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Genetic Engineering for Control of Dengue Fever Mosquito Vectors From A Bioethics Perspective

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ABSTRACT

Dengue Fever (DF) is a viral infectious disease transmitted by Aedes aegypti and Aedes albopictus mosquitoes, posing a major public health problem in tropical and subtropical regions, including Indonesia. Conventional control efforts, such as using insecticides, face challenges like mosquito resistance and negative environmental impacts. Therefore, innovative approaches such as genetic engineering in mosquitoes have been developed. This technology includes methods like the Sterile Insect Technique (SIT), the release of insects with dominant lethal genes (RIDL), and CRISPR-Cas9-based gene drive systems. This study uses a literature review method to explore the potential of genetic engineering in controlling dengue vector mosquitoes and the accompanying bioethical issues. The findings suggest that genetic engineering offers an effective solution to suppress mosquito populations and reduce DF transmission. However, operational challenges, infrastructure requirements, and high costs are obstacles in endemic countries. Additionally, bioethical issues such as ecosystem impacts, social equity, and community involvement in decision-making need to be addressed. Thus, while promising, the application of genetic engineering in mosquito control must carefully consider ethical and social aspects.

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1. INTRODUCTION

Dengue Fever (DF) is a viral infectious disease transmitted by mosquitoes, particularly Aedes aegypti and Aedes albopictus, which has become a major health issue in various tropical and subtropical regions. According to WHO (2021), the prevalence of DF continues to increase due to climate change, uncontrolled urbanization, and high human mobility. In many areas, DF often results in significant morbidity and mortality rates, especially in Southeast Asia, including Indonesia. Given its substantial impact on public health, effective and sustainable solutions are required to control the mosquito vectors of this disease.

Conventional vector control efforts, such as the use of insecticides, have limitations and adverse effects on human health and the environment. Insecticide resistance has been reported in various mosquito populations, ultimately reducing the effectiveness of conventional methods. Furthermore, excessive insecticide use can negatively affect local ecosystems and harm non-target organisms. These conditions highlight the need for safer and more sustainable approaches to address mosquito vectors of DF (4).

One innovative solution being developed is genetic engineering in mosquito control. This technology enables genetic modification of mosquitoes, such as releasing sterile mosquitoes or genetic modifications that render mosquitoes incapable of transmitting the DF virus. With this technology, it is hoped that mosquito populations can be controlled more effectively than conventional methods, ultimately reducing DF spread. This technology has the potential to provide a long-term solution to vector-borne disease control, particularly in DF-endemic areas (2).

Although genetic engineering offers a potential solution for mosquito control, it also raises significant ethical controversies. Genetic manipulation of specific species, such as mosquitoes, raises concerns about its impact on ecosystems, natural balance, and human responsibility toward nature. Additionally, the release of genetically modified organisms into the environment raises concerns about unpredictable consequences and potential future risks. Ethical aspects involve analyzing whether public health benefits from disease control outweigh potential ecosystem and environmental risks. Public education on the benefits and risks of this technology is crucial to ensure informed consent (3).

The concept of Dar'ul mafasid muqaddam 'ala jalbil mashalih (the prevention of harm takes precedence over the pursuit of benefits) is particularly relevant in the context of genetic engineering for controlling dengue fever mosquito vectors. This approach raises significant bioethical considerations, especially regarding potential risks versus benefits. This principle emphasizes that actions should be carefully considered, ensuring that potential negative consequences are minimized even if the intended outcome is positive. One relevant study by Kittayapong et al. (2021) discuss innovative strategies in their article, "Combating Mosquito-Borne Diseases Using Genetic Control Technologies." They review various genetic strategies aimed at reducing mosquito-borne diseases like dengue, discussing their potential efficacy and the ethical implications surrounding their use in natural ecosystems. This article reinforces the necessity of considering ethical frameworks when implementing new technologies in public health. The principle of Al-masyaqqah tajlibut taisir (hardship brings ease) aligns with the need for innovative and adaptive approaches in addressing dengue fever (DF). This concept emphasizes that solutions should simplify and alleviate difficulties faced by society, particularly in managing complex issues like vector-borne diseases. The challenges of increasing DF prevalence, insecticide resistance, and environmental impacts underscore the necessity of exploring alternative solutions, such as genetic engineering. By employing this principle, efforts to combat DF can prioritize ease and effectiveness while minimizing burdens on public health systems and the environment. This perspective is consistent with the guidance provided by The Islamic Bioethics Framework (20), which integrates ethical principles with practical solutions to address contemporary health issues.

