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Research

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Prevalence of Dengue virus among healthy blood donors in Mombasa County, Kenya

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Abstract

Introduction: *Dengue fever (DF) is a viral infection caused by a flavivirus called Dengue virus. The virus has four known serotypes (named DENV 1-4) that circulate between humans and Aedes mosquitoes throughout the tropical region of the world. The virus is transmitted primarily by the bite of an infected Aedes aegyptior, to a lesser extent, Aedes albopictus. Current evidence from published case studies shows that blood transfusions can transmit Dengue infection in hyperendemic regions in the tropics. It is important to note that 75% of people infected with DENV show no symptoms. Therefore, an infected individual could be accepted as a blood donor and spread the disease. In Kenya, frequent Dengue outbreaks have been reported in the coastal counties of Mombasa, Kilifi, and Kwale in recent years. This study aimed to determine the seroprevalence of Dengue virus among blood donors in a selected endemic region of the Republic of Kenya.* ***Methods:*** *the researchers used a cross-sectional research design to collect data from blood donors in two selected counties in Kenya in 2023. A self-directed questionnaire was used to collect sociodemographic data and risk factors associated with Dengue fever from consenting participants. Additionally, a 5-ml sample of blood was collected and serologically analyzed for anti-Dengue IgG, IgM, and NS1 using a commercial rapid Dengue testing duo kit (Bioline™ DENGUE DUO (Dengue NS1 Ag + IgG/IgM)). The data were summarized and presented using tables and bar graphs.* ***Results:*** *at the end of the study, the researchers recruited 103 participants from the selected study sites in Mombasa County. Most of the research participants were men between 20 and 30 years of age. The prevalence of Dengue virus seromarkers was 24%, 11%, and 2% for IgG, IgM, and NS1, respectively. These were detected among young adult donors between the ages of 20 and 30 years. Statistically, there was an association between anti-Dengue IgM positivity with a history of admission (p-value = 0.0015), fever in the last 6 months (p-value = 0.0015) and a history of living with a victim of DF in the last 6 months (p-value = 0.011). Similarly, there was a statistically significant association between anti-Dengue IgG positivity and length of stay in Mombasa County (p-value = 0.005), history of admission in the last 6 months (p-value =0.003), history of fever in the last 6 months (p-value = 0.004) and lived with a victim of Dengue fever in the last 6 months (p-value = 0.02) in a 95% confidence interval.* ***Conclusion:*** *according to the findings of our study, blood donors in Mombasa are susceptible to infection by the Dengue virus, some possibly carrying the virus without showing symptoms. The study identified IgG and IgM as the most prevalent serological markers. To protect blood recipients in Mombasa County and other Dengue-endemic counties such as Kilifi, Kwale, Lamu, and Taita Taveta, it is recommended that blood donors in these regions undergo regular screening, particularly during Dengue outbreaks.*

Introduction

Dengue fever is a viral infection that has recently been discovered to be transmissible through blood transfusions. Although Aedes mosquitoes are the primary vector of Dengue, they can also be transmitted via blood transfusions and organ transplants. This means that if a person receives blood from an infected donor, they can contract the virus through blood transfusions [1-3]. Various studies conducted in hyperendemic countries have reported five cases of Dengue hemorrhagic fever because of transfusion-transmitted Dengue [4-6]. The Dengue virus, a mosquito-borne disease, is endemic in tropical and subtropical areas of the world. Dengue fever has spread to 128 countries in the tropical and subtropical regions of the world. According to estimates, half of the world's population is at risk of contracting the Dengue virus. The symptoms of Dengue fever can range from mild to severe and include high fever, headache, muscle and joint pain, nausea, vomiting, and rash. In severe cases, Dengue fever can lead to Dengue hemorrhagic fever, which can be life-threatening. Each year, approximately

25,000 people die from the Dengue virus [7,8]. There is evidence that transfusions can spread Dengue infection in areas where the virus is persistent. Emerging infectious diseases are a problem for blood transfusion services right now. As a result, developed countries are required to perform additional tests that would be prohibitively expensive in developing countries such as Kenya [9]. Babesia, Chagas disease, chikungunya, zika virus, Dengue virus (DENV), hepatitis E virus, West Nile virus, human T lymphocyte virus, and Ross River virus are examples of emerging diseases in blood transfusions [10].

