

Molecular surveillance of Artemisinin resistance marker pfk13 prevalence in India

Search strategies run on 13/04/2022 by Eli Harriss, a librarian at the Bodleian Health Care Libraries, University of Oxford.

Search Results

Ovid Embase	1232
Ovid Medline	885
Scopus	927
Web of Science Core Collection	1489
IndMed	1
Clinicaltrials.gov	98
WHO ICTRP	0
Total	4632
Total after deduplication	1938

Search Strategies

Database: Embase 1974 to present

Search Strategy:

-
- 1 exp malaria/ (95255)
 - 2 exp Plasmodium/ (64595)
 - 3 (malaria or plasmodium).ti,ab,kw. (117440)
 - 4 1 or 2 or 3 (137359)
 - 5 (pfkelch* or pfk13* or k13 or kelch* or "artemisinin resistan*").ti,ab,kw. (4553)
 - 6 4 and 5 (1520)
 - 7 limit 6 to ((english or french or hindi or italian or spanish) and yr="2014 -Current") (1232)

Database: Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®) 1946 to present

Search Strategy:

-
- 1 exp malaria/ (71391)
 - 2 exp Plasmodium/ (50580)
 - 3 (malaria or plasmodium).ti,ab,kw. (103372)
 - 4 1 or 2 or 3 (112717)
 - 5 (pfkelch* or pfk13* or k13 or kelch* or "artemisinin resistan*").ti,ab,kw. (3794)
 - 6 4 and 5 (1070)
 - 7 limit 6 to ((english or french or hindi or italian or spanish) and yr="2014 -Current") (885)

Scopus

(TITLE-ABS-KEY (malaria OR plasmodium) AND TITLE-ABS-KEY (pfkelch* OR pfk13* OR k13 OR kelch* OR "artemisinin resistan*")) AND (LIMIT-TO (PUBYEAR , 2022) OR LIMIT-TO (PUBYEAR , 2021) OR LIMIT-TO (PUBYEAR , 2020) OR LIMIT-TO (PUBYEAR , 2019) OR LIMIT-TO (PUBYEAR , 2018) OR

LIMIT-TO (PUBYEAR , 2017) OR LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014)) AND (LIMIT-TO (LANGUAGE , "English") OR LIMIT-TO (LANGUAGE , "French"))

Web of Science Core Collection

malaria or plasmodium (Topic) AND pfkelch* or pfk13* or k13 or kelch* or "artemisinin resistan*" (Topic)

Refined by Publication Years: 2014 or 2022 or 2021 or 2020 or 2019 or 2018 or 2017 or 2016 or 2015

IndMed

<https://www.india.gov.in/gsearch?s=pfkelch&op=Search>

Pfkelch, pfk13, k13, kelch – no results

Artemisinin resistance – 1 result

Clinicaltrials.gov

Condition or disease: malaria

Other terms: pfkelch

All Studies

Condition or disease: malaria

Other terms: pfk13

All Studies

Condition or disease: malaria

Other terms: k13

All Studies

Condition or disease: malaria

Other terms: kelch

All Studies

Condition or disease: malaria

Other terms: artemisinin resistance

All Studies

WHO ICTRP <https://trialsearch.who.int/> Trials registered from 2014/01/01 - 2022

Condition: Malaria

Intervention: kelch13 or pfk13 or k13 or kelch or artemisinin resistance

ALL studies

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 - 6 4 and 5 (1520)
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 - 6 4 and 5 (1070)
 - 7 limit 6 to ((english or french or hindi or italian or spanish) and yr="2014 -Current") (885)

Scopus

(TITLE-ABS-KEY (malaria OR plasmodium) AND TITLE-ABS-KEY (pfkelch* OR pfk13* OR k13 OR kelch* OR "artemisinin resistan*")) AND (LIMIT-TO (PUBYEAR , 2022) OR LIMIT-TO (PUBYEAR , 2021) OR LIMIT-TO (PUBYEAR , 2020) OR LIMIT-TO (PUBYEAR , 2019) OR LIMIT-TO (PUBYEAR , 2018) OR

