Vital Surveillances

Cooperative Sentinel Surveillance of Malaria in Laiza and Nearby Areas of Myanmar and Importation Threat Monitoring — China, 2019–2023

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ABSTRACT

Introduction: Laiza and nearby areas (LNA) in Myanmar are identified as the primary malaria hotspots in the bordering regions of Yunnan Province, China.

Methods: Six sentinel surveillance sites were established at the China-Myanmar border in LNA to monitor malaria. Data from 2019 was used as a baseline to analyze malaria incidence and trends in LNA and Myanmar, as well as the importation of malaria cases into China from 2019 to 2023.

Results: *Plasmodium vivax* was the predominant species, representing 99.95% (14,060/14,066) of confirmed malaria cases in LNA. A total of 8,356 malaria cases were identified in 2023, with an annual parasite incidence (API) of 19.78 per 100 person-years. Compared to 2019, the incidence rate ratio was 21.47 (95% confidence interval: 18.84, 24.48), indicating that the API in 2023 was 21.47 times higher than that in 2019. In Yunnan, out of 1,016 reported cases, 545 imported cases (53.64%) originated from LNA and spread to 18 (13.95%) out of 129 counties. Ten provinces in China, including Yunnan, reported imported malaria cases from LNA in Myanmar.

Conclusions: The increase in population, particularly among internally displaced persons, along with inadequate healthcare services, has led to a notable resurgence of malaria in LNA. This resurgence poses a risk to preventing the re-emergence of malaria transmission in China. There is an urgent need for novel collaborative policies, as well as financial and technical assistance, to enhance malaria control efforts in LNA, Myanmar.

Malaria remains a significant global public health issue, with control efforts stagnating since 2015 and worsening during the coronavirus disease 2019 (COVID-19) pandemic. In 2022, an estimated 249 million malaria cases resulted in 608,000 deaths globally across 85 countries where malaria is endemic (*1*). China, having reported no indigenous malaria cases since April 2016, was officially declared malaria-free by the World Health Organization (WHO) on June 30, 2021. The unique ecological and epidemiological characteristics of malaria make the Yunnan border area highly susceptible to malaria transmission (*2*–*3*). Currently, the region including Laiza and nearby areas (LNA) in Kachin Special Region II (KR2) of Myanmar represents the most significant malaria hot spot along the China-Myanmar border (*4*–*5*). In the LNA, malaria incidence has escalated in recent years. Approximately 90% of malaria cases imported into Yunnan originate from Myanmar, predominantly from the LNA (*2*–*4*), with some cases spreading from LNA to other Chinese provinces. This study examines malaria trends in the LNA from 2019 to 2023 and the subsequent importation of cases into China.

METHODS

Study Site, LNA

The study site is located in LNA, within Kachin State, Myanmar, bordering Yunnan and Xizang, China. This region is known for its high malaria endemicity attributed to conducive ecological and vector conditions (*4*–*5*). The area is under the authority of the Kachin Independence Organization (KIO) and the Kachin Independence Army (KIA), making access to KR2 difficult due to political and military tensions with the Myanmar Government Defense Forces. Significant conflicts in 2011 resulted in a surge of internally displaced persons (IDPs) fleeing warfare to LNA, posing challenges for international health aid delivery into the region.

Laiza City, located on the China-Myanmar border, serves as the headquarters for KR2. The LNA in this study refers to areas on the Myanmar border that neighbor Yingjiang County in Dehong Prefecture, Yunnan Province, China. The region's hot climate, sufficient precipitation, and dense forests create an ideal habitat for mosquitoes, leading to malaria transmission. *Anopheles dirus* and *Anopheles minimus* are the primary vectors in a diverse vector population (*6*). Malaria transmission is continuous throughout the year, with all human malaria parasite species present in the area (*7*). Control measures have resulted in *Plasmodium vivax* (*P. vivax)* becoming the predominant malaria parasite over time (*7*–*9*).

Data Sources and Collection

The study received an approval from the Department of Health of KIO, Myanmar, and Yunnan Institute of Parasitic Diseases, China. In Myanmar, data were gathered from six malaria surveillance sentinel sites along the border. These sites included all health facilities equipped with malaria diagnosis capabilities through microscopy and rapid diagnostic tests (RDT) in LNA, namely Hpumlum Yang Camp, Je Yang Camp, Laiza City Hospital, Laiza Maternal and Child Hospital, Maisha Pa, and Jama. Three sites focused on local residents and IDPs, while the other three primarily served IDP camps. In China, data on imported malaria cases were obtained from the National Notifiable Disease Reporting System and individual case investigations detailed in epidemiological reports.

Data Analysis

The annual parasite incidence (API) and laboratory test positivity rate (microscopy and RDT) were calculated for each year. Using the 2019 data with the lowest API as a reference point, annual incidence rate ratios (IRR), risk ratios (RR), differences in API and test positivity rates, along with their 95% confidence intervals (*CI*), were computed using Epi Info 7.2. For imported malaria cases in China, the proportion of cases originating from LNA out of the total malaria cases reported in Yunnan was examined, and the distribution to counties in Yunnan and other provinces was mapped. Statistical significance was assessed using two-sided Fisher's Exact χ^2 test, with $P<0.05$ indicating significance.

