Vital Surveillances

Malaria Deaths — China, 2011–2020

Li Zhang[1]; Hong Tu[1]; Shuisen Zhou[1]; Zhigui Xia[1]; Jun Feng[1,2,#]

ABSTRACT

Introduction: The malaria deaths (MDs) caused by imported *Plasmodium falciparum* has become a great challenge. This article analyzed MDs in China in 2011–2020 to provide evidence-based data for further strategies and interventions adjustment.

Methods: Individual data via the National Notifiable Disease Reporting System (NNDRS) in 2011–2020 were collected. The *Plasmodium* species, case classification, temporal and spatial distribution, and source of MDs were analyzed to explore MD characteristics. The Parasitic Diseases Information Reporting Management System (PDIRMS) of MDs in 2013–2020 which explored clinical symptom and treatment was also collected and analyzed.

Results: A total of 165 MDs with a mortality rate of 0.5% were recorded in the NNDRS from 2011 to 2020. Among them, 164 (99.4%) died due to imported malaria cases, 1 (0.6%) died of indigenous case reported in Yunnan in 2013. The number of MDs showed a decreasing trend from 2011 (n=30) to 2020 (n=6). The MDs consisted of 160 (97.0%) *P. falciparum* cases, 1 (0.6%) mixed infection case, and 4 (2.4%) clinical diagnosed cases. The MDs were mainly reported in Guangdong (n=18, 10.9%), Sichuan (n=17, 10.3%), Beijing (n=15, 9.1%) and Henan (n=15, 9.1%). The PDIRMS had reported 121 MDs from 2013–2020, and 46.3% (n=56) of MDs exhibited severe brain damage, and most of the patients (n=95, 78.5%) were administrated by artemisinin combination therapy injection form.

Conclusions: The total MDs decreased in China, and a delay in diagnosis and treatment is the main causes of MDs. Therefore, two actions are needed to prevent MDs, including improving health education for key populations such as migrant workers who come to and return from endemic regions and maintaining malaria diagnosis and treatment capabilities of clinicians in medical facilities.

INTRODUCTIONS

China has eliminated indigenous malaria and reached this milestone for 4 consecutive years since 2017 (*1*–*2*). However, with globalization and economic integration, an increasing number of people come to or return from Africa and Southeast Asia, which also make imported malaria as a major challenge to malaria post-elimination stage in China (*3*–*5*). Severe malaria infections, or even fatalities, that are mainly caused by imported *Plasmodium falciparum* (*P. falciparum*), would be catastrophic if diagnosis and treatment could not be carried out promptly.

Therefore, the objective of this study was to characterize the epidemiological status of malaria deaths (MDs) and the clinical symptoms and treatments for deaths from 2011 to 2020, aiming to provide evidence-based data that could support the adjustment of appropriate control strategies and activities during the malaria post-elimination stage in China.

METHODS

Data from 31 provincial-level administrative divisions (PLADs) via the National Notifiable Disease Reporting System (NNDRS) were collected and carefully reviewed from January 1, 2011 to December 31, 2020. The NNDRS, which was set up in 2004 after the severe acute respiratory syndrome (SARS) outbreak, is a standardized platform that provides healthcare systems nationwide with the ability to detect, analyze, prevent, and respond to any communicable diseases in the country. The clinically diagnosed cases referred to individuals with malaria-related symptoms [fever (axillary temperature ≥ 37.5 °C), chills, severe malaise, headache, or vomiting] at the time of examination, and laboratory-confirmed cases referred to clinical cases confirmed by microscopy, polymerase chain reaction (PCR), or rapid diagnostic tests (RDT) in the laboratory, and both types of cases were included in this analysis. The clinical symptoms and treatments of all MDs from 2013 to 2020 were collected from the Parasitic Diseases Information Reporting Management System (PDIRMS). Data from Hong Kong, Macao, and

Taiwan were excluded in this study. Individual information including *Plasmodium* species, case classification, source of death cases, intervals from onset to diagnosis, intervals from onset to death, and treatment were used to analyze MD characteristics. The statistical analysis was evaluated by trend chi-squared tests (SPSS, version 21.0, IBM Corp.), and $P<0.05$ was considered as statistical significance.

