LSM) as Malaria Elimination

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ABSTRACT

Malaria is one of the infectious diseases that are still a problem in Indonesia and the world. The Indonesian government in collaboration with WHO had have guidelines to prevent malaria transmission through the distribution of mosquito nets (long-lasting insecticidal net), Indoor Residual Spray, use of repellents, and others. However, advances in malaria elimination measures had also been accompanied by rapidly growing resistance and changes in vector genetics. This study aimed to know the effectiveness of LSM for malaria elimination. This study used a literature review method using online-based databases including Google Scholar, Pubmed, Science Direct, and Springer, limited to the last 15 years, boolean operator "Malaria" OR "Malaria Control" OR "Malaria Elimination" AND "LarvalSource Management". There were 1,716 articles found and then excluded according to the restriction criteria, 8 articles were reviewed. Based on the 8 articles that had been obtained and analyzed, it was found that 1 article showed fully practised LSM and 7 articles had practised larviciding as representatives of the LSM program. Larval source management (LSM) can effectively reduce the number of Anopheles sp. mosquito larvae, whether used according to complete action or only one action. All articles stated that LSM was an effective program and can be used for malaria elimination in the future. Larval source management (LSM) was an effective program for malaria elimination.

1. Introduction

Malaria is one of the infectious diseases that are still a problem for people in Indonesia, even around the world.[1] By 2020, malaria will reach 229 million people worldwide, with a death toll of 409,000. In Southeast Asia, malaria cases reached 6,300,000 with a death rate of 9,000 people. Indonesia is reported to be the second-highest ranked country after India in Southeast Asia.[2] Total malaria cases in Indonesia reached 226,364 cases in 2020, whereas on September 3, 2021, malaria cases in Indonesia reached 94,610.[3]

The 60th World Health Assembly (WHA) in 2007 issued the Millennium Development Goals (MDGs) program on malaria elimination by each country. Therefore, the Indonesian government had a program as outlined in the Decree of the Minister of Health of the Republic of Indonesia No. 293 / MENKES / SK / IV / 2009 on April 28, 2009, on malaria elimination program in Indonesia, namely the program *"Menuju Indonesia Bebas Malaria 2030"* ("Towards Malaria-Free Indonesia 2030"), which Indonesia targets to be malaria-free by 2030. Malaria control held step by

step from one island to another until all of the Indonesian islands are malaria-free in 2030.[1,4]

The Indonesian government in collaboration with WHO had made guidelines to prevent malaria transmission through the distribution of mosquito nets (Long-Lasting Insecticidal Net), indoor residual spray, use of repellents, and others.[5] In the past decade, malaria elimination activities have achieved good results.[6] However, progress in malaria elimination measures has also been followed by rapidly growing resistance, changes in vector genetics, and human behaviour that can slow malaria control, such as non-compliance with eliminating programs.[7]

The current shortage of malaria interventions demonstrates the need for more effective strategies to reduce malaria transmission. According to WHO, larval source management (LMS), which controls malaria vector populations through reduction of the suitability of mosquito larva habitat, is recognized as an effective additional tool for malaria control under certain conditions.[8] LMS can provide dual benefits, where LSM not only reduce the number of mosquitoes that enter the house but also reduce mosquitoes that bite outside the home. This is due to the work of LMS that does eradication at a time when malaria vector mosquitoes have not developed into adults (stadium larvae), so it is expected that adult mosquitoes can be reduced. However, in some areas, LMS has not been introduced or evaluated for malaria control. This is due to several factors including a lack of local mosquito vector ecological data, a lack of local evidence for LSM in malaria control, and concerns about the cost of implementation on a large scale.[9]

2. Methods

The research design used for this research is a literature review or literature review. The technique of data retrieval in this literature review is to search for publication articles on databases such as Pubmed, Science Direct, Google Scholar, and Springer. Data searches using Boolean Logic with an "AND" component. The keywords used are "Malaria" OR "Malaria Control" OR "Malaria Elimination" AND "Larval Source Management."

This literature review is synthesized using narrative methods by grouping extraction data according to the results to answer the objectives. The data that has been obtained is then collected and made a summary of the article that includes the name of the researcher, the year of publication of the article, the country of the research, the title of the study, and a summary of the results or findings. Then, the summary is created in the form of a table, which is sorted according to the alphabet and the year the article is published. Summaries of articles are also created based on abstract analysis and discernment of full-text articles. After the summary of the article is made, then an analysis of the content, results, and findings is contained in the purpose of the research. Then screening with PRISMA method (Preferred Reporting Items for Systematic Reviews and Meta-analyses). The data that has been collected is then sought effectiveness conclusions against variables, then discussed to conclude. The research had ethical clearance from ethical commitee of Medical Faculty UMS No. 3886/C.1/KEPK-FKUMS/XI/2021.

