



Étude rétrospective des infections pédiatriques à *Plasmodium non falciparum* sur la période 2011-2023

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Déclaration de liens d'intérêt avec les industriels de santé
en rapport avec le thème de la présentation (loi du 04/03/2002) :

L'orateur ne
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☐

- **Intervenant** : NOM Prénom
- **Titre** : Intitulé de l'intervention

- Consultant ou membre d'un conseil scientifique ☐ OUI ☒ NON
- Conférencier ou auteur/rédacteur rémunéré d'articles ou documents ☐ OUI ☒ NON
- Prise en charge de frais de voyage, d'hébergement ou d'inscription à des congrès ou autres manifestations ☐ OUI ☒ NON
- Investigateur principal d'une recherche ou d'une étude clinique ☐ OUI ☒ NON



Déclaration d'intérêt de 2014 à 2025

- Intérêts financiers : Non
- Liens durables ou permanents : Non
- Interventions ponctuelles : Intervention Gilead (2022-2023)
- Intérêts indirects : Non

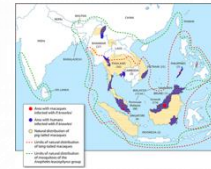
Epidémiologie, espèces de *Plasmodium* spp. responsables d'accès palustre

D'après les données de l'OMS

- ❖ 2024 : 282 millions de cas de paludisme, soit +9 millions (+3 %) par/à 2023.
- ❖ 2024 : 610 000 décès dus au paludisme, vs 598 000 en 2023 (+2%).
- ❖ Région africaine 95 % de l'ensemble des cas et des décès dus au paludisme

P. knowlesi

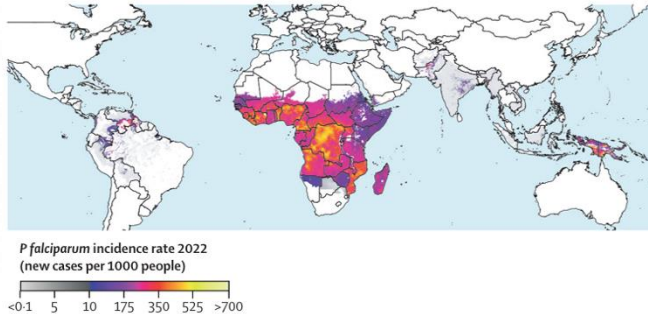
2 164 cas en 2024 (88% en Malaisie)



Répartition géographique et incidences

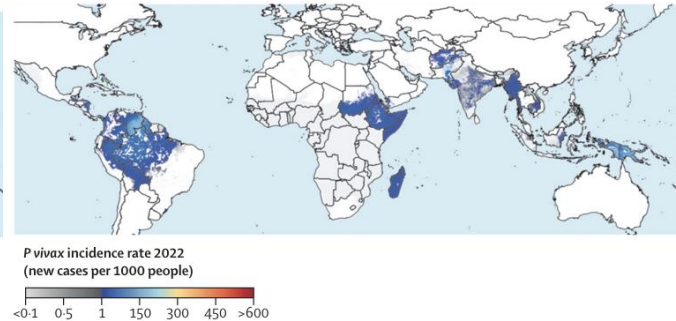
P. falciparum

244.4 (188.1–308.5) nouveaux cas par an (millions)



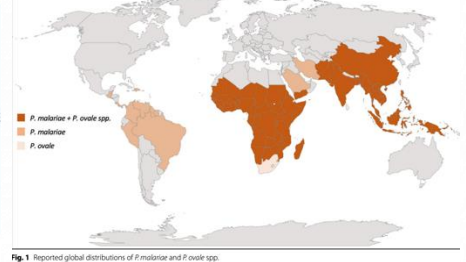
P. vivax

12.4 (10.7–14.8) nouveaux cas par an (millions)



P. ovale et *P. malariae*

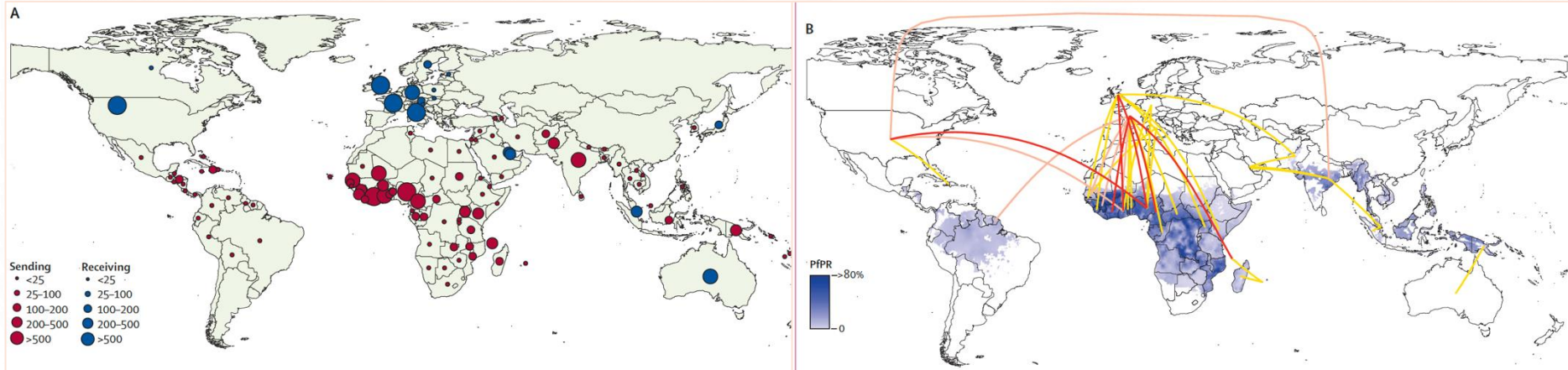
2.01% et 0.77% des cas totaux



Paludisme d'importation dans le monde

Meta analyse évaluant plus de 50 000 cas issus de 40 pays non endémique, 2005-2015