Studies conducted in countries such as Brazil, India, China, Saudi Arabia, Ghana, Tanzania, and Cameroon have concluded that the Dengue virus poses a threat to safety and availability in their respective countries [11-13]. The Dengue virus can now be spread through blood and tissue transplants, besides the traditional mosquito bite method. Several studies have shown that Dengue can be transmitted by blood transfusion. However, the first case was reported in China in 2002 and in Singapore in 2008 by Tambyah *et al.* [14], Chuang *et al.* [15]. According to their findings, patients who received blood transfusions from asymptomatic blood donors quickly developed Dengue-like symptoms. Comparable studies in Brazil, Puerto Rico, and Singapore during the 2016 outbreaks reported a 0.5% incidence rate of Dengue viremia among asymptomatic blood donors [6,16]. Ashshi [17] in their study among healthy blood donors in Saudi Arabia reported a seroprevalence between 1 and 7% for NS1, IgM, and IgG antibodies. Similarly, a study by Rodriguez Rodriguez *et al.* [18] using the enzyme-linked immunosorbent assay (ELISA) technique in blood donors in the northeastern region of Mexico discovered IgG and IgM levels of 59% and 2%, respectively. However, reverse transcription-polymerase chain reaction (RT-PCR) analysis did not find any evidence of viremia. These scenarios are most often observed in healed Dengue infections and are a technical limitation of the RT-PCR assay [19]. In India, the country most affected by the Dengue virus, a study by Kulkarni *et al.* [20] in the Pune region of western India reported seropositivity of 0.64 % and 6.4% for NS1 and IgM, respectively, in 2017.

Little is known about the prevalence of Dengue virus among blood donors in Africa, and the probability of Dengue fever caused by transfusion-transmitted Dengue (TTD) is high [21]. Studies conducted in some countries have detected Dengue markers in asymptomatic blood donors. For example, a study by Tchuandom *et al.* [22] among Cameroonian blood donors reported a prevalence rate of 5% for all serological markers using a simple immunochromatographic diagnostic kit. In Tanzania, a similar study by Vairo *et al.* [23] reported a prevalence of 50.6% anti-Dengue (IgG) among blood donors in Zanzibar. Unfortunately, there is less research output from African countries compared to other endemic regions of the world. To fill these gaps, a lot of effort and commitment are required to conduct research studies on blood safety in Africa [24].

The current problem is exacerbated in African countries because of limited resources, a high incidence of known transfusion-transmitted infection (TTI) a lack of blood supplies, and a shortage of blood transfusion specialists. As a result, the impact of these new infectious diseases on blood safety and the associated costs adds to the already significant financial burden on blood transfusion services in African countries [25]. Dengue fever is endemic in Africa in several countries, including Kenya, Tanzania, Sudan, Egypt, Nigeria, Cameroon, Burkina Faso, and Senegal. These countries have previously experienced outbreaks of Dengue fever, and the disease continues to be a major public health concern.

Prevention of Dengue fever involves taking measures to avoid mosquito bites, such as using insect repellent, wearing long-sleeve clothing, and staying in air-conditioned or well-screened areas. Currently, there is no specific treatment for Dengue fever, but supportive care can help

manage symptoms and prevent complications. To prevent Dengue fever transmitted by transfusions, some blood transfusion services in developed countries have added Dengue virus screens to their testing algorithm as a precautionary measure. This precautionary approach is intended to ensure the safety of the blood supply and the continuous availability of blood during outbreaks of Dengue fever [26,27].

The virus is prevalent in Kwale, Kilifi, Mandera, Lamu, Taita-Taveta, and Mombasa counties in Kenya. Dengue virus outbreaks have occurred since 2004, the most recent occurring in 2017. According to an epidemiological study conducted on febrile patients in Mombasa County using IgM as a marker, the prevalence of Dengue virus was 41% among febrile patients. According to the findings, DENV-1 was the most common serotype in samples collected between 2011 and 2014, followed by DENV-2 (38.5%) and DENV-3 (17.4%) [28]. Other major outbreaks have been observed in Kilifi, Lamu, Kwale, and Mandera between 2011 and 2018 [29,30]. Limited information is available on the impact of disease outbreaks on the safety of blood supplies in affected regions. This study addressed two research questions: (i) What is the prevalence of Dengue virus among blood donors in Mombasa County; and (ii) What are the demographic characteristics and risk factors associated with Dengue virus positivity among blood donors? Therefore, we aimed to investigate the prevalence of the Dengue virus among healthy blood donors in Mombasa County in Kenya and to analyze its potential implications for the safety of blood transfusions.