LIMIT-TO (PUBYEAR , 2017) OR LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR , 2015) OR LIMIT-TO (PUBYEAR , 2014)) AND (LIMIT-TO (LANGUAGE , "English") OR LIMIT-TO (LANGUAGE , "French"))

Web of Science Core Collection

malaria or plasmodium (Topic) AND pfk13* or pfk13* or k13 or kelch* or "artemisinin resistan*" (Topic)

Refined by Publication Years: 2014 or 2022 or 2021 or 2020 or 2019 or 2018 or 2017 or 2016 or 2015

IndMed

<https://www.india.gov.in/gsearch?s=pfkelch&op=Search>

Pfkelch, pfk13, k13, kelch – no results

Artemisinin resistance – 1 result

Clinicaltrials.gov

Condition or disease: malaria

Other terms: pfk13

All Studies

Condition or disease: malaria

Other terms: pfk13

All Studies

Condition or disease: malaria

Other terms: k13

All Studies

Condition or disease: malaria

Other terms: kelch

All Studies

Condition or disease: malaria

Other terms: artemisinin resistance

All Studies

WHO ICTRP <https://trialsearch.who.int/> Trials registered from 2014/01/01 - 2022

Condition: Malaria

Intervention: kelch13 or pfk13 or k13 or kelch or artemisinin resistance

ALL studies

Molecular surveillance of Sulfadoxine-Pyrimethamine resistance markers *pfdhps* and *pfdhfr* prevalence in India

Search strategies run on 09/03/2022 by Eli Harriss, a librarian at the Bodleian Health Care Libraries, University of Oxford.

Search Results

Ovid Embase	3646
Ovid Medline	2282
Scopus	4235
Web of Science Core Collection	3513
Clinicaltrials.gov	194
WHO ICTRP	34
Cochrane CENTRAL	369
Total	14278
Total after deduplication	6346

Search Strategies

Database: Embase 1974 to present

Search Strategy:

-
- 1 exp malaria/ (94183)
 - 2 exp Plasmodium/ (64026)
 - 3 (malaria or plasmodium or falciparum).ti,ab,kw. (116782)
 - 4 1 or 2 or 3 (136184)
 - 5 dihydrofolate reductase/ (7867)
 - 6 dihydropteroate synthase/ (971)
 - 7 ("dihydrofolate reductase" or dhfr).ti,ab,kw. (8512)
 - 8 ("tetrahydrofolate nadp oxidoreductase" or "tetrahydrofolate nicotinamide adenine dinucleotide phosphate oxidoreductase" or "dehydrofolate dehydrogenase" or "dehydrofolate reductase" or "dihydrofolate dehydrogenase" or "dihydrofolic acid reductase" or "dihydrofolic reductase" or "dihydropteroylglutamate reductase" or "e.c. 1.5.1.3" or "e.c. 1.5.1.4" or "folate reductase" or "folic acid reductase" or "folic reductase" or "reductase folate" or "tetrahydrofolate dehydrogenase" or "tetrahydrofolate reductase").ti,ab,kw. (1334)
 - 9 ("dihydropteroate synthase" or dhps).ti,ab,kw. (1698)
 - 10 ("dihydropteroate synthetase" or "dihydropteroate pyrophosphorylase" or "dihydropteroate synthetase" or "e.c. 2.5.1.15").ti,ab,kw. (155)
 - 11 molecular marker/ (15716)
 - 12 (molecular and (resistance or marker* or signature* or surveillance)).ti,ab,kw. (273520)
 - 13 (pfdhps or pfdhfr).ti,ab,kw. (513)
 - 14 pyrimethamine plus sulfadoxine/ (2086)
 - 15 (vivaxine or rimodar or suldox or fansidar or laridox or madomine or methamar or pyralfin or pyrimethamine* or sulphadoxine* or sulfadoxine*).ti,ab,kw. (6463)
 - 16 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 (294664)
 - 17 4 and 16 (8818)

18 limit 17 to ((english or french or hindi or italian or spanish) and yr="2014 - 2022")
(3646)

Database: Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®) 1946 to present

Search Strategy:

-
- 1 exp Malaria/ (71077)
 - 2 exp Plasmodium/ (50380)
 - 3 (malaria or plasmodium or falciparum).ti,ab,kw. (103350)
 - 4 1 or 2 or 3 (112384)
 - 5 Tetrahydrofolate Dehydrogenase/ (5916)
 - 6 Dihydropteroate Synthase/ (660)
 - 7 ("dihydrofolate reductase" or dhfr).ti,ab,kw. (7656)
 - 8 ("tetrahydrofolate nadp oxidoreductase" or "tetrahydrofolate nicotinamide adenine dinucleotide phosphate oxidoreductase" or "dehydrofolate dehydrogenase" or "dehydrofolate reductase" or "dihydrofolate dehydrogenase" or "dihydrofolic acid reductase" or "dihydrofolic reductase" or "dihydropteroylglutamate reductase" or "e.c. 1.5.1.3" or "e.c. 1.5.1.4" or "folate reductase" or "folic acid reductase" or "folic reductase" or "reductase folate" or "tetrahydrofolate dehydrogenase" or "tetrahydrofolate reductase").ti,ab,kw. (1145)
 - 9 ("dihydropteroate synthase" or dhps).ti,ab,kw. (1425)
 - 10 ("dihydropteroate synthetase" or "dihydropteroate pyrophosphorylase" or "dihydropteroate synthetase" or "e.c. 2.5.1.15").ti,ab,kw. (134)
 - 11 (molecular and (resistance or marker* or signature* or surveillance)).ti,ab,kw. (200534)
 - 12 (pfdhps or pfdhfr).ti,ab,kw. (380)
 - 13 (vivaxine or rimodar or suldox or fansidar or laridox or madomine or methamar or pyralfin or pyrimethamine* or sulphadoxine* or sulfadoxine*).ti,ab,kw. (5667)
 - 14 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 (215432)
 - 15 4 and 14 (6503)
 - 16 limit 15 to (yr="2014 -Current" and (english or french or hindi or italian or spanish))
(2282)

Scopus

(TITLE-ABS-KEY (malaria OR plasmodium OR falciparum)) AND ((TITLE-ABS-KEY ("dihydrofolate reductase" OR dhfr OR "tetrahydrofolate nadp oxidoreductase" OR "tetrahydrofolate nicotinamide adenine dinucleotide phosphate oxidoreductase" OR "dehydrofolate dehydrogenase" OR "dehydrofolate reductase" OR "dihydrofolate dehydrogenase" OR "dihydrofolic acid reductase" OR "dihydrofolic reductase" OR "dihydropteroylglutamate reductase" OR "e.c. 1.5.1.3" OR "e.c. 1.5.1.4" OR "folate reductase" OR "folic acid reductase" OR "folic reductase" OR "reductase folate" OR "tetrahydrofolate dehydrogenase" OR "tetrahydrofolate reductase" OR "dihydropteroate synthase" OR dhps OR "dihydropteroate synthetase" OR "dihydropteroate pyrophosphorylase" OR "dihydropteroate synthetase" OR "e.c. 2.5.1.15") OR TITLE-ABS-KEY ((molecular AND (resistance OR marker* OR signature* OR surveillance))) OR TITLE-ABS-KEY (pfdhps OR pfdhfr OR vivaxine OR rimodar OR suldox OR fansidar OR laridox OR madomine OR methamar OR pyralfin OR pyrimethamine* OR sulphadoxine* OR sulfadoxine*))) AND (LIMIT-TO (LANGUAGE , "English") OR LIMIT-TO (LANGUAGE , "French") OR LIMIT-TO (LANGUAGE , "Italian"))

AND (LIMIT-TO (PUBYEAR , 2022) OR LIMIT-TO (PUBYEAR , 2021) OR
LIMIT-TO (PUBYEAR , 2020) OR LIMIT-TO (PUBYEAR , 2019) OR LIMIT-TO (PUBYEAR , 2018) OR
LIMIT-TO (PUBYEAR , 2017) OR LIMIT-TO (PUBYEAR , 2016) OR LIMIT-TO (PUBYEAR , 2015) OR
LIMIT-TO (PUBYEAR , 2014))

Web of Science Core Collections (All Editions)