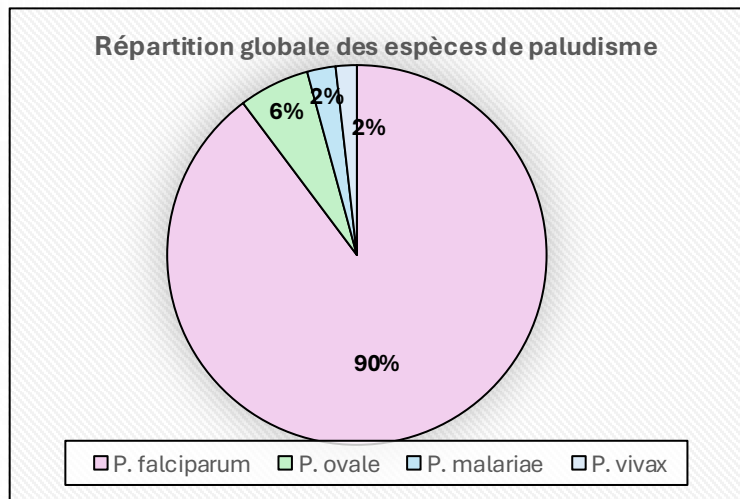
Afrique de l'Ouest 56%, France et UK : 4000 cas par an chaque année,



Epidémiologie, espèces de *Plasmodium* spp. responsables d'accès palustre

En France, rapport CNR: + 7% par rapport à 2022

Répartition globale des espèces de paludisme importés en France, CNRP, 1996-2016



Les enfants <5 ans = 75 % de l'ensemble des décès dus au paludisme en Afrique

Les enfants représentent environ 15 à 20 % de l'ensemble des importations

Reference	Plasmodium species					
	<i>P. falciparum</i>	<i>P. vivax</i>	<i>P. ovale</i>	<i>P. malariae</i>	Mixed	Unknown
Minodier et al ⁸	72%	9%	3%	2%	9%	5%
Ladhani et al ⁹	91%	6%	2%	0%	1%	0%
Parez et al ¹⁰	73%	2%	5%	4%	16%	0%
Begue et al ¹¹	77%	13%	0%	1%	1%	8%
Eloy et al ⁶	84%	5%	7%	0%	2%	2%
McCaslin et al ¹⁴	100%	0%	0%	0%	0%	0%
Huerga and Lopez-Velez ¹²	71%	2%	4%	4%	10%	9%
Miller and Banerji ¹⁵	7%	88%	0%	0%	0%	5%
Lynk and Gold ¹⁶	38%	60%	2%	0%	0%	0%
Rivera-Matos et al ¹⁷	56%	23%	0%	3%	0%	18%

Case series with fewer than 30 children were excluded. For year of study, location, and number of cases see tables 1 and 2.

Table 3: *Plasmodium* species in children with imported malaria

Qu'en est il des cas de paludisme d'importation à *P. non falciparum* chez l'enfant ?

Objectif: Caractéristiques des enfants atteints d'accès palustre à *P. non falciparum* en France

Objectif principal : caractériser les infections causées par les *Plasmodium* non *falciparum* et de comparer les cas dus à *P. ovale sensu lato*, *P. vivax* et *P. malariae*.

L'objectif secondaire : comparer ces infections aux infections à *P. falciparum*.
Appariement 1:1 (sur l'année d'infection, l'âge et le sexe).

Critères d'inclusion

- ❖ Cas pédiatriques (âgés de 0 à 18 ans) d'accès palustre à *Plasmodium* non *falciparum* survenus en France hexagonale
- ❖ Déclarés au Centre National de Référence du Paludisme
- ❖ Entre 2011 et 2023.

Critères d'exclusion

- ❖ *P. falciparum*
- ❖ Infection mixte
- ❖ Sans diagnostic d'espèce



Résultats

30626 cases of *Plasmodium* spp. declared to the French NRC for malaria
January 2011 - December 2023

25758 adults were excluded

4868 cases in children (0 - 18 years-old)

Were excluded
-4,138 cases of *Plasmodium falciparum*
-117 mixed infections
-17 cases not confirmed by the CNR
-15 cases without species diagnosis

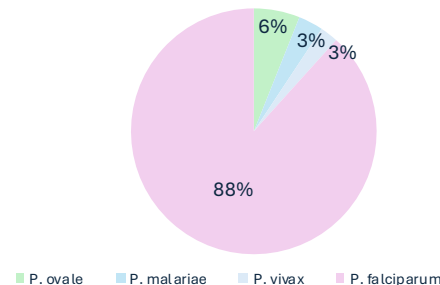
548 pediatric cases of *Plasmodium non-falciparum* in 531 patients