Methods

Study design and setting: the researchers used a cross-sectional study design guided by the STROBE guidelines [31] to collect data at a private blood donation center in Mombasa County. The donation center is located within a leading private tertiary healthcare institution in the county. The researchers collected their data between December 2022 and July 2023 using approved data collection tools. Validated questionnaires were used to collect study-related information from blood donors at the study site. Additionally, blood samples were collected from consenting donors after meeting the minimum qualification of a blood donor according to institutional guidelines. Convenient sampling was used to sample eligible blood donors for this study. The principal investigator (PI) of the study provided a self-administered questionnaire to all consenting blood donors during the field visit. The dependent variable for the study included the donor's residence, the duration of stay at the study site, travel history to countries in the Middle East, use of insect repellants, environmental conditions in his home space, sex, age, religion, medical history, and level of education. The independent variable for this study was seropositivity for Dengue IgG, IgM, and NS1 antigen. These samples received unique identifiers to conceal the identity of the research participants. This was followed by the test of three Dengue viral markers (IgG, IgM, and NS1 antigen) using a commercial rapid Dengue testing duo kit (Bioline™ DENGUE DUO (DENGUE NS1 Ag + IgG/IgM)).

Study population and sampling procedure: the target population for the study was individuals who presented themselves as voluntary blood donors during the study period. The study included blood donors who were between 16 and 65 years of age and gave their consent to participate. The study excluded people who had not lived in the study area for the last six months and those who had a fever in the last two weeks.

Sample size determination: the researchers used an online sample size calculator [32] where a prevalence of NS1 of 6.1% was used as reported by Tchuandom *et al.* [22], with a confidence level of 95% and a margin of error of 5. The minimum sample size for this study was 89 blood donors after the calculation.

Study variables and data sources/measurement: the dependent variables of interest for this study were ant-Dengue IgG, IgM, and NS1 antigen. The definition of Dengue fever was characterized by positivity for IgM or NS1. On the other hand, the independent variables were sociodemographic factors (age, sex, religion, level of education) and risk determinants (use of insect repellents, outdoor activities, history of travel to Dengue-endemic regions, stagnant water, and congested human dwellings) for the transmission of the Dengue virus. A self-administered questionnaire (English and Kiswahili) was used to capture relevant information (donor demographics and serology results). Aseptically collected blood samples were analyzed for the presence of the Dengue seromarkers IgM, IgG, and NS1. A commercial immunochromatography kit was used for this purpose.

Laboratory testing: at the study site, serum samples were serologically tested for NS1, IgM, and IgG using a combined Rapid test cassette (Bioline™ DENGUE DUO, Abbott Park, Illinois, United States) following the manufacturer's instructions. The results obtained were entered into the individual donor questionnaire and recorded as positive or negative for the markers.

Data management: the data collected were entered into an Excel spreadsheet, cleaned, and then entered into SPSS version 20. A Chi-square test (χ^2) at a 95 confidence interval was used to examine the relationships between binary or nominal variables. The Chi-square test was used to assess the characteristics of the relationship between the predictor variables and the outcome variables. The predictor variables were significant if their p-value was less than 0.05 at a 95% confidence interval.

Ethical considerations: the Aga Khan University Institutional Scientific Ethics Research Committee granted ethical approval with reference number 2022/ISERC-10(v3) (AKU-ISERC). Before data collection, a research permit with reference number 239512 was obtained from the National Commission for Science, Technology, and Innovation (NACOSTI).

Results

This study recruited 103 blood donors after meeting the minimum requirements for an eligible donor as described in the donor questionnaire. Most of them n-74 (71.8%) were between 21 and 30 years old. This was followed by people between 31 and 40 years of age at n=23 (22.3%). Males were the main blood donors at n= 87 (84.5%) who volunteered to donate blood during the study period. Lastly, n=74 (71.8%) of the blood donors indicated that they were Christians (Table 1).