RESULTS

A total of 165 MDs with a fatality rate of 0.54% were recorded in the NNDRS from 2011 to 2020 (Table 1). Among them, 164 (99.4%) MDs were due to imported malaria cases, and 1 death was an indigenous case (2013 in Yunnan). The number of MDs decreased from 2011 (n=30) to 2020 (n=6), a result which was statistically significant (evaluated by trend chi-squared test, $\chi^2=322.153$, $P<0.001$). The MDs consisted of 160 (97.0%) *P. falciparum* cases, 1 (0.6%) mixed infection case (2012 in Xinjiang), and 4 (2.4%) clinically-diagnosed cases. Most of the MDs (n=143, 86.7%) were reported in 22 endemic PLADs, and others (n=22, 13.3%) were reported in 5 non-endemic PLADs. The MDs were mainly reported in Guangdong (n=18, 10.9%), Sichuan (n=17, 10.3%), Beijing (n=15, 9.1%), and Henan (n=15, 9.1%) (Table 2). The distribution of MDs has been shrunken for reported cases from 14 PLADs in 2011 to 3 PLADs in 2020. The highest number of MDs was observed in the age group of 46 to 50 (n=32, 19.4%), followed by the age group of 40 to 45 (n=29, 17.6%). The highest number of MDs occurred in 2011 (n=30, 18.2%). The temporal distribution showed that MDs was reported throughout the whole year and monthly distribution showed that the highest number of MDs was reported in January (n=27, 16.4%) and February (n=23, 13.9%) (Figure 1). The MDs (n=156, 94.5%) were reported in hospitals and CDCs (n=9, 5.5%). In addition, the MDs were mainly reported by facilities at the prefecture level (n=95, 57.6%), at the provincial level (n=54, 32.7%), and at the county level (n=16, 9.7%). The average medium of interval from onset to diagnosis was 7 days, and the average medium of interval from onset to death was 8 days. Most of the MDs were from people of Chinese nationality (n=162, 98.2%).

The MDs due to imported cases were from 30 countries and 2 continents. Among them, 150 cases (90.9%) were from Africa and mainly from Central (n=59, 35.8%) and West Africa (n=47, 28.5%), including Angola (n=27, 16.4%), Nigeria (n=17, 10.3%), and Mozambique (n=10, 6.1%) (Table 3). For the MDs from Southeast Asia, they were mainly from Myanmar (n=8, 4.8%), Cambodia (n=1, 0.6%), and Indonesia (n=1, 0.6%).

TABLE 1. Malaria cases, deaths, and case-fatality rate reported in China (2011–2020).

Year	Total cases	Deaths	
		Total deaths	Case-fatality rate (%)
2011	4,450	30	0.67
2012	2,714	15	0.55
2013	4,137	21	0.51
2014	3,081	24	0.78
2015	3,277	21	0.64
2016	3,320	15	0.45
2017	2,861	7	0.24
2018	2,678	7	0.26
2019	2,674	19	0.71
2020	1,086	6	0.55
Total	30,278	165	0.54

The PDIRMS showed that among 121 MDs reported from 2013 to 2020, 46.3% (n=56) of them exhibited severe brain damage and 19.0% of them exhibited (n=23) severe liver and kidney damage. Most of the patients (n=95, 78.5%) were administrated by artemisinin combination therapy injection form.

DISCUSSION

Malaria mortality has declined over the past decades in China. The findings in this study revealed that most of the deaths were identified as imported malaria cases in returning migrant workers from Africa, and the findings were similar to a previously reported study (*6*). This result was consistent with expectations as *P. falciparum* was widespread in Africa, and Central and West Africa were the main source regions of imported deaths, which were regions with high disease burden of malaria mortality as reported by the World Health Organization (WHO) (*7*).

