Malaria Spatio-Temporal Patterns in Busia and Tororo Districts, Eastern Uganda

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Abstract

Malaria burden remains one of the major public health challenges in sub-Saharan Africa, Uganda inclusive. Uganda has the 3rd highest global disease cases estimated to be 225 million and the 8th highest level of deaths equivalent to 781,000 per year. Malaria remains a leading cause of morbidity and mortality in Uganda, accounting for 30-50% of outpatient visits at health facilities, 15-20% of all hospital admissions, and up to 20% of all hospital deaths with at least 27.2% of inpatient deaths among children under five years of age. Widely recommended *Plasmodium* vector control approaches include utilization of long-lasting insecticidal nets and indoor residual sprays which are insecticide-based. This study assessed a nine-year period malaria cases data (2012-2020) obtained from the health management database to depict malaria spatial and temporal patterns in Busia and Tororo districts pre and post-vector control interventions. The routine malaria surveillance data reported passively through public and high-volume private health facilities were entered and manipulated into MS Excel. This was done separately for each of the 9 years. Considering the malaria cases registered on annual basis, Mann- Kendal test revealed a drastic decline of malaria cases over the nine-year period (2012 -2020) in Tororo district with Sen's slope of -22, while for Busia district it revealed an increase of malaria cases (Sen's slope +28). Equally, these trends reveal varied spatial patterns over the two districts. Both Busia and Tororo revealed a high prevalence of malaria between May-November in respect to bimodal rainfall pattern, matching with the perennial transmission setting of Uganda. This study has shown that, for further epidemiological characterization, vector behavior, biology and physiology need consistent monitoring and surveillance while implementing new vector control interventions targeting outdoor biting *Plasmodium* vectors.

1.0 Background

Malaria, a disease caused by *Plasmodium* species, remains a public health burden worldwide with 40% of the world's population at risk of the disease, more so in the impoverished and developing regions including Africa (Collins et al., 2019). Malaria is endemic in tropical and subtropical regions where it causes over 300 million acute illnesses and at least one million deaths each year. Malaria is endemic in more than 30 countries in sub-Saharan Africa, including the eastern African countries of Uganda (Okia et al., 2018b). Uganda has the 3rd highest global disease cases estimated to be 225 million and the 8th highest level of deaths equivalent to 781,000 per year (Okia et al., 2013). Malaria remains a leading cause of morbidity and mortality in Uganda, accounting for 30–50% of outpatient visits at health facilities, 15–20% of all hospital admissions, and up to 20% of all hospital deaths with at least 27.2% of inpatient deaths among children under five years of age (MoH, 2014). Over the last two decades, there has been remarkable progress in malaria control in sub-Saharan Africa, due mainly to the massive deployment of long-lasting insecticidal nets and indoor residual spraying (Ochomo et al., 2014; Katureebe et al., 2016; Antonio-nkondjio *et al.*, 2018; Musiime et al., 2019; Tchouakui et al., 2021). These tools are insecticides based from four chemical classes: organochlorines, pyrethroids, carbamates and organophosphates. Whereas 14 formulations belonging to these classes are approved by the World Health Organization (WHO) for use in IRS, only pyrethroids are approved for use in LLINs because of their low human toxicity, repellent properties (Kenea et al., 2016) and rapid knock down and killing effect thus the community is protected from malaria (Helinski et al., 2015). Despite these gains, it is clear that in many situations, additional interventions are needed to further reduce malaria transmission. The

