

STUDY OF MALARIA CASES AMONG SEAFARERS IN CROATIA AND THE CAUSES OF INEFFECTIVE CHEMOPROPHYLAXIS AMONG THEM

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Abstract. Introduction: Malaria in Croatia was endemic until 1954, when the last autochthonous cases were reported. Now we have imported cases and the disease still most commonly affects seafarers and workers temporarily employed in malaria endemic countries.

The aim of this study was to investigate ineffective malaria chemoprophylaxis among Croatian seafarers.

Materials and methods: This study used the data collected by questionnaires that followed every imported case of malaria in Croatia. In addition, a survey was conducted among the seafarers attending the Special education program at the Faculty of Maritime Studies in Split, regarding their attitudes / reasons for not using chemoprophylaxis using a short questionnaire.

Results: From the 1st January 2007 to 31st December 2019 there was a total of 108 imported malaria cases in Croatia, of which 22 (20.37%) referred to seafarers. In situations reporting the information whether the infected seafarers used chemoprophylaxis, twenty seafarers (91% of the overall infected) responded that they had not used chemoprophylaxis, while two of them (9.0%) responded that they had used it incorrectly.

Conclusion: It appears that the main reason for avoiding chemoprophylaxis is the fear of side-effects. Some of the respondents, particularly the young ones, stated that they were not vaccinated – which is a proof of ignorance, as the vaccine does not exist. How to familiarise and motivate maritime students and seafarers to participate actively in protection against malaria – this is an issue that is important not only in Croatia but, presumably, in other countries as well.

Keywords: malaria; seafarers; chemoprophylaxis

Introduction

Malaria is a major international public health problem. 91 countries reported an estimated 216 million infections and 445,000 deaths in 2016, according to the World Health Organization (WHO) World Malaria Report 2017. Globally, there were an estimated 229 million malaria cases in 2019 in 87 malaria endemic

countries, declining from 238 million cases recorded in 2000¹⁾. Travellers going to malaria endemic countries are at risk of contracting the disease, and almost all of the approximately 1700 cases per year of malaria in the United States are imported (Tan et al. 2021). Although many studies have shown a significant reduction in morbidity from infectious diseases in recent years, malaria still remains one of the major health problems related to seafarers² (Palotta et al. 2019).

Malaria transmission occurs in large areas of Africa, Latin America, parts of the Caribbean, Asia (including south Asia, Southeast Asia, and the Middle East), and the South Pacific. The estimated number of malaria cases in international seafarers may be between 2000 and 3000 each year; and fatalities among them are reported. This has been an important health problem for seafarers and preventive interventions are essential² (Tan et al. 2021).

The risk for acquiring malaria differs substantially from traveller to traveller and from region to region, even within a single country. This variability is a function of the intensity of transmission within the various regions and the itinerary, duration, season, and type of travel. Risk also varies with travellers' adherence to mosquito precautions and prophylaxis recommendations² (Tan et al. 2021).

Human malaria is primarily caused by four species of *Plasmodium*: *Plasmodium falciparum*, *Plasmodium malariae*, *Plasmodium ovale* and *Plasmodium vivax*. Occasionally, malaria in humans can be caused by *Plasmodium knowlesi*ⁱⁱⁱ (Palotta et al. 2019; Mulić et al. 2000). Among these, the most lethal is *Plasmodium falciparum*, with the highest mortality rate among infested subjects, and mainly widespread in Sub-Saharan Africa^{1,2} (Tan et al. 2021).

Malaria is characterized by fever and influenza like symptoms, including chills, headache, myalgias, and malaise; these symptoms can occur intermittently. In severe disease, seizures, mental confusion, kidney failure, acute respiratory distress syndrome, coma, and death may occur. Malaria symptoms can develop as early as 7 days after being bitten by an infectious mosquito in a malaria-endemic area and as late as several months or more after exposure. Suspected or confirmed malaria, especially *P. falciparum*, is a medical emergency requiring urgent intervention, as clinical deterioration can occur rapidly and unpredictably² (Tan et al. 2021).

