Chapter

Dengue Virus Surveillance and Blood Safety: A One Health Perspective

Festus Mulakoli, George Gachara, Eric Ndombi and Samoel Khamadi

Abstract

The provision of blood products to save a life is a noble undertaking for any organization tasked with the duty. In addition to saving millions of lives, blood products pose health risks associated with adverse events. Much has been done to mitigate these challenges, but emerging new infectious diseases pose a public health challenge to both the safety of blood and its availability. The dengue virus an arbovirus is one such virus that is endemic in tropical and subtropical countries. The data emerging from the published papers show that dengue could be a major threat to blood safety and availability in the future. To address these threats, a collaborative approach through one health system is the only avenue to provide a last solution. One health has been implemented as a strategy to mitigate zoonotic diseases and its results are very impressive. This piece of work is a fraction of our larger project that aims to address threats to the dengue virus and blood safety in Kenya and the rest of Africa. In conclusion, adopting one health in the fight against the dengue virus in blood safety will be the best approach to ensure a safer supply of blood products.

Keywords: dengue virus, blood safety, surveillance, one health

1. Introduction

Dengue fever is a mosquito-borne disease endemic in the tropical and subtropical regions of the world. The highest burden of diseases is reported in the Asian and South American regions [1]. The virus has four serotypes (DENV 1–4) that are antigenically different, but with variations in their immunological response. The dengue virus inhabited primates before jumping into the human population. It is one of the main arboviruses associated with frequent disease outbreaks reported annually in endemic regions [2]. The rapid spread of the dengue virus has had a negative impact on blood safety and availability in endemic areas. For example, there is a reduction in the number of suitable donors during DENV outbreaks, as shown in studies conducted in India, China and Brazil. Affected countries have different strategies available to mitigate these threats, but with minimal success. The challenge has always been the lack of collaboration between entities involved in surveillance activities. The most critical limitation is the inability to share critical surveillance information on emerging disease patterns [3]. From an expert point of view, we believe that the adoption of one health in disease surveillance would be the best avenue to guarantee a safer blood supply.

One health, as is known, is a multidisciplinary platform where experts in human health, animal health, and environmental health work collaboratively to combat both human and animal diseases. These synergistic efforts put blood transfusion services in a better position to safeguard their blood supply in an era of the re-emergence of the dengue virus [4]. The Manhattan Principles, which outline relationships between infectious diseases, the environment, human health, and economic development activities, established the phrase "One Health" in 2003 [5]. This was after the outbreak of Ebola virus disease (EVD), a Filoviridae virus, in West Africa after the death of the great apes. Since then, high-level interest and acceptance of One Health initiatives have grown around the world [6]. The concept of One Health was adopted to allow the sharing of information and to foster collaboration between different sectors. It is a multidisciplinary initiative in which people working in different sectors within their countries, continents, and global regions come together to solve a common public health problem. The connectivity between humans, animals, and their ecosystems is agreed to play a significant role in the spread of infectious diseases [7–10]. This book chapter is a fraction of my Ph.D. project that seeks to highlight and evaluate the importance of adopting one health disease surveillance approach to safeguard blood supplies across the world. One aspect of one-health is helping different experts from different fields share information that can detect and suppress diseases upstream before they cause human disease [11].

2. Current evidence of transfusion-transmitted dengue

Transfusion-transmitted dengue (TTD) is a growing concern for many transfusion services in tropical and sub-tropical countries. These countries have experienced frequent outbreaks of dengue in the last ten years. The increasing number of dengue incidents increases the likelihood that blood components manufactured during dengue outbreaks could be infectious [12, 13]. The first documented cases of TTD in the literature were reported in two studies in Hong Kong and Singapore in 2008 and 2012, respectively. The cases involved blood recipients who received blood transfusions from asymptomatic blood donors. On evaluation of the transfused blood, the serotype detected in blood recipients was the same as the serotype present in blood donors. This became the first evidence of dengue transmitted by blood transfusions [14, 15]. Irrespective of this evidence, little was done to communicate this information to alert other regions where the dengue virus is endemic. With this evidence, it was important for all blood transfusion services in regions with frequent outbreaks of dengue virus to have taken urgent steps to secure their blood supply. This is a gap that needs to be filled by integrating one-health into our mitigation efforts to protect blood supply and availability.