#1 malaria OR plasmodium OR falciparum (Topic)

#2 "dihydrofolate reductase" OR dhfr OR "tetrahydrofolate nadp oxidoreductase" OR
"tetrahydrofolate nicotinamide adenine dinucleotide phosphate oxidoreductase" OR
"dehydrofolate dehydrogenase" OR "dehydrofolate reductase" OR "dihydrofolate
dehydrogenase" OR "dihydrofolic acid reductase" OR "dihydrofolic reductase" OR
"dihydropteroylglutamate reductase" OR "e.c. 1.5.1.3" OR "e.c. 1.5.1.4" OR "folate
reductase" OR "folic acid reductase" OR "folic reductase" OR "reductase folate" OR
"tetrahydrofolate dehydrogenase" OR "tetrahydrofolate reductase" OR "dihydropteroate
synthase" OR dhps OR "dihydropteroate synthetase" OR "dihydropteroate
pyrophosphorylase" OR "dihydropteroate synthetase" OR "e.c. 2.5.1.15" (Topic) or
molecular AND (resistance OR marker* OR signature* OR surveillance) (Topic) or pfdhps
OR pfdhfr OR vivaxine OR rimodar OR suldox OR fansidar OR laridox OR madomine OR
methamar OR pyralfin OR pyrimethamine* OR sulphadoxine* OR sulfadoxine* (Topic)

#3 #1 and #2 and English or French or Spanish (Languages) and 2014 or 2015 or 2016 or
2017 or 2018 or 2019 or 2020 or 2021 or 2022 (Publication Years)

Clinicaltrials.gov

Condition or disease: malaria

Other terms: dihydrofolate reductase

All Studies

Condition or disease: malaria

Other terms: dhfr

All Studies

Condition or disease: malaria

Other terms: dihydropteroate synthase

All Studies

Condition or disease: malaria

Other terms: dhps

All Studies

Condition or disease: malaria

Other terms: Sulfadoxine-pyrimethamine

All Studies

WHO ICTRP <https://trialsearch.who.int/>

Trials registered from 2014/01/01 - 2022

dihydrofolate reductase

Recruitment status is: ALL

dhfr

Recruitment status is: ALL

dihydropteroate synthase

Recruitment status is: ALL

dhps

Recruitment status is: ALL

Sulfadoxine-pyrimethamine

Recruitment status is: ALL

Cochrane Central Register of Controlled Trials

Issue 2 of 12, February 2022

- #1 MeSH descriptor: [Malaria] explode all trees 3265
- #2 MeSH descriptor: [Plasmodium] explode all trees 987
- #3 (malaria or plasmodium or falciparum):ti,ab,kw 7153
- #4 #1 or #2 or #3 7153
- #5 MeSH descriptor: [Tetrahydrofolate Dehydrogenase] explode all trees 23
- #6 MeSH descriptor: [Dihydropteroate Synthase] explode all trees 12
- #7 ("dihydrofolate reductase" or dhfr):ti,ab,kw 131
- #8 ("tetrahydrofolate nadp oxidoreductase" or "tetrahydrofolate nicotinamide adenine dinucleotide phosphate oxidoreductase" or "dehydrofolate dehydrogenase" or "dehydrofolate reductase" or "dihydrofolate dehydrogenase" or "dihydrofolic acid reductase" or "dihydrofolic reductase" or "dihydropteroylglutamate reductase" or "e.c. 1.5.1.3" or "e.c. 1.5.1.4" or "folate reductase" or "folic acid reductase" or "folic reductase" or "reductase folate" or "tetrahydrofolate dehydrogenase" or "tetrahydrofolate reductase"):ti,ab,kw 45
- #9 ("dihydropteroate synthase" or dhps):ti,ab,kw 60
- #10 ("dihydropteroate synthetase" or "dihydropteroate pyrophosphorylase" or "dihydropteroate synthetase" or "e.c. 2.5.1.15"):ti,ab,kw 4
- #11 (molecular and (resistance or marker* or signature* or surveillance)):ti,ab,kw 4318
- #12 (pfdhps or pfdhfr):ti,ab,kw 27
- #13 (vivaxine or rimodar or suldox or fansidar or laridox or madomine or methamar or pyralfin or pyrimethamine* or sulphadoxine* or sulfadoxine*):ti,ab,kw 1407
- #14 #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 5751
- #15 #4 and #14 1338