284 cases of *Plasmodium ovale* sensu lato included

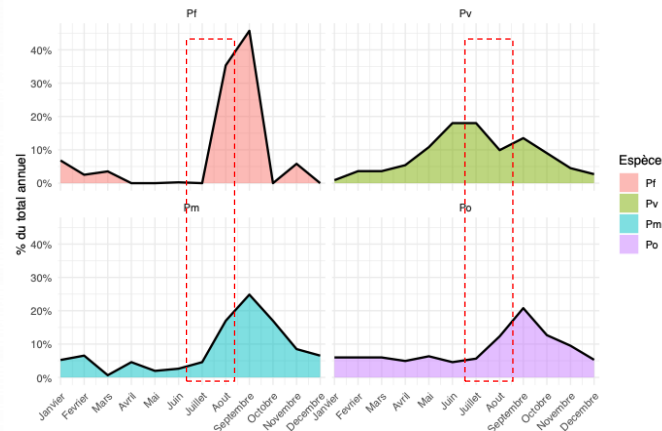
153 cases of *Plasmodium malariae* included

111 cases of *Plasmodium vivax* included

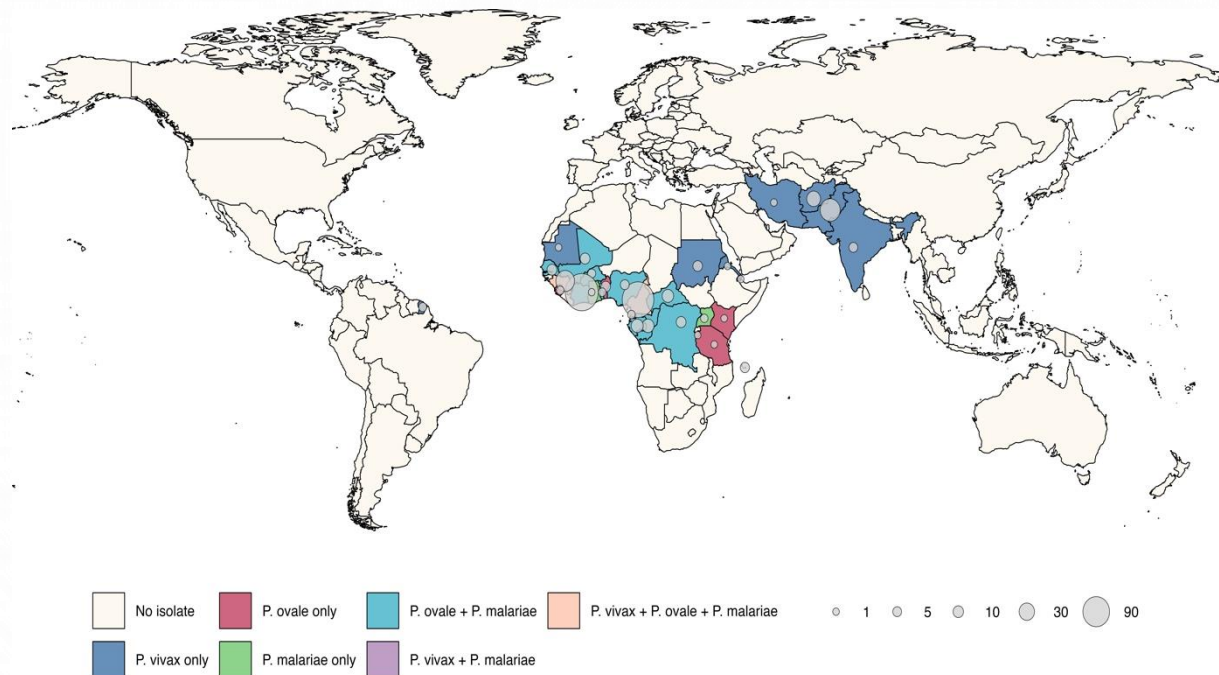
Répartition des cas d'accès palustre chez l'enfant



- Sex ratio MF= 1,7
- Enfants > 5ans : 88,7 %
- La plupart des cas déclarés pendant l'été.



Résultats



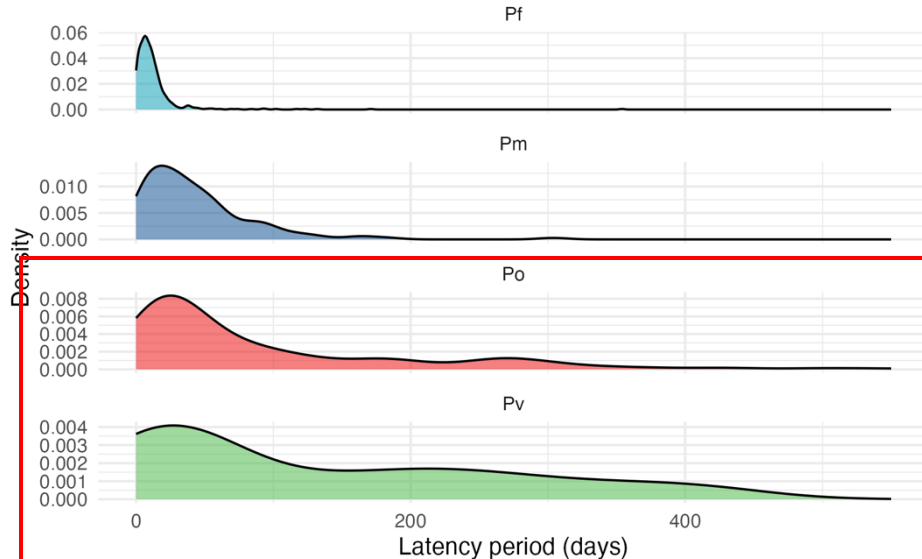
~ 85 % des patients
avaient voyagé en Afrique
P. vivax, principalement
en provenance du
Pakistan ou d'Afghanistan