In regions with widespread outbreaks of the dengue virus, the probability of receiving blood from asymptomatic donors is high and is easily missed by symptom-based exclusion criteria [16]. The high number of asymptomatic blood donors is the principal cause of the rising incidence of reported TT-DENV cases in dengue-endemic regions [17–20]. Asymptomatic individuals have a higher viral load on their peripheral blood circulation, but they do not exhibit signs and symptoms associated with dengue fever. This makes it difficult for an experienced blood donor recruiter to exclude such risky donors. Things have also been made worse by a regional variation in the incidence rate of dengue viremia from voluntary blood donors. The case at this point is Brazil with 0.04–0.81%, Puerto Rico with 0.02–0.19%, and Honduras with 0.3% [21–24]. Data gathered a few years ago depict a viral viremia that can last up to 24 hours before the manifestation of any clinical symptoms [25]. Unfortunately, minimal information is available during outbreaks, making it difficult for BTS to select donors during recruitment [26].

The dengue virus is rapidly spreading to new areas and significant outbreaks are becoming more common. **Figure 1** illustrates the global region with documented cases of dengue viral markers detected in healthy blood donors. The highest burden of dengue among eligible blood donors is seen in Brazil and India [17, 20, 27–35]. The burden from other regions is lower, probably masked by a lack of testing and surveillance initiatives. The susceptibility to the virus has recently changed as individuals targeted for donation have become vulnerable. Most potential blood donors would be rejected if they were subjected to pre-donation screening [36]. This has affected the blood supply because more blood donors are deferred from donating blood due to dengue infection or exposure. Blood transfusions from asymptomatic viremic donors will also increase the probability of transmission. Although effective disease reduction and dengue screening techniques have been implemented in developed countries, the initiative is costly for low-income countries. As the number of patients with DHF/DSS increases, so will the demand for blood products such as platelet rich plasma [37–39].

