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Cover Photo: China-UK Tanzanian Pilot Project for Malaria, China CDC Staff collecting blood sample for plasmodium in Rufiji, Tanzania, 2015.

Preplanned Studies

Evaluation of Malaria Standard Microscopy and Rapid Diagnostic Tests for Screening — Southern Tanzania, 2018–2019

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Summary

What is already known about this topic?

Microscopy is the gold standard for parasitological confirmation, but the accuracy of microscopic diagnosis is influenced by the skill of the technicians. An alternative is the immunologic-based malaria rapid diagnostic tests (mRDTs).

What is added by this report?

Our study evaluated standard microscopy in health system (SMHS) and mRDTs for focused screening and treatment of malaria (FSAT) in Southern Tanzania. We showed that mRDTs were more sensitive than local SMHS for diagnosing malaria infection.

What are the implications for public health practices?

Malaria rapid diagnostic tests can be useful as an alternative to SMHS for FSAT in the local context of Tanzania.

Focused screening and treatment for malaria (FSAT) is an epidemiological technique to identify and treat cases of malaria in a targeted geographic area. FSAT has been identified as a key approach for reducing the burden of malaria in southern Tanzania. The two main diagnostic tools in FSAT are local standard health system microscopy (SHSM) and malaria rapid diagnostic tests (mRDTs). However, performance and operating characteristics of SHSM and mRDTs in local practice conditions are not completely determined. To address this knowledge gap, we analysed paired mRDTs and SHSM results from individuals screened in FSAT during 2018–2019 by re-examining blood slides using the World Health Organization's (WHO) Level 1 Qualification for Malaria Microscopy as reference standard. We measured local SHSM and mRDTs operating characteristics of sensitivity, specificity, and concordance. We showed that in a low economic situation with a shortage of microscopy technicians and insufficient SMHS equipment in local health facilities, mRDTs can be useful as an alternative to standard microscopy in health system (SMHS) for FSAT in the local context of Tanzania.

Malaria remains one of the most serious vector-borne diseases impairing human health worldwide (*1*). In 2020, over 241 million cases of malaria were reported globally, 95% of which were in Africa. In Tanzania, as in many other countries in sub-Saharan Africa, national malaria prevalence decreased — from 18.1% in 2008 to 9.3% in 2017 (*2*). The "China-UK-Tanzania Pilot Project on Malaria Control" (the Pilot Project) was implemented in Southern Tanzania to explore a new model for reducing the malaria burden and for scaling up locally tailored approaches in similar areas in Africa and to share China's experiences of malaria control and elimination. The Pilot Project was initiated in 2015 in Rufiji District, Tanzania.

Microscopy is a convenient and direct diagnostic method for parasitological detection of *Plasmodium* species (*Plasmodium* spp.) and is the gold standard for parasitological confirmation. However, the accuracy of microscopic diagnosis is largely dependent on skills of the technicians. Microscopy tests only 50–100/μL blood for the presence of *Plasmodium* spp. and has a low rate of detection of asymptomatic carriers with their low-density infections (*3*). Use of anti-malarial drugs reduces *Plasmodium* spp. density and causes morphological changes in the parasite, both of which challenge parasite detection and species differentiation, leading to errors in microscopic detection (*4*).

mRDT is an immunological method for detecting specific antigens of *Plasmodium* spp. using peripheral blood. It has advantages of high sensitivity, simple operation, and rapid results, and requires only short-term training of local health staff. mRDTs are potentially ideal routine screening tools for detecting malaria in highly endemic countries with limited access to microscopy.

Progress of the Pilot Project highlighted the importance of evaluating performances of microscopy and mRDTs in Rufiji District, Tanzania. Our study aimed to analyze performance characteristics of SMHS and mRDTs to identify their relative suitability for malaria diagnosis in local settings.

We selected 1,497 blood slides from a FSAT that was implemented between 2018 and 2019 in seven villages in Ikwiriri that were classified as low transmission areas (LTA) (n=679 slides, 45.36% of the sample) and seven villages in Muhoro that were classified as high transmission areas (HTA) (n=818, 54.64%). Blood slide preparation and microscopy were done by local health staff.

Blood samples were collected from people with and without fever, and slides were prepared at field focal points. Samples were collected on clean, grease-free microscope slides. After staining films with 10% Giemsa solution for 10 minutes, slides were air-dried and then examined using light microscopy with an oil-immersion objective lens. A slide was declared negative only if 100 microscopic fields were examined and no parasites were observed. For each specimen, thick films were first examined for malaria parasite detection and then parasite species were differentiated in thin films. Results were recorded as positive when two microscopists recorded positivity for the same slides. Discrepancies were resolved by a third microscopist (*5*).

Re-examination of microscopy was considered the gold standard in our study. Following WHO guidelines, selected slides were re-examined by two experts from China with WHO Level 1 Qualification for malaria microscopy. The two expert microscopists re-examined each blood sample independently under double-blind conditions and recorded their results. Discrepancies were resolved by a third microscopist.

Chi-square tests (χ^2 test) were used for pairwise comparisons of diagnostic accuracy and concordance rates of the two methods (SMHS and mRDT) with a significance level of α=0.05. SMHS and mRDT results were evaluated for accuracy and reliability using the gold standard modality, described above, as the reference standard (*6*). Operating characteristics evaluated included sensitivity and specificity, where sensitivity=true positives/(true positives+false negatives)×100% and specificity=true negatives/(true negatives+false positives)×100%. Statistical analyses were performed using SAS software (version 9.3, Statistical Analysis System, NC, USA).

Of the 1,497 slides, 244 (16.30%), 382 (25.45%), and 309 (20.64%) were positive by SMHS, mRDTs, and the gold standard, respectively (Table 1).

mRDTs were more sensitive than SMHS in both HTAs and LTAs (χ^2=7.54, P=0.0105; χ^2=20.48, P<0.001). The difference in the sensitivity between mRDTs and SHSM was smaller in HTAs (87.10% *vs.* 76.88%) than in LTAs (86.99% *vs.* 65.04%). SMHS was more specific than mRDTs in both HTAs (χ^2=41.95, P<0.001) and LTAs (χ^2=21.76, P<0.001). The difference in specificity between mRDTs and SMHS was significantly greater in HTAs (87.83% *vs.* 98.38%) than in LTAs (92.52% *vs.* 98.13%) (P<0.05) (Table 2).

DISCUSSION

Our study showed that mRDTs were more accurate and reliable as a screening tool for malaria than SMHS, and were more sensitive in both HTAs and LTAs. The sensitivity gap between mRDTs and SMHS was smaller in HTAs than in LTAs, suggesting that mRDTs were more efficient in LTAs. The false

TABLE 1. Comparison of positive rates of three diagnostic modalities in Rufiji District of Tanzania during 2018–2019.

Ward	Diagnostic tools	Number of positive slides	Positive rate (%)
Ikwiriri (LTAs)	SMHS	93	11.37
	mRDTs	159	19.44
	Gold standard	123	15.04
Muhoro (HTAs)	SMHS	151	22.24
	mRDTs	222	32.70
	Gold standard	186	27.39
Both	SMHS	244	16.30
	mRDTs	382	25.45
	Gold standard	309	20.64

Notes: Ward is an administrative unit larger in area than a village and smaller than a county.
Abbreviations: LTAs=low transmission areas; HTAs=high transmission areas; SMHS=standard microscopy in health system; mRDTs=malaria rapid diagnostic tests.

TABLE 2. Comparison of performance of SMHS and mRDT in Rufiji District, Tanzania during 2018–2019.

Ward	Diagnostic tool	Sensitivity (%)	False negative rate (%)	Specificity (%)	False positive rate (%)
Ikwiriri (LTAs)	SMHS	65.04 (56.10–73.17)	34.96 (26.83–43.9)	98.13 (96.98–98.9)	1.87 (1.1–3.02)
	mRDTs	86.99 (80.49–92.68)	13.01 (7.32–19.51)	92.52 (90.5–94.39)	7.48 (5.61–9.5)
Muhoro (HTAs)	SMHS	76.88 (70.43–82.8)	23.12 (17.2–29.57)	98.38 (96.98–98.99)	1.62 (1.01–3.02)
	mRDTs	87.1 (82.26–91.94)	12.90 (8.06–17.74)	87.83 (84.99–90.67)	12.17 (9.33–15.01)
Both	SMHS	72.17 (67.31–77.02)	27.83 (22.98–32.69)	98.23 (97.47–98.91)	1.77 (1.09–2.53)
	mRDTs	87.06 (83.17–90.61)	12.94 (9.39–16.83)	90.57 (88.89–92.26)	9.43 (7.40–11.11)

Abbreviations: SMHS=standard microscopy in health system; mRDTs=malaria rapid diagnostic tests; LTAs=low transmission areas; HTAs=high transmission areas.

negative rates of mRDTs in LTAs (12.90%) and HTAs (13.01%) were less than respective SMHS false negative rates (23.12% and 34.96%). Together, these findings indicate that mRDTs demonstrated superior performance for identifying malaria infections in this Tanzania setting.

