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Status of *Plasmodium vivax* malaria in the Republic of Korea, 2008–2009: decrease followed by resurgence

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ABSTRACT

The number of *Plasmodium vivax* malaria cases in the Republic of Korea (ROK) in 2008 was 1009, a 54.2% decrease on the previous year. It then resurged to 1317 cases in 2009 (30.5% increase on 2008). One possible cause for the sharp decrease in 2008 might be the large-scale presumptive anti-relapse therapy with primaquine that was undertaken in the Democratic People's Republic of Korea in 2007. Of the 2326 cases of *P. vivax* malaria diagnosed in the ROK during 2008–2009, 599 cases (25.8%) were military personnel, 535 cases (23.0%) were veterans, and 1192 cases (51.2%) were civilians. Local transmission within the ROK appeared to increase gradually, and the length of the transmission period of *P. vivax* malaria extended during this period. Parasite clearance time after chloroquine treatment has increased in the late 2000s, which requires the introduction of countermeasures against the decreasing chloroquine susceptibility, including reduction of mass chemoprophylaxis with chloroquine in the ROK Army.

1. Introduction

Malaria is one of the most important parasitic diseases in the world, and of the four species of *Plasmodium* that infect humans *P. vivax* is the second most prevalent next to *P. falciparum*. While *P. falciparum* malaria occurs mainly in tropical and subtropical areas, *P. vivax* malaria is also found in temperate areas.[1] The Korean peninsula is the only temperate area where indigenous *P. vivax* malaria has occurred continuously and on a large scale.[2]

Plasmodium vivax malaria was endemic in the Korean peninsula for many centuries until the Republic of Korea (ROK; South Korea) was declared a 'malaria elimination' country in 1979.[3] *Plasmodium vivax* malaria re-emerged in 1993 in the ROK, and has remained endemic for nearly 20 years.[4–7] During the early period after the re-emergence, military personnel accounted for most annual cases,[4,8]

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however, civilian cases have gradually increased and have accounted for more than half of the total annual cases since 2003.[5–8] Although local transmission has increased in the ROK after 2000,[5–7] *P. vivax* malaria in the ROK has been directly influenced by areas of the Democratic People's Republic of Korea (DPRK; North Korea) that are adjacent to the demilitarized zone (DMZ), the border area between the two Koreas.[4–7]

The ROK government has undertaken various efforts to reduce *P. vivax* malaria cases, including mass chemoprophylaxis with hydroxychloroquine and presumptive anti-relapse therapy with primaquine (15 mg daily for 14 days) in the ROK Army since 1997, education programs for healthcare personnel in the civilian sector, and the provision of materials for malaria control to the DPRK via the World Health Organization.[8,9] As a result of these efforts, the number of *P. vivax* malaria cases decreased for four consecutive years after 2000,[5,6] however, there has been a resurgence in *P. vivax* malaria since 2005.[6,7] The nearly 20-year presence of *P. vivax* malaria since its re-emergence in the ROK tells of the continual failure of chloroquine prophylaxis in military personnel.[10] Chloroquine-resistant *P. vivax* malaria cases were recently reported in the ROK;[11] it is therefore important to monitor and analyze the status of *P. vivax* malaria in the ROK on an ongoing basis.

We collected a variety of epidemiologic data including the annual number of *P. vivax* malaria cases among military personnel, veterans, and civilians in the ROK, the mean daily incidence for each consecutive 10-day interval, the geographic distribution of cases among military personnel and civilians, the parasite clearance rates after chloroquine treatment in civilian patients, and the number of *Anopheles* mosquitoes detected in one of the malaria-risk areas in the ROK from 2008 through 2009. These data were used to analyze the epidemiological characteristics of *P. vivax* malaria in the ROK during 2008–2009.

2. Materials and methods

Malaria is classified as a group III communicable disease in the ROK. Cases detected in private hospitals and clinics are reported to local public health centers operated by the national government. The case definition of malaria includes any febrile illness with demonstration of *P. vivax* parasites in peripheral blood smears.[3] Each case report usually contains the patient's name, age, sex, address, date of onset of illness, date of malaria diagnosis, and the possible area where infection occurred. Data collected in public health centers are sent to the Division of Infectious Disease Surveillance (DIDS) at the Korea Centers for Disease Control and Prevention (KCDC). Most of the cases reported through this system are civilians and veterans, although soldiers who are diagnosed while on vacation may also be included. The DIDS directly contacts every reported patient to obtain exact epidemiological information, so any incorrect information reported by hospitals and clinics is usually corrected.

All malaria cases among military personnel must be reported to the Korean Armed Forces Medical Command and the Korean Ministry of National Defense. The Korean Armed Forces Medical Command sends military malaria data to DIDS at KCDC.

Cases among military veterans were defined as those who had a malaria attack within 24 months of discharge from military service, and who had been stationed in a malaria-risk area. Veterans stationed outside of malaria-risk areas were classified as civilians because it is almost certain that they were not infected during their military service but via some other route, based on the fact that malaria incidence outside of the risk areas is just marginal.

All reported cases were classified as civilian/veteran/soldier, and the exact numbers of reported cases were finalized by DIDS at KCDC.

The annual geographic distribution of *P. vivax* malaria in ROK military personnel, veterans, and civilians was determined by the location where they were stationed or where they lived when the diagnosis was made. The seasonal change in malaria incidence was analyzed by dividing each month into three intervals, i.e. from first to 10th (early), from 11th to 20th (mid), and from 21st to the last day of the month (late). The number of days included in the late intervals varies from 8 to 11 days depending on the number of days in the month. For fair comparison of such uneven intervals, data were presented in terms of mean daily incidence that was calculated by dividing the total number of cases during an interval with the number of days included in the interval.

Numbers of *Anopheles* mosquitoes were monitored using a black light trap in Cheolwon County, one of the high malaria-risk areas in the ROK, during the malaria transmission seasons of 2008 and 2009. Trapping was conducted twice a week on Tuesdays and Thursdays in 2008, and every day in 2009. Trapping time was between 18:00 h and 06:00 h on the following day from May until October in both years. A trap was set up at the same location and the length of trapping time was kept constant to ensure consistency. *Anopheles* mosquitoes were separated morphologically and counted regardless of blood-fed status or sporozoite content. The average of the daily numbers of trapped *Anopheles* mosquitoes was taken as a representative value of the week.

Parasite clearance rates were observed among civilian patients with *P. vivax* malaria who were admitted to five different civilian hospitals located in Goyang City or Incheon Metropolitan City, parts of the malaria-risk areas in the ROK, from 2003–2009. The numbers of observed patients from 2003–2009 were 71, 37, 63, 107, 91, 37 and 32, respectively. All patients were initially given 800mg of hydroxychloroquine and 400mg given 6, 24, 48 hours after the initial dose. Microscopic examinations were performed 24 hours after completion of chloroquine treatment to determine the clearance of asexual cycle parasites.

Annual parasite incidence (API; number of microscopically proven malaria cases/1000 population/year) of the civilian malaria cases from 2007–2009 were calculated. Risk ratios were calculated between 2007–2008 and 2008–2009. Statistical significance of the trend in the proportion of patients in whom asexual parasites were cleared 24 hours after the completion of chloroquine treatment over time during 2003–2009 were tested using χ^2 test