3. Results and Discussion

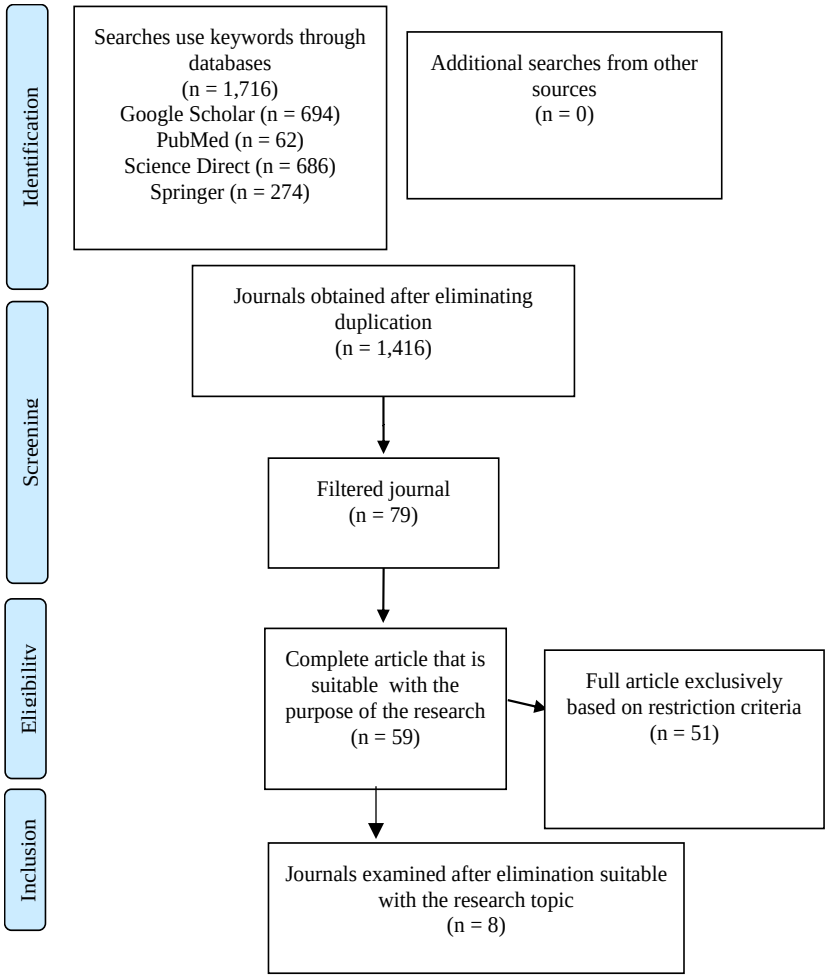

Figure 1. Flowchart of PRISMA diagram

The study was conducted using searches for published articles on the PubMed, ScienceDirect, Google Scholar, and Springer databases using Booelian Logic. The search results showed the findings of 1,716 journals and as many as 59 journals conducted further reviews. Obtained 8 journals selected to fit into the criteria.

Larval source management (LSM) is a technique of managing aquatic larvae habitat to prevent the completion of mosquito development reaching the immature stage. LSM include any changes in the water environment that have the potential to become mosquito habitat to prevent the completion of the development of immature stage.[10,11] LSM consists of four types, they are habitat modification, habitat manipulation, larvaciding and biological control.[12] Table 1 shows 8 article characteristic from article review the role of LSM to malaria elimination.

Table 1. Article characteristic from article review the role of larval source management (LSM) to malaria elimination