Our findings are consistent with those of Shakeley and colleagues who reported that mRDTs enhance performance for detecting malaria infections compared with microscopy, favouring their use in community cross-sectional malaria surveys, where microscopy expertise is difficult to find (*7*). Judith Kahama-Maro and colleagues proposed that microscopy should be replaced by mRDTs as the first-line diagnostic tool for malaria in all medical institutions because of poor quality of routine malaria microscopic examinations at different levels of the health system in Tanzania (*8*). The main findings from our study were similar to those of other studies. Fançony and colleagues used polymerase chain reaction (PCR) as the gold standard and compared screening performance of microscopy and mRDTs in Angola (*9*). They concluded that mRDTs were more sensitive than microscopy. Harchut and colleagues evaluated the cost efficiency of microscopy and mRDTs for malaria diagnosis in Southern Tanzania and found that use of mRDTs reduced government expenditure and facilitated rapid diagnosis of malaria (*10*).

Our study had some limitations. Samples were not tested by PCR. Hence, some patients with low-density parasitemia, particularly individuals with asymptomatic infection, may have been missed. The sample size was relatively small. If the sample size could be expanded, results could be more representative. However, the strategy of initial screening using mRDTs in HTAs followed by malaria microscopy confirmation should be a good strategy for improving the efficiency of local malaria detection.

In conclusion, mRDTs could be a useful alternative to SMHS for FSAT in local health facilities in Tanzania that, due to poor economic conditions, have a shortage of certified microscopy technicians and lack some equipment necessary for conducting SMHS.

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Preplanned Studies

Plasmodium vivax in the Elimination Phase — China, 2013–2020

Li Zhang[1]; Boyu Yi[1]; Zhigui Xia[1]; Fang Huang[1,#]

Summary

What is already known about this topic?

Plasmodium vivax (*P. vivax*) was the most widely distributed and major human malaria parasite in China, considered the last parasite to be eliminated.

What is added by this report?

The last domestic *P. vivax* case was reported in 2016, while hundreds of imported cases were reported annually from 2013–2020, predominantly from Southeast Asia.

What are the implications for public health practice?

In the post-elimination phase, adaptive and practical strategies focusing on imported *P. vivax* cases should be updated and adopted to prevent malaria resurgence.

Plasmodium vivax (*P. vivax*) is the most geographically distributed malaria parasite, and causes severe morbidity (*1*). Historically, *P. vivax* was the dominant parasite species in China for several decades (*2*). Since the National Action Plan for Malaria Elimination was launched in 2010 (*3*), domestic vivax malaria cases have steadily declined, while the proportion of imported vivax malaria cases has increased. To date, the epidemiological status and characteristics of *P. vivax* in the malaria elimination phase have not been adequately studied. The objective of this study was to analyze the epidemiological characteristics of *P. vivax* between 2013 and 2020 in China. The individual data of vivax malaria cases were collected to analyze the demographic characteristics, time distribution of cases and source infection countries of imported cases. The results revealed that the last domestic vivax malaria case was reported in Yunnan Province in 2016, and that hundreds of imported vivax cases were still reported every year, mainly from Southeast Asia. Men who worked outdoors were at high risk of *P. vivax* infection. This study suggests that *P. vivax* remains a key point of focus in the elimination or after elimination phase. Adaptive and updated strategies focusing on *P. vivax* should be considered.

Although *P. vivax* was endemic in China, the incidence of malaria had decreased to an estimated 2/100,000 in 2000, due to the widespread use of antimalarial drugs, unprecedented socioeconomic changes, and urbanization implemented nationwide since the 1980s (*4*). From 2004 to 2012, vivax malaria cases accounted for 76.9% of all reported malaria cases. Between 2001 and 2006 there was a resurgence of *P. vivax* malaria in central China, mainly caused by climate warming, which led to extending malaria transmission, with increasing vectorial capacity of *Anopheles sinensis* (*An. sinensis*) and low capacity of diagnosis leading to an accumulation of infectious sources (*5*). This resurgence was controlled by targeted mass drug administration (MDA) and case management (*5*). As most areas in central and southern China are susceptible areas where *An. sinensis* is prevalent, the imported *P. vivax* malaria may pose a high risk of malaria transmission re-establishment in these malaria-free localities during the transmission season (*6*).

Data on vivax malaria cases, including demographic information (age, sex, and occupation), diagnosis, case classification, interval between onset and diagnosis, and source infection of malaria from 31 provincial-level administrative divisions (PLADs), were collected via the Parasitic Diseases Information Reporting Management System (PDIRMS) during 2013–2020. Data from Hong Kong, Macao, and Taiwan were not included in the study. Demographic data were analyzed using Microsoft Excel 2010 and SAS (version 9.4, SAS Institute Inc, NC, USA). Differences between groups were evaluated by chi-squared test and Kruskal-Wallis test. Differences were considered statistically significant at $P<0.05$.

From January 1, 2013 to December 31, 2020, a total of 23,114 malaria cases were recorded from 31 PLADs via PDIRMS, among them 4,817 vivax malaria cases were reported, including 138 domestic cases and 4,679 imported cases. Meanwhile, 120 malaria-associated deaths were reported during this period (Figure 1A). Yunnan Province reported the last domestic *P. vivax* case in 2016, which was also the last

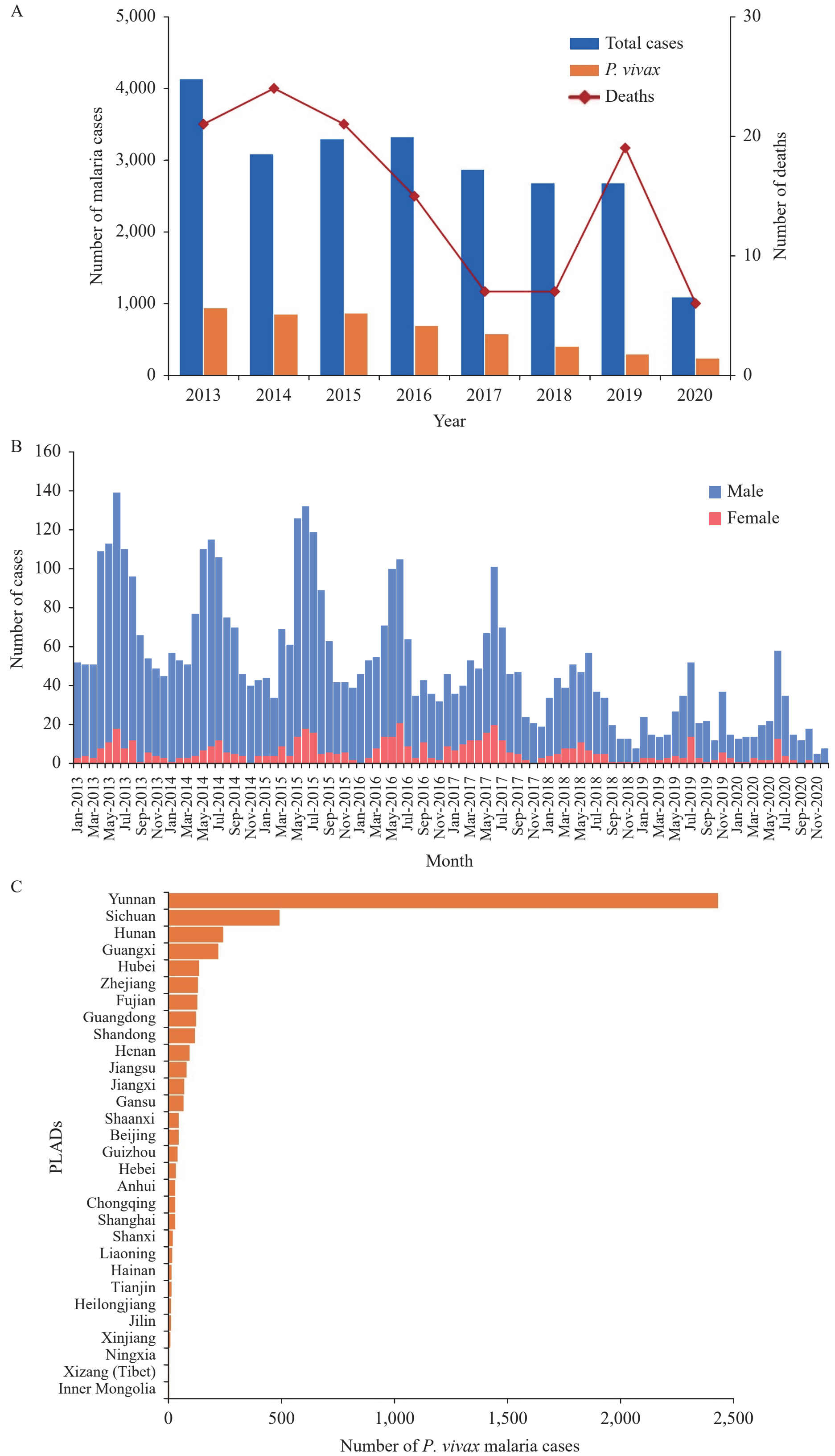

FIGURE 1. The PLADs of *P. vivax* malaria in China, 2013–2020. (A) Number of total malaria cases, vivax malaria cases, and deaths in China, 2013–2020. (B) Monthly distribution of imported and domestic vivax malaria cases based on sex, 2013–2020. (C) Provincial distribution of reported *P. vivax* in China, 2013–2020.