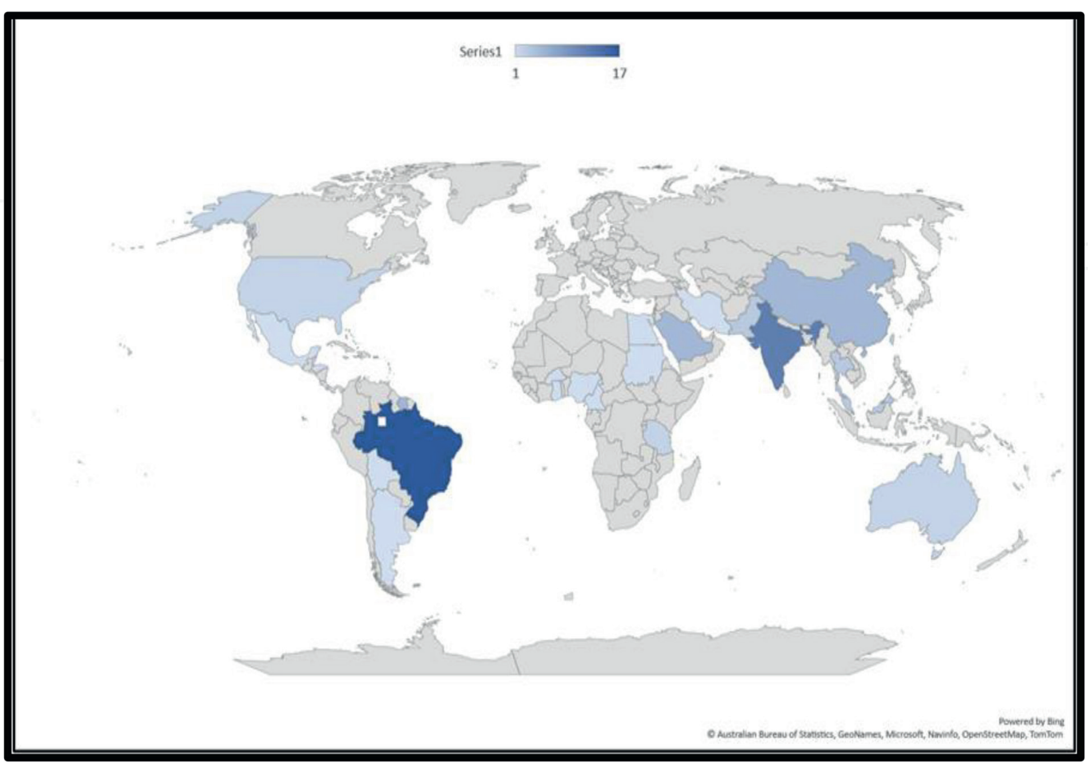

Figure 1.
Regions with documented cases of dengue virus among blood donors.

3. Dengue virus and blood safety: one health perspective

Past outbreaks of emerging infectious diseases have highlighted the close relationship between human and animal health and their environment. A broader understanding of health and disease dynamics demands an integrated approach, which can only be achieved through a convergence of humans, domestic animals, wildlife, and the ecosystem through one health magnifying lens [40–43]. Many include the extinction of some animal species, environmental degradation, environmental pollution, jumping microbial species, and global warming. These are examples of natural drivers of nature that have positively or negatively impacted life on planet Earth and its ecosystems. The emergence and reemergence of infectious diseases endanger not only humans and their livelihood, but other biospheres that support life on earth [44]. Holistic care for our environment and the future of our health has a close connection with what happens in the ecosystem we live in. To safeguard the blood supply that supports the general health of human beings, an interdisciplinary and multi-sectoral approach is paramount. In all measures to protect blood recipients through surveillance systems, disease monitoring, vector control, and environmental conservation, no effort is directed toward an integrated approach through one health system [45].

One Health-One World perception advocates for well-coordinated approaches that will enable a better understanding and management of a complicated health crisis [46, 47]. The only way to solve such problems is to initiate a strategy that integrates all activities in human health, animal health, and environmental preservation into a single system. Different professional leaders and decision-making organs come together collectively to establish an interdisciplinary approach to the treatment of health issues in different communities [48]. Other stakeholders, including global organizations, national governments, and the research community, apply the One-Health approach as a holistic mechanism to combat the spread of infectious diseases. This is one of the best platforms for addressing complex health issues such as emerging and reemerging infectious diseases in blood transfusions [49]. The One-Health and One-World principle focuses on improving our disease surveillance systems in terms of epidemiological trends of diseases and their impact on our economy. It is hoped that one health approach will improve our knowledge of health issues and provide an avenue to develop interventions that are pocket friendly to most counties. A variety of technical, organizational, and sociological factors are an impediment to the long-term implementation of One Health surveillance [50].

In the current world, the world has become a global village and infectious diseases spread rapidly from one nation to another. This is promoted by the interconnectivity of countries through modern transport networks and human movements. This uncomplicated mobility of people around the world shows clearly that no single professional discipline or sector has enough knowledge and resources to prevent the emergence or resurgence of diseases in blood transfusion [51]. The only way to face the future is to eliminate barriers between organizations, individuals, specialities, and sectors. The world requires innovation and collaboration between various sectors to mitigate the frequent threats to human health, livestock health, wildlife, and the integrity of our ecosystem. Current threats and future problems cannot be solved with outdated interventions. The world has become a "One World, One Health" era, and we must develop new mechanisms to handle these threats. Forecasting future threats and working collaboratively in a multidisciplinary approach is the only way to overcome the challenges that arise from emerging infectious diseases in blood transfusions. **Figure 2** is an example of a probable approach through one health that