RESULTS

From 2019 to 2023, a study tested 104,262 febrile patients for malaria across six sites, with 14,066 (13.49%) testing positive. Among the positive cases, 99.95% were due to *P. vivax*, while only six cases were confirmed as *P. falciparum* (Table 1). The peak incidences were typically observed in June and July, with occasional smaller peaks in November in certain years.

Malaria experienced a resurgence after 2019, with the API in LNA increasing significantly from 0.92 per 100 person-years in 2019 to 19.78 per 100 person-years in 2023. The IRR in 2023 compared to 2019 was 21.47, indicating a substantial rise (Table 1). Additionally, the positivity rate of laboratory tests also surged to 31.40% in 2023, marking a 28.43 percentage point increase from 2019. The RR for this increase was 10.58, showing that the positivity rate in 2023 was 10.58 times higher than in 2019 (Table 2).

From 2019 to 2023, Yunnan Province documented a cumulative total of 1,016 malaria cases. Among these cases, 545 (53.64%) were identified through epidemiological surveys as imported malaria from LNA. Furthermore, 18 (13.95%) counties in Yunnan Province reported cases of imported malaria from LNA. Additionally, nine other provinces in China also reported cases of imported malaria from LNA (Table 3).

TABLE 1. API and malaria trends in Laiza and nearby areas of Myanmar, 2019–2023.

Year	Population	No. cases	No. *P. vivax* (%)	API (%)	RR (95% *CI*)	Difference of percentage points (95% *CI*)	*P*-value
2019	24,640	227	227 (100.00)	0.92	Reference	Reference	Reference
2020	25,470	745	743 (99.73)	2.93	3.18 (2.74, 3.68)	2.00 (1.76, 2.24)	<0.0001
2021	39,781	1,533	1,531 (99.87)	3.85	4.18 (3.64, 4.80)	2.93 (2.71, 3.16)	<0.0001
2022	40,200	3,205	3,203 (99.94)	7.97	8.65 (7.57, 9.89)	7.05 (6.76, 7.34)	<0.0001
2023	42,238	8,356	8,356 (100.00)	19.78	21.4 (18.84, 24.48)	18.86 (18.46, 19.26)	<0.0001

Abbreviation: API=annual parasite incidence; *Pv*=*Plasmodium vivax*; IRR=incidence rate ratio; *CI*=confidence interval.

TABLE 2. Testing results for malaria in Laiza and nearby areas of Myanmar, 2019–2023.

Year	No. tested	Coverage (%)*	No. Positivity (%)	RR (95% *CI*)	Difference of percentage points (95% *CI*)	*P*-value
2019	7,644	31.02	227 (2.97)	Reference	Reference	Reference
2020	18,126	71.17	745 (4.11)	1.38 (1.20, 1.60)	1.14 (0.66, 1.62)	<0.0001
2021	25,199	63.34	1,533 (6.08)	2.05 (1.79, 2.35)	3.11 (2.63, 3.60)	<0.0001
2022	34,329	85.40	3,205 (9.34)	3.14 (2.75, 3.59)	6.37 (5.88, 6.86)	<0.0001
2023	26,608	63.00	8,356 (31.40)	10.58 (9.29, 12.04)	28.43 (27.76, 29.11)	<0.0001
Total	104,262	70.60	14,066 (13.49)			

Abbreviation: RR=risk ratio; *CI*=confidence interval.
* The numerator is the number of febrile patients tested, and the denominator is the population at the middle of each year for malaria.

TABLE 3. Imported malaria and spread from Laiza and nearby areas of Myanmar, 2019–2023.

Year	No. imported cases in YN	No. cases from LNA in YN (%)	No. counties with malaria from LNA in YN* (%)	Other provinces in China with number of cases from LNA
2019	188	119 (63.30)	7 (5.43)	Guangdong 1, Shanxi 1
2020	163	103 (63.19)	5 (3.88)	Fujian 1
2021	131	90 (68.70)	5 (3.88)	Fujian 1
2022	136	79 (58.09)	5 (3.88)	Zhejiang 2, Guangdong 2, Henan 1
2023	398	273 (68.59)	9 (6.98)	Jiangsu 1, Shandong 1, Hainan 1
Total	1,016	545 (53.64)	18 (13.95)	9 provinces, 12 cases

Abbreviation: YN=Yunnan Province; LNA=Laiza and nearby areas, Myanmar.
* The denominator =129 (the number of counties in Yunnan Province).

DISCUSSION

Kachin State in Myanmar has the highest malaria endemicity, with KR2 being the most affected area within Kachin (*5*,*7*). LNA, within KR2, has the highest malaria prevalence. In 2016, the API in LNA was twice that of the entire KR2, with rates of 5.10 and 10.68 per 100 person-years, respectively (*7*). Due to ongoing military conflicts, there has been an influx of IDPs, leading to a population increase in LNA from 19,470 in 2016 to 42,238 in 2023. The rise in population is a contributing factor to the increased malaria cases and resurgence.