Abbreviations: PLADs=provincial-level administrative divisions; *P. vivax*=*Plasmodium vivax*.

domestic malaria case in China. No domestic cases have been reported in the country since 2017. From 2013 to 2020, the proportion of *P. vivax* remained above 20%, except in 2018 and 2019. The number of vivax malaria cases gradually declined, from 935 in 2013 to 234 in 2020 (Figure 1A). The number of domestic *P. vivax* cases decreased from 68 in 2013 to 1 in 2016. In addition, among all the reported vivax malaria cases, 179 were recurrent cases, accounting for 3.7% of the total. The interval from last malaria infection to recurrence among different sources was significantly different (P<0.01).

The monthly distribution of imported and domestic vivax malaria cases exhibited a seasonal trend (Figure 1B). The peak was in the period from May to August. Most *P. vivax* cases occurred in males (88.2%, 4,249/4,817) and in the 19–59 age group (91.8%, 4,421/4,817). The proportion of males among domestic cases (72.5%, 100/138) was lower than that among imported cases (88.7%, 4,149/4,679), which indicated that the majority of the population working abroad was male. Furthermore, most vivax malaria cases occurred among people working outdoors (43.0%, 1,307/4,817), who were at high risk of exposure to outdoor biting vectors including construction workers, farmers, open mine workers, drivers, field engineers, etc. Of the 4,817 reported malaria cases, 68.1% (n=3,281) were diagnosed in a health facility of a city or county center for disease control and prevention (CDC)/hospital, while 19.4% were diagnosed in a township hospital (Table 1). Moreover, 89.8% were diagnosed and confirmed by PCR in the provincial malaria diagnosis reference laboratory. The median interval between the illness onset and the first visit to the doctor was different between domestic cases and imported cases (P<0.05), which were 3 days [interquartile range (IQR): 1–6] and 2 days (IQR: 0–4), respectively. The median interval between the first visit to the doctor and the final diagnosis was 0 days (IQR: 0–4).

Most imported vivax malaria cases were from Southeast Asia (63.8%, 2,986/4,679), followed by East Africa (16.1%, 753/4,679), Central Africa (6.5%, 304/4,679), West Africa (5.1%, 240/4,679), and South Asia (5.1%, 237/4,679) (Supplementary Table S1, available in https://weekly.chinacdc.cn/). Among these cases, the major source countries were Myanmar, Ethiopia, and Indonesia, accounting for 54.5%, 13.0%, and 5.2%, respectively. In addition, most vivax malaria cases were reported from Yunnan Province (52.7%), followed by Sichuan (10.3%), Henan (5.0%), and Guangxi (4.6%) PLADs (Figure 1C).

DISCUSSION

The results of this study showed that the number of vivax malaria cases in China declined significantly during 2013–2020 (Figure 1A and Table 1). The last domestic vivax case was reported in 2016 and hundreds of imported vivax cases have been recorded annually. China was certified malaria-free by the World Health Organization (WHO) in 2021 since there had been no domestic cases for more than three years. Malaria elimination in China has largely been achieved through China's "1-3-7" approach along with an adaptive malaria elimination strategy (*6*–*7*). *P. vivax* is more difficult to eliminate or control than *P. falciparum* and other species because it has dormant liver forms (hypnozoites) in its lifecycle (*8*). *P. vivax* patients may relapse due to the activation of hypnozoites and become a new source of transmission, even after the schizonts of *P. vivax* have been removed from the blood.

P. vivax remained the predominant species in China, and several interventions focused primarily on *P. vivax* elimination in the journey of malaria elimination phase, such as radical cure in the following spring, target MDA and adaptive case finding, and a focus-based surveillance system (*4*). The last domestic *P. vivax* case was reported in 2016, and since then there have been no reported domestic cases. However, hundreds of imported vivax malaria cases have been reported annually (Table 1), mainly due to the increasing number of Chinese workers or business people working abroad, especially from Southeast Asia and Africa, where malaria is highly endemic (Supplementary Table S1, available in https://weekly.chinacdc.cn/). In addition, the difference in sex ratio between domestic and imported cases indicated the population working abroad was predominantly male, especially those working outdoors, which was consistent with the previous study (*6*). The decrease in imported cases in 2020 was caused by the COVID-19 international travel restrictions (*9*). Additionally, a proportion of recurrent imported vivax malaria cases were identified in this study, which may be due to differences in radical treatment strategies, glucose-6-phosphate dehydrogenase (G6PD) deficiency rate, treatment adherence, and drug resistance in the infection source countries (*10*), suggesting that G6PD

TABLE 1. Demographic characteristics of the reported vivax malaria cases in China (2013–2020).

Item	2013		2014		2015		2016		2017	2018	2019	2020	*P*-value†
	IMP	IND	IMP	IND	IMP	IND	IMP	IND	IMP	IMP	IMP	IMP	
Total	867	68	798	45	836	24	685	1	573	397	289	234	
Sex													<0.001
Female	61	20	47	11	86	7	97	0	105	57	47	30	
Male	806	48	751	34	750	17	588	1	468	340	242	204	
Age group (years)													0.072
<5	3	0	6	3	9	0	9	1	10	4	1	2	
5–18	28	14	17	3	35	5	38	0	35	20	10	17	
19–59	832	47	766	37	776	18	615	0	510	353	263	204	
≥60	4	7	9	2	16	1	23	0	18	20	15	11	
Occupation													<0.001
Outdoors	NA	NA	NA	NA	80	1	233	0	379	272	190	152	
Indoors	NA	NA	NA	NA	13	0	34	0	34	39	33	13	
Unclear*	NA	NA	NA	NA	21	1	84	0	125	77	63	38	
Missing	NA	NA	NA	NA	722	22	334	1	35	7	3	31	
Diagnosis health facility													<0.001
Provincial-level CDC	38	3	21	0	1	0	7	0	5	2	1	0	
Provincial-level hospital	48	2	45	0	49	2	58	0	38	33	23	12	
City-level CDC	37	1	25	0	18	0	11	0	9	3	3	2	
City-level hospital	140	6	124	3	125	5	141	0	135	104	72	53	
County-level CDC	307	16	301	19	253	11	166	1	98	68	33	22	
County-level hospital	133	17	149	13	152	1	143	0	106	96	83	76	
Township hospital	90	20	73	8	197	5	153	0	170	89	68	62	
Village clinic	12	1	4	1	5	0	0	0	1	1	5	6	
Private clinic	61	2	56	1	36	0	6	0	11	1	1	1	
Missing	1	0	0	0	0	0	0	0	0	0	0	0	
PCR confirmation													<0.001
Yes	625	51	714	38	772	22	647	1	547	385	289	233	
No	242	17	84	7	64	2	38	0	26	12	0	1	

Abbreviations: NA=not available; IMP=imported cases; IND=domestic cases; PCR=polymerase chain reaction.

* Unclear indicates that the risk exposure could not be estimated in populations such as children, retirees, students, unemployed persons, etc. Missing data were not included in the statistical analysis.

† *P* value was calculated by chi-squared test or Kruskal-Wallis test.

detection before treatment and supervised medication for imported vivax malaria cases are required.

China has been a malaria-free country, however *An. sinensis*, the major malaria vector in China, is prevalent in most parts of country (*4,6*). In the post-elimination phase, several challenges need to be considered to prevent re-transmission of vivax malaria through imported malaria cases. First, this study showed that the duration between disease outbreak and first doctor visit was slightly longer in areas with reported domestic cases, such as Yunnan Province, reflecting the residents' lack of knowledge, attitudes, and practices regarding malaria treatment-seeking. Health education on malaria among the high-risk population is needed. Second, the capability for malaria diagnosis in health facilities was unbalanced at different levels. More training and refresher training should be conducted for case detection and diagnosis, especially in health facilities at the city or county levels. In addition, submicroscopic or asymptomatic patients with lower parasitemia were not diagnosed using RDT or microcopy, which is still a challenge in malaria elimination. Third, early detection and diagnosis with appropriate treatment and radical cure in the following spring should be maintained for imported *P. vivax* patients to prevent relapse or recurrence. The radical cure rate was relatively higher in China, which might be caused by the spring radical treatment in the following year, although the dosage of 8-day primaquine in China was different compared with 14-day primaquine recommended by WHO. Fourth, the "1-3-7" approach was well implemented nationwide, and made an important contribution to achieving the national goal of elimination. However, the strategies and approaches should be updated or adapted, with a focus on imported cases, to prevent recurrence of malaria in the post-eradication phase.