Prevalence of Dengue virus among selected research participants:the prevalence of Dengue virus was 11%, 24%, and 2 % for IgM, IgG, and NS1, respectively. The most dominant marker for Dengue fever was anti-Dengue IgG, followed by anti-Dengue IgM. Only a few donors had detectable NS1 antigens in their blood (Figure 1). During the study period, these markers were distributed differently between various age groups of blood donors. Blood donors between the ages of 21-30 and 41-50 years had a higher prevalence of anti-Dengue IgM and IgG (Figure 2).

Sociodemographic characteristics and risk factors are associated with Dengue virus positivity:to determine the association between independent variables (age, gender, education, use of insect repellant use, etc.) and dependent variable (Dengue seropositivity), we performed a Chi-square analysis (χ^2). The analysis showed that there was a significant association between anti-Dengue IgM positivity with a history of admission (p=0.0015), having had a fever in the last six months (p=0.0015), and a history of living with a victim of Dengue fever in the last six months (p=0.011) at 95 CI (Table 2). However, there was no correlation between the dependent variable NS1 positivity and the independent variables of interest in this study (Table 3). Similarly, there was a statistically significant association between anti-

Dengue IgG positivity and length of stay in Mombasa County (p=0.005), history of admission in the last six months (p=0.003), history of fever in the last six months (p = 0.004) and lived with a victim of DF in the last six months (p= 0.02) (Table 4).

Discussion

The prevalence of Dengue virus infection among unpaid voluntary donors in an endemic region around the world is a matter of great concern for the safety and availability of blood products. The rapid spread of the virus is the subject of discussion among scholars involved in blood safety. In this study, our findings show that a good number of blood donors were exposed to the Dengue virus at the time of data collection. This confirms that Mombasa County is an endemic region of the Dengue virus in the Republic of Kenya [33]. This finding is similar to the 13% that was reported in the 2013 household survey by Ellis *et al.* [34]. Exposure to Dengue virus (IgG) was higher than that reported by Koech [35] among blood donors in Nairobi (11.1%), Kisumu (5.4%), and Eldoret (2.2%). This difference is because of the regional variation in the prevalence of different counties in Kenya.

Regionally, our findings were higher than the 2.2 % reported in a study by Muhibi *et al.* [13] among blood donors in Nigeria and 0.0% among Egyptian blood donors by Abd El-Wahab *et al.* [36]. Similarly, our findings were reported to be less than 24.8% among blood donors in Cameroon, where the prevalence of IgM, IgG, and NS1 was reported at 12.3%, 4.5%, and 6.1% [22]. Our exposure [37] to Dengue virus was also less than 50.6% reported in Zanzibar by Vairo *et al.* [23], and 43.6% in Ghana by Narkwa *et al.* [38]. Variation in exposure to Dengue virus could be attributed to the test method used in these studies that predispose to cross-reactivity with other flavivirus infections [39]. Therefore, it is important to exercise caution when interpreting the results of these studies before concluding on the implications of the Dengue virus on blood safety and availability.

Globally, our findings for anti-Dengue IgG were higher than 1.4% reported in a study in Brazil by Ribas-Silva [40], 4.21% in another study by Slavov *et al.*[41] the same country, 3.4% in donor blood samples in China [42], and 2.25% in the same country [43]. Similarly, our findings were comparable to 26.53% reported among blood donors in Yunnan province by Li *et al.* [44]. However, our findings were lower than the 17.9% reported in a study in Jordan by Swedan [45]. Our prevalence rate of 2% was less than NS-1 0.54% reported in India by Jain *et al.* [46]. A similar observation was observed in anti-Dengue IgM, where our findings were similar to 11.23%, but less than 6.74% reported in two studies among donors in India [47,48]. However, our findings were higher than the 0.78% reported in China by Gao *et al.* [49], and 5.5% by Ashshi *et al.* [27]. These findings suggest that, if the plasma sample tests were positive for IgM, it is likely that the infection occurred between one and two months before the sample was collected. This indicates that the virus is still actively circulating in the community and that more aggressive measures are needed to contain its spread. The presence of DENV-NS1 antigen and/or anti-DENV IgM antibody in the tested donors indicates that they are in the asymptomatic viremic infectious stage with DENV during donation time, while the high prevalence of anti-DENV IgG suggests that Dengue disease is highly prevalent in this region.