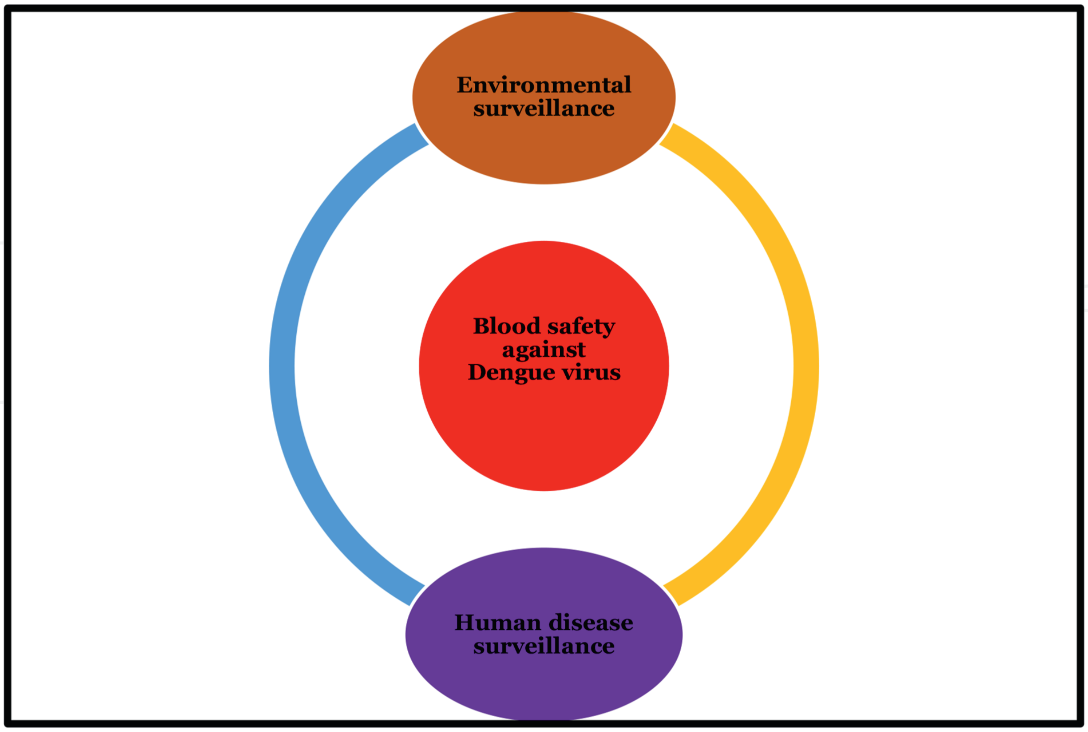

Figure 2.
One health perspective on protecting the blood supply against the dengue virus and other emerging infectious diseases.

will help blood banks keep pace with new threats. A similar approach to address challenges in the fight against diseases in the general human population and in the animal population has yielded good results [52, 53].

3.1 Human disease surveillance

3.1.1 Epidemiological surveillance

A robust surveillance structure is critical for disease prevention for any country in an era full of emerging disease outbreaks. Communication of early warning signs through one health surveillance system helps in preparedness for blood transfusion services. Traditionally, surveillance system models are structured at three levels: event-based, active, and passive surveillance systems [54]. All three systems are applied based on the prevailing circumstances, but with various limitations. One health is the best link to connect all three to address emerging infectious diseases in blood transfusion. Identification of new threats and the ability to share information on risks from passive surveillance would help secure our blood supplies [55]. However, for diagnostic and clinical laboratories, all three surveillance components will be essential to generate surveillance data on viral, bacterial, and parasitic diseases. The basis of disease surveillance is not to investigate all agents, but to investigate data on disease patterns across the world. From a personal understanding, the three surveillance strategies seem inadequate, but they are better than nothing. When used effectively and integrated into our disease mitigation programs, they help predict future disease outbreaks [56].