No	Author (year)	Title of article	Design	Method	Result
1	(Imbahale et al., 2012)	Integrated Mosquito Larval Source Management Reduces Larval Numbers in Western Kenya	Quasi Experiment, Nonequivalent Control Group Design	• LMS are carried out in two villages namely Fort Ternan and Lunyerere • Intervention strategies implemented, among others, environmental management through - Habitat modification - Habitat manipulation - Larviciding - Use of predators • Number of stages of Anopheles sp. and Culex sp. Adults in interventional habitats are compared to non-interventional habitats.	• At Fort Ternan LSM can reduce the number of larvae in intervention areas • In Lunyerere LSM can reduce the number of larvae in intervention areas • The overall NGO strategy undertaken can reduce the number of malaria vector larvae • NGO strategy targets immature adult mosquitoes outdoors (larvae). • LSM will be beneficial for malaria elimination.
2	(Dambach et al., 2019)	Reduction of Malaria Vector Mosquitoes in a Large-Scale Intervention Trial in Rural Burkina Faso Using Bti Based Larval Source Management	Quasi Experiment, Nonequivalent Control Group Design	• 127 rural and semi-urban communities were distributed into three study groups that received different larvacides: 1. Full treatment throughout the larval breeding site, 2. Selective care only in places that have the highest larval breeding rate, and 3. Control group. • Each subsequent study group was distributed into three groups, bringing the total to nine groups. • Larvacide performed with Bti VectoBac ® WG, AM65-52 strain (Valent Bio-Sciences Corporation, IL, USA)	• In villages that receive selective treatment, the number of Anopheles sp. Females were down 61% compared to the pre-intervention period. • In villages where they receive full treatment, the number of Anopheles sp. Females were reduced by 70% compared to the pre-intervention period. • The number of malaria vectors can be dramatically reduced through larvacide in breeding habitats • Larvacide is a viable addition to current malaria control measures.
3	(Geissbühler et al., 2009)	Microbial Larvicide Application by a Large-Scale, Community-Based Program Reduces Malaria Infection Prevalence in Urban Dar Es Salaam, Tanzania	Non – Randomized Community – Based, Quasi Experiment, Nonequivalent Control Group Design	• Larvicidal Bti is applied weekly in the urban city of Dar es Salaam, Tanzania. • Random cluster sampling of the prevalence of malaria infection and non-randomized program surveillance of entomological inoculation (EIR) are primary and secondary results surveyed in the population.	• Implementation of Bti for one year reduces the annual transmission forecast • Larvicidal reduces the risk of malaria infection among children ≤5 years (OR [CI] = 0.284 [0.101 to 0.801], P = 0.017) • Larvacides reduce the prevalence of malaria.
4	(Mpofu et al., 2016)	Field effectiveness of microbial larvicides on mosquito larvae in malaria areas of Botswana and Zimbabwe	Quasi Experiment, Nonequivalent Control Group Design	• Two villages are selected in each of the two countries, one as an intervention and the other as a control. • Intervention using commercial products VectoBac® WG (Valent BioSciences Corporation, IL, USA) containing the active ingredient Bacillus thuringiensis var. israelensis (Bti), a WHO-recommended bio-larvicide, is applied at a dose of 300 g per hectare. • Intervention is carried out with a 2-week pause of 8 periods. • Compared intervention with control location with respect to the number of larvae.	• The effects of larviciding reduced 92% of larvae in Bostwana and 65% in Zimbabwe, with an early stage larva reduction of 77% and late-stage larvae by 91%. • Overall, the number of larvae at the beginning before the intervention had a 5x amount of control area, and after the intervention had 26x less larval number than the control area after 16 weeks. • Larvicidal can be used to control mosquito vector populations
5	(Obopile et al., 2018)	Did Microbial Larviciding Contribute to a Reduction In Malaria Cases	Quasi Experiment, Nonequivalent Control Group	• Test against the efficacy of Bacillus thuringiensis subsp. israliensis vs. Anopheles	• Larvicidal reduced larval density by 95% in Bobirwa in 2012, with two cases of malaria, while in 2013 the decrease in