World Health Organization (WHO) has promoted the Integrated Vector Management (IVM) approach through its Global Vector Control Response 2017–2030. However, prior to roll-out of larval source management (LSM) as part of IVM, knowledge on ecology of larval aquatic habitats is required. LLINs are widely recommended because the insecticide incorporated can retain effectiveness against susceptible *Anopheles* species vectors for up to 20 standard WHO laboratory washes and 3 years of recommended usage under field conditions unlike conventional ITNs which lose effective insecticide after one or two washes and maintain bioefficacy for a maximum of 6–12 months (Okia et al., 2013; Musiime et al., 2019). However, these methods have been noted to be ineffective against exophagic malaria vectors, decreased susceptibility, and increased resistance to pyrethroids (Hakizimana et al., 2016; Musiime et al., 2019; Ochomo et al., 2014). Additionally, mosquito vector species dynamics have been reported to change, where, for example, the most susceptible to a specific vector control approach becomes less common, leaving vector species that are less susceptible (Sherrard-smith et al., 2019). Despite the deployed vector control approaches, malaria status of Busia and Tororo districts is particularly high as the area is characterised by numerous and recurrent bushes, persistent stagnant water around homesteads, long rain seasons, low altitude and high temperatures. Busia and Tororo also accommodates two important boarder points of Busia and Malaba along the famous Trans-Africa highway, characterised by heavy traffic of people and merchandise from, through and to many other countries. All these factors favours the proliferation of *Anopheles* mosquitoes and reproduction of the parasites within them (Oguttu et al., 2017). Additionally, limited surveillance and monitoring of mosquitoes for behavioural adaptations and changes in vector species' composition is the common challenge (Katureebe et al., 2016). Together with the fact that there is also oscillation of mosquito vectors and the human-plasmodium carriers within the area, it could explain why amidst the intensified vector control measures, the regions still experience active *Plasmodium* transmission, especially during the peak of malaria vector breeding season that spans the summer months (Ssempiira et al., 2017).Therefore, there was a need to examine the effect of vector control interventions on trends of malaria over the nine year period in the hotspot and cold spot areas in Busia and Tororo in order to implicate the role of variabilities of the different control frameworks in the two districts.

2.0 Materials And Methods

2.1 Description of Study Area

The study was conducted in two purposively selected districts of Busia and Tororo in Eastern Uganda, regarded as among the sentinel regions sharing eco-epidemiological features and characterized strata of high malaria transmission with the presence of mosquito species and higher insecticide pressure (Hakizimana et al., 2016; Tchouakui et al., 2021).

Busia and Tororo districts have a stable perennial malaria transmission with malaria prevalence rates ranging from 39 to 68% (Okia et al., 2018a). Busia district is located to the southeast and lies between 0^{o} 46'N, 34^{o} 0'E of Uganda near Kenya boarder and bordering Tororo district to the north (Githinji et al., 2020). Tororo town is approximately 10 kms west of the town of Malaba at the border between Uganda and Kenya, located 205 km northeast of Kampala and lies between 0° 45'N, 34° 5'E (Latitude: 0.692780; Longitude: 34.181655) in Eastern Uganda and lies at an average elevation of 1,278 m above sea level.

2.2 Research Design

This study used an observational and retrospective data for malaria cases in the study area for the past nine year's period (from 2012 to 2020).

2.3 Sampling Design

Times-series data on malaria cases (2012–2020) from Health Centre level II, III, IV, private and government health facilities occurring across two districts of the study were obtained from the data base. The routine malaria surveillance data reported passively through public and high-volume private health facilities from the year 2012–2020 were accessed from the data base. Weekly and monthly malaria case reports made to the MoH by all health facilities through district health information management system (DHMIS) and entered and manipulated into MS Excel. This was done separately for each of the 9 years.

2.4 Statistical Analysis

To detect the effect of vector control interventions on trends of malaria over the study period in the hotspot and cold spot areas of both districts, the annual Malaria cases data (2012–2020) for both Busia and Tororo districts were subjected to a Makesens 1.0 Toolkit in Ms. Excel. A nonparametric Mann-Kendall test was run using the toolkit to estimate trend in time series of annual cases trend thereafter a nonparametric Sen's method was used to estimate the slope of trend. A positive value of S indicates an 'upward trend' (increasing values with time), while a negative value of S indicates a 'downward trend. For each of the hospital, location data (coordinates) was obtained through mapping of hospitals using a Geographical Positioning System (GPS). The coordinates and the malaria cases were matched in Microsoft Excel. The data were exported to the GIS environment then interpolated using kriging method to generate the Geotif maps. A total of 500 random values were extracted from the Geotif and re-interpolated to generate spatial distribution maps for malaria cases.

3.0 Results

3.1 Malaria Patterns in Busia and Tororo Districts

Considering the malaria cases registered on annual basis, the results revealed more malaria cases in Busia than Tororo. Mann- Kendal test revealed a drastic decline of malaria cases over the nine-year period (from 2012 to 2020) in Tororo district with Sen's slope of -22 ($p < 0.05$), while for Busia district it revealed an increase of malaria cases with Sen's slope of + 28 ($p < 0.001$) as shown in Table 1.