The interval from onset to diagnosis was 7 days in this study, which was longer than that reported in other non-endemic countries, whose median diagnosis delays were 4 or more days (*8*). Reasons that are likely to cause delays from onset to diagnosis are as follows. First, the patients failed to recognize the harm of malaria to the human body, which led to poor

TABLE 2. Malaria deaths in 31 provincial-level administrative divisions (PLADs) in China (2011–2020).

PLADs	Malaria endemicity	Total cases	Deaths		Proportion of deaths (%) in the whole country
			Total	Case-fatality rate (%)	
Guangdong	Endemic	1,686	18	1.07	10.9
Sichuan	Endemic	2,163	17	0.79	10.3
Henan	Endemic	1,903	15	0.79	9.1
Beijing	Non-endemic	769	15	1.95	9.1
Shandong	Endemic	1,702	13	0.76	7.9
Fujian	Endemic	880	11	1.25	6.7
Hunan	Endemic	1,298	9	0.69	5.5
Anhui	Endemic	1,645	8	0.49	4.8
Jiangsu	Endemic	2,797	7	0.25	4.2
Hubei	Endemic	1,248	7	0.56	4.2
Yunnan	Endemic	5,415	6	0.11	3.6
Liaoning	Endemic	460	6	1.30	3.6
Guangxi	Endemic	3,193	5	0.16	3.0
Chongqing	Endemic	290	5	1.72	3.0
Shanghai	Endemic	409	4	0.98	2.4
Hebei	Endemic	456	3	0.66	1.8
Jilin	Non-endemic	131	3	2.29	1.8
Zhejiang	Endemic	1,723	2	0.12	1.2
Xinjiang*	Endemic	63	2	3.17	1.2
Inner Monglian	Non-endemic	33	2	6.06	1.2
Shannxi	Endemic	606	1	0.17	0.6
Jiangxi	Endemic	399	1	0.25	0.6
Gansu	Endemic	203	1	0.49	0.6
Shanxi	Endemic	119	1	0.84	0.6
Hainan	Endemic	99	1	1.01	0.6
Tianjing	Non-endemic	92	1	1.09	0.6
Ningxia	Non-endemic	40	1	2.50	0.6
Qinghai	Non-endemic	17	0	0.00	0.0
Tibet	Endemic	30	0	0.00	0.0
Guizhou	Endemic	340	0	0.00	0.0
Heilongjiang	Non-endemic	69	0	0.00	0.0
Total	NA	30,278	165	0.54	100

* Xinjiang includes Xinjiang Uygur Autonomous Region and the Xinjiang Production and Construction Corps.

awareness of medical treatment. After the appearance of symptoms such as chills and fever, patients did not pay attention on them. They often obtained infusions in small clinics and even self-administered medication to relieve symptoms, which could lead to delays in diagnosis and treatment, worsen conditions, and even death. These factors were found in some MDs reported recently in Beijing, Sichuan, Shanghai, Jiangsu, and Shandong (*9*–*13*).

Second, the clinicians had insufficient experience in the diagnosis and treatment of malaria, and some of them did not take the initiative to ask the patient's epidemiological history, so patient who had symptoms of *P. falciparum* could not be promptly diagnosed. Third, low-level hospitals for first visits were also main factors influencing malaria deaths. In this study, 47.9% of MDs were first diagnosed in county-level hospitals or below, which need to be strengthened on capacity

TABLE 3. Source of imported malaria cases contributing to deaths reported in China, 2011–2020.