The study was subject to some limitations. First, the source countries of 31 imported vivax cases were not available. Second, recurrent vivax cases were not analyzed in this study because no methods were available to distinguish recurrent vivax cases from new infections or recrudescence.

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SUPPLEMENTARY TABLE S1. Source of imported vivax malaria cases reported in China (2013–2020).

Region	Country	2013	2014	2015	2016	2017	2018	2019	2020	Total
Asia		613	587	591	453	402	243	209	147	3,245
Southeast Asia		582	559	571	412	335	211	180	136	2,986
	Myanmar	478	418	502	358	297	190	171	134	2,548
	Indonesia	48	115	32	23	13	8	2	0	241
	Laos	35	16	22	26	13	4	2	1	119
	Cambodia	18	6	12	3	11	9	2	0	61
	Thailand	3	3	2	0	0	0	1	1	10
	Vietnam	0	1	1	1	1	0	2	0	6
	Malaysia	0	0	0	1	0	0	0	0	1
South Asia		29	27	18	39	65	31	23	5	237
	Pakistan	17	14	11	27	59	24	20	5	177
	India	12	12	7	12	4	7	3	0	57
	Bangladesh	0	0	0	0	1	0	0	0	1
	Bhutan	0	0	0	0	1	0	0	0	1
	Sri Lanka	0	1	0	0	0	0	0	0	1
East Asia		1	0	1	1	1	1	6	6	17
	Republic of Korea	0	0	0	0	1	1	6	6	14
	Democratic People’s Republic of Korea	1	0	1	1	0	0	0	0	3
West Asia		1	1	1	1	1	0	0	0	5
	Palestine	0	1	0	0	1	0	0	0	2
	The United Arab Emirates	0	0	0	1	0	0	0	0	1
	Saudi Arabia	1	0	0	0	0	0	0	0	1
	Armenia	0	0	1	0	0	0	0	0	1
Africa		246	202	241	219	147	134	71	50	1,310
East Africa		79	123	144	132	94	100	47	34	753
	Ethiopia	42	106	117	117	79	85	40	22	608
	Sudan	21	13	15	0	5	2	3	2	61
	Uganda	0	1	3	6	1	3	1	6	21
	Tanzania	4	0	3	2	6	0	1	0	16
	Mozambique	6	1	1	2	0	2	0	1	13
	Djibouti	0	0	0	0	2	5	1	1	9
	Rwanda	0	0	0	1	0	2	1	2	6
	South Sudan	3	1	0	1	0	0	0	0	5
	Kenya	0	1	2	0	0	0	0	0	3
	Zambia	2	0	0	0	1	0	0	0	3
	Egypt	1	0	0	1	0	0	0	0	2
	Eritrea	0	0	1	0	0	1	0	0	2
	Malawi	0	0	1	1	0	0	0	0	2
	Madagascar	0	0	1	0	0	0	0	0	1
	Somalia	0	0	0	1	0	0	0	0	1

TABLE S1. (Continued)

Region	Country	2013	2014	2015	2016	2017	2018	2019	2020	Total
West Africa		113	35	23	19	20	16	10	4	240
	Ghana	91	7	5	7	5	2	2	0	119
	Nigeria	10	13	10	5	10	6	5	3	62
	Liberia	4	5	1	3	1	4	1	0	19
	Sierra Leone	2	3	4	1	1	1	1	1	14
	Cote d'Ivoire	0	1	1	3	1	2	1	0	9
	Togo	2	3	0	0	1	0	0	0	6
	Mali	3	0	0	0	1	1	0	0	5
	Benin	1	1	0	0	0	0	0	0	2
	Mauritania	0	1	1	0	0	0	0	0	2
	Niger	0	1	1	0	0	0	0	0	2
Central Africa		52	41	71	65	32	18	13	12	304
	Equatorial Guinea	16	16	21	21	7	2	4	1	88
	Angola	17	8	14	12	2	3	0	1	57
	Democratic Republic of Congo	5	4	10	16	8	6	1	7	57
	Cameroon	2	7	18	8	6	1	2	1	45
	Republic of Congo	4	3	4	7	4	3	4	0	29
	Gabon	5	1	2	0	0	1	1	1	11
	Burundi	0	0	1	0	5	1	1	0	8
	Chad	2	2	1	0	0	0	0	1	6
	The Central African Republic	1	0	0	1	0	1	0	0	3
South Africa		1	1	3	1	0	0	1	0	7
	South Africa	1	1	3	1	0	0	0	0	6
	Comoros	0	0	0	0	0	0	1	0	1
North Africa		1	1	0	0	1	0	0	0	3
	Libya	0	0	0	0	1	0	0	0	1
	Algeria	1	0	0	0	0	0	0	0	1
	Tunisia	0	1	0	0	0	0	0	0	1
Africa (other regions)		0	0	0	2	0	0	0	0	3
Oceania		5	8	2	11	17	10	8	8	69
	Papua New Guinea	4	8	2	9	15	10	8	8	64
	Solomon Islands	1	0	0	2	2	0	0	0	5
America		2	2	1	2	7	5	2	4	25
South America		2	2	1	2	7	4	2	4	24
	Guyana	1	2	1	1	5	1	0	3	14
	Venezuela	0	0	0	1	2	3	2	1	9
	Ecuador	1	0	0	0	0	0	0	0	1
Latin America	Nicaragua	0	0	0	0	0	1	0	0	1
Unknown sources		1	0	1	0	0	4	0	25	31
Total		867	798	836	685	573	396	290	234	4,679

Preplanned Studies

Epidemiological Characteristics of Visceral Leishmaniasis — Shanxi Province, China, 1950–2019

Yingze Zhao[1]; Ping Tie[2]; Yongfei Bai[2]; Liping Wang[3]; Yuhua Zheng[2]; Jiaojiao Zhang[4]; Xiao Qi[3,#]; Canjun Zheng[3]; Xiao-nong Zhou[5]

Summary

What is already known about this topic?

Visceral leishmaniasis (VL) is the most serious form of leishmaniasis. In recent years, reported cases of VL have been gradually increasing in Shanxi Province, China.

What is added by this report?

The report describes the epidemiology of VL from 1950 to 2019 in Shanxi Province and the recent trend of VL reemergence.

What are the implications for public health practice?

Measures to prevent and control VL, such as health education, improving clinical diagnostics, strengthening epidemiological investigation capacity for VL cases, monitoring surveillance, and use of other evidence-based preventive measures, should be undertaken in Shanxi Province.

In recent years, the number of reported cases of visceral leishmaniasis (VL) has gradually been increasing in Shanxi Province, China. Using surveillance data from the Chinese Center for Disease Control and Prevention from 1950 to 2019, we analyzed and described trends and epidemiological characteristics of VL in Shanxi Province. Study results showed that the VL epidemic was reemerging, with a gradually expanding epidemic scope and evident aggregation in Shanxi Province. Among reported VL cases, 41.4% were among children under three years old and 15.7% were among adults over 60 years of age. It is necessary, therefore, to pay high attention to the reemergence of VL and take action to curb this trend in Shanxi Province.

VL data from 1950 to 2004 came from infectious disease report forms (paper version) that were delivered from agencies at each level to China CDC. These reports only provided annual summaries for each province and lacked detailed information about individual cases. Case-level data from 2005 to 2019 came from the National Notifiable Disease Reporting System, and included detailed information such as age, gender, occupation, date of onset, and address of each case. Demographic data came from the public website of the Chinese Statistics Bureau (https://data.stats.gov.cn/). VL cases reported from 2005 to 2019 were diagnosed using the Criterion of Visceral Leishmaniasis Diagnosis of China (WS 258–2006) and based on clinical manifestations and rk39 test results (*1*). Early case diagnosis was based on pathogenic examination of bone marrow smears and clinical manifestations. SPSS software (version 22.0, IBM, New York, USA) was used for data processing and analysis. We estimated prevalence trends from 1950 to 2019 and analyzed season, population, and regional distribution data for 2005 to 2019.

The data showed that the prevalence of VL in Shanxi Province was very high in the 1950s, but decreased sharply after the 1960s, although there was an outbreak in 1972. From 1974 to 2004, VL was almost nonexistent in Shanxi Province, with only sporadic cases and an annual case count that never exceeded five. Since 2014, reported cases of VL had increased rapidly in Shanxi, with an annual rate of increase of 63.7%. The number of VL cases reported each year had been over 20 in the last three years, and was 47 in 2019 (Figure 1).

From 2005 to 2019, 140 VL cases were reported in Shanxi Province; 96 among males and 44 among females for a male∶female ratio of 2.2∶1. The youngest case was a 19-day infant, the oldest was 85 years old, and the median age was 21 years old. There were 58 cases under the age of 3, accounting for 41.4% of reported cases, and 22 were older than 60 years, accounting for 15.7%. Among 6 occupational groups, “children at home” had the most cases, with 43.6% of reports (Table 1).

Between 2005 and 2019, VL cases were reported every month of the year, with a peak reporting incidence in May and a second peak in January (Supplementary Figure S1, available in https://weekly.chinacdc.cn/).