Table 1
Sen’s Method Estimating the Slope of Malaria Trend over a Nine Year Period in Busia and Tororo

Number	**1**	**2**
Name	Malaria cases Tororo	Malaria Cases Busia
Years	2012–2020	2012–2020
N	9	9
Test S	-22	28
Significant.	*	**
Q	-3.97E + 04	4.67E + 04
B	4.24E + 05	1.64E + 05

The red colour in the maps reveal areas with high malaria cases regarded as hot-spots, while the cloudy blue colour reveals the lowest malaria cases regarded as cold-spots recorded in a given year.

According to Fig. 3, the malaria cases registered on annual basis, the results revealed more malaria cases in Busia than Tororo. There was a general increase in number of malaria cases in Busia ($R^2 = 0.8136$) and a general decline in malaria cases in Tororo district ($R^2 = 0.8435$).

According to Table 2, the average malaria cases in both Busia and Tororo varied between years ($p < 0.05$). For Tororo, the highest mean number of cases were recorded in 2013 (537 ± 340.322). For Busia, the highest number of cases were recorded in 2019 (1213.08 ± 841.561).

Table 2
Mean Malaria Cases in Tororo and Busia for the year 2012 to 2020

District		N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	F	p-value
Tororo	2012	864	491.12	308.659	10.501	0	2091	224.943	0.000
	2013	792	537.00	340.322	12.093	0	2174		
	2014	792	464.68	299.625	10.647	0	2667		
	2015	840	293.90	230.150	7.941	0	1483		
	2016	840	299.41	339.862	11.726	0	4822		
	2017	792	362.24	357.644	12.708	0	1935		
	2018	792	160.68	160.633	5.708	0	1420		
	2019	793	184.88	209.251	7.431	0	1964		
	2020	936	157.59	201.408	6.583	0	1400		
	Total	7441	325.80	311.284	3.609	0	4822		
Busia	2012	261	627.33	373.824	23.139	11	2606	47.306	0.000
	2013	348	636.03	584.455	31.330	0	4715		
	2014	348	584.88	477.522	25.598	19	3248		
	2015	360	695.16	626.131	33.000	0	4916		
	2016	432	903.97	703.131	33.829	0	3002		
	2017	432	1074.35	808.403	38.894	0	3742		
	2018	432	862.70	661.722	31.837	0	3979		
	2019	432	1213.08	841.561	40.490	0	3899		
	2020	420	1151.60	754.365	36.809	0	3686		
	Total	3465	887.13	716.295	12.169	0	4916		

The average malaria cases for both Busia and Tororo varied between months ($p < 0.05$). For Tororo, the highest mean number of cases were recorded in June (460.89 ± 416.466). For Busia, the highest mean number of cases were recorded in May (1088.63 ± 763.353) as per Table 3.

Table 3
Monthly mean malaria cases in Tororo and Busia 2012 to 2020

District		N	Mean	Std. Deviation	Std. Error	Minimum	Maximum	F	p-value
Tororo	Jan	621	332.95	324.506	13.022	0	2306	30.838	0.000
	Feb	619	299.68	272.398	10.949	0	1580		
	Mar	620	281.92	250.781	10.072	0	1533		
	Apr	620	311.16	300.869	12.083	0	1726		
	May	620	390.86	352.348	14.151	0	1935		
	Jun	620	460.89	416.466	16.726	0	4822		
	July	620	424.61	368.539	14.801	0	2667		
	Aug	620	342.15	287.279	11.537	0	1692		
	Sept	620	253.73	243.808	9.792	0	1770		
	Oct	620	272.86	262.558	10.545	0	1636		
	Nov	621	292.11	283.382	11.372	0	2174		
	Dec	620	246.70	236.787	9.510	0	1762		
	Total	7441	325.80	311.284	3.609	0	4822		
Busia	Jan	296	854.74	689.304	40.065	0	3040	7.204	0.000
	Feb	267	832.15	654.318	40.044	0	3470		
	Mar	231	800.80	626.958	41.251	0	3322		
	Apr	296	876.31	726.736	42.241	0	4715		
	May	303	1088.63	763.353	43.853	0	3681		
	Jun	296	1065.13	887.842	51.605	0	3742		
	July	296	864.34	755.433	43.909	0	3748		
	Aug	296	966.79	814.612	47.348	0	3979		
	Sept	296	710.03	552.529	32.115	0	3412		
	Oct	296	825.84	646.398	37.571	0	4916		
	Nov	296	932.40	684.143	39.765	0	3275		
	Dec	296	799.30	619.318	35.997	0	3146		
	Total	3465	887.13	716.295	12.169	0	4916		