The case of Croatia

Since 1964, when the World Health Organization declared Croatia a “malaria free” country, there have been a number of imported cases, some of which transmitted by Croatia's seafarers. Given the fact that the country is still home to a malaria-transmitting mosquito, Croatia has introduced a continuous monitoring of the travellers arriving from malaria affected endemic areas (Mulić et al. 2000; Perić et al. 2009; Aleraj 2008), in addition to the law on the protection of the population from infectious diseases. Reporting malaria disease is mandatory in the Republic of Croatia.

Prevention

The recommended prevention includes education, general mosquito bite protection and chemoprophylaxis. Preventing malaria involves striking a balance between effectiveness and safety: ensuring that all people at risk of infection use the recommended prevention measures and preventing rare occurrences of adverse effects.

As malaria and other diseases are spread by mosquito bites, the Center for Disease Control and Prevention (CDC) recommends that travellers take mosquito avoidance measures. These measures include using insect repellent when outdoors, wearing protective clothing, staying in an air-conditioned or well-screened area, and sleeping under an insecticide-treated bed net (Tan et al. 2021; Kurečić et al. 2018).

The reason for giving priority to prevention rather than treatment lies in the fact that malaria can be lethal even when treated. Preventive measures are obligatory for persons who have recovered from the illness. In Croatia, all travellers are offered individual consultation with an epidemiologist in order to assess the risk of visiting a destination and seek advice on prevention. Individual counselling is available at the local branches of Croatian Institute of Public Health (Kurečić et al. 2018).

Risk assessment of the exposure to malaria

An individual's exposure to malaria depends on the amount of bites of malaria-carrying mosquitos. The factors affecting the amount of infected mosquitoes include temperature, altitude and season. Environment temperatures ranging from 20 to 30°C are considered as optimal for the transmission of malaria. Maturing of parasites in mosquitoes does not usually occur at altitudes above 2000 m, although this may happen at altitudes up to 2500 m in some countries. Rainy seasons encourage the reproduction of mosquitoes and in some regions, malaria is mainly a seasonal disease. The risk of infection also depends on the very area: the incidence rate is typically higher in rural than in urban areas, especially in Africa where the transmission rate is, on average, about 8 times higher in villages than in towns.

If the accommodation is not air-conditioned, people should use impregnated nets (treated with pyrethroids) above beds. People in poorer accommodation facilities are at higher risk of exposure to mosquito bites than people in better, air-conditioned facilities.

It is useful to apply mosquito repellents to the clothing and on skin. Travellers camping in tents should use a combination of mosquito repellents and fine-mesh screens. When outdoors, the risk is higher between dusk and dawn, as this is the time when female *Anopheles* mosquitoes, which transmit the malaria parasite, bite.

General protective measures against mosquitoes

Due to nocturnal activity of *Anopheles* mosquitoes, the transmission of malaria typically takes place at night (from dusk to dawn). Therefore, one should:

- Fit the windows and doors with anti-mosquito mesh;
- Protect the bed with a net against mosquitoes;
- Stay in air-conditioned rooms;
- Wear clothes with long sleeves and legs;
- Use repellents (when using sun cream at the same time, first apply the sun cream then the repellent);
- In addition to the repellent applied on the skin, products containing permethrin can be applied to the bed net and clothing.

Chemoprophylaxis

All recommended primary prophylaxis regimes involve taking a medicine before, during, and after travel to an area with malaria. Taking the drug before travel allows the antimalarial agent to be in the blood before the traveller is exposed to malaria parasites. The medications recommended for prophylaxis of malaria may be available at overseas destinations. However, combinations of these medications and additional drugs that are not recommended may be commonly prescribed and used in other countries^{1,2}.

Nowadays there are a number of antimalarials, so the choice of drug may vary with a number of factors: length of travel, activities, drug resistance in a specific area, age, and so on. Therefore, an individual medical consultation is advised prior to travelling.

