

Research Article

Risk Factors Associated With Malaria Mortality in Tshwane District, South Africa: A Retrospective Cohort Study, 2011-2014

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Abstract

Background: Tshwane District in Gauteng Province identifies malaria cases from endemic provinces and neighbouring countries as well as Odyssean malaria cases.

Objectives: To assess changes in malaria morbidity and mortality and to determine risk factors associated with malaria mortality in Tshwane District during 2011-2014.

Methods: A retrospective cohort study was conducted using malaria surveillance data collected by the Communicable Disease Control Directorate in Tshwane district over a period of four years. Only laboratory confirmed cases were enrolled in the study. Secondary death audits were reviewed. Logistic regression determined risk factors associated with malaria mortality.

Results: During 2011-2014, 964 cases were identified. Of these, the median age was 28 years (range: 4 months to 79 years), 71.7% (n=691) were males. The majority of cases, 96.6% (n=931), had travelled to malaria endemic areas within South Africa and neighbouring countries. Of those who travelled to endemic malaria provinces in South Africa, 62.5% (40/64) went to Limpopo. Malaria cases decreased from 333 in 2011 to 229 in 2014. There were 20 deaths (2.1%) and 19 (2.0%) Odyssean malaria cases. Age, gender and malaria season were not associated with mortality. History of travel to a malaria endemic area was a protective factor for mortality (aOR 0.2, 95%CI: 0.36 to 0.78, p=0.021).

Conclusion: In this non-endemic district, a number of malaria cases have been reported. Public awareness regarding uptake of antimalarial prophylaxis before and during travel to endemic areas could lead to a reduction in mortality and morbidity in South Africa.

Keywords: Malaria; Tshwane district; Mortality; Risk factors; Endemic; Surveillance

1. Introduction

Malaria is a life threatening parasitic disease which is transmitted to humans by the bite of an infected female anopheles mosquito [1]. It is one of the leading causes of morbidity and mortality in endemic countries [2]. There has been a global decline of malaria incidence by 17% and malaria mortality by 26% since 2000 [3]. There was an estimated 214 million cases of malaria and 438 000 deaths in 2015 and a global decrease of 37% in malaria incidence and 60% in malaria deaths between 2000 and 2015 [1]. There are potential risk factors which may have a significant impact on malaria transmission such as the level of mosquito control measures, population immunity, social and economic status (housing conditions), and environmental factors including rainfall and temperatures. Resistance to antimalarial drugs has been attributed to an increase in mortality [4]. In Africa, malaria is mostly caused by *Plasmodium falciparum* (*P. falciparum*) as opposed to *P. ovale*, *P. vivax*, *P. malariae*, and *P. knowlesi* [3, 5]. 90% of malaria infections in South Africa are caused by *P. falciparum*, which is more virulent [6, 7]. Previous studies have shown that people who are at high risk of dying from malaria are pregnant women whose immunity is decreased by pregnancy, children <5 years of age with immature immune systems, immunocompromised people and travellers from non-endemic areas into malaria endemic areas [8]. Malaria is under surveillance and is a notifiable condition in South Africa [9]. The number of reported malaria cases and deaths is used to guide public health interventions to inform policy decision making and to track progress of malaria control programmes. There are three malaria endemic provinces: Limpopo, KwaZulu-Natal and Mpumalanga [9].

Due to increased travel, Tshwane District in Gauteng Province is identifying malaria cases from endemic neighbouring countries and provinces within South Africa [10]. Odyssean malaria refers to a case of malaria that does not have a travel history to malaria endemic areas and there is no mechanical transmission, either by blood transfusion, needle stick injury or injection. Odyssean malaria can be caused by translocated mosquitoes from endemic provinces or countries and is usually called taxi malaria, baggage malaria or airport malaria [10]. Diagnosis of these cases of malaria is often delayed or missed, resulting in severe complications and death because malaria is not endemic or expected in Gauteng province. The relevance of being able to identify cases of malaria in Tshwane District using surveillance data is that epidemiological investigations will be done for Odyssean cases to identify mosquito breeding sites. As South Africa aims to eliminate malaria in 2018, it is important to understand the factors associated with malaria mortality, so that mosquito control programs can be strengthened [11]. The aim of the study was to assess changes in occurrence of malaria morbidity and mortality over a period of four years, 2011-2014 and to determine the risk factors associated with malaria mortality in Tshwane district.