Regions	Country	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	Total
Africa		25	12	19	25	20	11	7	6	19	6	150
Southeast Africa		2	6	7	9	4	4	0	2	3	2	38
	Mozambique	1	0	3	3	0	2	0	0	0	1	10
	Uganda	0	0	2	1	3	1	0	0	1	1	9
	Tanzania	0	2	0	4	0	0	0	1	0	0	7
	Zambia	1	1	0	1	0	0	0	0	1	0	4
	Madagascar	0	2	0	0	1	0	0	0	0	0	3
	Malawi	0	1	0	0	0	0	0	0	1	0	2
	South Sudan	0	0	0	0	0	1	0	1	0	0	2
	Kenya	0	0	1	0	0	0	0	0	0	0	1
	Egypt	0	0	1	0	0	0	0	0	0	0	1
West Africa		9	2	4	7	6	2	3	4	7	3	47
	Nigeria	5	1	1	2	1	1	2	2	1	1	17
	Guinea	1	0	2	1	2	0	0	0	0	2	8
	Côte d'Ivoire	0	0	0	1	1	0	0	1	3	0	6
	Sierra Leone	0	1	0	0	1	0	1	1	2	0	6
	Ghana	1	0	0	2	0	1	0	0	1	0	5
	Benin	1	0	1	1	0	0	0	0	0	0	3
	Mali	1	0	0	0	0	0	0	0	0	0	1
	Mauritania	0	0	0	0	1	0	0	0	0	0	1
Central Africa		13	3	7	7	10	5	4	0	9	1	59
	Angola	8	1	6	2	4	1	2	0	3	0	27
	Cameroon	0	0	0	2	5	0	0	0	1	0	8
	Equatorial Guinea	3	0	1	0	0	1	0	0	2	0	7
	Democratic Republic of the Congo	0	0	0	0	1	3	2	0	0	0	6
	Republic of Congo	1	1	0	1	0	0	0	0	2	1	6
	Gabon	1	0	0	2	0	0	0	0	0	0	3
	Chad	0	1	0	0	0	0	0	0	0	0	1
	The Central African Republic	0	0	0	0	0	0	0	0	1	0	1
South Africa		0	1	0	1	0	0	0	0	0	0	2
	South Africa	0	1	0	1	0	0	0	0	0	0	2
Africa (Other regions)		1	0	1	1	0	0	0	0	0	0	3
Asia		3	3	1	1	1	0	0	1	0	0	10
Southeast Asia		3	3	1	1	1	0	0	1	0	0	10
	Myanmar	3	3	1	0	0	0	0	1	0	0	8
	Indonesia	0	0	0	1	0	0	0	0	0	0	1
	Cambodia	0	0	0	0	1	0	0	0	0	0	1
Unknown source		2	2	0	0	0	0	0	0	0	0	4
Total		30	17	20	26	21	10	7	7	19	6	164

building, particularity for malaria diagnosis and treatment. A study by Tu et al. has also proved this point by learning the experience and lessons on 16 MDs reported in China (*14*). Finally, most patients who were infected with *P. falciparum* were diagnosed with malaria abroad in private clinics had previously