Generally speaking, medicines used for malaria chemoprophylaxis are well tolerated but, as with other drugs, side-effects may appear. In case of mild side-effects, there is no need for stopping the chemoprophylaxis, but in the event of serious side-effects, a doctor should be consulted for changing the regimen. No antimalarial drug achieves 100% protection against malaria, but personal protection measures in combination with chemoprophylaxis increase the level of safety.

The goal of this paper was study of malaria cases among seafarers in Croatia and the causes of ineffective chemoprophylaxis among them.

Methods and materials

This study used the data collected by questionnaires that followed every imported case of malaria. The data have been obtained from the Epidemiological service of the Croatian Institute for Public Health.

From 1st June 2020 to 31st December 2020, a survey was conducted among the seafarers attending the Special education program at the Faculty of Maritime Studies in Split, regarding their attitudes / reasons for not using chemoprophylaxis. The authors of this study created a short anonymous questionnaire, explained its purpose to the respondents and received their approval. The questionnaire was filled in on voluntary basis, there were no conditions. 71 seafarers agreed to complete the questionnaire. 58 among them met the necessary requirement for taking part in the research: sailing to malaria-affected endemic areas over the previous year. The question about taking

chemoprophylaxis referred to their last voyage to malaria-affected endemic areas (Central and South Americas, the Caribbean, Africa, Asia). We wanted to find out why the seafarers did not use chemoprophylaxis or used it irregularly. In addition to gathering basic socio-demographic data, we asked the seafarers:

1. Do you sail on inter-continental routes, including South America, Asia and Africa?
2. Have you ever been ill with malaria (proven case)?
3. Do you use chemoprophylaxis regularly when sailing to malaria-affected endemic areas?
4. Do you use chemoprophylaxis irregularly when sailing to malaria-affected endemic areas?
5. Who recommends you to take a specific drug?
 - Recommendation / proposal of the shipping company
 - Recommendation of the Epidemiological service of Croatian Institute for Public Health
 - Recommendation of the occupational medicine specialist.
6. In case of not taking chemoprophylaxis, the following reasons were offered:
 - a) I am not afraid that I will get ill with malaria
 - b) Taking drugs is more dangerous than getting malaria
 - c) Taking chemoprophylaxis causes damage to the liver
 - d) Taking chemoprophylaxis adversely affects male potency
 - e) I am concerned for my health as these drugs should be taken continuously
 - f) Sometimes I take the medicines, sometimes I forget
 - g) No special reason, but I don't want to take medicines
 - h) Those medicines do not protect against malaria anyway
 - i) Because I have been vaccinated.
7. Did you read the instructions on the use of the antimalarial medicine? The following responses were offered:
 - a) Yes, I did, thoroughly.
 - b) No.
 - c) Not thoroughly.
 - d) My colleagues shared their experience / attitude with me.

All respondents were male, their age ranging from 28 to 59 (see Table 1).

Table 1. Sociodemographic indicators of the surveyed seafarers

	M	F	%	median
Gender	58	0		
Age	28-59			48.3
Work experience at sea, in years	8-31			24.5

Married / single	51/7			
Officers	58			
Ratings	0			
Malaria in anamnesis	1		1,7%	

Results

From the 1st January 2007 to 31st December 2019 there was a total of 108 imported malaria cases in Croatia, of which 22 (20.37%) referred to seafarers. All infected seafarers contracted the disease along the shores of West Africa (Angola, Guinea, Equatorial Guinea, Ghana, Sierra Leone), and the infection was largely caused by *Plasmodium falciparum*, with two cases where a mixed infection was recorded: *P. falciparum* and *P. vivax* (see Table 2).