2. Methods

2.1 Study design

Ethical approval was obtained from University of Pretoria Ethics Committee. Permission to use the surveillance data was obtained from Tshwane research committee and Communicable Diseases Control (CDC) programme manager. A retrospective cohort study was conducted using malaria surveillance data collected by the Communicable Disease Control Directorate in Tshwane district during 2011-2014. The surveillance data was received from both private and public health facilities. The reporting sites included eight public hospitals, 35 private hospitals, 22 municipal clinics and 49 public clinics. Only laboratory confirmed malaria cases were enrolled in the study. For each malaria death in Tshwane district, an audit is conducted using a special tool to assess risk factors associated with malaria mortality, therefore, secondary death audits were reviewed. The secondary death audit data were used to describe the risk factors associated with malaria mortality in Tshwane district.

2.2 Study site and population

The study was conducted in Tshwane district, which is one of five districts in Gauteng province. Tshwane is the second largest municipality in Gauteng with a population of approximately 2.9 million [12]. The study included individuals who resided in urban and rural settlements within the seven sub-districts of Tshwane, both males and females and all age groups who consulted in health facilities and were laboratory confirmed malaria cases.

2.3 Data management

Data was cleaned and validated including identification of duplicates using Microsoft Excel 2013. Information collected during research was kept confidential. The names of participants involved in the study were not mentioned during report writing. Data was stored on a password protected computer.

2.4 Data analysis

Time series plots were constructed to analyze changes in malaria cases over the period of four years (2011-2014). Univariate and multivariate logistic regression analysis was used to determine risk factors for malaria mortality. The potential risk factors including age, gender, travel history and malaria season were considered. Risk factors with p-values less than 0.2 in the univariate logistic regression models were introduced into the multivariate model. Statistically non-significant risk factors were removed using the manual forward stepwise procedure, starting with those that were highly significant. In all statistical tests, a p value less than 0.05 was considered to be statistically significant. Data was analysed using STATA version 13 and Microsoft Excel 2013.

3. Results

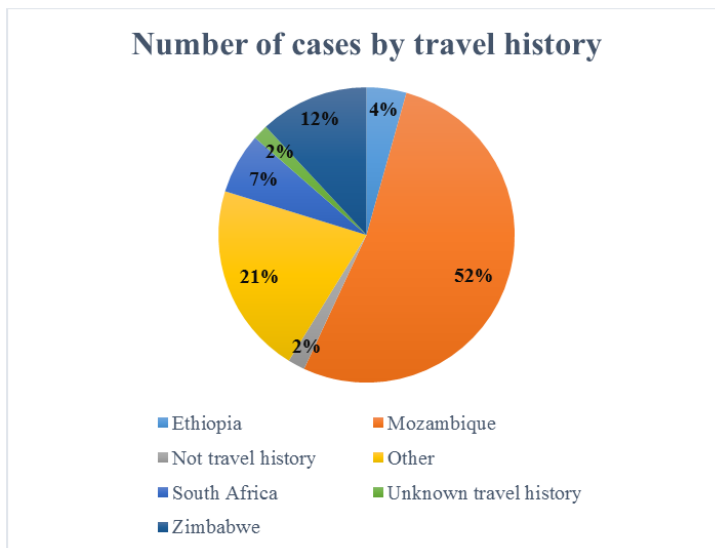
Between 2011 and 2014, a total of 964 cases were diagnosed with malaria and were notified by public and private hospitals to the Tshwane district Communicable Disease Control (CDC) Directorate. Of these, 19 cases, including one death were Odyssean malaria cases. The median age was 28 years (range: 4 months to 79 years). The age group 25-34 years was more affected compared to other age groups. Males were more affected than females in all the years of study (2011-2014) (Table 1). Almost all cases (99.8%) were caused by *P. falciparum*. The majority of cases,

96.6% (n=931) had travelled to malaria endemic areas within South Africa and neighbouring countries predominantly Mozambique (52.6%) (Figure 1). Of all cases, 19 did not have travel history. None of the cases had taken chemoprophylaxis before they travelled as indicated on the notification forms received by the CDC directorate.

Age (years)	2011	2012	2013	2014	N	%
0-5	21	32	30	32	115	12%
6-14	25	12	14	14	65	7%
15-24	67	23	31	35	156	16%
25-34	117	58	60	58	293	30%
35-44	52	41	33	32	158	16%
45-54	30	18	19	29	96	10%
55-64	8	8	6	15	37	4%
65+	8	0	3	9	20	2%
Unknown	5	4	10	5	24	2%
Gender						
Males	253	139	135	164	691	72%
Female	80	57	71	65	273	28%
Travel history						
To endemic areas and provinces	320	186	199	225	930	96.47%
No travel history	9	7	3	1	20	2.07%
Unknown travel history	4	3	4	3	14	1.45%
Total	333	196	206	229	964	100%

Table 1: Demographic characteristics of reported cases, Tshwane District: 2011-2014.

