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Epidemiological analysis of 133 malaria cases in Shanxian county, Shandong Province, China

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ABSTRACT

Objective: To conduct an analysis of the epidemiological changes in malaria that have occurred in Shanxian county from 2002 to 2016.

Methods: A retrospective study was conducted and data were collected from web-based reporting system to explore the epidemiological characteristics in Shanxian county from 2002 to 2016. All individual case information was obtained from village malaria servicers organized by the local Shandong Institute of Parasitic Diseases.

Results: A total of 133 cases were identified as malaria in Shanxian county during this period, including 124 indigenous cases (93.2%) and 9 imported cases (6.8%). The 124 indigenous malaria cases were infected with *Plasmodium vivax (P. vivax)*, whereas 7 of the 9 confirmed imported cases were infected with *Plasmodium falciparum (P. falciparum)*, 1 was infected with *Plasmodium ovale* (*P. ovale*) and 1 patient was infected with *P. falciparum* mixed with *P. vivax*. The total number of malaria cases included 86 males (64.7%) and 47 females (35.3%). Age of the patients ranged from 1 to 83 years, although most (64.7%) infections occurred in the 21-to 60-year-old age group. Remarkably, 117 of the total malaria cases (98.0%) were reported from 2006 to 2011. The epidemic season was from June to October, with the peak occurring yearly from July to September. The most common occupation of the infected patients was farmer. In total, 58.1% of the cases occurred in 3 townships, namely, Fugang, Huanggang and Caozhuang.

Conclusions: In Shanxian county, the local malaria incidence experienced an emerge-peak-control-eliminate status. However, due to the numbers of migrant labourers returning from Africa, imported cases were continuous and presented an increasing annual trend, which became a non-negligible and a significant impediment for malaria elimination. Therefore, the need to eliminate instances of malaria reintroduction to receptive malaria-free areas should drive strategies to align with the epidemiological changes.

1. Introduction

Malaria is one of the most important parasitic diseases and is widely endemic in tropical, subtropical, and temperate regions [1]. Updated estimates have indicated that 212 million cases occurred globally in 2015, leading to 429 000 deaths, most of which were in children under 5 years of age in Africa [2]. Although great success has been achieved since the launch of the national malaria control programme in 1955, malaria remains a serious public health problem in China [3], where *Plasmodium vivax* and *Plasmodium falciparum* have historically been present at high frequencies [4]. Shandong Province underwent two large malaria outbreaks during the

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1960s and 1970s with more than 6 million and 4 million annual cases, respectively [5].

Shanxian county lies in the southwest of Shandong Province at the border of Jiangsu, Henan and Anhui provinces between 115°48′–116°24′ east longitude and 34°34′–34°56′ north latitude. The sixth census in 2010 showed that Shanxian county had a population of 1.06 million people. The total area is 1 650 km^2 and belongs to the Yellow River alluvial plain of the north temperate zone. According to the local meteorological department website, the annual mean temperature and rainfall of this country are 13.9 °C and 737.1 mm, respectively. In the 1970s, Shanxian County was considered a high incidence area of *P. vivax* malaria via its single vector [*Anopheles sinensis (A. sinensis)*]. This county was subsequently incorporated into the south Shandong malaria integrated prevention and control area and contributed to a powerful epidemic rebound through an established surveillance system, improved environment and vector control. Since 1988, the area has achieved the standard of almost completely eliminating malaria, and no malaria cases have been reported. Few cases emerged after 2002. However, the morbidity has increased substantially each year since 2005. The numbers of cases detected in the continuous 4 years between 2007 and 2010 were greater than 20, and the proportion of indigenous cases that accounted for all cases in Shandong province increased yearly during this period. Therefore, the malaria prevention and control efforts in Shanxian county are vital to determining whether Shandong province can achieve the goal of eliminating malaria in 2018. The objective of this study was to characterize the malaria situation and development trends in Shanxian county from 2002 to 2016, which was a very important transition period from the control to elimination phases in Shanxian county, and to provide scientific insights for the improvement of regional control strategies and acceleration of the elimination goal in Shandong Province.