Table 2. Imported cases of malaria in Croatia, period 2007-2019

Vocation / exposure conditions	N	%	Taking chemoprophylaxis				Causative agent (confirmed)	Destination
			Regularly	Irregularly	NO	No data		
Seafarer	22	20.37	0	2	18	2	<i>P. falciparum</i> <i>P. falciparum</i> + <i>P. vivax</i>	Angola, Guinea, Equatorial Guinea, Ghana, Sierra Leone
Work abroad (including children and family members, 4 in total)	49	45.37	5	7	33	4	<i>P. falciparum</i> <i>P. malariae</i> <i>P. vivax</i> <i>P. ovale</i> Mixed infections	Sub-Saharan Africa Peru
Military mission	2	1.85	2	-	-	-	<i>P. falciparum</i>	Sierra Leone
Tourism	28	25.93	2	2	23	1	<i>P. falciparum</i> <i>P. malariae</i> <i>P. vivax</i> Mixed infections	Sub-Saharan Africa Peru
Unknown / no data	7	6.48	4	3	1	1	<i>P. falciparum</i>	Nigeria Sudan Congo
TOTAL	108	100.00	13	14	75	8		

One fifth of the imported cases refer to the seafaring population. It is interesting to note that, out of 108 imported cases, not a single one comes from Asia, while

just one case refers to South America (Peru). These data were obtained through anonymous questionnaires, and were therefore liable to errors, deviations and modifications of responses provided by the respondents who had experienced malaria.

Most of the sick seafarers did not take chemoprophylaxis or used it irregularly. Those who had been ill with malaria could not be subsequently surveyed again, due to technical reasons, but we had the opportunity to examine the attitude and behaviour of the seafarers who, during the period indicated above, attended the Special education program at the Faculty of Maritime Studies in Croatia.

The survey was conducted from 1st June 2020 to 31st December 2020. The seafarers were given a short anonymous questionnaire to be completed on voluntary basis. There were no conditions, the seafarers were familiar with the objective of the research and they gave their consent for using the gathered data. 71 seafarers agreed to complete the questionnaire.

The responses of 58 seafarers – those who sailed in malaria-affected endemic areas – were considered. The research did not consider the responses of 12 seafarers in coastal trade in the Adriatic Sea, and the responses of 1 seafarer who regularly used chemoprophylaxis in compliance with his epidemiologist's recommendations. Out of 58 seafarers who sailed in malaria-affected endemic areas, one got sick with malaria. Most of the respondents took chemoprophylactic drugs that were offered by the shipping company.

As for not using chemoprophylaxis, the seafarers were offered nine explanations of which they could select more than one – Table 3.

Table 3. State the reasons for not taking chemoprophylaxis or for taking it irregularly

Answer to question No. 6. Please explain why you did not use chemoprophylaxis against malaria	Number of respondents	%
a) I am not afraid that I will get ill with malaria	8	13.8
b) Taking drugs is more dangerous than getting malaria	3	5.2
c) Taking chemoprophylaxis causes damage to the liver	45	77.6
d) Taking chemoprophylaxis adversely affects male potency	48	82.8
e) I am concerned for my health as these drugs should be taken continuously	48	82.8
f) Sometimes I take the medicines, sometimes I forget	22	37.9
g) No special reason, but I don't want to take medicines	42	72.4
h) Those medicines do not protect against malaria anyway	37	63.8
i) Because I have been vaccinated	3	5.2
Total respondents	58	
Total responses	256	

58 respondents provided a total of 256 responses, which implies that each respondent selected 4 out of 9 explanations on average.

We were interested in how the respondents developed their viewpoints regarding chemoprophylaxis, and how they were informed about it (see Table 4).

Table 4. Answer to the question: Did you read instructions on using the antimalarial drug?

Possible answer	N	%
Yes, thoroughly	3	5.2
b) No	51	87.9
c) Not thoroughly	7	12.1
d) My colleagues and acquaintances shared their experience / attitude with me	53	91.4

Again, the question allowed multiple responses, so that 114 responses were obtained from 58 respondents. And again, the responses revealed a passive attitude: most of the respondents acquired their attitude and information about antimalarial medicines from their colleagues and acquaintances, whose attitude was negative. Only 5% of the respondents actually read the instructions on using the antimalarial drug. This corresponds to the results of our previous studies where the seafarers' passive attitude towards health issues was identified (Russo et al. 2020).

Discussion

The analysis of the reported malaria cases in the seafaring population revealed that the most common reason for getting malaria was failure to take chemoprophylaxis, irregular use of chemoprophylaxis or using inadequate medicine as chemoprophylaxis.