Résultats

Variable		P. ovale (n=284)	P. vivax (n=111)	P. malariae (n=153)	p	P. non falciparum	P. falciparum	p
Parasitémie, M [IQR]		0.1 [0.3]	0.3 [0.5]	0.14 [0.3]	<0.001	0.15 [0.3]	1 [2.3]	<0.001
Parasitémie, catégorie, n ()	<0.1	63 (30.4)	12 (13.8)	32 (29.6)		107 (26.6)	63 (13.1)	
	[0.1-0.5]	122 (58.9)	51 (58.6)	60 (55.6)		233 (58.0)	127 (26.4)	
	(0.5-1]	16 (7.7)	14 (16.1)	13 (12.0)		43 (10.7)	67 (13.9)	
	>1	6 (2.9)	10 (11.5)	3 (2.8)	0.0015	19 (4.7)	224 (46.6)	<0.001
Plaquettes (G/L), M [IQR]		128 [79.5]	109 [76.8]	168 [86]	<0.001	135 [91.3]	125.5 [114.8]	NS
Plaquettes <50G/L, n ()		10/270 (3.7)	13/112 (11.6)	4/138 (2.9)	0.011	27 (5.2)	62 (12.2)	
Globules blancs (G/L), M [IQR]		5.5 [2.2]	5.1 [2.6]	5.7 [2.8]	NS	5.5 [2.6]	6.42 [3.3]	<0.001
Hémoglobine (g/L), M [IQR]		110.5 [21]	117.5 [23]	108 [22]	<0.001	111 [23]	113 [26]	NS
Fièvre, n ()	Oui	205 (99)	77 (97.5)	104 (99)		386 (98.7)	390 (95.6)	
	Non	2 (1)	2 (2.5)	1 (1)	NS	5 (1.3)	18 (4.4)	NS
Céphalées, n ()	Oui	121 (68.4)	28 (57.1)	48 (55.8)		197 (63.1)	214 (63.1)	
	Non	56 (31.6)	21 (42.9)	38 (44.2)	NS	115 (36.9)	125 (36.9)	NS
Délai de latence*, M [IQR]		44 [107]	70 [205]	33 [46.3]	<0.001	42 [98.5]	9 [9]	<0.001
Délai diagnostic**, M [IQR]		4 [6]	4 [5.3]	7 [11]	0.003	5 [7]	3 [4]	<0.001
Type d'accès, n ()								
	Accès simple sans v ^t	203 (74.1)	67 (63.8)	108 (72)		378 (71.5)	273 (51.5)	
	Accès simple avec v ^t	57 (20.8)	36 (34.3)	30 (20)		123 (23.3)	165 (31.1)	
	Accès grave	4 (1.5)	2 (1.9)	0	0.0012	6 (1.1)	79 (14.9)	<0.001
Prise en charge	Ambulatoire	114 (44.9)	23 (24.2)	60 (44.4)		197 (40.7)	127 (24.9)	
	Hospitalisation	140 (55.1)	72 (75.8)	75 (55.6)	0.001	287 (59.3)	383 (75.1)	<0.001

Résultats : les reviviscences

Distribution des délais de latence par espèce



		Latence < 50 jours	Latence > 50 jours	Test statistique
P. ovale sensu lato	N	110	107	/
	Plq	134.5 [81.5-170.2]	121 [90-161.5]	NS
	% plq < 150	61.8% (68/110)	69.2% (74/107)	NS
P. vivax	N	39	47	/
	Plq	120 [99-154.5]	88 [66-134]	0.026
	% plq < 150	69.2% (27/39)	80.9% (38/47)	NS

Résultats, cas graves

Résumé sur le paludisme grave à *P. non falciparum*

ID Patient	Diagnostic	Comorbidités	Caractéristiques cliniques ou radiologiques graves	Caractéristiques biologiques graves	Plaquettes (G/L)	Évolution
S2 – Femme, 4 ans	<i>P. vivax</i> 1 %	Aucune	Aucun	Anémie sévère (Hb = 4,3 g/dL)	194	Survie
S3 – Homme, 8 ans	<i>P. ovale</i> 0,3 %	Drépanocytose	Ictère clinique	Anémie sévère (Hb = 4,9 g/dL) Bilirubine sérique élevée (83,4 mmol/L)	557	Survie
S1 – Homme, 10 ans	<i>P. ovale</i> 0,3 %	Drépanocytose	Coma (Glasgow = 4) Ictère clinique Détrousse respiratoire aiguë Hémorragie pulmonaire	Anémie sévère (Hb = 4,2 g/dL) Hyperlactatémie (7,13 mmol/L) Bilirubine sérique élevée (695 mmol/L)	117	Décès
S4 – Homme, 15 ans	<i>P. ovale</i> 0,3 %	Aucune	Aucun	Bilirubine sérique élevée (98 mmol/L)	52	Survie
S5 – Homme, 17 ans	<i>P. ovale</i> 0,3 %	Épilepsie	Confusion (Glasgow = 13)	Aucun	85	Survie