There was a variation in the prevalence of NS1 reported in our study compared to what is reported elsewhere. For example, our findings were higher than 0.56%, 0.9%, and 0.54%, as reported in three studies from India by Raj, Shashindran *et al.* [47] Jain, *et al.* [46], Remakanth *et al.* [48]. However, our findings were lower than the 5.3% reported in a study in Saudi Arabia by Ashshi *et al.* [27]. The presence of NS1, a protein associated with Dengue virus infection, in Mombasa blood donors, poses a serious threat to the safety of donated blood in this region. This

indicates that individuals could have potentially transmitted the virus to recipients of these blood products. As Dengue infection can have severe consequences, including death, it is essential to implement strict screening procedures to prevent infected blood from entering the blood supply. The findings on the NS1 protein are consistent with those of a previous study, indicating the reliability of our research. This provides further evidence for the existing body of knowledge on NS1. The congruent results of both investigations suggest that NS1 plays a crucial role in the biological processes studied and can be considered a significant factor in the development of potential treatments or therapies [50-53].

Dengue fever is a pressing issue in numerous regions of the world and poses a grave threat to public health. Blood transfusion is a known mode of transmission that poses a significant hazard to blood recipients. Although the Aedes mosquito is the main vector of Dengue transmission, studies indicate that the virus can also be transmitted by blood meals. As such, people who donate or receive blood may be at risk of contracting the virus and subsequently developing Dengue fever [1,36,48,49].

Study limitations and bias: this study was conducted during a dry season in the study area and in a single blood donation center in the vast coastal region of the Republic of Kenya. Therefore, the prevalence obtained cannot be generalized to present the entire coastal region.

Conclusion

There is a high prevalence of Dengue virus among blood donors in Mombasa County, with a majority having previously been exposed to the Dengue virus. Therefore, screening of blood donors in this region for Dengue virus will be a good measure to protect blood recipients from Dengue fever.

What is known about this topic

- *Mombasa County is a known endemic region of Dengue fever in the Republic of Kenya;*
- *Studies in other global regions have shown a varying prevalence of the Dengue virus among blood donors.*

What this study adds

- *Documented the first study of Dengue virus among blood donors in Mombasa County, Kenya;*
- *Illustrated the need to introduce Dengue virus screening among blood donors in all endemic counties of the Republic of Kenya and other African countries.*

Competing interests

The authors declare no competing interests.

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Authors' contributions

The initial concept of the study was developed by Festus Mulakoli. George Gachara and Eric Ndombi reviewed the concepts and made additional amendments to the final concept. Samoel Khamadi reviewed the method section of the manuscript. The four authors critically reviewed and co-authored the final manuscript before submission for publication.

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Tables and figures

Table 1: sociodemographic data of blood donors for the study

Table 2: correlation between sociodemographic/risk factors and anti-Dengue IgM positivity

Table 3: correlation between sociodemographic/risk factors and NS1 positivity

Table 4: correlation between sociodemographic/risk factors and anti-Dengue IgG positivity

Figure 1: prevalence of Dengue seromarkers among blood donors in Mombasa County

Figure 2: distribution of Dengue seromarkers among different age groups of selected blood donors in Mombasa County

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Table 1: sociodemographic data of blood donors for the study		
	Frequency (n)	**Percent (%)**
Age group		
21-30	74	71.8
31-40	23	22.3
41-50	6	5.8
Level of education		
None	6	5.8
Primary	11	10.7
Secondary	66	64.1
Tertiary	20	19.4
Sex		
Female	16	15.5
Male	87	84.5
Religious belief		
Muslim	29	28.2
Christian	74	71.8

Table 2: correlation between sociodemographic/risk factors and anti-dengue IgM positivity