4.0 Discussion

4.1 Malaria patterns in Busia and Tororo Districts

The declined annual malaria cases and trend through the period 2012 to 2020 in Tororo compared to Busia as indicated in Table 2, Fig. 1&2 are generally attributed to the synergistic control strategies of LLINS and IRS (Kigozi et al., 2020) practiced in Tororo unlike the lonely LLINs used in Busia. There is increased maximum protection of individuals indoors both in and outside bed. More often people stay in houses doing many other things other than sleeping during which the IRS prevent from mosquito bites, then while asleep the LLINs protect them against the mosquito bites. Additionally, the use of IRS to supplement LLINs is known to rapidly reduce *Plasmodium* vectors and protect communities from infective bites (were et al;.2009) and might have protected all people who did not sleep under LLINs and gave additional protection to those who slept under treated nets (Oguttu et al., 2017). The distribution of IRS in Tororo was 90% in 2015, according to a report by the District Health Office (WHO,.2015). Similar studies by Mawejje *et al*., (2021) and Kleinschmidt et al., (2018) found out that, the combination of the two interventions achieved greater reduction of malaria vectors which resulted into significant reduction in *Plasmodium* transmission.The consistent spatial expansion of malaria patterns in Busia revealed by Fig. 1 demonstrates the ecological importance of water bodies in the transmission of malaria parasites. The southern part of the district is contagious with the Lake Victoria that provides constant breeding ground for *Anopheles* mosquitoes particularly *Anopheles funestus* is known to breed all year round and prefer permanent, stagnant water bodies Lake Victoria (Kabbale 2013, 2016). Given *Anopheles funestus* one among the constant effective and competent vectors, it plays a prominent role in the transmission of the most dangerous malaria parasite species *Plasmodium falciparum* explained in the growing burden of malaria cases in Busia (Ekoko et al., 2019).Tororo maps on the other hand, reveal a general temporal and spatial decline in malaria. There is no doubt the complementary vector control approaches combining LLINS and IRS are working synergistically to eliminate malarial parasite (West et al., 2014), hence the noted reduction. Similar studies attest to this phenomenon in other parts of Uganda and elsewhere. For example, Mawejje *et al*. (2021) noted malaria burden decline in children from 40% in 2009 to 19% in 2015 and further to 9% in 2019 in northern Uganda where both LLINs and IRS were concurrently used. Abongo *et al*. (2020) recorded a decline of 50% in malaria prevalence between 2000 and 2015 in Migori County in Kenya, where LLINs were supplemented with IRS.

Combining LLINs with IRS based on bendiocarb for three rounds in Tororo district in 2015 shown in Fig. 2 was followed by steep decline of malaria cases, as well as when IRS chemical was changed to Actellic (pirimiphos-methyl) in 2017 (West et al., 2014; Oguttu et al., 2017). This means that for the first-time multiple non-pyrethroid IRS products are available with different modes of action that achieve broadly equivalent reductions in malaria burden across Africa (Haji et al., 2015). Bendiocarb is known to have a shorter residual life on sprayed surfaces of three months when compared to Actellic® 300CS (Abong'o et al., 2020), which has a longer residual life efficiency up to six to ten months (Haji et al., 2015). Similar studies corroborate to this observation in Northern Uganda whereby Raouf *et al*. (2017) found rapid malaria reduction when IRS and LLINs were being utilized. These findings are also consistent with Fullman *et al*;.(2013) which described LLIN and IRS combination as synergistic malaria control strategies.

The study further revealed a distinct monthly distribution of average malaria cases of all years across the two regions from May-November in respect to bimodal rainfall pattern, matching to the considered perennial transmission setting of Uganda (Katureebe et al., 2016; Oguttu et al., 2017).

5.0 Conclusion

The introduction of three rounds of IRS based on bendiocarb in Tororo district in 2015 was followed by steep decline of malaria cases, as well as when IRS chemical was changed to Actellic (pirimiphos-methyl) in 2017. It is therefore imperative that their use in mosaics is implemented to maintain the efficacy of both insecticides. However, there is an urgent need to better assess product efficacy and mode of action to help decision makers choose effective and relevant tools for mosquito control for cost efficiency purposes.