Résultats, 1 décès

- ❖ M, 10 ans, drépanocytaire homozygote, séjour en Côte d'Ivoire un an auparavant
- ❖ Hb de base < 7g/dL, sous hydrea
- ❖ Fièvre, douleurs abdominale et gêne respiratoire depuis midi avec Hb 4g/dL
- ❖ Polypnée 60c/min, tachycarde 125 bpm, GSG 15
- ❖ Ictère conjonctival, tableau d'hémolyse aigue, fièvre et douleur abdominale
- ⇒ *P. ovale* 0.3% ayant pu favoriser la décompensation fébrile et l'hémolyse

- ❖ Hb: 4.2g/dL, GB 13G/L, PNN 8.5G/L
- ❖ Plaquettes: 117 G/L
- ❖ CRP: 104 mg/L
- ❖ ASAT: 623 UI/L ASAT: 262 UI/L, TP 54%,
- ❖ GGT 82 UI/L, Bili tot 685 μmol/L, bili conjuguée 425 μmol/L Lactates 7mmol/L
- ❖ Urines hémoglobinuriques

- ❖ Transfusion
- ❖ Quinine-> relais Artesunate
- ❖ Oxygénothérapie haut débit
- ❖ Clarofan-Genta-Flagyl

- ❖ SDRA
- ❖ Insuffisance hépatocellulaire
- ❖ CVD, syndrome hémorragique, HITC HIC
- ❖ Parasitémie de contrôle 0.1%

Discussion

Méta-analysis

2000-2020

113 études

En Afrique

P. malariae (2%) adults (2.13%), enfants (2.90%) et femmes enceintes (2.77%)

P. ovale (0.7%) spp. + fréquent chez les femmes enceintes (2.90%) que chez les enfants <15 ans (0.97%) et chez les enfants de plus de 15 ans (0.39%) (p=0.021)

Diminution au cours des 20 dernières années, mais pas de manière significative.

Très souvent des co-infections avec d'autres espèces de *Plasmodium* spp.

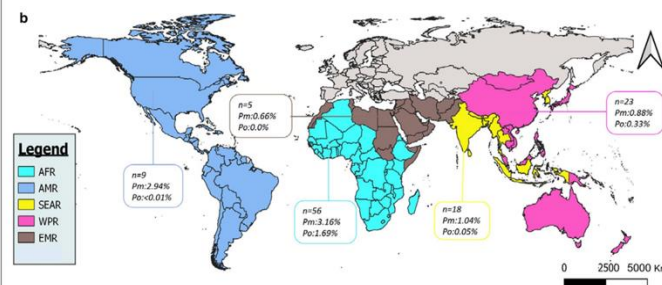


Fig. 2 a Distribution of included studies depending on the year. b Map of WHO regions where included studies were conducted. The regionalization used on this map is that of the WHO Global Health Observatory map. WHO Member States are grouped into six regions. The European region is not represented here, as it was not included in our study. (AFR: African Region, WPR: Western Pacific Region, AMR: Region of the Americas, SEAR: South-East Asia Region, EMR: Europe Region)

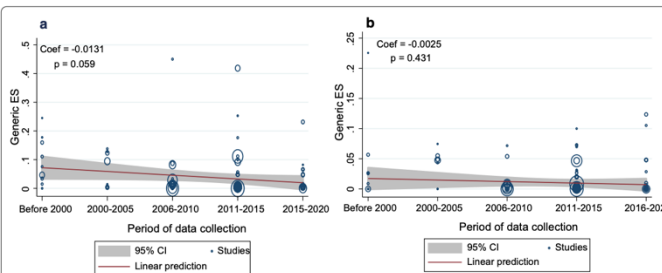


Fig. 5 Meta-regression of prevalence over the period of data collection: a meta-regression of *P. malariae* prevalence, b meta-regression of *P. ovale* spp. prevalence

Conclusion

- ❖ 1^{er} étude sur le paludisme à *Plasmodium non falciparum* pédiatrique hors zone endémique
- ❖ Le délai de retour d'endémie pas de bon marqueur pour les *P. non falciparum* à rechercher en systématique... penser aux reviviscences, la thrombopénie est un marqueur de *P. vivax*
- ❖ Nette diminution des cas de *P. vivax*
- ❖ Les patients drépanocytaires avec une infection à *P. non falciparum* peuvent présenter des critères de sévérité avec l'anémie au premier plan

Un grand MERCI

- ❖ CNRP : Pr Sandrine Houzé, Dr Marc Thellier, Dr Frédérick Gay, Dr Lise Musset, Dr Valentin Joste
- ❖ Task Force: Dr Frederic Sorge, Pr Julie Toubiana, Pr Olivier Lortholary, Dr Paul-Henry Consigny, Dr Claire Ferruat, Dr Bruno Pradines
- ❖ Pr Pierre Buffet

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Discussion

RESEARCH

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Molecular epidemiology of non-falciparum *Plasmodium* infections in three different areas of the Ivory Coast

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Abstract

Background Malaria is a major public health problem, particularly in the tropical regions of America, Africa and Asia. *Plasmodium falciparum* is not only the most widespread but also the most deadly species. The share of *Plasmodium* infections caused by the other species (*Plasmodium ovale* and *Plasmodium malariae*) is clearly underestimated. The objective of the study was to determine the molecular epidemiology of plasmodial infection due to *P. malariae* and *P. ovale* in Côte d'Ivoire.