		IgM status		Chi-square	P value
		Negative (n)	Positive (n)		
Level of education	None	6	0	3.854	0.248
	Primary	9	2		
	Secondary	61	5		
	Tertiary	16	4		
Age	21-30	67	7	0.476	0.801
	31-40	20	3		
	41-50	5	1		
Gender	Female	16	0	2.265	0.140
	Male	76	11		
Religion	Muslim	25	4	0.41	0.499
	Christian	67	7		
Length of stay in Mombasa	1-2	8	0	4.150	0.62
	2-5	11	0		
	56-10	7	0		
	Above 10	66	11		
History of vomiting in the last six months	No	88	9	3.428	0.123
	Yes	4	2		
History of pain in the last six months	No	81	9	0.345	0.627
	Yes	11	2		
History of admission	No	89	8	10.326	0.015
	Yes	3	3		
History of bleeding	No	90	11	0.244	1
	Yes	2	0		
History of fever	No	64	3	7.730	0.015
	Yes	28	8		
Use of insect repellant	No	46	5	0.081	1
	Yes	46	6		
Relax and play outdoors during the day	No	27	2	0.606	0.724
	Yes	65	9		
Visited dengue-endemic countries	No	87	11	0.628	1
	Yes	5	0		
Lived with a DF patient	No	86	7	9.981	0.011
	Yes	6	4		
Empty and stagnant water	No	82	10	0.033	1
	Yes	10	1		
Congested housing	No	63	8	0.83	1
	Yes	29	3		

Table 3: correlation between sociodemographic/risk factors and NS1 positivity					
		NS1 Status		**Chi-square**	**P value**
		Negative (n)	**Positive (n)**		
Level of education	None	6	0	1.382	0.700
	Primary	11	0		
	Secondary	65	1		
	Tertiary	19	1		
Age	21-30	73	1	0.954	0.636
	31-40	22	1		
	41-50	6	0		
Gender	Female	16	0	0.375	0.712
	Male	85	2		
Length of stay in Mombasa	1-2	8	0	0.689	0.759
	2-5	11	0		
	56-10	7	0		
	Above 10	75	2		
History of vomiting in the last six months	No	95	2	3.428	0.123
	Yes	6	0		
History of pain in the last six months	No	81	9	2.584	0.238
	Yes	11	2		
History of hospital admission to the hospital	No	95	2	0.126	1
	Yes	6	0		
History of bleeding	No	99	2	0.040	1
	Yes	2	0		
History of fever	No	67	0	3.796	0.120
	Yes	34	2		
Use of insect Repellant	No	50	1	0.000	1
	Yes	51	1		
Relax and play outside during the day.	No	28	1	0.481	0.486
	Yes	73	1		
Visited dengue-endemic countries.	No	96	2	0.104	1
	Yes	5	0		
Lived with a dengue fever patient	No	91	2	0.219	1
	Yes	10	0		
Empty and stagnant water in the Living Environment	No	91	1	3.306	0.203
	Yes	10	1		
Congested housing	No	71	0	4.525	0.094
	Yes	30	2		

Table 4: correlation between sociodemographic/risk factors and anti-dengue IgG positivity					
		IgG Status		**Chi-square**	**P value**
		Negative (n)	**Positive (n)**		
Level of education	None	6	0	7.750	**0.040**
	Primary	5	6		
	Secondary	52	14		
	Tertiary	15	5		
Age	21-30	53	21	3.983	0.98
	31-40	21	2		
	41-50	4	2		
Gender	Female	14	2	1.428a	0.193
	Male	64	23		
Religion	Muslim	20	9	1.004	0.32
	Christian	58	16		
Length of stay in Mombasa	1-2	8	0	8.462	0.005
	2-5	11	0		
	56-10	6	1		
	Above 10	53	24		
History of vomiting in the last six months	No	75	22	2.294	0.152
	Yes	3	3		
History of pain in the last six months	No	69	21	0.342	0.512
	Yes	9	4		
History of hospital admission to the hospital	No	77	20	12.091	0.003
	Yes	1	5		
History of bleeding	No	76	25	0.654	1
	Yes	2	0		
History of fever	No	57	10	9.111	0.004
	Yes	21	15		
Use of insect Repellant	No	40	11	0.401	0.647
	Yes	38	14		
Relax and play outside during the day.	No	22	7	0.000	1
	Yes	56	18		
Visited dengue-endemic countries.	No	74	24	0.628	1
	Yes	4	1		
Lived with a dengue fever patient	No	75	18	12.6	0.02
	Yes	3	7		
Empty and stagnant water in the Living Environment	No	71	21	0.98	0.455
	Yes	7	4		
Congested housing	No	53	18	0.145	0.807
	Yes	25	7		