Annual malaria cases were more in Busia than Tororo, with a general trend increase being witnessed in Busia and a drastic trend decline in Tororo district. This is attributed to the complementary efficiency of long-lasting insecticidal nets and indoor residual spraying practiced in Tororo. Additionally, the use of IRS to supplement LLINs is known to rapidly reduce *Plasmodium* vectors and protect communities from infective bites. Therefore, routine surveillance should be undertaken for planning and timely action towards control.

The Busia maps revealed a generally growing number and spread of malaria with time towards the southern part closer to Lake Victoria, *Anopheles* species are known to breed all year in presence of stagnant water which favours their proliferation and reproduction of parasite within them. Whilst Tororo maps, revealed a generally declining malaria cases in time and space attributed to intensified use of LLINs and IRS put into practice in the region. These findings provide further evidence of identifiable candidate area for targeted control interventions among the high-risk district. Although, there's need to develop an approach assessing possible impacts of vector control approaches practiced in the two districts. In conclusion a progressive reduction in cases and spatial distribution of malaria through the last nine years in Tororo District is consistent with the utilisation of the complementary interventions of LLINs and IRS. Omission of similar practice in Busia district explains the contradictory increase in cases and distribution of the disease, hence the relevance of combining the two control strategies for optimal results.

Declarations

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Competing Interests

The Authors declares that they have no competing interests in terms of financial or non-financial status.

Data Availability

The routine malaria surveillance data reported passively through public and high volume private health facilities for the nine year period (2012-2020) were entered and manipulated and subjected to a Makesens 1.0 Toolkit in Ms. Excel.

Authors Contribution Statement

F.C designed the study, collected data for research, analysed the data and manuscript writing

C.O.O assisted with the design of the study

J.K and A.E supported in designing the study, data analysis and manuscript writing

