EVALUATION OF PREGNANT WOMEN ANTIMALARIAL INTERMITENT PRESUMPTIVE TREATMENT AND PREVALENCE OF SULFADOXINE-PYRIMETHAMINE RESISTANCE MARKERS IN FOUGAMOU, A GABONESE RURAL AREA

Fleuramie MIREMBOU BOUKOUMBA[1,2], Nancy Diamela MOUKODOUM[1], Pierre Blaise MATSIEGUI[2], Jean Bernard LEKANA-DOUKI[1,3]

ABSTRACT:

Pregnant malaria remains one of complexes forms of malaria. Despite the adoption of intermittent preventive treatment with Sulfadoxine-Pyrimethamine (IPT-SP), SP resistance emerged and haplotypes of *P. falciparum Dihydropteorate synthase (PfDHPS)* and *P. falciparum Dydrofolate reductase (PfDHFR)* associated with resistance increased.

Retrospective and cross sectional survey were done to investigate the IPT adhesion. Malaria was diagnosed using rapid diagnostic test and *PfDHFR* and *PfDHPS* were genotyped using PCR-RFLP.

We included 427 women at the time of delivery. The rate of adhesion to IPT-SP was 94.37% (n=403). For pregnant women including during cross sectional survey, only 8.7% (n=14) were infected with plasmodium.. The prevalence of triples mutations of PfDHFR VIRNI and AIRNI were 12.07% and 84.48% respectively. An undescribed profile of genotype 59 of PfDHFR was reported. The prevalence of mutant haplotypes of PfDHPS were SGEA, SGKA and AGEA was 37.93%, 25.86% and 12.07% respectively.

Data call for clinical trials to investigate the efficacy of ITP-SP.

INTRODUCTION

Despite upgrade of malaria fight, pregnant associated (PAM) malaria remains one of complex forms of malaria. PAM induces severe consequences for mother and newborn. So, several African countries adopted Intermitent Presumtive Treatment with Sulfadoxine Pyrimethamine (IPT-SP) to roll back PAM. But, some data reported highest level of markers of SP resistance in Africa: Haplotypes PfDHFR-(16- 51-59-108-164) VIRNI and AIRNI and SGEA, SGKA and AGEA of PfDHPS.

In Gabon, decrease of PAM burden were reported in urban areas, after implementation of IPT-SP. Nothing is known about pregnant women IPT-SP adhesion and prevalence of SP resistance markers in rural areas.

MATERIAL AND METHODS

Study site: Health Center of Fougamou (HFC)

Study population and inclusion criteria

Pop1: Pregnant women and after labour

- **Delivery at HCF**
- **Seeing in antenatal consultation at HCF**

Pop2: febrile patients

- **Fever (T° ≥ 37,5°C)**
- **Fever story during lasted 48H before consultation**

Statistical analysis: Epi Info sofware

RESULTS

I. IPT-SP Adhesion level of pregnant women at the delivery

Among 427 women who deliveried at HCF 403 (94.4%) took IPT-SP during pregnancy. The distribution of the number of taking doses is showing in table 1.

Table 1: DISTRIBUTION OF WOMEN ACCORDING TO THE NUMBER OF TAKING DOSES

Number of ttaking Doses	1	2	3	ND
Women	65 (16.12%)	119 (29.52%)	193 (47.89%)	26 (6.45%)

The socio-demographical parameters of these included women correspond to the rural area: 74.53% without work and 47.2% live in villages around Fougamou.

II. IPT-SP and pregnant malaria

During the cross sectionnal study, 161 pregnant women were included. The prevalence of malaria was 8.7% (n=14). A positive impact of IPT-SP was observed. The prevalence of malaria was higher in women with parity ≤ 1 (17.65%) than whose with parity ≥ 2 (2.15%), p=0.001. (Table 2).