		in Eastern Botswana in 2012–2013?	Design	• Larval density was measured before the intervention, 24 hours, and 48 hours after treatment at seven locations in Bobirwa district, eastern Botswana, in 2012 and 2013. • Vector densities and malaria cases were compared between Bobirwa and Ngami, and without larvacide in the control group were performed in Shorobe.	larval density was 81%, with 11 cases. • There were no cases of malaria in Robelela in either year, but in Shorobe there were 20 and 70 cases, respectively, in 2012 and 2013. • Larvicidal can reduce the density of mosquito larvae and reduce malaria transmission in Botswana.
6	(Maheu-Giroux & Castro, 2013)	Impact of Community-Based Larviciding on the Prevalence of Malaria Infection in Dar es Salaam, Tanzania	Randomized Cluster Sampling, Cross – Sectional Study, Experiment	• Larvicidal was carried out in 3 of the 15 target areas of Dar es Salaam • This intervention was later increased to 9 regions a year later, and to 15 target areas	• Research shows a significant protective effect from larvacide intervention. • Individuals living in areas treated with malaria-infected larvacide were 21% lower (Odds Ratio = 0.79; 95% Credible Interval: 0.66-0.93) than those living in untreated areas. • Large-scale larvacide intervention significantly reduced the prevalence of malaria infection in urban Dar es Salaam.
7	(Fontoura et al., 2021)	Monthly Biological Larviciding Associated With a Tenfold Decrease in Larval Density in Fish Farming Ponds and Reduced Community-Wide Malaria Incidence in Northwestern Brazil	Single Group Interurupted Time Series Analysis	• The study was conducted at Vila Assis Brasil (VAB). • The intervention consists of monthly treatment with 20 kg/ha of VectoMax FG from all water-filled fish ponds in VAB with a surface area between 20 and 8000 m2 • The study compared monthly larval density measurements in fish ponds during the pre-intervention period, with interventions, and shortly after 12-month interventions.	• • Average larval density decreased tenfold in treated fish farming ponds, from 0.467 anopheles larvae per pre-intervention dip to 0.046 larvae per dipping after intervention • Average malaria incidence rate decreases by 0.08 cases per 100 people • Larviciding on a regular basis can lead to a dramatic decrease in larval density and a modest but significant decrease in the incidence of malaria across communities.
8	(Fontoura et al., 2020)	Field Efficacy of VectoMax FG and VectoLex CG Biological Larvicides for Malaria Vector Control in Northwestern Brazil	Stratified Block Randomization with Controlled Group	• The study was conducted in rural Nova Cintra, using two formulations of biological larvacide granular, namely - VectoMax FG - VectoLex CG. • The trial aims to test the effectiveness and residual activity of both larvacides, as well as determine the optimum dose. • The study was conducted on 24 fish ponds, the density of early and late-stage larvae was monitored for 48 hours and 72 hours after the first larvacide application.	• There was a >95% decrease in the density of late-stage larvae up to 7 days after the first application of VectoMax FG or VectoLex CG up to 21 days after larvacide re-application in fish ponds located in the main pond of Brazil's residual malaria pouch regardless of formulation or dosage (10 or 20 kg/ha) used. • The results support the use of biological larvacides to reduce the larval density of Anopheles sp.

Based on 8 articles that have been obtained and analyzed, 1 article that has practiced LSM fully by Imbahale et al. (2012), and 7 article that practice larviciding as representatives of LSM programs by Dambach et al. (2019), Geissbühler et al. (2009), Mpofu et al., (2016), Obopile et al. (2018), Maheu-Giroux & Castro (2013), Fontoura et al. (2021), Fontoura et al. (2020). The entire article stated that LSM are an effective program in their use, and can be used for malaria elimination in the future.

Research by Imbahale et al. used LSM program by habitat modification, habitat manipulation, larviciding, use of predator. Biological control is an attempt to incorporate natural enemies into the

habitat of larvae, including predatory fish, predatory invertebrates, and parasites or other disease-causing organisms. The LSM program was effective to control the amount of larvae.[12,13]

Study of LMS using larvasiding by researchers showed good results. It can reduce transmision of Anopheles sp, reduced the incidence of malaria in children.[7,14]

Larvaciding used *Bacillus thuringiensis subsp. israelensis* (Bti) by Mpofu et al. and Obopile et al. showed good outcome. It could reduce larvae density so it can control mosquito population.[15,16] *Bacillus thuringiensis subsp. israelensis* (Bti), and *Bacillus sphaericus* (Bs) produce insecticide crystal proteins, which after ingested by mosquito larvae, these proteins are modified by enzymes in the larval intestine and then bind to receptors in the intestinal epithelium, resulting in the formation of pore holes and causing impaired eating and homeostasis, resulting in death.[12]

Larvaciding was the best used in dry season. It have sinergic effect with malarial net. Vector-based malaria elimination efforts carried out in Indonesia, and can be used to assist LMS programs include the use of insecticidal nets (LLINs), and insecticide spraying using the indoor residual spraying (IRS) method. Biological larvacide can reduce density of *Anopheles* larvae, and continous larvaciding can reduce the incidence of malaria.[17,18,19,20]

From 8 articles taken it is known that larval source management (LSM) can effectively reduce the larvae of Anopheles sp., either by using the actions of LSM in full, or one of the actions of LSM only, for example larviciding. There are fewer articles discussing the implementation of LSM or conducting research related to the effectiveness of LSM, more articles that examine people's interest in LSM.

4. Conclusion

Based on a systematic review of 8 articles obtained and analyzed, it can be concluded that Larval Source Management (LSM) was an effective program for malaria elimination.

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