2. Material and methods

2.1. Study setting

Shanxian county is located in a warm temperate zone with a semi-humid continental monsoon climate. Rainfall is concentrated mostly in the summer when the southeast monsoons carry rainwater into the county. Many rivers present in Shanxian county belong to the ancient Yellow River canal and include the Fuxin River and Dongyu River, which are drainage clearance rivers. Rural economics is drought crop oriented, and planting fast-growing poplar is prevalent as a means to increase incomes in the villages and their surroundings.

2.2. Data collection

A retrospective study was conducted to explore the changing characteristics of endemic malaria in Shanxian county from 2002 to 2016. Daily disease surveillance data were obtained from the web-based reporting system (WBRS). The parameters included the type of disease, diagnostic approach and reporting institution. Other parameters were collected for individual cases by village malaria servicers (VMS) who were organized by the Shandong Institute of Parasitic Diseases, including age, gender, occupation, residential address, and recent travel/time spent outdoors history.

2.3. Diagnostic approach

Clinically diagnosed cases were defined as a patient with malaria-like symptoms but no parasites detected in the blood examination. Laboratory-confirmed cases were those defined by the use of any laboratory test, including polymerase chain reaction (PCR), rapid diagnostic tests (RDTs), and microscopy examination [6,7].

2.4. Case definition

Imported malaria must meet all of the following criteria: (1) the patient was given a malaria diagnosis; (2) the patient had a travel history to malaria-endemic areas outside of China during malaria transmission season; and (3) the onset time was less than 1 month after returning to China during the local transmission season. This definition is based on the reasonable latent period for all Plasmodium species reported in China [6]. Indigenous malaria was defined as any case infected within the province where the case was diagnosed [8].

2.5. Statistical analysis

A descriptive analysis was performed using the Microsoft Excel and SAS software (SAS Institute Inc., Version 9.2, Cary, NC, USA).

2.6. Ethical approval

Ethical approval for this study was obtained from the Ethics Committee of the China CDC. Permission was also obtained from the Municipal Government, the Municipal Health Bureau and the CDC in Heze city.

3. Results

3.1. Indigenous and imported case surveillance

From 2002 to 2016, Shanxian county had 133 malaria cases overall, including 124 indigenous cases and 9 imported cases. Most of the indigenous malaria cases occurred during the period from 2006 to 2011 (117 cases accounting for 88.0% of the total cases). Although no malaria cases were found in 2003, indigenous malaria cases began to increase gradually after a one-year silent period until the peak was reached (2006–2011). In 2012, no malaria cases were reported (neither local nor non-local cases). The year 2012 seemed to be a turning point for local and imported cases, because after this time point, no indigenous cases occurred. However, imported cases began to rise. Although one imported case per year was reported in 2011, 2013, 2014 and 2016, 5 cases were reported in 2015 (Figure 1).

3.2. Malaria case types

From 2002 to 2016, 124 *P. vivax* malaria cases were reported, which accounted for 93% of the total cases. Additionally, 7 *P. falciparum* malaria cases accounted for 5% of the total cases, and 1 *Plasmodium ovale* (*P. ovale*) malaria and 1 mixed malaria case both accounted for 1% of the total cases (Table 1). The mixed malaria case was infected with *P. vivax* and *P. falciparum*. Among the total cases, 26 were confirmed by a clinical diagnosis, and 107 were confirmed by a laboratory diagnosis (Table 1).