The malaria burden in northern Myanmar was significantly reduced by 89% in 2013 compared to 2008 due to the China malaria programs within the Global Fund to fight AIDS, Tuberculosis and Malaria, with a specific reduction of 92.40% in KR2 (*7*–*8*). However, following the conclusion of these programs, malaria cases started to increase. To ensure malaria elimination in the Yunnan border area, local health authorities collaborated with the Health Department of KIO, resulting in the detection of only 227 malaria cases in LNA by 2019. *Anopheles minimus* was the predominant malaria vector in LNA, with an 85.87% prevalence among *Anopheles* spp in 2018. It was reported to have a 1.69% sporozoite infection rate of *P. vivax* (*9*). Any slight decrease or inadequacy in interventions could trigger a resurgence of malaria. The resurgence of malaria was observed due to reduced control measures during the COVID-19 pandemic.

Cross-border movements of humans and anopheline mosquitoes can lead to the importation of malaria. The WHO has reported that malaria can spread across international borders from endemic border areas to neighboring countries. This phenomenon is termed "border-spill malaria," which denotes the introduction of imported malaria by infected anopheline mosquitoes flying across boundaries from endemic regions of neighboring countries. Studies have shown that the presence of malaria parasite reservoirs and the distance traveled by female anopheline mosquitoes are key factors contributing to border-spill malaria (*4*,*10*–*11*). Even during the border closure period from 2000 to 2022, hundreds of malaria cases continued to cross the border into frontier communities in China from the LNA region, resulting in approximately one-third of Chinese provinces, including Yunnan, reporting imported malaria from the LNA region.

Drug resistance in *Plasmodium* spp. poses a significant challenge to malaria control and eradication efforts. The LNA is notably a hotspot for mutations and drug-resistant molecular markers near the China-Myanmar frontier. Research has indicated a high incidence of *pfk13* mutations linked to artemisinin

resistance, along with other markers indicative of drug resistance. Specifically, the *pfk13* mutations P574L, N458Y, and G533S have been associated with diminished parasite clearance rates and treatment failure in *P. falciparum* patients receiving dihydroartemisinin-piperaquine therapy (*12*). Moreover, Integrated Drug Efficacy Surveillance carried out in Yunnan has revealed a decline in *P. vivax*'s susceptibility to chloroquine. This is evidenced by the persistence of parasitemia on day 2 in 50.00% (22 out of 44) of the imported vivax malaria cases from the LNA, with two patients (4.55%) still exhibiting parasitemia on day 3 in 2023. The waning efficacy of antimalarial drugs against *Plasmodium* spp. may heighten the risk of malaria reintroduction in China and complicate the disease course, potentially leading to severe outcomes and fatalities.

Effective cross-border collaboration has significantly reduced the malaria burden in the border area of Northern Myanmar, and has advanced malaria elimination efforts in China (*3*–*5*,*8*). Conversely, a resurgence of malaria in LNA could heighten the risk of re-establishing transmission in the Yunnan border area. *Anopheles sinensis* is prevalent in 10 Chinese provinces where malaria cases are imported from LNA (*13*). Failure to promptly detect cases could lead to the re-establishment of transmission. Despite vector control efforts lowering mosquito density in Yunnan border areas, *Anopheles* mosquitoes carrying *Plasmodium* spp. infections can still cross over from LNA to bite individuals in Chinese frontier communities. Between January and November 2021, Yingjiang County in Dehong Prefecture, Yunnan, documented 70 malaria cases, with 63 (70%) classified as border-spill malaria (*4*).

P. vivax prevails in the regions (*7*,*10*). Gametocytes of *P. vivax* appear earlier in the infection's progression compared to *P. falciparum*. Moreover, under equivalent temperatures, *P. vivax* sporozoites mature faster in mosquitoes than *P. falciparum*. This implies that *P. vivax* gametocytes are more effectively transmitted to *Anopheles* mosquitoes than *P. falciparum* ones, even at lower parasite densities. Radical cure treatment with primaquine is necessary to disrupt transmission (*14*–*15*); however, primaquine is currently unavailable in China, posing acquisition challenges.

This study is limited by two facts. First, the data was collected solely from six surveillance sites along the border. Second, there are two methods for malaria surveillance, namely, active detection and passive detection. This is just a passive detection based on patient visits to the surveillance sites. A large proportion of *P. vivax* infections are asymptomatic with low parasite densities at submicroscopic and sub-RDT levels. This study has no data on malaria infections among people who did not visit the six health facilities. Consequently, these findings may not fully represent the extent of malaria in the LNA region, potentially indicating a more severe situation than portrayed.

In conclusion, the malaria situation in LNA has seen a significant deterioration. To prevent the resurgence and decrease the risk of transmission re-establishment in China, there is a critical need for innovative collaborative policies, financial support, and technical assistance for border malaria control.

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