

Malaria infection and resistance-associated mutations in pregnant women receiving sulfadoxine-pyrimethamine prophylaxis



NEAR EAST
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MALARIA IS 100% TREATABLE AND PREVENTABLE

each year

655,000 people die from **MALARIA**

200,000 of these deaths are **NEWBORNS**

10,000 **MOTHERS DIE**

SIMPLE INTERVENTIONS can save **LIVES**



PREVENTIVE MALARIA MEDICINE & ANEMIA
SCREENING DURING PRENATAL CARE



USE OF BED NETS



PROMPT DIAGNOSIS, TREATMENT AND
COUNSELING FOR MALARIA ILLNESS & ANEMIA



INVEST IN THE FUTURE
DEFEAT MALARIA


innovating to save lives

Jhpiego

an affiliate of Johns Hopkins University



Sources: WHO (2012). *World Malaria Report*. Geneva, Switzerland; http://www.who.int/malaria/high_risk_groups/pregnancy/en/

A photograph of a pregnant woman's bare belly, which is being gently touched by two hands. The background is dark, and the lighting is soft, highlighting the contours of the abdomen.

WHO: Intermittent preventive treatment in pregnancy with sulfadoxine-pyrimethamine (IPTp-SP)

Increasing SP resistance...

Mutations in *Plasmodium falciparum* dihydrofolate reductase (*Pfdhfr*) and dihydropteroate synthase (*Pfdhps*) genes

Aim of the study: to detect the infection rates and *Pfdhfr/Pfdhps* mutations in pregnant women from Democratic Republic of Congo (DRC)

250 pregnant women from Bandundu city, the DRC, who received two doses of SP during pregnancy

Following delivery, blood samples were collected and applied onto Whatman filter papers

Nested PCR for identification
Plasmodium species

DNA sequencing of (+) samples for detection of mutations in *Pfdhfr* and *Pfdhps* genes



92 (36.8%) of 250 samples: *Plasmodium* spp. positive

<i>Plasmodium</i> species	n	(%)
<i>P. falciparum</i>	87	94.5
<i>P. falciparum</i> + <i>P. vivax</i>	2	2.2
<i>P. falciparum</i> + <i>P. malariae</i>	1	1.1
<i>P. vivax</i>	2	2.2
<i>P. ovale</i>	0	0.0
<i>P. knowlesi</i>	0	0.0
Total	92	100.0

P. falciparum (+) samples (n: 90) → DNA sequencing

56 samples: successfully sequenced for *Pfdhfr*

56 (100.0%) samples: one or more mutations

<i>Pfdhfr</i> mutation	Mutation number	
	n	(%)*
N51I	46/56	82.1
C59R	35/56	62.5
S108N	56/56	100.0

*Row percentage

N: Asparagine (Asn), I: Isoleucine (Ile), C: Cysteine (Cys), R: Arginine (Arg), S: Serine (Ser)

Resistance to pyrimethamine (*Pfdhfr* gene):

Primary mutation at codon 108

Augmented by mutations at codon 16, 51,59 and 164¹

N51I, C59R and S108N mutations are widespread in Africa²

Our results are consistent with previous findings

¹Sharma et al., 2015

²Heinberg and Kirkman, 2015

67 samples: successfully sequenced for *Pfdhps*

66 (98.5%) of 67 samples: one or more mutations

<i>Pfdhps</i> mutation	Mutation number	
	n	(%)*
A437G	66/67	98.5
K540E	1/67	1.5
A581G	1/67	1.5

*Row percentage

A: Alanine (Ala), G: Glycine (Gly), K: Lysine (Lys), E: Glutamic acid (Glu)

Resistance to sulfadoxine (*Pfdhps* gene):

Primary mutation at codon 436 or 437

Augmented by mutations at codon 540, 581 and 613¹

A437G and K540E mutations are widespread in Africa²

Our results are consistent with previous findings

¹Sharma et al., 2015

²Heinberg and Kirkman, 2015

48 samples: sequenced for both *Pfdhfr* & *Pfdhps*

48 (100.0%) of samples carried multiple mutations

<i>Pfdhfr</i> gene	<i>Pfdhps</i> gene	Mutation no	
		n	(%)
N51I, S108N	A437G, K540E, A581G	1/48	(2.1)
N51I, C59R, S108N	A437G	22/48	(45.8)
N51I, S108N	A437G	17/48	(35.4)
C59R, S108N	A437G	6/48	(12.5)
N51I, C59R, S108N	No mutation	1/48	(2.1)
S108N	A437G	1/48	(2.1)
Total		48/48	(100.0)

Multiple mutation combinations in *Pfdhfr* and *Pfdhps* are associated with treatment failure¹

Triple mutation in *Pfdhfr*, plus A437G mutation in *Pfdhps* were detected at high rates (45.8%)^{2,3}

Triple mutation in *Pfdhps* (A437G, K540E and A581G)⁴ was detected at low levels (2.1%)

¹Sharma et al., 2015

²Chico et al., 2015

³Heinberg and Kirkman, 2015

⁴Taylor et al., 2014

Conclusions:

SP prophylaxis failed to protect 36.8% of the pregnant women against malaria

Continuous monitoring of SP resistance is important

Number of SP doses may be increased to have better outcomes of the IPTp-SP^{1,2}

More effective drugs should be considered

¹WHO, 2014

²Likwela et al., 2012



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Thank you for your attention...