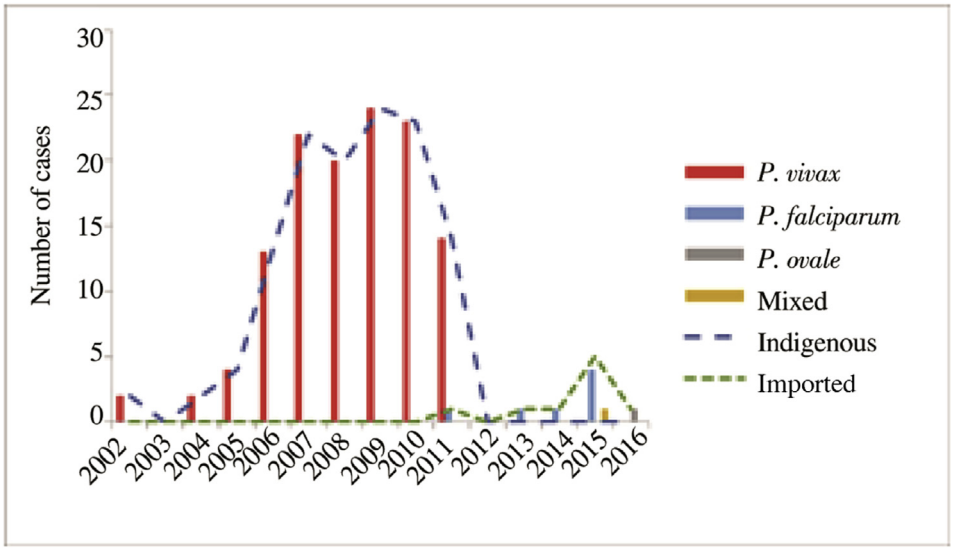

Figure 1. Malaria cases occurred during the period in Shanxian county, Shandong province from 2002–2016.

Table 1
Malaria case classification for Shanxian County from 2002 to 2016 by year.

Year	Vivax malaria	Falciparum malaria	Ovale malaria	Mixed malaria	Clinical diagnosis	Laboratory diagnosis	Total
2002	2	0	0	0	0	2	2
2003	0	0	0	0	0	0	0
2004	2	0	0	0	0	2	2
2005	4	0	0	0	3	1	4
2006	13	0	0	0	2	11	13
2007	22	0	0	0	7	15	22
2008	20	0	0	0	1	19	20
2009	24	0	0	0	7	17	24
2010	23	0	0	0	6	17	23
2011	14	1	0	0	0	15	15
2012	0	0	0	0	0	0	0
2013	0	1	0	0	0	1	1
2014	0	1	0	0	0	1	1
2015	0	4	0	1	0	5	5
2016	0	0	1	0	0	1	1
Total	124	7	1	1	26	107	133

Additionally, the major *P. vivax* malaria cases were centred around the period from 2006 to 2011 when 116 cases occurred, accounting for 93.5% of all *P. vivax* malaria cases (Table 1). Before October of 2011, all malaria cases were *P. vivax* malaria and were indigenous cases. However, since October of 2011, *P. falciparum* malaria, *P. ovale* malaria, and mixed malaria have begun to emerge, and imported malaria cases have appeared. In other words, the indigenous cases in Shanxian county from 2002 to 2011 were vivax malaria, whereas the imported cases that occurred from 2011 to 2016 consisted of falciparum malaria, ovale malaria and mixed malaria (Figure 2).

3.3. Demographic characteristics

From 2002 to 2016, there were 47 female and 86 male malaria patients, accounting for 35.3% and 64.7% of the total cases, respectively. There were more male patients than female patients in all age groups except the 51–60-year-old age group and the 81-year-old age group; the female and male patients were equal (14 cases) in the 51–60-year-old age group, whereas the 81-year-old age group only included 1 female patient. The 51–60-year-old age group had the most patients (28), followed by 31–40-year-old age group (24) and the 21–30 and 41–50-year-old age groups, which had the same number of cases (17). The 21–60-year-old age group (86) accounted for 64.7% of the total cases (Figure 2).

From 2002 to 2011, the cases included 105 farmers, who accounted for a large proportion (78.9%) of all *Plasmodium*

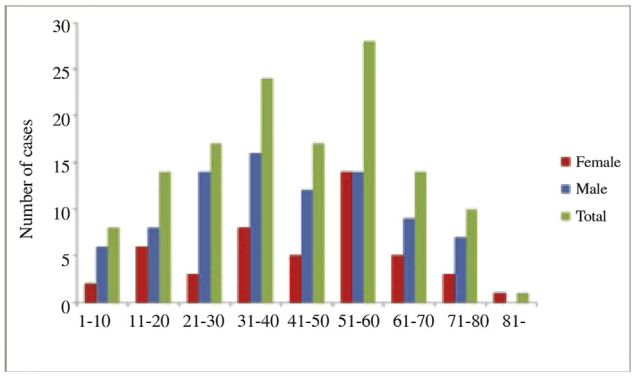

Figure 2. Female and male malaria cases occurred in Shanxian county, Shandong province from 2002–2016.

Table 2
Indigenous malaria cases of Shanxian County from 2002 to 2011 by year and month.