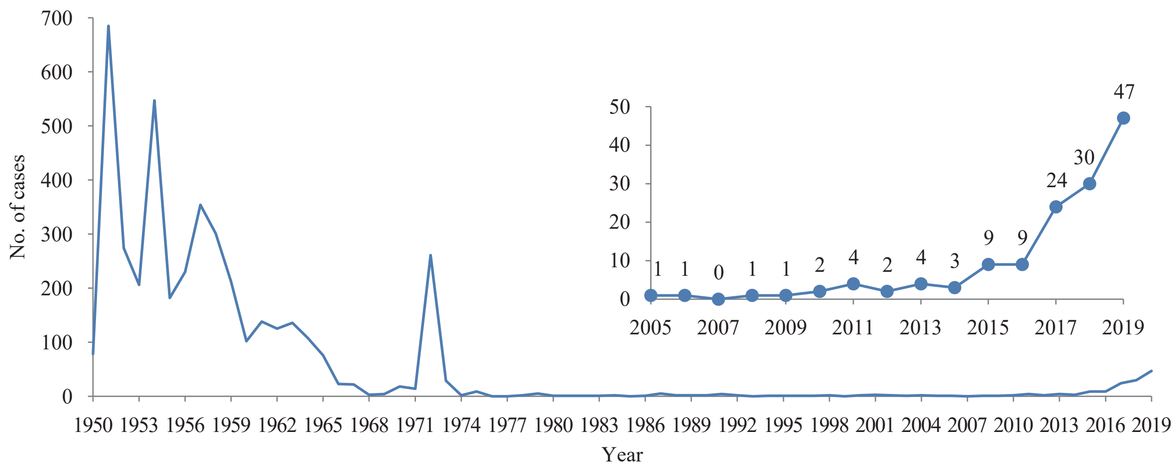

FIGURE 1. Prevalence trend of visceral leishmaniasis in Shanxi Province, 1950–2019.

TABLE 1. The reported visceral leishmaniasis cases by age and occupation in Shanxi Province, 2005–2019.

Item	Group	No. of male	No. of female	Total	Proportion (%)
Age (years)	0–2	31	27	58	41.4
	3–9	6	2	8	5.7
	10–19	3	1	4	2.9
	20–59	38	10	48	34.3
	60–	18	4	22	15.7
Occupation	Children at home	33	28	61	43.6
	Farmers	29	9	38	27.1
	Houseworkers	10	3	13	9.3
	Workers	8	0	8	5.7
	Students	6	2	8	5.7
	Others	10	2	12	8.5

There are 11 prefectures, 117 counties, and 1,390 townships in Shanxi Province. From 2005 to 2019, reported cases were seen in all 11 prefectures and in 29 counties and 67 townships. The number of townships, counties, and prefectures where cases were reported increased each year (Figure 2). Cases were aggregated. At the prefecture level, 89.9% of cases were distributed in Yangquan Prefecture (73 cases, 52.1%), Changzhi Prefecture (29 cases, 20.7%), and Linfen Prefecture (24 cases, 17.1%). At the county level, 57.1% of cases were distributed in 4 counties, including Suburb District of Yangquan (32 cases), Pingding County of Yangquan (19 cases), Wuxiang County of Changzhi (17 cases), and Urban District of Yangquan (12 cases). However, on a smaller scale, there was a sporadic trend. Of the 67 townships with reported cases during 2005–2019, the number of cases in each township varied from 1–5, with an average of 1.3 cases per township. Only 15 townships reported 2 or more cases in the same year.

DISCUSSION

Our study showed a VL resurgence in Shanxi Province. Historically, Shanxi Province was an epidemic area of zoonotic type VL, which is mainly transmitted from dogs to humans through sandfly bites — a common occurrence in infants and young children (*2*). VL prevalence is related to local distribution of sandflies and animal hosts in endemic areas. Changes in the natural and social environment often lead to outbreaks or reemergences of VL. Because large-scale actions such as controlling dogs, spraying insecticides, promoting the use of mosquito nets, and conducting health education were adopted in the 1970s, VL was almost eliminated in Shanxi Province (*3*). However, in recent years, the number of family dogs in Shanxi Province has been increasing (*4*). Since

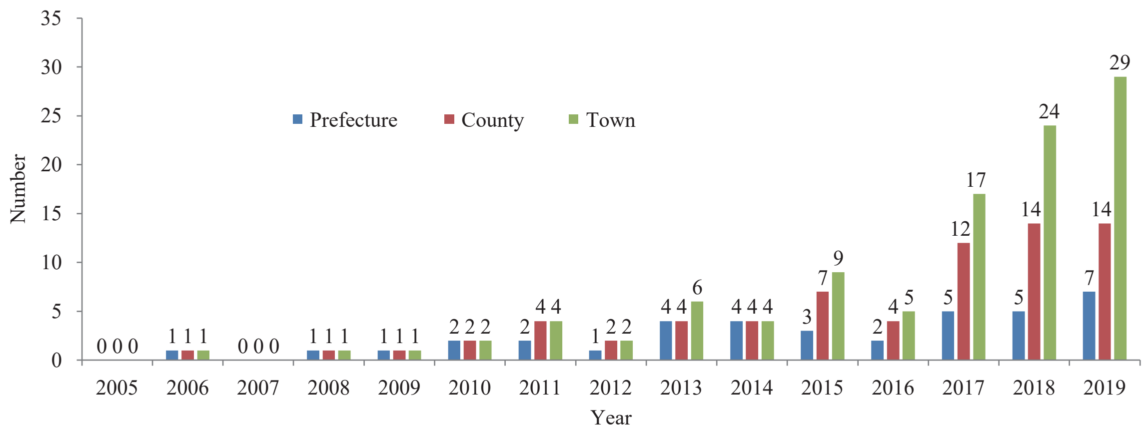

FIGURE 2. Changes of the number of towns, counties, and prefectures reported visceral leishmaniasis in Shanxi Province, 2005–2019.

China started implementing a policy of returning farmland to forests in 2000, Shanxi Province had returned 1.82 million hectares of farmland to forests by 2018 (*5*). This change may provide suitable conditions for an increase in density of wild animal hosts and growth in population of the main vector, the sandfly. The reemergence in recent years is likely related to these changes.

In our study, the infection rate in males was higher than in females, which is consistent with the epidemic characteristics in endemic areas in Gansu Province and Xinjiang Uygur Autonomous Region in China (*6*). It is generally believed that because males have more field activities, they have a higher exposure risk to sandflies, which leads to a higher incidence. Children under 3 years old accounted for a large proportion (41.4%) of cases. This is consistent with the characteristics of zoonotic VL caused by *Leishmania infantum*, which was historically epidemic in Shanxi Province. However, half of the cases were more than 20 years old, and 15.7% were among individuals over 60 years of age, which is significantly different from endemic areas in Gansu and Xinjiang (*7*–*8*). This phenomenon may be related to lack of immunity and high susceptibility to VL in adults, or to changes of VL type, infectious sources, routes of transmission, and vector habitats in those areas. The epidemiological history of these adult cases should be further investigated, including occupations, outdoor working conditions, and dog breeding activities.

VL cases reported from 2005 to 2019 were concentrated in a few prefectures in Shanxi Province, such as Yangquan, Linfen, and Changzhi prefectures. These three prefectures were previously severely endemic areas based on records in the 1950s. Sporadic VL cases had been reported every year since the 1980s, indicating the existence of VL circulation in the local mountainous wild environments (*9*). Although the incidence in Shanxi Province has increased rapidly in recent years, a sporadic pattern of local VL at the community level has been seen in the last three years. This indicates that the VL epidemic is still at an early stage. The density of vector sandflies and the number of infection sources have not yet accumulated to the point of causing large-scale epidemics. A retrospective investigation and analysis of VL cases in Yangquan City in 2021 showed that eliminating sandflies, preventing sandfly bites, managing sick dogs, and strengthening clinical diagnostic abilities are the main measures to control *Leishmania infection* (*10*). It is necessary to take effective measures as soon as possible to curb the epidemic trend.

This study had several limitations. Available data lacked detailed laboratory and epidemiological information related to cases, including VL typing, occupational characteristics, and living habits. We were unable to evaluate the ecological relationship between natural or social environmental changes and VL incidence. Therefore, this study cannot provide related prevention and control suggestions.

In summary, VL control and prevention should be paid attention to in Shanxi Province. Health education on VL prevention and control knowledge for clinicians, patients, and high-risk populations should be strengthened. Detection, diagnosis, and epidemiological investigation capacity of medical staff should be improved. VL vector and host monitoring should be strengthened. Finally, proven preventive measures, such as use of mosquito nets, spraying insecticide against sandflies, and management of sick dogs should be used to curb the expansion of reemergence of VL in Shanxi Province.