There were 20 deaths (2.1%) out of 964 cases. Of these, 17 secondary death audits were reviewed, 94.1% (n=16) of deaths had travelled to malaria endemic countries and provinces. Over a third of the deceased patients had comorbidities, including HIV infection (n=2), pre-eclampsia (n=1), hypertension (n=2), diabetes mellitus (n=1), asthma (n=1) and 5.9% (n=1) was pregnant. They all died in a health facility. The majority of the deceased patients (n=11) were diagnosed within a day, (range: 10 minutes to 4 days). Of all deaths, 35.3% (n=6) had co-morbidities and 4.8% (n=1) were pregnant. The length of stay in the hospital before death varied from one to 25 days (median: 4 days). The majority of the cases 47.1% (8/17) presented at a facility between three days and one week after onset of symptoms. The total number of malaria cases decreased from 333 in 2011, to 196 in 2012 and then increase slightly to 206 in 2013 to 229 in 2014 (Figure 2). A total of 19 Odyssean malaria cases have been reported. The majority (90.0%, n=18) of cases that died had travelled to malaria endemic areas. There was a decrease in the total number of deaths during the study period with the highest case fatality rate in 2012 (Figure 2). The number of malaria cases peaked in January each year for the period of study (2011-2014) (Figure 3).



*Other refers to countries with fewer cases

Figure 1: Number of cases by travel history, Tshwane District: 2011-2014 (n=964).

In univariate analysis, cases aged 45-64 years (OR 2.9, 95%CI: 1.10 to 8.09, p=0.046) were more likely to die from malaria relative to cases of younger age groups of 0-5 years (Table 2). Gender (OR 0.6, 95%CI: 0.24 to 1.45, p=0.257) and malaria season (OR=0.7, 95% CI: 0.21 to 2.49, p=0.613) were not statistically significant (Table 2). Age, gender and malaria season were not statistically significant in multivariable analysis. History of travel to a malaria endemic area was found to be protective (OR 0.2, 95%CI: 0.36 to 0.78, p=0.02) (Table 2).

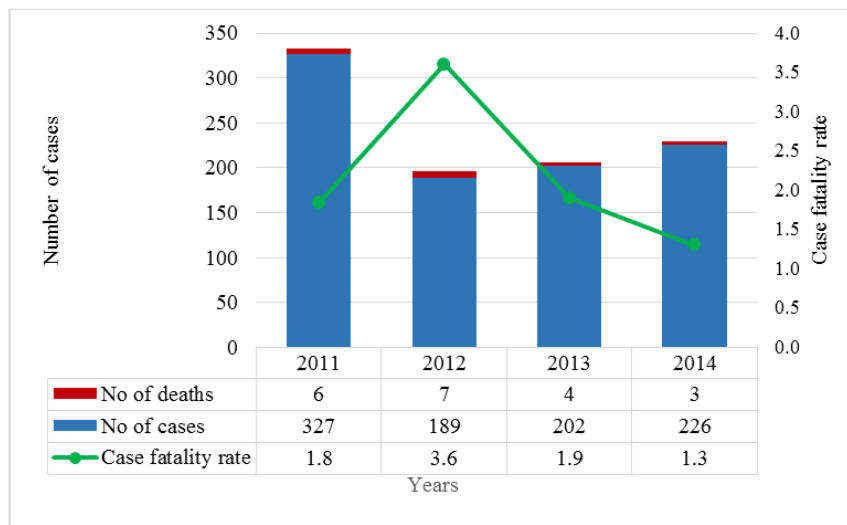


Figure 2: Changes in the occurrence of malaria cases and deaths reported in Tshwane District by year (2011-2014).

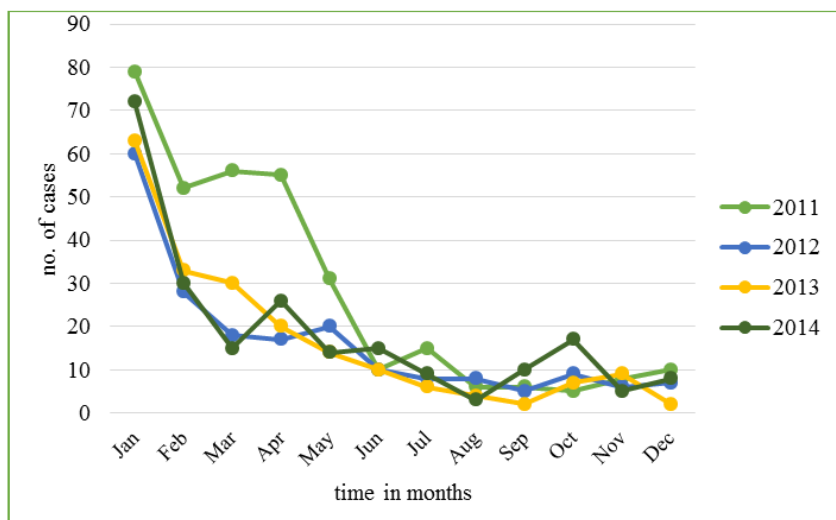


Figure 3: Trends in malaria cases reported in the Tshwane District month by month (2011-2014).