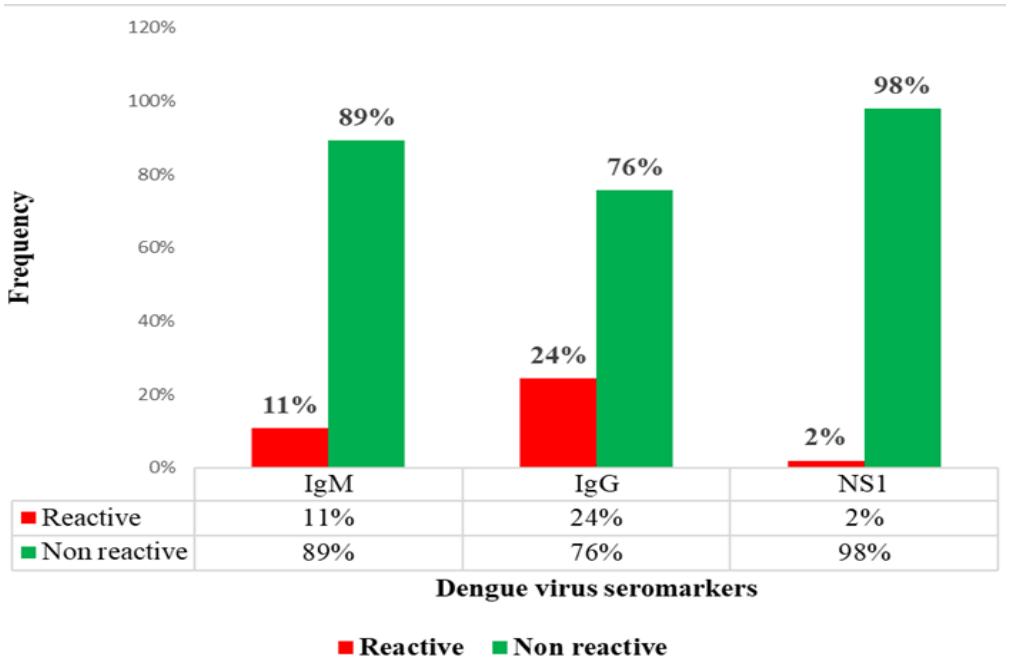

Figure 1: prevalence of Dengue seromarkers among blood donors in Mombasa County

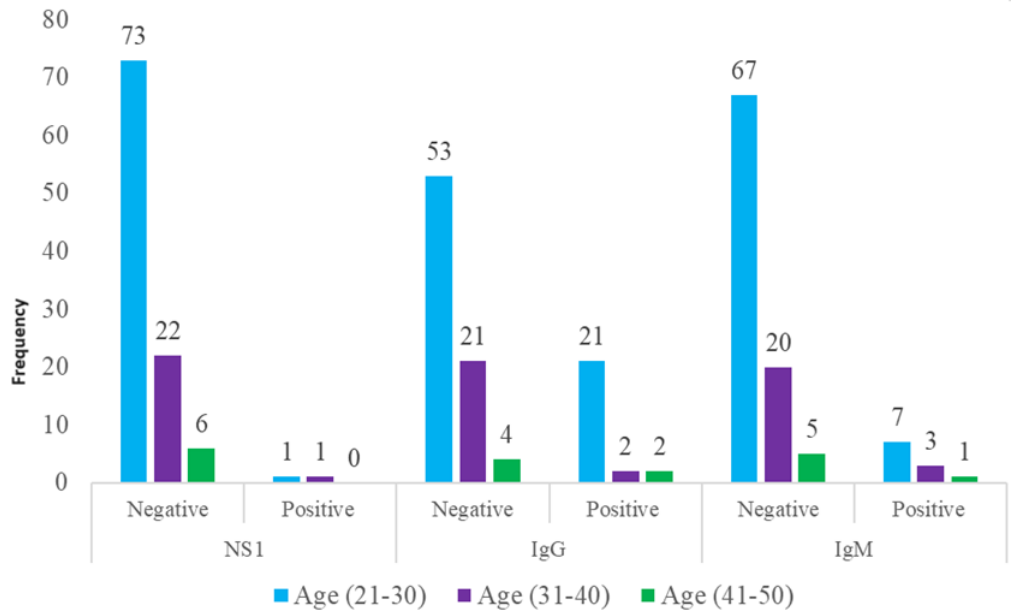

Figure 2: distribution of Dengue seromarkers among different age groups of selected blood donors in Mombasa County