F.K supported with the manuscript write up

All the authors reviewed the article

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Figures

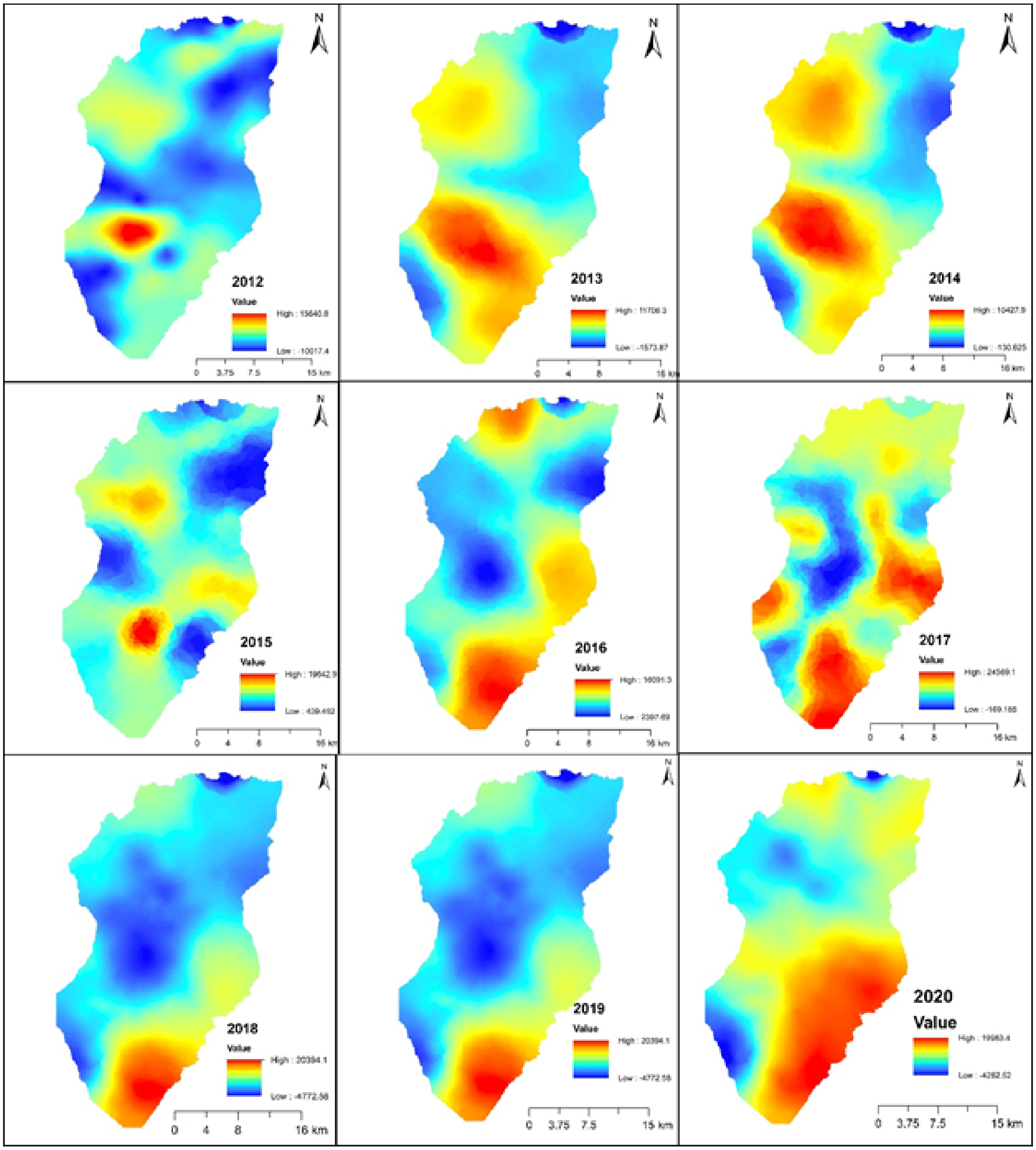

Figure 1

Spatial Variation of Malaria Cases in Busia district from 2012 to 2020

The Busia maps revealed a generally growing number and spread of malaria with time whilst the Tororo maps, revealed a generally declining malaria cases in time and space as illustrated in Figure 1&2.

