Journal of Infectious Diseases & Therapy

Coulibaly, J Infect Dis Ther 2023, 11:7

Mini-Review Open Access

An Insight into Imported Malaria in Canada: Travellers Visiting Family/Friend and Originated from Sub-Saharan Africa Perspectives

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Received: 07-Nov-2023, Manuscript No. JIDT-23-119400; **Editor assigned:** 10-Nov-2023, Pre QC No. JIDT-23-119400(PQ); **Reviewed:** 24-Nov-2023, QC No. JIDT-23-119400; **Revised:** 01-Dec-2023, Manuscript No. JIDT-23-119400(R); **Published:** 08-Dec-2023, DOI: 10.4172/2332-0877.1000572

Citation: Coulibaly KS, Hawkes M, Gnidehou S (2023) An Insight into Imported Malaria in Canada: Travellers Visiting Family/Friends and Originated from Sub-Saharan Africa Perspectives. J Infect Dis Ther 11:572.

Abstract

Malaria caused by *Plasmodium (P.) falciparum* is the deadliest parasitic disease worldwide and Sub-Sahara Africa (SSA) where this species is prevalent is the most affected region. Promoted by population movements, Imported Malaria (IM) is a growing public health issue in many industrialized non-endemic countries including Canada. Despite being largely treatable and preventable, travellers Visiting Friends/Relatives (VFR) and originated from malaria endemic areas, especially from SSA, accounted for a significant portion of IM cases in Canada. While the number of immigrants originally from SSA and the number of IM cases have been increasing across Canada for the last decade, studies focusing on the trend of IM cases and disease management among immigrants from SSA and particularly VFR from SSA (VFRSSA) are limited.

Keyword: Imported malaria; Canada; Immigrants VFR; Sub-Saharan Africa; Prevention measures; Research priority

Abbreviations IM: Imported Malaria; P: *Plasmodium*; SSA: Sub-Saharan Africa; VRF: Visiting Friends and Relatives; VFRSSA: Visiting Friends and Relatives from Sub-Saharan Africa

Introduction

Travel-related malaria or Imported Malaria (IM) refers to malaria infection acquired in a malaria-endemic setting and diagnosed in a non-endemic region [1]. Increased travel and migration lead to a heightened risk of IM cases resulting in an average of 30,000 IM cases in non-endemic regions globally [2]. This makes IM a growing public health threat in several industrialized non-endemic countries. Globally, SSA, where the most lethal infecting species P. falciparum is prevalent, is the region where most travellers contract malaria [3-8]. Moreover, strong pieces of evidence have highlighted that the "Visiting Friends and Relatives" (VFR) traveler (immigrant who is ethnically and/or racially distinct from the majority population in their current country of residence and who returns to their homeland to visit friends and relatives) from or returning from travel to the tropics and particularly SSA, accounted for approximately 50% and 90% of annual IM cases and severe cases respectively [3,6,9-12].

Canada has experienced a steady growth of immigrants originating from SSA. While several studies have reported an increase in the number of IM cases since the end of the 1980s and demonstrated the high risk among VFR travellers from SSA (VFRSSA), [4,13,14], further research is needed to characterize this unique population and identify strategies that will help to reduce the incidence and improve the management of IM across the country.

Here we discuss the data from studies on IM cases among VFRSSA. We discuss the lack of compliance to appropriate preventive measures against malaria among a unique population, French-speaking VFRSSA residing in a minority language setting. Finally, we define research gaps and consider priorities to better raise awareness of preventive measures in VFRSSA populations and improve the management of IM in Canada.

Literature Review

Epidemiology of IM among VFRSSA in Canada

Research focusing mainly on the epidemiology of IM within immigrants originating from SSA is scarce. When available, many studies combined either data from all VFR [3,6,15], or all newcomers and refugees [3,6], originating from SSA, Latin America and Southeast Asia. Other studies combined VFRSSA results from European and North American countries [8,16]. Moreover, while some studies did not report the proportion of VFRSSA among the number of travellers who were positive for malaria infections [6], others lacked the stratification of data based on the purpose of travel [4,17,18].

Yet, some studies conducted in Ontario, Quebec, Saskatchewan, Alberta and British Colombia provided insight into IM in VFRSSA. Few studies have demonstrated that regardless of the province, a high proportion of malaria infections among VFR were VFRSSA (Table 1) [5,7,13,19]. The relative proportion of malaria-positive VFRSSA ranged from 35% [13] to more than 70% [5,7,20]. Countries including

Ghana, Nigeria [1,7,9], Ivory Coast and Cameroon [7,9] were identified as the most likely sources of malaria exposure, with the greatest number in Ghana (up to 22%) and Nigeria (up to 20%). Males were more affected than females [5,7] Most importantly, all studies have found that P. falciparum accounted for more than 85% of IM cases in this group of travellers.