An active surveillance system is one of the most effective methods used in China to monitor the circulation of infectious diseases in the endemic region of the disease of the disease [57]. Health officials monitor dengue transmission at the local level and can accurately pinpoint the exact pattern of the disease in their locality. These generate data on the serotypes of viruses that are circulating, the burden of the disease, and the complications associated with dengue infection at any time. The strategy here is to have dengue virus surveillance integrated into routine diagnostic laboratory operation [58]. When properly managed, disease surveillance systems can predict and provide early warning before disease outbreaks. However, due to resource constraints, this is not achievable in low-middle-income countries. Additional active surveillance integrated into BTS will increase the overall cost of blood transfusions [59, 60].

With this approach, disease epidemics can be easily predicted and necessary measures are taken to combat the situation. This initiative-taking surveillance system must have at least two elements focusing on the epidemic or interepidemic period. A sentinel site/physician collaboration, a fever vigilant structure that uses peripheral health workers, and a sentinel hospital system are some types of active surveillance systems [61–63]. The main objective of this surveillance mechanism is to assess and detect disease patterns before there is a rise during the interepidemic period. However, once an epidemic occurs, the focus should be on reducing the spread of infectious diseases. Surveillance strategies must be redesigned and directed toward a contextualized region [64].

Countries with evidence of the presence of dengue virus should have disease surveillance mechanisms as part of their disease prevention intervention. They should also be required to develop a legal framework to recognize dengue as a reportable infectious disease [65–68]. The best place to have this approach would be within the BTS, provided that there are standardized case definitions and a formalized mandated reporting system. Although passive systems are less accurate in prediction and have low specificity because cases are not laboratory confirmed, this can be improved by having them integrated into blood transfusion services. Blood transfusion centers are strategically located and may serve a useful purpose in monitoring and monitoring dengue circulation within a community [69].

The clinical continuum of dengue virus infection illnesses ranges from asymptomatic to the most severe form of DHF/DSS. Clinically, it is usually a difficult task to differentiate between fevers associated with DF and other infectious diseases. As a result, laboratory diagnosis should supplement surveillance. Reporting of dengue disease is best when clinical diagnosis, epidemiological data, and laboratory confirmation are combined [70, 71].

Case reports should be requested from all hospitals, clinics, private physician offices, and other facilities that treat the susceptible population as part of passive surveillance [72]. Because not all clinical cases are accurately detected during low transmission, passive surveillance is insensitive even when required by law [73, 74]. Several individuals who suffer from a mild, non-specific viral condition self-medicate at home without consulting a doctor. Under a passive surveillance approach, considerable transmission has already occurred and may have reached its peak by the time doctors identify and record dengue cases [75].

However, passive monitoring for DF/DHF has two drawbacks. The reporting criteria are uneven, to begin with. Although some nations only report DHF, others also report DF. Second, when reporting instances, the CASE definitions are not always followed. These problems lead to under- and over-reporting, making monitoring systems less effective [76].

Last but not least, the purpose of event-based monitoring is to investigate a strange health occurrence, including fevers with unexplained causes and clustering of cases [77]. Unlike the conventional surveillance system, event-based surveillance should be an investigation carried out by an epidemiological unit with the support of a microbiologist, an entomologist and other personnel pertinent to the particular event. This will allow the implementation of interventions to stop the further spread of the infection [78].

3.2 Environmental surveillance

3.2.1 Entomological surveillance

To prioritize areas and seasons for mosquito control, it is essential to carry out regular surveillance of Aedes aegypti to identify its distribution, population density, major larval habitats, spatial and temporal risk factors related to dengue transmission and susceptibility or insecticide resistance levels [79]. This information will make it possible to choose and use the most effective mosquito control methods while also keeping track of their effectiveness. Adult and larval populations can be found and tracked using a variety of techniques. Based on monitoring goals, infestation levels, and resource availability, the best techniques [80] are selected. Information about such activities will be of help if shared with blood transfusion services. A risk mitigation strategy that is helpful for transfusion services by providing adequate time to make risk-based decisions.