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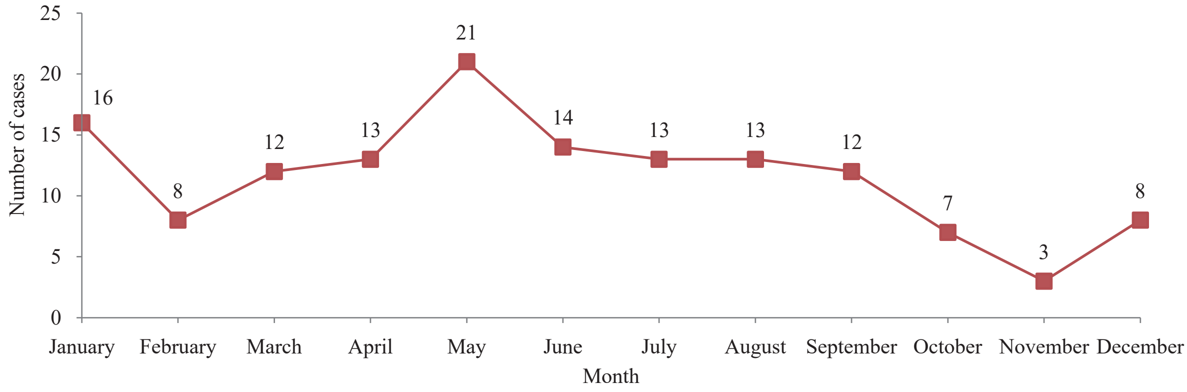

SUPPLEMENTARY FIGURE S1. Seasonal distribution of reported visceral leishmaniasis in Shanxi Province, 2005–2019.

Preplanned Studies

Assessment of the Health-Related Quality of Life in Neurocysticercosis Patients in Hot Spot Areas — China, 2017–2018

Yingjun Qian[1]; Xinzhong Zang[2]; Huanzhang Li[3]; Zhaoyu Guo[1]; Changhai Zhou[1]; Menbao Qian[1]; Yingdan Chen[1]; Hongkun Liu[4]; Yuhua Liu[4]; Shizhu Li[1,#]

Summary

What is already known about this topic?

Neurocysticercosis is the most severe form of infection caused by ingesting cysticerci, the larval cysts of the pork tapeworm, *Taenia solium.* Approximately 50 million people worldwide have neurocysticercosis, which is the leading cause of acquired epilepsy in many endemic countries.

What is added by this report?

The health of neurocysticercosis patients can be seriously impaired, including through loss of mobility, inability to do self-care, impairment of usual activities, pain/discomfort, anxiety/depression, and impaired cognition. Cognitive impairment is the major consequence of neurocysticercosis and significant contributor to decreased health-related quality of life. Our study made the first estimate of disability weight from neurocysticercosis as a key parameter for disease burden assessment in China.

What are the implications for public health practice?

To prevent severe health outcomes from neurocysticercosis in China, it is necessary to improve public awareness of neurocysticercosis and relevant health behaviors.

Cysticercosis is considered by the World Health Organization (WHO) to be a neglected tropical disease. It is a parasitic tissue infection caused by cysticerci, the larval cysts of the pork tapeworm *Taenia solium* in an intermediate host. Humans are the definitive hosts of *T. solium*, which is acquired via ingestion of cysticerci in undercooked pork. Human cysticercosis is only acquired from ingestion of *T. solium* eggs through fecal-oral transmission: either autoinfection or swallowing eggs from carriers. When cysticerci encyst in the central nervous system, neurocysticercosis (NCC) can occur (*1*). WHO estimated that in 2015 there were 2.5–8.3 million NCC cases resulting in a loss of 2.8 million disability-adjusted life years (DALY) (*1*). NCC is endemic in southeast China; Dali Prefecture in Yunnan Province is a hot spot (*2*–*3*). However, there are few domestic studies of NCC patients' quality of life and burden of disease. To fill this knowledge gap, our study assessed health outcomes and estimated disability weight (DW) in NCC inpatients through a hospital-based survey in Dali that was conducted in 2017–2018. The study showed that human health was seriously damaged in six dimensions, among which cognitive impairment was the most serious. We estimated DW to illustrate the urgency of increasing public awareness of NCC and improving relevant health behaviors.

From September 2017 to September 2018, inpatients in the affiliated hospital of Dali Prefectural Institute of Research and Control on Schistosomiasis, Dali City, Yunnan Province, were enrolled into the study if they met inclusion criteria and had no exclusions. Confirmed NCC cases were included if they met national cysticercosis diagnostic criteria (WS 381-2012), but patients with combined cysticercosis or who were below 5 years of age were excluded. Participants were categorized into two groups — a first-visit group and a follow-up group. The first-visit group was patients who received standard, hospital-based anti-cysticercosis treatment for the first time. The follow-up group was patients who received standard in-hospital treatment for their second-or-more time.

Health-related quality of life (HRQoL) was assessed in face-to-face interviews. We obtained demographic, diagnostic, and treatment data and administered the EQ-5D+C* survey. EQ-5D is a standardized measure

* EQ-5D+C is the abbreviation of European Quality of Life Scale (EQ) consisting of five dimensions (5D) with the additional dimension cognition (+C), which are rated with three levels (3L): no health problems, moderate health problems and extreme health problems. The 5D are: mobility, self-care, usual activities, pain/discomfort and anxiety/depression.

of health status developed by the EuroQol Group. This instrument provides a simple, generic measure of health for clinical and economic appraisals and for population surveys. It has 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has 3 levels: no problems, some problems, and extreme problems (*4*). EQ-5D+C was developed from EQ-5D and is used in disease burden research to assess cognitive impairment (*5*). We included cognitive impairment assessment as the 6th health dimension because cognitive loss is commonly seen with NCC (*6*). DW was calculated with the formula, DW=1–EQ-VAS[†]/100. EQ-VAS uses the EuroQol Visual Analogue Scale and records the respondent's self-rated health on a vertical, visual analogue scale where 100 is "the best imaginable health state" and 0 is "the worst imaginable health state." We used EpiData (version 3.1, The EpiData Association, Odense, Denmark) to correct logic errors. Statistical analyses were performed with SPSS (version 19, IBM, Armonk, NY, USA).

Our study enrolled 210 participants. The average age was 38.9±15.5 years; 32.9% (69/210) of participants were 30–44 years of age. Eighty-four subjects were in the first-visit group and 126 were in the follow-up group. The most prominent clinical manifestations were headache (68.10%), memory impairment (61.43%), and epilepsy (37.1%). Epilepsy was more prominent in the first-visit group than in the follow-up group (54.76% *vs.* 25.40%; χ^2=18.52, P<0.001). Headache was reported by 76.19% in the first-visit group and 62.70% in the follow-up group (χ^2=8.76, P<0.05). Memory impairment was reported by 52.38% in the first-visit group and 67.46% in the follow-up (χ^2=8.76, P<0.05) (Supplemental Table S1, available in http://weekly.chinacdc.cn).

Table 1 shows EQ-5D+C survey results; 93.33% patients (196/210) had at least one health problem; 83.33% (175/210) had moderate health problems; and 10.0% (21/210) had extreme health problems. Cognitive impairment was the most frequently reported health problem (71.9%, 151/210). Of the six health indicator dimensions, pain/discomfort ranked the highest (77.38%) in the first-visit group followed by cognitive impairment (67.86%) while cognitive impairment was highest in the follow-up group (74.60%). No statistically significant differences were seen between the two groups in the six health dimensions. Logistic regression analysis showed statistically significant differences by age group. Compared to the 5–14 year old group, the risk of cognitive impairment was 16.33 times greater among 45–59 year old group (Supplementary Table S2, available in http://weekly.chinacdc.cn/).

The median EQ-VAS score was 70 (interquartile interval: 60–80; range: 20–96). Multiple linear regression showed that EQ-VAS was negatively correlated with problems with usual activities, pain/discomfort, anxiety/depression, and cognitive impairment. Standardized regression coefficients showed that the greatest impact on EQ-VAS was cognitive impairment (–0.32), followed by problems with usual activities (–0.27), and pain/discomfort (–0.25) (Table 2). Multi-factor analysis showed that

TABLE 1. NCC patients' 6 health dimensions of health problems.

Dimension	No. having health problems			Participants with health problems (%)*	Having health problems*		χ^2	P
	None (%)	Moderate (%)	Extreme (%)		First-visit group (N[†]=84) n[§] (%)	Follow-up group (N[†]=126) n[§] (%)		
Mobility[¶]	201(95.71)	9(4.29)	0(0.00)	9(4.29)	5(5.95)	4(3.17)		>0.05
Self-care[¶]	204(97.14)	6(2.86)	0(0.00)	6(2.86)	2(2.38)	4(3.17)		>0.05
Daily activities	124(59.05)	83(39.52)	3(1.43)	86(40.95)	38(45.24)	48(38.10)	1.06	>0.05
Pain/discomfort	61(29.05)	147(70.00)	2(0.95)	149(70.95)	65(77.38)	84(66.67)	2.81	>0.05
Anxiety/depression	80(38.09)	118(56.19)	12(5.71)	130(61.90)	53(63.10)	77(61.11)	0.03	>0.05
Cognitive impairment	59(28.1)	144(68.57)	7(3.33)	151(71.90)	57(67.86)	94(74.60)	1.14	>0.05
Any dimension[¶]	14(6.67)	175(83.33)	21(10.00)	196(93.33)	80(95.24)	116(92.06)		>0.05

Abbreviation: NCC=neur ocysticercosis.
* health problems=having moderate and extreme health problems.
[†] N=No. of participants in the first-visit group and follow-up group.
[§] n=No. of participants having health problems in first-visit group and follow-up group.
[¶] Fisher exact probability test was used.