It was not clear why the seafarers avoid using malaria chemoprophylaxis.

The authors of this study tried to find the answer through a survey. Although the sample of the surveyed seafarers was limited (58), the respondents produced relevant and indicative answers.

This study used the data collected by questionnaires that followed every imported case of malaria, also. The data have been obtained from the Epidemiological service of the Croatian Institute for Public Health.

However, the drawback of this procedure is that the questionnaires were not always completed in a correct way.

As a rule, all passengers and seafarers are advised to use malaria chemoprophylaxis if they travel in malaria endemic areas. Ship management companies must provide chemoprophylaxis for their seafarers. Irregular or non-existent application of

chemoprophylaxis is the cause of contraction of imported malaria (Mulić et al. 2000; Aleraj 2008).

The World Health Organization observes the resistance of *Plasmodium* species to antimalarial drugs and is well familiar with the distribution of this phenomenon across the endemic regions in the world. For instance, resistance to chloroquine is widespread in Africa and Asia, so that using this drug will not result in protection against malaria there^{1,2} (Tan et al. 2021).

Although there is no written proof, it turns out that shipping companies meet their chemoprophylaxis requirements by offering the cheapest medicines to their employees. As a rule, causal agents are resistant to those medicines. This information was disclosed through informal talks with the seafarers who stated the name of the medicine offered by the company. The results / responses in this survey reveal the seafarers' fear of possible side-effects ("taking chemoprophylaxis causes damage to the liver"; "taking chemoprophylaxis adversely affects male potency"; "I am concerned for my health as these drugs should be taken continuously") but also their passive attitude, reflected in the fact that they obtained most information about chemoprophylaxis from their colleagues and acquaintances, not from professional services or, at least, by reading the instructions included in every medicine package.

Due to the nature of their work, seafarers cannot avoid malaria risk areas. That is why the right prevention and surveillance must be considered mandatory onboard ships navigating in endemic zones².

Malaria is a maritime problem for the following reasons: unawareness of the fact that malaria is a serious and potentially fatal disease; insufficient information regarding the clinical picture of malaria; lack or insufficient use of anti-mosquito measures and the classical protective medication; increasing resistance of many new malaria strains to the medication; the fluctuating frequency of malaria occurrence in the most dangerous areas, which leads to miscalculation of the real risk.

Even if the risk seems small, a brief visit to a country where malaria is endemic may be sufficient to contract the disease. It is important to note that even frequent travel to endemic areas does not convey useful immunity against malaria².

Compared to the period before 2007, it can be noted that the percentage of malaria-affected seafarers has decreased (Mulić et al. 2000; Aleraj 2008). The reasons may include a shorter stay / exposure or an increased tourist travel over the last years (before COVID 19 pandemic). The information on the overall Croatian seafarers who have been ill with malaria cannot be completed – due to the nature of their work and life, it is likely that not all malaria-affected seafarers have been recorded. In case of illness, they are treated in the nearest adequate health facility. However, the number of seafarers who have got ill with malaria because they had failed to use chemoprophylaxis is a matter of concern.

When responding to the question "Did you read the instructions on the use of the antimalarial medicine?", the seafarers once again confirmed their passive

attitude: most of the respondents acquired their attitude and information about antimalarial medicines from their colleagues and acquaintances whose attitude was negative. Only 5% of the respondents actually read the instructions on using the antimalarial drug. This corresponds to the results of our previous studies where the seafarers' passive attitude towards health issues was identified (Russo et al. 2020).

The results of the survey reveal the poor health awareness in seafarers (at least as far as malaria is concerned) and their passive attitude towards health issues.

Conclusions

Therefore, in Croatia at least, the possibility of additional efforts of the occupational medicine specialists should be considered, as they are in direct contact with the seafarers during their necessary health checks. We believe that these specialists should advise the seafarers on taking necessary measures against malaria. It is hard to expect that a seafarer, in addition to the bulk of administrative and other obligations prior to boarding, would seek advice on the needed and suitable chemoprophylaxis on his/her own, from the dedicated epidemiological service of the Croatian Institute for Public Health.

NOTES

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