Children under 5 years old are at particular risk of severe malaria infections [21]. VFR travellers also include children of foreign-born parents (second-generation immigrants) who return to their parents' homeland to visit friends and relatives [16]. In Canada, children represent 15 to 20% of IM cases and are more likely to die compared to adults [21,22]. Since P. falciparum is the most lethal cause of malaria in SSA, complicated and severe malaria cases have been reported among VFRSSA and their children in Canada. Studies conducted in Ontario, Quebec, Manitoba, Saskatchewan, Alberta, and British Columbia (Table 1) have found that P. falciparum accounted for 75% to 94% [1,7,9] of IM cases among VFRSSA and their children. Fifty-six percent and 85% of malaria-positive VFRSSA were adult males and children, respectively. While severe malaria was globally overrepresented among children under 5 years old [23,24], two studies have demonstrated that severe malaria affected both adult VFRSSA (average of 33 years old) and child VFRSSA of various ages (children under 18 years old and children with a median age of 6.7 years old) [1,9]. Interestingly, the highest frequency was identified in VFRSSA originated from Ghana (12-22%) Nigeria (11-20%), Cameroon (7%) and Uganda (7%). Ontario, which has the highest proportion of immigrants originating from Ghana and Nigeria, has the highest number of severe malaria cases across the country. This is consistent with studies that showed that Ghana and Nigeria were the top destinations of VFRSSA who were diagnosed with positive malaria infections (Table 1).

Study site	[a]Sample size	Percent (%) of malaria positive		Region or country of exposure	*Plasmodium* species (%)c	Diagnosis	Distribution category (%)d	References
		VFR	bVFRSSA					
Quebec	n=157	53	85%	SSA	*P. falciparum* (86.4)	Malaria	Male (68) children < 20 yr, (16.9)	[20]
Quebec	n=92	25.5	32.5	SSA	*P. falciparum* (84.8), *P. ovale* (5.4), *P. malariae* (4.3)	Malaria	Male	[13]
Quebec Ontario Manitoba Alberta British Colombia	n=437	38.7	78.7	Nigeria	*P. falciparum*	Malaria	Male	[7]
Alberta	n=219	49.7	79.7	SSA	*P. falciparum*	Malaria	Male Children <16 yr	[5]
Ontario	n=104	46	51	Ghana Nigeria Ivory Coast	*P. falciparum* (71)	Severe malaria	Children	[1]
Quebec Ontario Manitoba Saskatchewan Alberta British Colombia	n=248	65	91	Ghana Nigeria Cameroon Uganda	*P. falciparum* (94)	Severe malaria	Adult male (56) Children <18 yr (18)	[9]

Note:aSamples that were diagnosed positive for or malaria; bBased on the percent of VFR; c*Plasmodium* species percentage; dPercent were indicated when available in the original article.

Abbreviations: P: *Plasmodium*; VFR: Visiting Family and Relatives; SSA: Sub-Saharan Africa; Yr: Years

Table 1: Distribution of Imported Malaria among VFRSSA.

While no deaths were noted among VFRSSA (adults and children) presenting with severe malaria, studies have observed that 25% of them were hospitalized. As expected, children were hospitalized more frequently than adults (73% versus 62%) [1,9].

Lack of appropriate adherence to preventive measures against IM in VFRSSA populations

For travellers from North America, preventive measures against malaria include awareness of malaria exposure, seeking pre-travel medical advice and using appropriate preventive chemoprophylaxis. However, preventive care provided in Canada to VFRSSA seems to not be paying off. While 67% of VFRSSA (adults and children) with P. falciparum severe malaria infections have not sought pre-travel visits [1], only 23% of VFRSSA reported taking chemoprophylaxis [9]. In addition, we have recently demonstrated that only 48% of francophone VFRSSA residing in Edmonton, a predominantly English-speaking city, have booked a pre-travel medical consultation before travelling. Chemoprophylaxis was taken by only 37% of travellers and of this, 59% was prescribed by a health professional in Canada [25].