[†] EQ-VAS means European quality of life visual analogue scale.

the regression model was statistically significant overall (*F*=16.99, *P*<0.001). R^2 was equal to 0.46, indicating that the included variables could account for 46% of the total variation in EQ-VAS scores. The first-ever assessment in China of the overall NCC DW was 0.3 (0.2–0.4), with no statistically significant differences between gender (*Z*=–0.15, *P*>0.05) or group (*Z*=0.62, *P*> 0.05).

DISCUSSION

NCC is the most severe form of cysticercosis and is often characterized by headaches and epileptic seizures. We found that the most prominent clinical manifestations in NCC patients were headache, impaired memory, and epilepsy. Comparison of first-visit and follow-up groups showed that the proportion of NCC patients with epilepsy in the follow-up group was significantly lower than the proportion with epilepsy in the first-visit group, suggesting that standardized treatment was helpful to decrease this major health outcome for NCC patients. Over 60% (129/210) of NCC patients reported impaired memory. Although little attention was attached to memory impairment, it is common in cysticercosis, and long-term memory impairment causes great psychological pressure and seriously affects quality of life (*7–8*). The average EQ-VAS was 70, which is lower than the 80.91 score found in the National Health Service survey (*9*), indicating that HRQoL is heavily degraded in NCC patients.

Of the six dimensions of health, we found that the top-reported problem in NCC patients was cognitive impairment, showing that cognitive impairment is a prominent health problem for both first-visit and follow-up groups and implying that more attention should be paid to cognition problems in NCC. The risk of impaired cognitive ability increased with age. Risk of impaired cognitive ability was 16.33 times higher in the 45–59 age group compared to the 5–14 age group. Therefore, more attention should be paid to cognitive impairment in this age group, considering that cognition is a mainstay of productivity.

Disability weight is a critical parameter for estimating disease burden. Our study estimated DW at 0.3 in NCC patients through an assessment of quality of life, highlighting significant health loss in this population. Impaired memory is a cause of cognitive disorders (*7*), and we found significantly more memory impairment in the follow-up group than in the first-visit group. Since memory impairment is a key contributor to DW, this finding suggests that follow-up treatment did not improve the overall health status of NCC patients. Health education has been proved a robust intervention tool leading to knowledge improvement and improvement in community hygiene practices (*10*). Our study showed a poor quality of life in terms of six health dimensions measured in the standard EQ-5D assessment tool. Cognitive impairment was responsible for most health loss among NCC patients, calling for consistent health education in this population.

The study was subject to at least two limitations.

TABLE 2. Linear regression analysis of factors influencing EQ-VAS score.

Influencing factors	Partial regression coefficient	SE	*t*	*P*	Standardized coefficients
Intercept	87.44	2.94	29.72	<0.0001	
Age group (years)					
15–29	−1.39	3.47	−0.40	>0.05	−0.05
30–44	−0.33	3.43	−0.10	>0.05	−0.01
45–59	−0.09	3.48	−0.03	>0.05	0.00
≥60	−3.20	3.90	−0.82	>0.05	−0.07
Occupation	2.62	1.56	1.68	>0.05	0.10
Mobility	−0.38	3.43	−0.11	>0.05	−0.01
Self-care	−6.19	4.16	−1.49	>0.05	−0.08
Usual activity	−7.13	1.46	−4.88	<0.001	−0.27
Pain/discomfort	−6.97	1.50	−4.66	<0.001	−0.25
Anxiety/depression	−5.42	1.52	−3.56	<0.001	−0.20
Cognitive impairment	−9.12	1.65	−5.52	<0.001	−0.32

Abbreviations: EQ-VAS=European quality of life visual analogue scale; SE=standard error.

First, it was a retrospective study. There may have been recall bias in this face-to-face survey. Second, EQ-VAS records respondents' self-assessment of health status and may not be representative of the general population. Participants were recruited in Dali, which may not be representative of the entire NCC population. A large-scale study is needed to fully assess the NCC disease burden in China.

In conclusion, our study documented great health losses in NCC patients, with cognitive impairment being the most serious health outcome. Standardized treatment was not associated with improvement in cognitive impairment. Patients 45–59 years of age are at the highest risk of cognitive impairment. Strengthening health education targeted populations with a custom of eating raw pork may reduce the health impact of NCC in China.

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SUPPLEMENTARY TABLE S1. Clinical manifestations in NCC patients between first-visit group and follow-up group.

Group	No. of NCC patients	Epilepsy (%)*	Headache (%)†	Impaired memory (%)†	Muscle paresthesia (%)§	Eye discomfort (%)§
First-visit	84	46(54.76)	64(76.19)	44(52.38)	26(30.95)	12(14.29)
Follow-up	126	32(25.40)	79(62.70)	85(67.46)	37(29.37)	11(8.73)
Total	210	78(37.14)	143(68.10)	129(61.43)	63(30.00)	23(10.95)

Abbreviation: NCC=neurocysticercosis.
* P<0.001.
† P<0.05.
§ P>0.05.

SUPPLEMENTARY TABLE S2. Cognitive impairment in NCC patients among different age groups.

Age group (years)	n	No. with cognitive impairment (%)	β	P	OR
5–14	10	2(20.00)			
15–29	51	34(66.67)	2.08	<0.05	8.00
30–44	69	51(73.91)	2.43	<0.01	11.33
45–59	61	49(80.32)	2.27	<0.01	16.33
≥60	19	15(78.94)	2.71	<0.01	15.00

Abbreviation: NCC=neurocysticercosis.

Preplanned Studies

Surveillance and Response to Imported Malaria During the COVID-19 Epidemic — Anhui Province, China, 2019–2021

Tao Zhang[1]; Jingjing Jiang[1]; Xiaofeng Lyu[1]; Xian Xu[1]; Shuqi Wang[1]; Zijian Liu[1]; Jianhai Yin[2,#]; Weidong Li[1,#]

Summary

What is already known about this topic?

China was certified malaria-free on June 30, 2021. However, imported malaria continuously threatens the effort to prevent re-establishment of malaria in China.

What is added by this report?

Measures such as international travel restrictions, entry quarantine, and screening in fever clinics during the coronavirus disease 2019 (COVID-19) period were associated with a significant decrease of imported malaria cases in Anhui Province, a higher proportion of non-*Plasmodium falciparum* (non-*P. falciparum*) malaria reported infections, and a higher proportion of cases requiring medical attention at their initial visit.

What are the implications for public health practices?

It is necessary to be vigilant about imported malaria during the COVID-19 epidemic, especially for non-*P. falciparum* infections which are more difficult to detect, and to promote research, development, and introduction of more sensitive and specific point-of-care detection methods for non-*P. falciparum* species.

Malaria is one of the most serious global public health problems. In 2020, there was an estimated 241 million malaria cases, up from 227 million in 2019, and primarily due to health service disruptions during the coronavirus disease 2019 (COVID-19) pandemic (*1*). The World Health Organization (WHO) certified China as malaria-free on June 30, 2021 (*2*) — a great inspiration to progress in global malaria elimination, which had unfortunately stalled. Anhui Province is in the eastern part of China; local transmission of malaria in Anhui has been interrupted since 2014 (*3*). In May 2021, long-term work for malaria elimination in the province was evaluated and affirmed by an independent Malaria Elimination Certification Panel organized by the WHO. Presently, prevention of malaria re-establishment is the priority in the province. However, this effort faces serious challenges from the COVID-19 epidemic. In this paper, we reported a case-based retrospective study of surveillance and response to imported malaria in Anhui Province from 2019 to 2021, including the time of COVID-19, with the aim of providing evidence for refinement of strategies and development of targeted interventions.

Every suspected malaria case in China is mandatorily reported through the China Information System for Disease Control and Prevention (CISDCP). We extracted data on malaria cases reported in Anhui Province between January 1, 2019 and December 31, 2021 from CISDCP and the Information System for Parasitic Disease Control and Prevention. Extracted data included demographic, epidemiological, diagnostic information of cases, and indicators of malaria surveillance and response. Reported cases were divided into two groups — reported before (first stage) or reported after (second stage) January 24, 2020, when the first-level response to COVID-19 was launched in Anhui Province. We compared malaria surveillance and response data between the first stage (January 1, 2019 – January 23, 2020) and the second stage (January 24, 2020 – December 31, 2021). Normally distributed quantitative variables were presented as means and standard deviations, and categorical data were presented as percentages. Differences in proportions were tested for statistical significance using Pearson's chi-square (χ^2) test or Fisher's exact test, as appropriate. *P* values less than 0.05 were considered statistically significant.