The Breateau index is the most insightful indicator that shows a connection between homes and positive containers but does not account for container productivity [81]. However, it is desirable to profile larval habitat characteristics while collecting basic information for the Breateau index by simultaneously logging the relative abundance of the different container types, either as potential or actual mosquito production sites, for example, the number of positive drums per 100 houses, number of positive tires per 100 houses [82]. These facts are crucial for concentrating efforts on managing or eliminating the most typical habitats. The rate at which newly emerging adults from different container types contribute to the adult mosquito population can vary significantly. Counting all pupa in each container allows one to estimate the relative adult production [83].

To assess the relative significance of larval habitats, the Pupal index can be broken down into "useful", "nonessential", and "natural" containers or by particular habitat types such as tires, flower vases, drums, and clay pots [84, 85]. This method may not be used for routine monitoring or in every Aedes aegypti population survey because of the practical challenges and labor-intensive efforts needed to achieve pupal counts, especially from large containers. Instead, it can be saved for special studies or used twice in each locality, once during the wet season and once during the dry season, to identify the most productive containers. For practical purposes, the Pupal index has been the most widely used strategy [84, 86]. The basis for making the greatest use of a few resources can be laid by identifying the classes of containers in the neighborhood that have the highest rates of adult emergence. These classes can then be selectively targeted for source reduction or other mosquito control treatments [87, 88]. The pupal/demographic survey is a technique to determine the most important epidemiological container types. Unlike conventional indices previously discussed, pupal/demographic surveys count all pupae in various types of containers in each community [89, 90].

In real practice, a pupal/demographic survey comprises going to a selection of randomly chosen homes. The number of occupants in the house is noted. With the homeowner's consent, the field employees search for the contents of each water-filled container at each place, strain the contents through a sieve, and then resuspend the sieved contents in a small amount of clean water in a white enamel or plastic pan. Put every pupa in a vial with a label. Large containers provide a great challenge in pupal/demographic surveys, as it is difficult to identify the precise number of pupae in them [86, 90, 91].

Sweep-net techniques with calibration factors have been devised in such circumstances to estimate the overall quantity of pupae in particular types of containers. When returning to the lab, the contents of each vial are moved to tiny cups and covered with mosquito nets fastened with a rubber band if there are any other species except Aedes aegypti in the region. They are maintained until adult emergence, when taxonomic identification and counting can be performed [92]. The collection of demographic data allows us to calculate the ratio of pupae, as reported by Ha and León [85] (a proxy for adult mosquitoes) to people in the community. There is increasing evidence that, when combined with other epidemiological parameters, such as seroconversion rates and temperature specific to dengue serotypes, it is possible to determine the level of mosquito control required in a specific location to prevent virus transmission. This is still an important area of research that needs to be validated. Procedures for sampling adult mosquitoes can provide valuable information for studies on seasonal population patterns, transmission dynamics, transmission risk, and evaluation of adulticide interventions [93].

Planning and evaluating control measures requires knowledge of the sensitivity of Aedes aegypti pesticides. The status of resistance in a population must be carefully monitored in several representative sentinel sites based on the history of insecticide usage and eco-geographical situations to ensure that timely and appropriate decisions on matters like the use of alternative insecticides or the change of control strategies are made [94, 95]. Over the past 40 years, chemicals have been routinely used to prevent mosquitoes and other insects from dispersing illnesses that are crucial to public health. DDT, temephos, malathion, fenthion, permethrin, propoxur, and fenitrothion are only a few of the insecticides widely used that Aedes aegypti and other dengue mosquitoes have become resistant to. The operational influence of resistance on dengue control has not yet been extensively evaluated [96–98]. In countries where DDT resistance has been pervasive, pyrethroid compound precipitated resistance, which is increasingly employed for space spray, is a problem. The voltage-gated sodium channel and mutations in the Kdr gene have been related to resistance to DDT and pyrethroid insecticides in Aedes aegypti because both types of pesticides act at the same target location [99]. Therefore, it is recommended to obtain baseline information on insecticide susceptibility before starting insecticide control operations and to check the susceptibility levels of mosquito larvae or adults [100]. WHO kits to assess the susceptibility of adults and larvae mosquitoes continue to be the accepted approach to assess the susceptibility of Aedes populations. Techniques for analyzing an individual mosquito's biochemistry and immune system have also been created and are currently being used in the field [101].