Table 2: DISTRIBUTION OF MALARIA ACCORDING TO THE PARITY

Parity	0	1	2	3	≥ 5
numbers	36	32	30	26	18
P. falciparum infected women (%)	3 (8,33)	9 (28,12)	0 (0)	1 (3,85)	1 (5,55)

17.65% 2.7%

Data showed that antimalarial prevention measures were highly followed: 80.2 % (n=129) slept under bed net, 66.45% (n=107) received information and education on malaria basis

III. Malaria in all febrile patients

We investigated malaria in all febrile consulted patients at HCF. We included 101 patients. The malaria prevalence was 60.4% (n=61) with a mean of parasitemia of 52,374±81,151 Pf/µL. In this context, malaria affected blood cell level (Table 3). TABLE 3: COMPARISON OF BLOOD CELLS LEVELS ACCORDING MALARIA

Blood cells	Mean ± SD		
	Plasmodium +	Plasmodium -	*p-value*
White cells .10^3 / mm^3	8.13 ± 4.22	8.25 ± 5.49	0.85
Red blood 10^6/ mm^3	4.03 ± 0.78	4.46 ± 0.67	0.003
Haemoglobin (g/dl)	9.61 ± 1.71	11.18 ± 1.96	0.0001
Platelet.10^3/ mm^3	121.76 ± 73.32	190.99 ± 125.53	0.002

IV. High level of molecular markers of SP resistance

TABLE 4: PREVALENCE OF RESISTANCE PfDHFR AND PfDHPS GENOTYPES

Genes	Codons	Genotypes	Prevalences
PfDHFR	16	A16	91,37%(n=53/58)
		V16	8,62%(n=5/58)
	51	I51	100% (n=58/58)
	59	R59	96,55% (n=56/58)
		X59	3,44% (n=2/58)
	108	N108	100%(n=58/58)
	164	I164	100%(n=58/58)
PfDHPS	436	A436	15,51% (n=9/58)
		S436	77,58% (n=45/58)
		A/S436	6,89% (n=4/58)
	437	G437	100%(n=58/58)
	540	E540	53,44%(n=31/58)
		K540	37,93%(n=22/58)
		E/K540	8,62%(n=5/58)
	613	A613	98,27% (n=57/58
		S613	1,72% (n=1/58)

High levels of mutation associated with SP resistance was found! In the codon 59 of PfDHFR, we found 2 isolates with undescribed genotype, named X59 which gave undescribed profil by previously described PCR-RFLP assay.

TABLE 5: PREVALENCE OF HAPLOTYPES

Genes	Haplotypes	Prevalences % (n)
PfDHFR	$V_{16}I_{51}R_{59}N_{108}I_{164}$	12,07 (7/58)
	$A_{16}I_{51}R_{59}N_{108}I_{164}$	84,48 (49/58)
	$A_{16}I_{51}X_{59}N_{108}I_{164}$	3,45% (2/58)
PfDHPS	$S_{436}G_{437}E_{540}A_{613}$	37,93% (n=22/58)
	$S_{436}G_{437}K_{540}A_{613}$	25,86% (n=15/58)
	$A_{436}G_{437}E_{540}A_{613}$	12,07% (n=7/58)

CONCLUSION:

Data showed the high IPT-SP adhesion is next to 100%. The highest prevalence of genotypes associated with SP drug resistance found call for clinical trials to investigate the efficacy of ITP-SP.

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1 : Unité d'Evolution, Epidémiologie et Résistances Parasitaires (UNEEREP), Centre International de Recherches Médicales de Franceville (CIRMF) B.P. 769 Franceville Gabon. Phone : 00241 06 25 95 90.
2 : Centre de Recherches Médicales de la Ngounie (CRMN), de Fougamou. B.P. 133 Fougamou, Gabon
3: Département de Parasitologie-Mycologie Médecine Tropicale, Faculté de Médecine, Université des Sciences de la Santé, B.P. 4009 Libreville Gabon. Phone/Fax: 00241 70 48 96.