2. METHOD

This study employed a literature review methodology. The literature review in this research involves a series of activities related to the collection of library data, reading and noting, as well as managing research data objectively, systematically, and critically. The data collected and analyzed are secondary data derived from research results such as books, journals, articles, internet sites, and other relevant sources. Subsequently, the data analysis technique used in this study is content analysis.

3. RESULT AND DISCUSSION

Genetic engineering is a technology for manipulating DNA molecules, also known as recombinant DNA technology. Several terminologies are often used to describe genetic engineering techniques, including gene manipulation, recombinant DNA technology, gene cloning, and genetic modification.

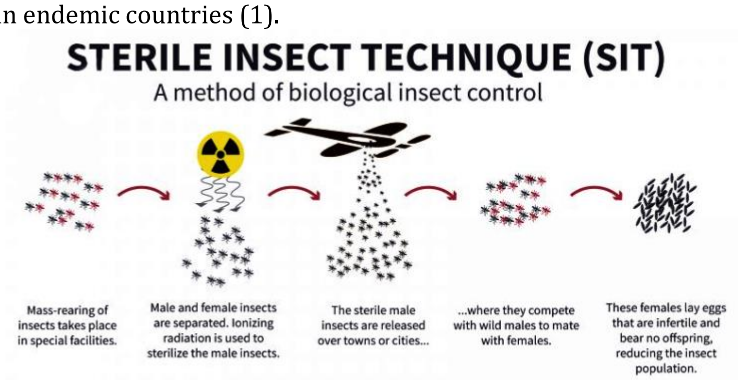
Genetic engineering offers potential solutions in controlling Aedes aegypti mosquitoes, which are vectors of th dengue virus, through approaches such as using genetically modified mosquitoes to produce sterile offspring or those incapable of spreading the virus. Although these strategies have shown positive results in reducing vector populations in some locations (2), complex bioethical issues must be addressed. Firstly, there are concerns about the long-term impacts of releasing modified organisms on biodiversity and local ecosystems, including risks to non-target species (8).

Moreover, social justice related to access to this technology is a concern, particularly in developing countries most affected by mosquito-borne diseases, where the benefits of the technology must be available to all societal groups (14). Finally, transparency and public participation in decision-making are also essential to ensure that public voices are accommodated in the development and implementation of this technology. Therefore, while genetic engineering provides new opportunities in vector control, its application must be carried out cautiously and consider various bioethical aspects to ensure fair benefits for all parties.

In the field of mosquito vector biotechnology, genetic engineering is also developed to control disease transmission by mosquito vectors. In the context of vector control, most efforts have focused on genetic constructs to suppress mosquito population density, including:

1. Sterile Insect Technique

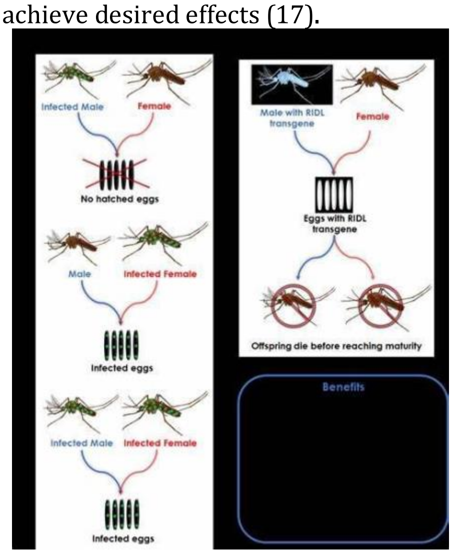
The sterile insect technique (SIT) involves releasing sterilized male insects, usually through radiation exposure, to suppress vector mosquito populations. SIT induces mutations that randomly deactivate germ cells, preventing fertilization. Sterile males mate with wild females without producing offspring. Challenges in the field include the availability of adequate infrastructure to support large-scale vector breeding. New technologies for mosquito rearing, particularly Aedes species, are available in various countries, but sterilization procedures require further development to avoid somatic damage, resulting in shorter lifespans, mating issues, and male mosquito activity problems. Although SIT has shown satisfactory results in A. albopictus, high operational costs remain a barrier for large-scale maintenance facilities in endemic countries (1).