Integrated community-oriented pest control solutions need the routine monitoring of additional metrics to assess elements such as the number and spread of mosquitoes. These include things such as population density and distribution, settlement traits, land tenure situations, dwelling types, and educational attainment [98, 102, 103]. The planning and evaluation of dengue risk must monitor these characteristics. It is also crucial to understand how home water storage and solid waste disposal techniques have changed over time, as well as how water supply services are distributed, their quality, and their dependability.

Weather data are also crucial in monitoring dengue activities within endemic regions. This information helps to structure epidemic intervention strategies and the planning of focused source reduction and management operations [104]. Some of these data sets are produced by the healthcare industry, so it may be necessary to use additional data sources. For program management, annual or even less frequent updates are generally sufficient. If meteorological data, in particular rainfall patterns, humidity, and temperature, are to be predictive in identifying seasonal trends in mosquito populations and their short-term changes, a more frequent study is necessary [105, 106].

3.2.2 Why one health approach?

One health intervention is a system-thinking approach that helps low- and middle-income countries address threats from dengue and emerging viral diseases in blood transfusion. With limited resources to support their healthcare systems, affected countries will allocate financial resources appropriately where they are needed most. Proper allocation of resources within the different sectors would help most countries deal with collective threats from the dengue virus to blood safety. The avenues available are the establishment of a common laboratory testing facility and an information sharing platform for all sectors involved in dengue surveillance in endemic regions [107, 108].

One health program is an asset to struggling countries that will help them use resources properly to safeguard their blood supply. The challenges facing most blood banks around the world are the lack of adequate financial resources and technology to conduct additional testing of their testing algorithms. The only way to properly use resources is to integrate a system-thinking approach through one health. This approach has had a positive impact on other interventions where one health was implemented to address disease surveillance [109].

Dealing with a complex health problem is a big investment that is not sustainable if only one sector approaches it. Different sectors working collaboratively to address threats to blood safety from emerging infectious diseases provide a sustainable intervention. One Health offers a platform through which different players in blood safety can work with a common goal in mind [110].

Improvement and well-coordination of health systems through one health system is easier than in different sectors working separately. Having a common well-coordinated approach is more impactful and easier to monitor compared to having different players working separately [111–113]. A well-coordinated communication channel between blood transfusion services and other sectors involved in disease surveillance will ease the threats of emerging infectious diseases.

4. Conclusions

In summary, emerging infectious diseases such as the dengue virus threaten the safety of blood transfusions in endemic regions. Necessary measures are required to protect blood recipients from emerging infectious diseases. One Health provides a platform through which various stakeholders, working collaboratively, can ensure that information is available on disease trends in a particular geographic region. Integrating one health into the main disease surveillance system will save most countries millions of dollars in terms of preparation within the blood transfusion sector.

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Conflict of interest

The three authors declare that they have no conflict of interest.

Author details

Festus Mulakoli[1,2]*, George Gachara[3], Eric Ndombi[4] and Samoel Khamadi[5]

1 Aga Khan University, Nairobi, Kenya

2 Kenyattta University, Nairobi, Kenya

3 Department of Medical Laboratory Sciences, Kenyatta University, Nairobi, Kenya

4 Department of Pathology, Kenyatta University, Nairobi, Kenya

5 KEMRI-Centre for Virus Research, Nairobi, Kenya

*Address all correspondence to: mulakolifesto@gmail.com

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