Methods The study was cross-sectional. The study participants were recruited from Abengourou, San Pedro and Grand-Bassam. Sample collection took place from May 2015 to April 2016. Questionnaires were administered and filter paper blood samples were collected for parasite DNA extraction. The molecular analysis was carried out from February to March 2021. A nested PCR was used for species diagnosis. The data was presented in frequencies and proportions.

Results A total of 360 patients were recruited, including 179 men (49.7%) for 181 women (50.3%). The overall *Plasmodium* positive rate was 72.5% (261/360). The specific index was 77.4% and 1.5% for *P. falciparum* and *P. malariae* in mono-infection, respectively. There was also 15% *P. falciparum* and *P. malariae* co-infection, 3.4% *P. falciparum* and *P. ovale* co-infection and 2.3% *P. falciparum*, *P. malariae* and *P. ovale* triple-infection. Typing of *P. ovale* subspecies showed a significant predominance of *P. ovale curtisi* (81.2% of cases).

Conclusion *Plasmodium falciparum* remains the most prevalent malaria species in Côte d'Ivoire, but *P. malariae* and *P. ovale* are also endemic mostly in co-infection. Malaria elimination requires a better understanding of the specific epidemiological characteristics of *P. malariae* and *P. ovale* with a particular emphasis on the identification of asymptomatic carriers.

Keywords *Plasmodium*, Nested PCR, Ivory Coast

Table 1 Socio-demographic characteristics of the study population (non-falciparum cases)

	Number (n)	Percentage
Age range (years)		
0–5	4	6.8
6–10	38	64.4
10–16	17	28.8
Sex		
Female	32	54.2
Male	27	45.8
Locality		
Abengourou	26	44.1
Grand-Bassam	7	11.9
San-Pedro	26	44.1
Season		
Rainy	39	66.1
Dry	20	33.9
Total	59	100.0

Table 2 Clinical characteristics of the study population (non-falciparum cases)

	Number (n = 59)	Percentage
Body temperature (°C)		
35–36.9	40	67.8
37–37.4	12	20.3
≥ 37.5	7	11.9
Clinical status		
Asymptomatic	38	64.4
Symptomatic	21	35.6
Clinical signs		
Clinical signs	12	20.3
Headache	5	8.5
Pale conjunctivitis	8	13.6
Abdominal pain	1	1.7
Arthralgia	4	6.8
Nausea	2	3.2
Vomiting	3	5.1
Diarrhoea	1	1.7

Table 3 Distribution of plasmodial species (non-falciparum cases)

Parasite species	Number (n)	Percentage
<i>Plasmodium falciparum</i> + <i>P. malariae</i>	39	66.1
<i>P. falciparum</i> + <i>P. malariae</i> + <i>P. ovale</i>	6	10.2
<i>P. falciparum</i> + <i>P. ovale</i>	9	15.2
<i>P. malariae</i>	4	6.8
<i>P. malariae</i> + <i>P. ovale</i>	1	1.7
Total	59	100.0

Miezan, *Malaria Journal*, 2023

Discussion-Severe malaria

- ❖ 1995-2015
- ❖ Analyse de 2793 En Suède
- ❖ Sévère malaria : *P. falciparum* (9.4%), *P. vivax* (7.7%), *P. ovale* (5.3%), *P. malariae* (3.3%), and mixed *P. falciparum* épisodes (21.1%).

Table 1. Characteristics of Patients Diagnosed With Malaria in Sweden

Characteristic	All n = 2653 ^a	<i>P. falciparum</i> n = 1548, 58.3%	<i>P. vivax</i> n = 776, 29.2%	<i>P. ovale</i> n = 188, 7.1%	<i>P. malariae</i> n = 61, 2.3%	Mixed ^b n = 44, 1.7
Age, y, mean (range)	32.6 (0.2–83)	34.4 (0.2–83)	29.9 (1–79)	30.4 (3–70)	30.2 (3–65)	28.0 (1–68)
Children <18 y, No. (%)	448 (16.9)	220 (14.2)	166 (21.4)	31 (16.5)	11 (18.0)	13 (29.5)
Male gender, No. (%)	1773 (66.8)	1009 (65.2)	536 (69.1)	128 (68.1)	44 (72.1)	33 (75.0)
Patient origin, No. (%)						
Sub-Saharan Africa	1391 (52.4)	902 (58.3)	325 (41.9)	83 (44.2)	37 (60.7)	26 (59.1)
Other endemic ^c	150 (5.6)	21 (1.4)	118 (15.2)	7 (3.7)	3 (4.9)	0 (0)
Nonendemic	1100 (41.5)	616 (39.8)	331 (42.6)	98 (52.1)	20 (32.8)	18 (40.9)
Missing data	12 (0.5)	9 (0.6)	2 (0.3)	0 (0)	1 (1.6)	0 (0)
Travelers ^d length of stay in endemic area, days, median (IQR)	30 (20–60)	30 (16–60)	45 (21–90)	45 (23.5–149)	45 (30–75)	30 (20–90)
Chemoprophylaxis, No. (%)						
Regular	530 (20.0)	282 (18.2) ^b	150 (19.3)	71 (37.8)	11 (18.0)	11 (25.0)
Irregular	349 (13.1)	213 (13.8)	75 (9.6)	33 (17.5)	15 (24.6)	5 (11.4)
No prophylaxis	1674 (63.1)	1003 (64.8)	514 (66.3)	79 (42.0)	34 (55.8)	27 (61.3)
Missing data	100 (3.8)	50 (3.2)	37 (4.8)	5 (2.7)	1 (1.6)	1 (2.3)