Variables	Univariate analysis				Multivariable analysis			
	Odds ratio	95% Confidence interval		p-value	Odds ratio	95% Confidence interval		p-value
		Lower	Upper			Lower	Upper	
Gender: Males	(reference)							
Females	0.6	0.24	1.45	0.257	0.9	0.32	2.73	0.898
Age groups 0-5	(reference)							
6-24	0.9	0.35	2.78	0.973	2.0	0.38	10.66	0.407
25-44	0.7	0.22	2.03	0.454	1.3	0.21	7.60	0.809
45-64	2.9	1.10	8.09	0.046	4.9	0.96	24.97	0.055
65+	2.7	0.34	21.19	0.411	6.3	0.54	73.38	0.143
Travel history: No	(reference)							
Yes	0.2	0.04	0.78	0.036	0.1	0.03	0.75	0.021
Malaria season: Low	(reference)							
High	0.7	0.21	2.49	0.207	0.9	0.17	3.64	0.766

Table 2: Logistic regression predicting the likelihood of malaria mortality in Tshwane District (2011-2014).

4. Discussion

The surveillance data indicates that malaria incidence has been decreasing from 2011 to 2014 with a decrease in the total number of deaths. Age was found to be a risk factor for mortality. Mortality was higher in older people (45-65 years). Most deaths were not in the <5 age group. This is in contrast with other studies where majority of deaths occur in children under five years of age [13]. The incidence of malaria was high in the age group 24-34 as compared to other age groups. This supports findings of other studies [11]. This is an economically productive age

group. They are more likely to migrate to Tshwane district in Gauteng province for employment opportunities. Majority of cases occurred in rainy season with a highest peak in January. This may be due to people who are travelling during December holidays to locations that are malaria endemic resulting in an increased number of cases when they return from those areas. There was an increased number of cases in 2014 between August and November which may be due to high temperatures as a result of global warming. Previous studies have shown that there has been a steady decline in the number of cases in South Africa which resulted in decreased morbidity and mortality [9, 14]. Males were more affected than females. This is similar to previous studies conducted in Mpumalanga and Limpopo provinces, South Africa and United Kingdom [8, 15, 16]. All the patients did not take chemoprophylaxis as indicated on the notification forms. However, the reasons for low prophylaxis uptake were not investigated in this study. The findings of a study conducted in the United Kingdom found that low prophylaxis uptake was associated with cost and fear of side effects [17]. Research shows that pregnancy and co-morbidities may lead to severe malaria and are significant causes of malaria mortality [18-20]. However, in this study, statistical significance could not be established due to insufficient risk factor data among those who did not die. These results are similar to the results of the study conducted in Tamale hospital, Northern Ghana [21].

Travel history to a malaria endemic area was found to be protective. The study indicated that those who did not travel to malaria endemic provinces were more at risk of dying as compared to those who travelled. The reason for this might be that malaria is unlikely to be suspected in those without a travel history and diagnosis might be missed. The study showed that the odds of dying from malaria increases with age. This is similar to the results of the study conducted in United Kingdom in 2012 [22]. This study had some limitations. Our study focused on cases which were reported to the Communicable Disease Control office in Tshwane District. Those who were not reported would have caused underrepresentation of the total number of cases in Tshwane District. The results are not generalizable because the surveillance system looked at was only that from Tshwane. A risk factor audit was done only for the patients who died, hence there was insufficient risk factor data for those patients who did not die. The outcome of this study was malaria mortality and the sample size of the deceased was small hence the statistical significance of other variables could not be established. The other limitation of this study is that we were not able to analyse some potential risk factors such as occupation, pregnancy, chemoprophylaxis during travel, time interval between illness and presentation at the health facility, comorbidity, length of stay in hospital, doctors training about malaria, availability of malaria guidelines due to insufficient risk factor information for those patients who did not die.

5. Conclusion

In Tshwane district, malaria cases were reported throughout the year during the study period with seasonal peaks. Majority of cases were imported. Therefore, public awareness regarding uptake of antimalarial prophylaxis before and during travel to endemic areas could lead to a reduction in mortality and morbidity in South Africa. There is a need to investigate any case of fever for malaria infection to avoid complications and to reduce morbidity and mortality. Malaria surveillance should be strengthened in non-endemic provinces for early detection of malaria cases, including Odyssean cases to reduce morbidity and mortality associated with malaria.

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