Month	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Total
Apr	0	0	0	0	0	0	2	0	0	1	3
May	0	0	0	0	0	1	1	0	0	3	5
Jun	1	0	0	1	1	2	2	2	0	6	15
Jul	0	0	0	1	0	4	2	11	1	2	21
Aug	0	0	0	1	5	8	3	10	9	2	38
Sep	1	0	0	1	6	5	4	0	8	0	25
Oct	0	0	2	0	1	1	6	1	4	0	16
Nov	0	0	0	0	0	1	0	0	1	0	2
Total	2	0	2	4	13	22	20	24	23	14	124

infections, 15 students, who accounted for a smaller proportion (11.3%) of the total patients, 5 labourers, who accounted for a relatively lower risk (3.8%) compared to the students, and 5 children, 1 infant and 2 others, who accounted for approximately 6.0% of the total cases.

3.4. The incidence time of the indigenous cases

Table 2 shows that the local malaria cases were mostly (115) reported between June and October from 2006 to 2011, which accounted for 92.7% of all local cases. Local cases first appeared in April, subsequently arose slowly in May, grew quickly in June, and reached a peak after entering summer in July, August, and September. August accounted for the maximum in terms of the numbers of malaria patients. After October, the malaria incidence declined gradually, and malaria patients were rare (2 cases) up to November (Table 2).

3.5. General features of the imported cases

Among the 9 overseas-acquired cases, 3 came from West African countries: Nigeria (2011, 1 *P. falciparum* case), Guinea (2013, 1 *P. falciparum* case), and Liberia (2015, 1 mixed infection case). Five cases derived from central African countries: Cameroon (2015, 4 *P. falciparum* cases) and the Congo (2016, 1 *P. falciparum* case), and 1 patient was infected with *P. falciparum* malaria in Sudan in 2014. The majority of the malaria cases (7) were *P. falciparum* malaria, which was the most prevalent malaria type in Sub-Saharan Africa [9].

4. Discussion

We report several findings based on analysis of data from the malaria cases in Shanxian county from to reported by the WBRS and VMS. First, local cases were concentrated on both sides of the major rivers, including Fugang, Huanggang and Caozhuang Townships. Second, most of the patients were farmers, and most of the imported cases from 2013 to 2016 occurred in 21–31-year-old adult men. Third, the local cases mainly occurred between June and October and peaked in August from 2006 to 2011. Fourth, males were more vulnerable than females to some extent, particularly in the 31–40-year-old age group. For females, the 51–60-year-old age group was at a high risk for plasmodium infection. Fifth, *P. vivax* malaria was dominant in the indigenous malaria cases, whereas falciparum malaria was the leader in the imported malaria cases. Moreover, according to the malaria elimination definition of the WHO (one area with 3 consecutive years with zero indigenous cases [2]), Shanxian county is considered an eliminated malaria region. However, although local malaria cases have disappeared, overseas-acquired malaria cases have increased successively. Obviously, malaria importation to eliminated regions has increasingly become a critical obstacle to achieving malaria elimination [10].

Shanxian county has many small river systems that are the best breeding sites for *A. Sinensis*. *A. sinensis* is the sole vector of *P. vivax* malaria in Shanxian county. *A. sinensis* is partially endophilic and tends to rest outdoors. The eggs of this mosquito develop on the water surface with floating impurities. Mark-release-recapture methods have certified that the flying distance of *A. sinensis* is usually 500–1000 m, although the mosquitoes can fly several kilometers under advantageous geographical, wind velocity, and other meteorological conditions [11]. Furthermore, malaria cases were distributed on both sides of the breeding sites, which demonstrated a positive correlation between the endemicity of malaria and the distance of the households of the cases to the nearest larval habitats [12,13]. The ancient canal of the Yellow River traverses the Shanxian southern border via Fugang and Huanggang Townships, whereas Caozhuang Township adjoins the Donggou River. These locations could explain why the indigenous malaria cases mainly occurred in these three townships.