Several studies have suggested that non-compliance with pre-travel malaria preventive measures among VFR is multifactorial [6,22,26]. These factors include overestimation of prior immunity, costs associated with visiting travel clinics, advice, drug prescription, the opportunity to access a pharmacy for cheaper antimalarial without prescription when febrile during the stay in endemic areas, level of education, lack of knowledge and malaria risk assessment, language barrier, lack of healthcare coverage, cultural beliefs, and most importantly, lack of trust in malaria-related knowledge and the ability of Canadian physicians to efficiently manage IM. We have reported

that although 65% of francophone VFRSSA had a personal or familial past malaria history and a high perceived risk of contracting malaria in SSA (95%), a large proportion (42%) of them travelled and stayed in SSA for more than 30 days without malarial precautions. Of note, no significant associations were found between language barrier and having had a pre-travel consultation or using preventive measures upon arrival [25]. While one study has reported the geographic and individual determinants of malaria incidence in Ontario [17], those characterizing the determinants of uptake of pre-travel malarial prevention methods among VFRSSA are scarce.

Delays in post-travel presentation for medical care

A prompt diagnosis of IM is the cornerstone of effective management [21]. Several diagnostic modalities are available, including microscopy, malaria Rapid Diagnosis Tests (mRDTs), and Polymerase Chain Reaction. However, before these diagnostic tools can be applied, an important question is the timing of the patient's assessment after developing symptoms post-travel. Barriers to prompt diagnosis may arise at the level or the traveller or the health system.

Among VFRSSA travellers, we have previously found that, despite being well-educated (76% of them had a post-secondary degree), recognizing fever as the main symptoms of the disease (97%), and knowing that malaria is a lethal disease, approximately 22% of francophone VFRSSA still didn't inform their physician about a trip to SSA or go to hospital emergency/family doctor when they or their child was febrile. Furthermore, although 83% of francophone VFRSSA found that access to medical treatment was easy and 77% were satisfied with the care they previously received, only 39% of them had confidence in the healthcare system's ability to treat malaria effectively [27].

VFRSSA with mild symptoms after travelling may not seek medical attention, which may lead to a delayed diagnosis [28]. To develop tailored intervention strategies, more community outreach activities focusing on specific tropical diseases in the SSA community are needed. Such studies should include SSA community leaders, students in medicine, health practitioners and knowledge users.

With respect to health system barriers, a lack of recognition of malaria may lead to delayed diagnosis. A previous study in Canada found that the diagnosis of malaria was initially missed in 59% of cases [22]. The average delay before treatment was 7.6 days for P. falciparum malaria and 5.1 days for P. vivax malaria [22]. Clinicians in Canada may not be familiar with malaria, including variations in the clinical presentation. For example, although fever is a key symptom of malaria, only 40% of children with IM had a fever documented in the emergency room in one previous study [1]. Systematic diagnosis of malaria using an appropriate diagnosis method should be encouraged in all VFRSSA if they develop symptoms compatible with malaria post-travel.

Canadian physicians may not be up to date on emerging challenges to malaria diagnosis and treatment, including hrp2/hrp3 mutant parasites which escape detection by mRDTs, and resistance to commonly used antimalarial medications. Furthermore, the epidemiology of malaria continues to evolve. While P. falciparum is classically recognized as the dominant pathogen in most SSA countries, there is growing evidence of acute P. vivax autochthonous cases across SSA regions among Duffy-negative blood group 3 [29-32]. Contrary to P. falciparum, P. vivax displays a dormant liver form that can cause clinical relapses after several months and requires accurate species-level diagnosis [33].

Future research priorities

Although knowledge related to IM has expanded, there remain many gaps. More research is needed among VFRSSA, given the strong association between IM and the SSA region, the increased number of immigrants originating from this region in Canada, and the fact that many VFRSSA do not adopt preventive recommendations against IM. Studies of IM in immigrants originating from SSA across Canada are required to better study the trend of the epidemiology of IM cases, provide specific IM incidence and characterize the determinants of pre-travel visits and the use of chemoprophylaxis in this specific population.

This mini-review was limited by the fact that only studies with detailed precision on the frequency of IM, the severity of the diseases and information on pre-travel precautions within the VFRSSA population were included. Nevertheless, it shows the relevance of studying VFRSSA and research priorities worth pursuing.

Conclusion

Collectively, in terms of IM, VFRSSA results that were discussed in this mini-review reveal that exposure to P. falciparum in SSA places VFRSSA at high risk. VFRSSA represent a group that need careful surveillance. In minority settings, factors other than education, risk assessment, knowledge of fever as malaria symptoms and language might impact compliance with the pre-travel medical visits.

Acknowledgment

We thank Dr. Stan Houston for his valuable comments on this manuscript.

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