(International Atomic Energy Agency, 2024)

2. Release of Insects with Dominant Lethal Gene

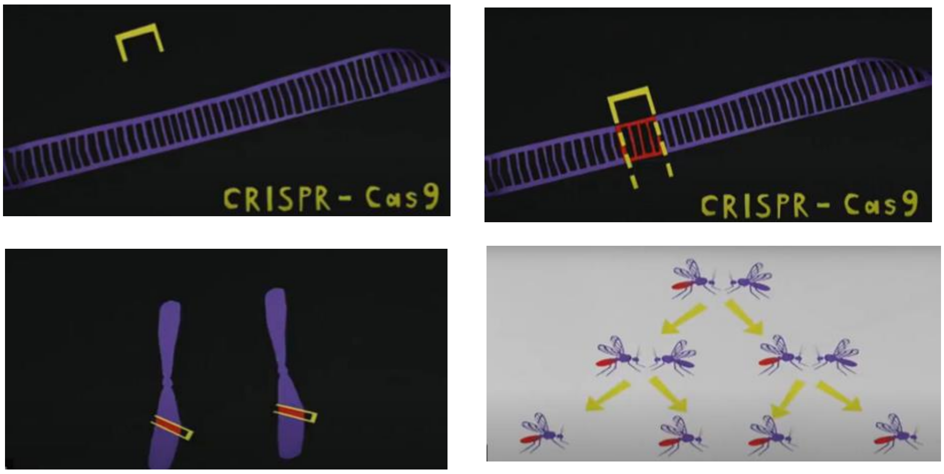
The release of insects with dominant lethality (RIDL) aims to suppress vector populations (self-limiting approach) using individuals carrying transgenic genes, which refer to late larval and pupal stages to reduce imago survival. Unlike SIT and Wolbachia-based population suppression, RIDL requires egg fertilization at an early stage to achieve desired effects (17).



(Dickens, et.al, 2016)

3. Gen drives

Gene drives involve transgenic constructs with the ability to target specific species populations. This strategy was introduced by Austin Burt in 2003 and later developed by experts to construct and modify desired traits in mosquito species. The design uses Palindromic Repeats—CRISPR-associated protein 9 (CRISPR-Cas9) systems. The principle is that transgenic elements must be precisely inserted into predetermined sequences. A "cassette" is integrated with a "knock-in gene." This technique aims to introduce and inactivate fertility genes in specific sexes to reduce populations and generate sterility alleles. Laboratory studies have demonstrated the potential for adapting this approach to African malaria vector Anopheles gambiae and quickly applying it to A. aegypti and A. albopictus. However, gene drives have proven less effective in the field than in the lab. If gene drives function efficiently in the field as theoretically proposed, this control approach has the potential to eradicate target species without complete depopulation (1).



(Swiss Academy of Science, 2024)

Genetic engineering for mosquito vectors, particularly Aedes aegypti, which spreads dengue fever, offers great potential for controlling mosquito populations. One widely researched approach involves developing genetically modified mosquitoes that can produce sterile offspring or those incapable of transmitting the virus (10). Although this technique shows promising results in field trials, bioethical challenges remain a central issue.

Firstly, risks to broader ecosystems must be thoroughly evaluated, including potential negative impacts on non-target species and ecological balance (9). Additionally, social equity must be considered, particularly regarding access and distribution of this technology. Genetic engineering applications must ensure that benefits are accessible to all community groups, including those most vulnerable to disease (12).

Finally, it is crucial to engage communities in discussions about the risks and benefits of this technology so decisions reflect public interests and build trust in implementing innovative solutions in vector control. Thus, while genetic engineering offers promising solutions, this approach must be balanced with in-depth ethical and social considerations.

In the context of genetic engineering for mosquito vectors, several bioethical issues need attention:

1 Safety and Risk One

The major question is the safety of using genetically modified mosquitoes. Potential negative impacts on ecosystems and other species must be thoroughly evaluated. Research by Eidschun et al. (2015) warns that invasive interventions can have unforeseen long-term consequences.

2. Social Justice

The social implications of this technology also need consideration. Access to this technology may not be evenly distributed, potentially widening gaps between wealthy and poor nations. According to Liao et al. (2017), ensuring all community groups, especially vulnerable ones, benefit from this innovation is critical.

3. Informed Consent Applying

This technology must involve community participation and informed consent. This aligns with bioethical principles emphasizing individual autonomy and transparency. Research by Fishman et al. (2019) demonstrates that public engagement in decision-making processes increases trust and acceptance of new technologies.

4. Long-Term Consequences

Bioethics also demands consideration of the long-term consequences of genetic engineering. Do we fully understand the impacts of genetic modifications on mosquitoes? This aligns with the views of Tait and Barlow (2019), highlighting the importance of ongoing research to assess ecological impacts.