The age, gender and occupation distributions implied that males who were 31–40 years old and females who were 51–60 years old were at a high risk for plasmodium infection. In Shanxian county, farmers account for a large proportion of the total population. Males 31–40 years old have a higher occupational risk because they often work in the mines, fields, or forests at the peak biting times and have more opportunities to expose their bodies to the environment than other groups. Females 51–60 years of age have a high frequency of walking after dinner, which unfortunately caters to the peak biting time of *A. sinensis*. Additionally, some farmers and engineers work abroad to obtain higher rewards, and a few of them work in malaria-endemic areas. Many migrants work in high-risk environments, such as natural forests, palm oil or rubber plantations, and fish farms [14]. Their mobile behaviour, together with a range of social, legal, economic, and geographic factors, limits their access to and contact with healthcare delivery systems [15].

The majority of the local cases occurred between June and October with a peak in August from 2006 to 2011. The seasonal activity of *A. sinensis* ranges from June to October in Shandong Province due to the suitable rainy and hot weather conditions [16]. Mosquito breeding largely depends on appropriate climatic conditions. If the rivers have not received integrated control at the time of year when the rainy season is approaching and the temperatures are increasing, the larvae multiply rapidly and

became a hazard to the local people. Environmental factors associated with seasonal changes and human outdoor activities have enormous impacts on malaria transmission.

Thus, to interrupt transmission, ecological factors facilitating *A. sinensis* breeding sites (*i.e.*, dams, irrigation canals, floods on shorelines, agricultural field puddles, wetlands, man-made pools, and rain pools) [17,18] or resting places for adult mosquitoes (i.e., surrounding vegetation and housing characteristics) should receive effective integrated management. Conditions that increase exposure to infectious mosquito bites (e.g., agriculture and livestock economic activities) [19] and human behavioural factors that limit the coverage and effectiveness of malaria control interventions (*e.g.*, outdoor sleeping habits, low utilization of long-lasting insecticidal nets, poor treatment seeking behaviours, and low treatment adherence) [20] should also be reduced significantly.

In the 1970s, Shanxian county had the highest incidence of vivax malaria in Shandong Province. From 2002 to 2011, the indigenous cases were both vivax malaria. Typically, plasmodium vivax occurs across the widest geographic area of the human malarias, extending well beyond the limits of *P. falciparum* into temperate climates [21]. The levels of *P. vivax* endemicity vary widely among the World Health Organization (WHO) regions. Outside of Africa, *P. vivax* is the dominant species, with a relatively high prevalence of infection in the Southeast Asian and Western Pacific regions [22]. Furthermore, *P. vivax* was the predominant species in countries in the pre-elimination and elimination phases, which had low total annual malaria incidence rates [23,24]. Therefore, vivax malaria was unsurprisingly dominant in the indigenous malaria cases in Shanxian county, whereas falciparum malaria was the leader in the imported malaria cases.

In 2012, the "1-3-7" strategy (which refers to reporting of malaria cases within 1 day, case confirmation and investigation within 3 days, and foci investigation and response to prevent further transmission within 7 days) was launched [25,26]. However, many residual potential reservoirs from migrants or working-abroad labourers were not detected in a timely manner and thus represented an important source of infection. Therefore, an intensified and targeted context-specific prospective training and education system should be built for the overseas population before they travel abroad. A detection system for asymptomatic infections after individuals return should also be enforced. Local assessments of the risk factors for malaria infection are necessary to reduce secondary case detection [27].

In conclusion, although eliminating countries reduce their malaria burdens, strategies that address the changing epidemiology—specifically, in adult men, from imported transmission and migration, and in hard-to-reach populations (travellers)—need to be developed, validated, and adopted. To achieve elimination in the at-risk malaria-free districts, a comprehensive monitoring and prevention system is needed, and an understanding of the risk factors for malaria infection is critical to inform strategic planning and implementation. Ultimately, a coordinated malaria control effort with endemic neighbours should be a component of all strategic plans implemented by malaria-eliminating countries.

Authors' contributions

QQS and PC conceived the study and drafted the manuscript. CQZ, XXG, LJL and HFW analysed the data. XDH, JXK and HWW gave good suggestions on improving the quality of the tables and figures. MQG initiated the study and made major contributions to drafting the manuscript. All authors contributed to the writing of the manuscript and approved the submitted version of the manuscript. All authors read and approved the final manuscript.

Conflict of interest statement

The authors declare that they have no competing interests.

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