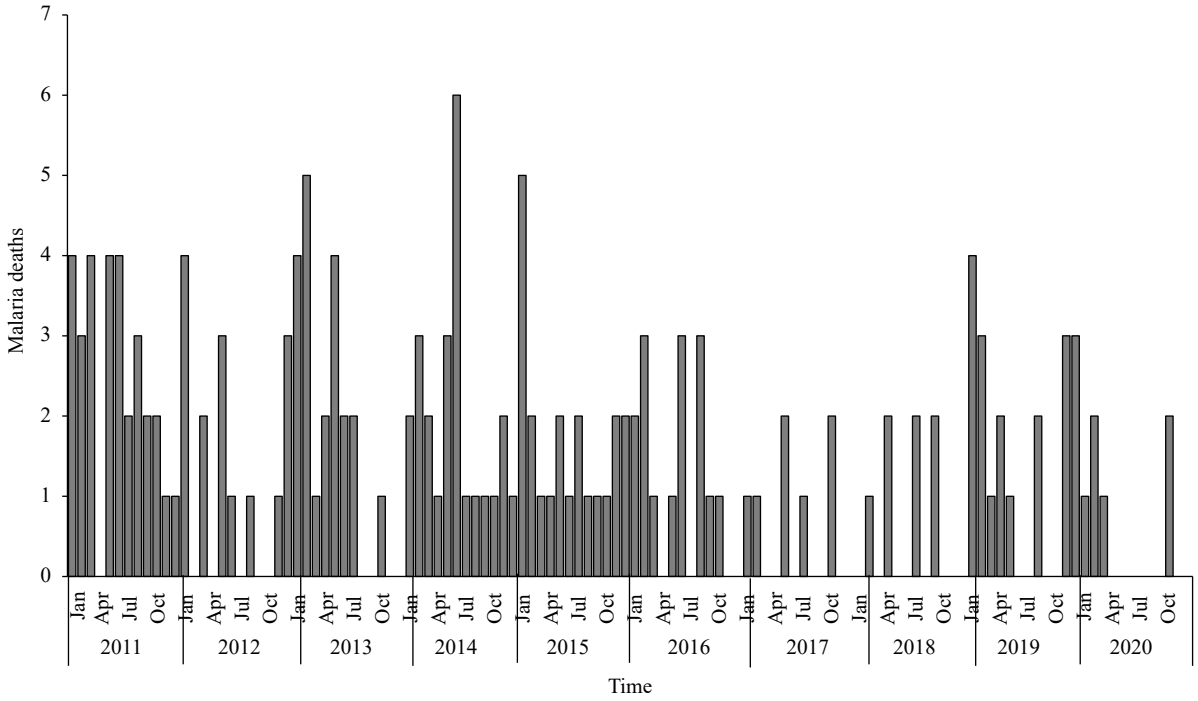

FIGURE 1. Temporal distribution of malaria deaths (MDs) in China, 2011–2020.

received improper treatments such as aspirin, which added the risk of recurrence of *P. falciparum* when they returned from African countries. This was similar to *P. vivax* and *P. ovale*. For example, in 2014, 78.6% of all imported *P. vivax* and *P. ovale* in Guangxi were individuals who had been given aspirin instead of antimalarial agents (*15*).

The results indicated that MDs occurred in returning migrant workers from January and February because most of the migrant population came back from abroad at this period due to the Chinese Spring Festival, and delays in diagnosis and treatment were the main causes of MDs. Since imported *P. falciparum* was now reported in every PLAD in China, timely detection, proper treatment, and deaths prevention caused by imported *P. falciparum* were major challenges faced by post-elimination stage in China. Therefore, some strategies and interventions should be carried out as follows: 1) health education through cooperation with customs and CDCs for the targeted populations such as migrant workers who come to and return from endemic regions; 2) maintain malaria diagnosis and treatment capabilities of clinicians in medical facilities above county levels, especially in the COVID-19 prevention and control process since both malaria and COVID-19 harbored the same clinical symptom at the initial onset stage; and 3) improve the ability to treat severe malaria cases. Expert panels at the national and provincial level could use these recommendations derived from tracking the reasons for MDs and provide suggestions for preventing MDs caused by imported malaria.

The study was subject to some limitations. Not all MDs were well recorded with the exact epidemiological information in 2011–2020. The study still has 5 unknown MDs imported from abroad. In addition, not all MDs were confirmed in the laboratory as 4 clinically diagnosed cases were found in this study.

Acknowledgement: Provincial and county-level CDCs in China.

Conflict of interest: No conflicts of interest were reported.

Funding: The key techniques in collaborative prevention and control of major infectious diseases in the Belt and Road (2018ZX10101002-004)

doi: 10.46234/ccdcw2021.098

[#] Corresponding author: Jun Feng, fengjun@nipd.chinacdc.cn.

[1] National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention (Chinese Center for Tropical Diseases Research); NHC Key Laboratory of Parasite and Vector Biology; WHO Collaborating Centre for Tropical Diseases; National Center for International Research on Tropical Diseases, Shanghai, China; [2] School of Global Health, Chinese Center for Tropical Diseases Research, Shanghai Jiao Tong University School of Medicine, Shanghai, China.