There were 151 imported malaria cases reported in Anhui Province during the study period. The mean age was 44.0±10.3 years, and 148 cases (98.0%) were among males. There were 111 cases of *Plasmodium falciparum* (*P. falciparum*) infection and 36 cases of infection with other *Plasmodium* species including 4 *Plasmodium vivax* (*P. vivax*) cases, 24 *Plasmodium ovale* (*P. ovale*) *cases*, 8 *Plasmodium malariae* (*P. malariae*) cases, and 4 mixed infections (Figure 1). The number of imported malaria cases decreased from 98 in 2019 to 18 in 2021. The proportion of non-*P. falciparum* malaria increased from 17.3% in 2019 to 61.1% in 2021 (χ^2=16.065, *P*<0.001).

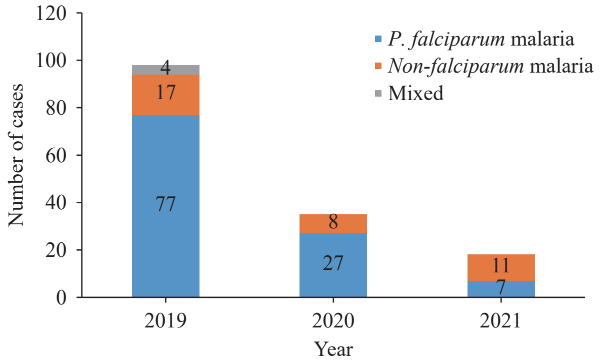

FIGURE 1. Imported malaria cases reported in Anhui Province, 2019–2021.

A total of 110 cases were reported in the first stage. The time between arrival in China to symptom onset was shorter in the first stage than in the second stage (χ^2=28.115, P<0.001). The percent of patients who received medical care during their first visit to a prefectural and county-level medical facility was 57.3% (63/110) in the first stage and 80.5% (33/41) in the second stage. Case profiles from onset to diagnosis were shown in Table 1.

The percentages of cases reported within 1 day, of epidemiological investigation performed within 3 days, and investigated and disposed of within 7 days were 100% (110/110), 95.5% (105/110), and 98.1% (102/104), in the first stage, respectively, compared with of 100% (41/41), 95.1% (39/41), and 100% (40/40) during the second stage. Among first-stage cases, 98.2% (108/110) were initially detected parasitologically, 85.5% (94/110) were accurately identified by *Plasmodium* species, and all were confirmed by both PCR and microscopy. In contrast, 100% (41/41) of second-stage cases were detected parasitologically and confirmed, but only 70.7% (29/41) were correctly identified by species, significantly lower than in the first stage (χ^2=4.286, P=0.038) (Table 2).

DISCUSSION

The COVID-19 pandemic has become one of the world's most important public health concerns. Many malaria symptoms are similar to COVID-19 symptoms. The epidemic has disrupted health service delivery and timely malaria detection, reporting, diagnosis, and treatment (*1*). As China adheres to its dynamic zero-COVID policy to tackle imported and domestic SARS-CoV-2 infections, several strict measures have been implemented across the nation

TABLE 1. Profile of imported malaria cases from onset to diagnosis in Anhui Province, 2019–2021.

Characteristics	First stage, n (%)	Second stage, n (%)	χ^2	*P*
Time from arrival in China to symptom onset			28.115	<0.001
≤30 days	102 (92.7)	23 (56.1)		
>30 days	8 (7.3)	18 (43.9)		
Time from onset to the first medical visit			0.016	0.901
≤3 days	93 (84.5)	35 (85.4)		
>3 days	17 (15.5)	6 (14.6)		
Time from the first medical visit to diagnosis			0.108	0.743
≤1 day	72 (65.5)	28 (68.3)		
>1 day	38 (34.5)	13 (31.7)		
Species			14.682	<0.001
P. falciparum	89 (84.0)	22 (53.7)		
Non-*P. falciparum**	17 (16.0)	19 (46.3)		
Level of medical facilities at the first medical visit			6.951	0.008
County or prefectural level	63 (57.3)	33 (80.5)		
Other†	47 (42.7)	8 (19.5)		
Diagnosis at the first medical visit			0.003	0.953
Other diseases	37 (33.6)	14 (34.1)		
Malaria	73 (66.4)	27 (65.9)		

* non-*P. falciparum* includes *P. vivax*, *P. ovale,* and *P. malariae*.
† medical facilities at provincial and township levels, and private facilities.

TABLE 2. Surveillance and response to imported malaria in Anhui Province, 2019–2021.

Stages	Case management			Laboratory detection		
	Reported within one day n (%)	Case investigation within three days n (%)	Focus investigation and action within seven days* n (%)	Parasite detection¶ n (%)	Species identification** n (%)	Rate of laboratory confirmation n (%)
First stage	110 (100.0)	105 (95.5)	102 (98.1)*,†	108 (98.2)	94 (85.5)	110 (100.0)
Second stage	41 (100.0)	39 (95.1)	40 (100.0)*,§	41 (100.0)	29 (70.7)	41 (100.0)
χ^2	NA				4.286	NA
P		1.000††	1.000††	1.000††	0.038	

Abbreviation: NA=not applicable.

* Focus investigation and disposal within seven days: calculated according to the number of the current address in Anhui province.

† A total of 104 foci in the first stage.

§ A total of 40 foci in the second stage.

¶ Parasite detection: calculated according to whether or not malaria parasites were detected initially.

** Species identification: calculated based on the number of correctly identified species.

†† Fisher's exact test.

that affect case management of imported malaria.

Our study found that the number of imported malaria cases decreased dramatically in Anhui Province during the study period, with only 18 cases reported in 2021 — a reduction of 81.6% compared to the 98 cases reported in 2019, which is similar to the national trend (*4–5*). This decrease is likely due to international travel restrictions. Therefore, after the COVID-19 epidemic subsides and international population movement resumes, there may be a sharp increase in imported cases. It is essential to formulate scientific emergency plans to ensure effective management of imported malaria.

The larger percent of imported cases of non-*P. falciparum* (especially *P. ovale*) malaria was different from earlier studies that showed most cases imported into Anhui to be *P. falciparum* infections of people returning from endemic African countries (*6*). The change in imported malaria type is potentially attributed to the 14-or-more day quarantine for COVID-19 upon entry to China, which facilitates detection and reporting of *P. falciparum* infection during the quarantine period in the port of entry (*7*). Non-*P. falciparum* species such as *P. vivax* and *P. ovale* have a dormant hypnozoite stage that can trigger multiple episodes of malaria with longer latency. Some infected individuals do not develop symptoms until a year after returning to China (*8*), resulting in most non-*P. falciparum* cases being less likely to be detected during the quarantine period but being found and reported after returning to Anhui Province. Non-*P. falciparum* cases require more sensitive detection techniques for early identification. It is worth noting that the species identification rate during the second stage was lower than in the first stage (70.7% *vs.* 85.5%). This was possibly caused by the increased proportion of imported malaria cases infected with non-*P. falciparum*, which is difficult to identify by light microscope owing to similarities in morphology, especially between *P. ovale* and *P. vivax* (*8*), and by malaria rapid diagnostic tests, which are most efficient for detection of *P. falciparum*. Therefore, more sensitive and specific point-of-care detection methods for non-*P. falciparum* species need to be developed and introduced.

We found that 80.5% of cases received care during the first medical visit at prefectural and county-level facilities in the second stage, which was higher than the 57.3% rate in the first stage. This may be due to prohibition of primary medical institutions from dealing with fever cases, instead referring them to medical institutions with standardized fever clinics during the COVID-19 period. This turned out to also be beneficial for prompt diagnosis and appropriate treatment of malaria cases, because it was found that misdiagnosis rates in the first medical visits at primary medical institutions were high (*9*).

Our study also evaluated the implementation of the "1-3-7" approach. This approach was developed in 2012 and has guided malaria elimination in China. It includes three steps: case reporting within 24 hours, case investigation within 3 days, and focus investigation and disposal within 7 days to reduce the risk of secondary local transmission (*10*). In the post-elimination phase, the "1-3-7" approach is still used as a core indicator to evaluate the quality of malaria surveillance and response activities in China. In our study, all cases were reported within 24 hours and all foci were investigated and disposed of within 7 days, but there were 2 cases whose investigation took longer than 3 days due to staff involvement in the COVID-19 response. In general, malaria surveillance and response during the COVID-19 epidemic in Anhui Province remained sensitive, however, it is necessary to pay attention to a reasonable allocation of human resources for disease control and prevention.

In summary, due to international travel restrictions, entry quarantine, and the use of fever clinics during the COVID-19 period, imported malaria cases in Anhui Province decreased significantly, but a higher proportion of non-*P. falciparum* malaria infections were reported and a higher proportion of cases received medical care at the first visit. It is necessary to be vigilant about imported malaria during the COVID-19 epidemic, especially for non-*P. falciparum* infections, which are more difficult to detect.

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