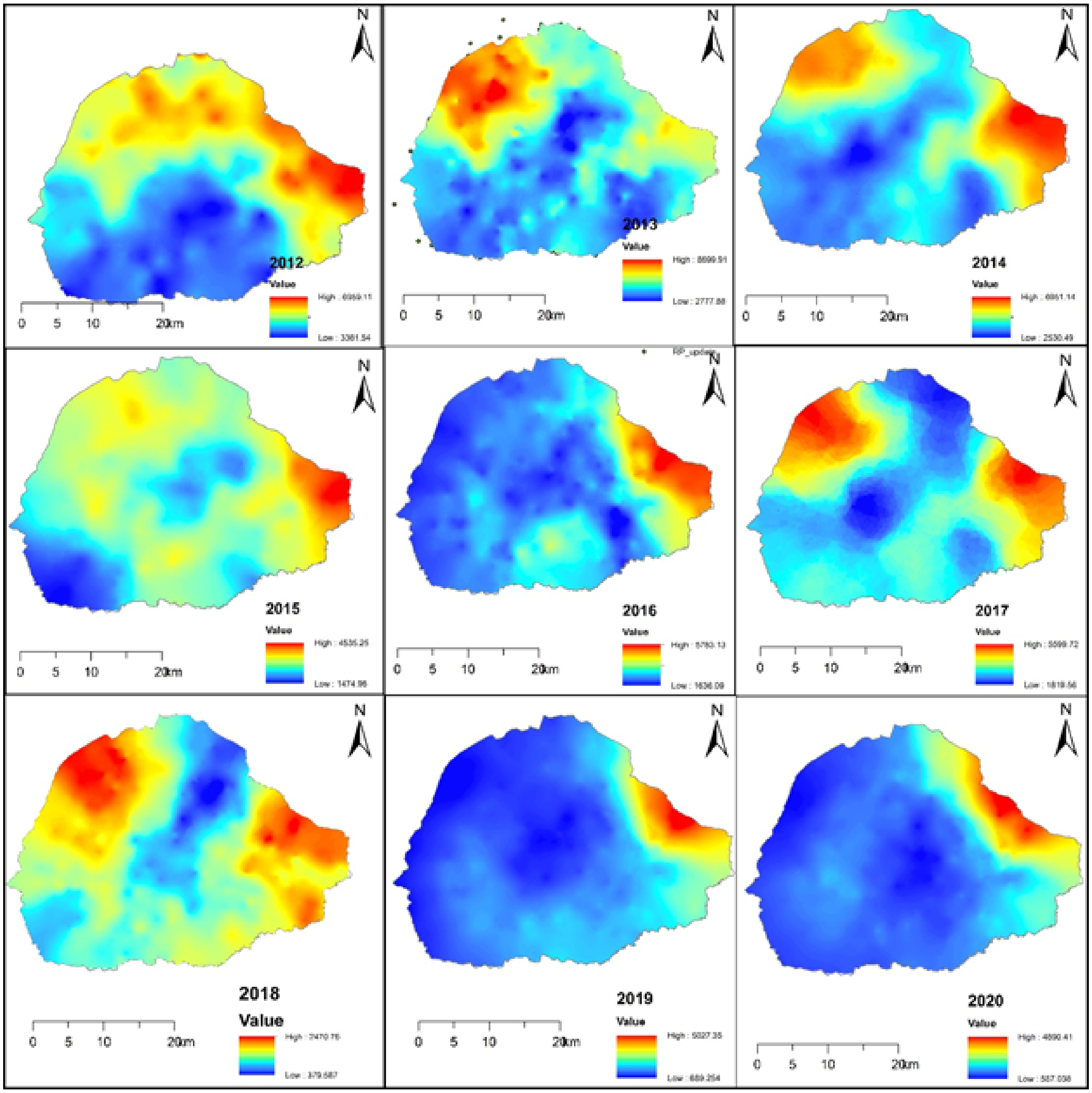

Figure 2

Spatial Variation of Malaria Cases in Tororo district from 2012 to 2020

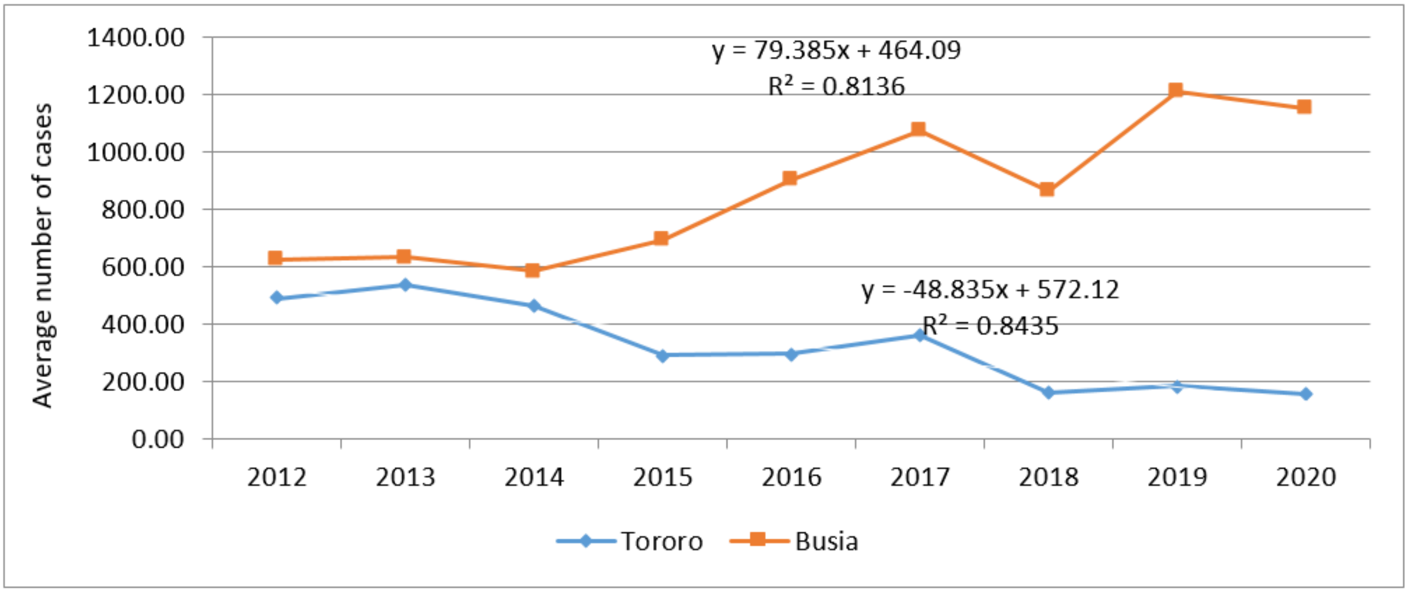

Figure 3

Combined Annual Malaria Cases Trend for a Nine-Year Period in Busia and Tororo