Submitted: March 16, 2021; Accepted: April 19, 2021

REFERENCES

1. Feng J, Zhang L, Huang F, Yin JH, Tu H, Xia ZG, et al. Ready for malaria elimination: zero indigenous case reported in the People's Republic of China. Malar J 2018;17(1):315. http://dx.doi.org/10.1186/s12936-018-2444-9.
2. Feng J, Zhou SS. From control to elimination: the historical retrospect of malaria control and prevention in China. Chin J Parasitol Parasit Dis 2019;37(5):505 – 13. http://dx.doi.org/10.12140/j.issn.1000-7423.2019.05.001.
3. Feng J, Xia ZG, Vong S, Yang WZ, Zhou SS, Xiao N. Preparedness for malaria resurgence in China: case study on imported cases in 2000-2012. Adv Parasitol 2014;86:231 – 65. http://dx.doi.org/10.1016/B978-0-12-800869-0.00009-3.
4. Feng J, Tu H, Zhang L, Xia ZG, Zhou SS. Vital surveillances: imported malaria cases —China, 2012–2018. Chin CDC Wkly 2020;2(17):277 – 84. http://dx.doi.org/10.46234/ccdcw2020.072.
5. Feng J, Xiao HH, Xia ZG, Zhang L, Xiao N. Analysis of malaria epidemiological characteristics in the People's Republic of China, 2004-2013. Am J Trop Med Hyg 2015;93(2):293 – 9. http://dx.doi.org/10.4269/ajtmh.14-0733.
6. Zhang Q, Geng QB, Sun JL, Zhang ZK, Lai SJ, Zhou S, et al. Epidemiological analysis of the deaths of malaria in China, 2005-2014. Chin J Prev Med 2016;50(4):302 – 5. http://dx.doi.org/10.3760/cma.j.issn.0253-9624.2016.04.004. (In Chinese).
7. World Health Organization. World malaria report 2020. Geneva: World Health Organization. 2020. https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2020.[2020-11-30].
8. Bastaki H, Carter J, Marston L, Cassell J, Rait G. Time delays in the diagnosis and treatment of malaria in non-endemic countries: a systematic review. Travel Med Infect Dis 2018;21:21 – 7. http://dx.doi.org/10.1016/j.tmaid.2017.12.002.
9. Song YG, Ji AP, Wang F, Ren J. Epidemiological and clinical features of imported malaria cases in Beijing. Chin Trop Med 2013;13(2):198 – 200,203. http://dx.doi.org/10.13604/j.cnki.46-1064/r.2013.02.029. (In Chinese).
10. Xu GJ, Kang Y, Lai Q, Lei Y. Death due to imported falciparum malaria: 4 cases. Chin J Parasitol Parasit Dis 2006;24(3):165. http://dx.doi.org/10.3969/j.issn.1000-7423.2006.03.023. (In Chinese).
11. Li Y, Zou PP, Lu L, Jin LF. One death due to imported falciparum malaria in Fengxian of Shanghai. Chin J Parasitol Parasit Dis 2010;28(2):88. (In Chinese).
12. Jia CY, Yang WZ, Wang WM, Tang Y. Analysis of two cases of malaria death in Huai'an. Chin Trop Med 2018;18(7):675 – 7. http://dx.doi.org/10.13604/j.cnki.46-1064/r.2018.07.11. (In Chinese).
13. Liu SZ, Ji FY, Li XK, Dou XJ. A case of malaria death in Qingdao, 2018. Chin Trop Med 2019;19(6):600 – 2. http://dx.doi.org/10.13604/j.cnki.46-1064/r.2019.06.25. (In Chinese).
14. Tu H, Feng J, Zhang L, Zhang SS, Xia ZG, Zhou SS. The analysis of deaths due to malaria in China, 2016. Chin Trop Med 2018;18(7):650 – 3. http://dx.doi.org/10.13604/j.cnki.46-1064/r.2018.07.05. (In Chinese).
15. Lin KM, Wei HY, Jiang WK, Li J, Zhang WW, Wei SJ, et al. Malaria in the Guangxi Zhuang Autonomous Region in China: a twelve-year surveillance data study. Am J Trop Med Hyg 2017;97(4):1163 – 9. http://dx.doi.org/10.4269/ajtmh.16-0260.