3.1 Ethical Matriks

The ethical matrix is a specific schema that provides meaning to recognized ethical principles from the perspective of stakeholders. This approach first emerged in medical ethics by Beauchamp and Childress and was later developed by Ben Mepham concerning biotechnology issues. The ethical matrix relates to decision-making processes, involving parties like families, patients, future generations, test animals, and more, encompassing aspects of justice, dignity, and welfare, in line with the ethical matrix structured by Mepham (2005).

	Justice	**Welfare**	**Autonomy**
Civil Society	Justice Ensures that the benefits of using genetic engineering for DF vector control are widely and equitably distributed, enabling society to experience its positive impacts comprehensively.	Welfare Ensure that genetic engineering for DF vector control provides clear benefits, such as improving public disease surveillance and enabling earlier DF diagnosis.	Autonomy Ensure that the public understands the risks, benefits, and objectives of using genetic engineering for DF vector control.
Test animal	Focus on the rights and fair treatment of animals used in experiments. This includes limiting the disproportionate use of animals by considering the type and number of animals utilized. Ensure that experiments conducted have clear and significant benefits, not solely for human interests, but also with regard to the sustainability of the species involved.	Experiments should not cause excessive suffering. Researchers must commit to minimizing pain, stress, or injury to animals, as well as providing proper environmental conditions and adequate care. This principle is often integrated into the 3R concept (Replacement, Reduction, Refinement) to reduce the number of animals used and ensure experiments are conducted in a more humane manner.	It is essential to evaluate the cost-effectiveness of experiments, ensuring that the benefits derived from the experiments are proportional to the expenses incurred and that the experiments do not impose excessive economic burdens.
Future Generations	Genetic engineering in mosquito vector control offers opportunities to create a healthier environment by reducing the spread of dengue fever. In the context of justice, it is crucial to ensure that access to this technology is not limited to specific groups or countries. This technology should be designed and disseminated in a way that allows people from diverse socio-economic backgrounds to equally benefit. Inequities in access can exacerbate health disparities between developed and developing countries, so the implementation of this technology must consider distributive justice principles aligned with bioethical values.	Genetic engineering technologies, such as the release of genetically modified mosquitoes, have great potential to improve the social welfare of future generations. By reducing the incidence of mosquito-borne diseases, the public health burden will decrease, allowing resources to be reallocated to support other aspects of social development. However, implementation requires comprehensive planning, including risk assessments for the environment and indirect impacts on ecosystems. The bioethical perspective emphasizes the importance of the principle of beneficence, which seeks to provide maximum benefits to society as a whole.	The application of genetic engineering technology not only brings benefits but also poses challenges related to respecting the autonomy of individuals and communities. Communities must be provided with clear and transparent information about the benefits, risks, and long-term impacts of this technology. Decisions to accept or reject its use must be based on informed consent. The bioethical perspective demands that affected communities be given opportunities to participate in decision-making processes, avoiding top-down approaches that may violate the principle of respecting individual and collective rights.

From the matrix above, genetic engineering approaches to controlling mosquito vectors causing dengue fever (DF) must consider bioethical aspects, including justice, welfare, autonomy, and treatment of test animals. This technology should be designed to ensure its benefits are equitably distributed among all community groups, help reduce public health burdens broadly, and prevent socio-economic inequalities.

Respect for individual and community rights should be prioritized by ensuring clear information delivery and community involvement in decision-making. Regarding test animals, the 3R principle (Replacement, Reduction, Refinement) must be applied to ensure ethical and humane treatment. Comprehensive planning should also consider long-term impacts on the environment and ecosystems, allowing this technology to provide optimal benefits for society and support the sustainability of future generations' welfare.

4. CONCLUSION

Genetic engineering in *Aedes aegypti* mosquito vectors offers significant opportunities to control dengue virus transmission through methods such as the Sterile Insect Technique (SIT), RIDL (release of insects with dominant lethal genes), and CRISPR-Cas9-based gene drives. These techniques have shown positive results in suppressing mosquito populations in some locations. However, these successes face challenges including infrastructure availability and high operational costs, especially in endemic countries. Additionally, while effective in laboratories, the efficacy of some techniques in the field requires further evaluation and development.

On the other hand, applying genetic engineering raises significant bioethical issues. Concerns about long-term impacts on ecosystems and non-target species necessitate thorough research to ensure environmental safety. Social justice is also a key concern, particularly regarding access to this technology in developing countries most affected by the disease. Transparency in decision-making and community involvement are crucial to building public trust in this technology. Thus, while genetic engineering offers innovative solutions in vector control, this approach must be balanced with careful ethical and social considerations.

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