Table 2. Severe Malaria Criteria in Episodes of Different Species (n=227)^a

Criteria	<i>P. falciparum</i> n = 146/1548, 9.4%	<i>P. vivax</i> n = 60/776, 7.7%	<i>P. ovale</i> n = 10/188, 5.3%	<i>P. malariae</i> n = 2/61, 3.3%	Mixed ^b n = 8/44, 18.2%
WHO criteria					
Impaired consciousness	28	1	1	0	1
Prostration	9	1	0	0	0
Multiple convulsions	9	0	0	0	0
Acidosis	21	0	0	0	0
Hypoglycemia	2	0	0	0	0
Severe anemia	16 ^c	15	0	1	4
Renal impairment	31	1	0	0	3
Hyperbilirubinemia	66 ^c	28	6	0	4
Pulmonary edema	15	4	2	0	0
Significant bleeding	17	5	1	0	1
Shock	33	8	2	1	3
Hyperparasitemia	57	0	0	0	3
Numbers of criteria fulfilled per episode of severe malaria, No. (%) ^d					
1	79 (59.4)	57 (95.0)	8 (80)	2 (100)	4 (50.0)
2	25 (18.8)	3 (5.0) ^e	2 (20) ^f	0 (0)	1 (12.5)
3	15 (11.3)	0 (0)	0 (0)	0 (0)	0 (0)
4	5 (3.7)	0 (0)	0 (0)	0 (0)	2 (25.0)
≥5	9 (6.8)	0 (0)	0 (0)	0 (0)	1 (12.5)
Criteria prognostic of unfavorable outcome, No. (%) of all cases ^g	84 (5.4)	18 (2.3)	4 (2.1)	1 (1.6)	5 (11.4)
Fatal outcome, No. (%) of the severe	3 (2.1)	0 (0)	0 (0)	0 (0)	1 (12.5) ^h

La fièvre bilieuse hémoglobininurique (FBH)

- ❖ Hémolyse intravasculaire (100%), hémoglobinurie (100%), insuffisance rénale aigüe (77%), Post quinine, Documenté à *P. falciparum*

Table 1. Relevant data that concerns 21 cases of blackwater fever, at presentation in France.

Case no., reference	Age, y	Year	Prior antimalarial treatment	Presumed trigger	Temp., °C	Hemoglobin level, ^a g/dL	Platelet count, ^b ×10 ³ cells/mm ³	Total bilirubin level, ^c mg/dL	LDH, ^d U/L	Plasma creatinine level, ^e mg/dL	G6PD deficiency	Direct antiglobulin test result
1 [8]	52	1989	Q, C, SP	M	40.0	6.0	37	9.5	4805	4.5	No	Neg
2 [8]	67	1990	Q	M	40.0	5.6	116	4.0	ND	3.4	No	ND
3 [8]	28	1990	M	M	39.0	6.9	ND	ND	ND	ND	No	ND
4 [7]	48	1990	H	H	38.5	4.5	33	ND	ND	3.8	No	Neg
5 [7]	18	1990	Q, C	H	38.0	3.4	37	11.2	4523	7.1	ND	Pos (Cpt/IgG)
6	48	1992	H	H or Q	38.2	5.8	59	5.5	7840	7.5	ND	Pos (Cpt/IgG)
7	39	1992	Q, H, SP	H	37.8	4.5	55	4.0	8540	6.2	No	Pos (Cpt/IgG)
8	37	1993	H	H	39.3	5.5	18	4.9	ND	8.8	No	Pos (Cpt)
9	42	1993	Q, M, SP, H	H or Q	37.5	5.5	137	6.3	7870	10.6	ND	Pos (Cpt)
10	56	1994	Q, H, C	Q	39.0	6.3	37	3.9	1486	11.9	No	ND
11	37	1995	Q	Q	37.0	9.0	117	3.9	3800	1.3	No	Pos (Cpt)
12	55	1996	Q	Q	39.7	5.0	ND	33.6	5325	2.8	No	Pos
13	48	1996	ND	M	39.5	6.2	47	4.2	2579	1.2	ND	ND
14	35	1996	H	H	39.1	5.7	106	7.3	2081	1.3	ND	Pos (Cpt)
15	60	1997	Q	H	36.0	3.0	103	4.1	ND	2.7	No	ND
16	54	1997	H, C	H	37.0	4.5	46	10.3	ND	9.0	No	Pos
17	57	1997	Q, H	H	37.0	6.1	ND	0.5	660	3.2	No	Neg
18	60	1997	Q, H	H or Q	39.5	4.8	214	3.7	6081	3.4	No	ND
19	51	1997	Q	M	38.4	3.0	77	42.6	7000	2.7	ND	Pos (Cpt/IgG)
20	67	1997	Q, H, A	Q	39.0	3.0	129	11.3	ND	ND	ND	Pos (Cpt/IgG)
21	78	1999	Q	Q	37.3	7.1	57	5.9	3336	1.5	No	Neg
Mean ± SE	49.4 ± 14.1	NA	NA	NA	38.4 ± 1.1	5.3 ± 1.5	80 ± 51	9.3 ± 10.7	4712 ± 2531	4.9 ± 3.3	NA	NA

NOTE. A, artemisinin; C, chloroquine; Cpt, complement; G6PD, glucose-6-phosphate dehydrogenase; H, halofantrine; LDH, lactate dehydrogenase; M, mefloquine; NA, not applicable; ND, not determined; Neg, negative; Pos, positive; Q, quinine; SP, sulfadoxine-pyrimethamine; temp., temperature.

^a Normal range, 13–18 g/dL.

^b Normal range, 150–400 × 10³ cells/mm³.

^c Normal range, 0.1–1.4 mg/dL.

^d Normal range, <470 U/L.

^e Normal range, 0.6–1.2 mg/dL.

Discussion

Table 3. Relevant data in 13 cases of blackwater fever identified by a literature review.

Reference	Age in y, sex	Country of residence	Presumed trigger	Clinical feature(s)	Hemoglobin level, ^a g/dL	Total bilirubin level, ^b mg/dL	Plasma creatinine level, ^c mg/dL	Parasitemia (level at admission)	G6PD deficiency	Direct antiglobulin test	HD	Outcome
[13]	41, M	Mali	H	MH, nausea, jaundice, fatigue	5.0	ND	ND	Neg	ND	Pos	No	Survived
[16]	57, F	Cameroon	Mef or H	MH, jaundice, fatigue, fever	4.9	17.5	ND	Pos (0.5%)	No	Neg	No	Survived
[17]	64, F	Mali	Q	MH, nausea, jaundice, fever	4.9	3.5	1.8	Neg	No	Neg	No	Survived
[17]	54, F	Congo	Q or H	MH, jaundice, fatigue	5	11.4	8.9	Neg	ND	Neg	Yes	Survived
[17]	53, F	Congo	Q or Mef	MH, nausea, jaundice, fever	5.2	68.5	4.4	Neg	No	Pos (Cpt)	Yes	Survived
[17]	67, M	Congo	Q	MH	6.3	1.7	2.5	Neg	No	Pos (IgG)	No	Survived
[17]	39, F	Guinea	Q or H	MH, nausea, fever	3.5	ND	Normal	Neg	ND	Pos (IgG)	No	Survived
[14]	44, M	Central Africa	Q	MH, jaundice, fever	3.9	40.0	Anuria	Neg	No	Pos	Yes	Died
[18]	49, F	Central Africa	Q then H	MH, jaundice, fever	7.5, then 4.1	4.1	ND	Neg, then Pos (<0.1%)	ND	Neg	No	Survived
[18]	59, F	Ivory Coast	Mef	MH, jaundice, fever	4.8	ND	ND	Pos (<0.1%)	No	Pos	No	Survived
[18]	44, M	Congo	Q	MH, jaundice	7.5	ND	ND	Neg	ND	ND	No	Survived
[18]	74, M	Central Africa	Q or H	MH	ND	ND	Transient anuria	ND	ND	ND	No	Survived
[18]	44, M	Angola	Q	MH, fever	5.4	ND	1.9 (anuria)	Neg	ND	ND	Yes	Survived

NOTE. Cpt, complement; F, female; G6PD, glucose-6-phosphate dehydrogenase; H, halofantrine; HD, hemodialysis; M, male; Mef, mefloquine; MH, macroscopic hemoglobinuria; ND, not determined; Neg, negative; Pos, positive; Q, quinine.

^a Normal range, 13–18 g/dL.

^b Normal range, 0.1–1.4 mg/dL.

^c Normal range, 0.6–1.2 mg/dL.

Discussion

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COMMENTARY

Haemoglobinuria in a 38-year-old French expatriate man living in Cameroon following artemisinin-based antimalarial treatment

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Summary

Massive haemoglobinuria is encountered rarely during the course of malaria. It is usually considered a diagnostic criterion for severe malaria, together with anaemia, acute renal failure and jaundice. Haemoglobinuria can also present among expatriates travelling to endemic areas following repeated exposure to quinoline or arylaminoalcohol drugs. A case is described of haemoglobinuria developing in a 38-year-old French expatriate diagnosed concurrently with numerous tropical infections, and treated on presumptive basis with an antimalarial regimen containing artemisinin derivatives. Haemoglobinuria resolved spontaneously within a few days. Although this case does not definitely indicate a causal link between haemoglobinuria and artemisinin derivatives, the risk of such infrequent side-effects should be taken into account in pharmacovigilance monitoring. Moreover, the patient illustrates the multifaceted pathology that can be encountered with tropical infections.
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