Limited by date: 2014 to 2022

<i>P. falciparum</i> resistance markers	Study inclusion criteria	Study exclusion criteria
<i>pfk13</i>	<ul style="list-style-type: none"> • Indian Studies involving humans of all age groups and gender • <i>pfk13</i> genotypes assessed by sequencing at least one <i>P. falciparum</i> isolate/infection • Original data • Baseline/pre-treatment infections • Marker prevalence must be linked to the geographical site 	<ul style="list-style-type: none"> • Non-human <i>P. falciparum</i> infections • Publication not accessible • Publications in other languages than English, French, Spanish, Italian, or Hindi • Non-primary research studies/Review • Cultured strains, genetically manipulated strains, strains that have been adapted to long-term culture in vitro (not representative of original infection) • Parasites isolated from other tissues than blood (for example placenta) • Post-treatment infections • Biased selection of baseline samples (e.g. only treatment failures, half resistant and half sensitive in vitro tested isolates) • Regionally pooled marker prevalence data, where the origin of infection cannot be linked to a geographical site. • Marker prevalence (%) presented in the article without sample size. • Full text could not be found
<i>pfdhps/pfdhfr</i>	<ul style="list-style-type: none"> • Indian studies involving humans of all age groups and gender • At least one <i>pfdhps</i> or <i>pfdhfr</i> genotype/haplotype/copy number from isolate/infection • Original data • Baseline/pre-treatment infections • Marker prevalence must be linked to the study site/country 	<ul style="list-style-type: none"> • Non-human <i>P. falciparum</i> infections • Publication not accessible • Publications in other languages than English, French, Spanish, Italian, or Hindi • Non-primary research studies and Review articles • Cultured strains, genetically manipulated strains, strains that have been adapted to long-term culture in vitro (not representative of original infection) • Parasites isolated from other tissues than blood (for example placenta) • Post-treatment infections • Biased selection of baseline samples (e.g. only treatment failures, half resistant and half sensitive in vitro tested isolates) • Regionally pooled marker prevalence data, where the origin of infection cannot be deduced on at least the country level. • Marker prevalence (%) presented in the article without sample size.

Supplementary Table 1: Inclusion and exclusion criteria for selection of *pfk13* and *pfdhps/pfdhfr* resistance marker prevalence studies for the systematic review.

<i>P. falciparum</i> resistance markers	PubMed Id	Studies excluded at the full-text screening stage	Brief reasons
<i>pfk13</i>	NA	1. Molecular evidence for <i>Plasmodium falciparum</i> resistance to sulfadoxine-pyrimethamine but the absence of k-13 mutations in Mangalore, southern India	Missing information
	NA	2. Slow parasite clearance, absent k-13 propeller gene polymorphisms and adequate artesunate levels among patients with severe malaria: a prospective observational cohort study from south India	Missing information on the number of sequenced samples
	NA	3. High-throughput genomic surveillance Plasmodium infections in India	Missing information
<i>Pfdhps/pfdhfr</i>	26068343	4. Population genetic study of Plasmodium falciparum parasites pertaining to <i>pfdhps</i> gene sequence in malaria-endemic areas of Assam	Marker prevalence data is not available
	NA	5. Analysis of sulphadoxine-pyrimethamine drug resistance in Plasmodium falciparum from Khurda District of Odisha, India	RFLP, not a sequencing method in inclusion criteria
	30428283	6. Evidence of artemisinin-resistant Plasmodium falciparum malaria in Eastern India	Does not contain <i>pfdhps</i> or <i>pfdhfr</i> genotypes
	27448953	7. Polymorphisms in <i>pfert</i> and <i>pfmdr-1</i> genes after five years of withdrawal of chloroquine for the treatment of Plasmodium falciparum malaria in West Bengal, India	Does not contain <i>pfdhps</i> or <i>pfdhfr</i> genotypes
	31548652	8. Characterization of drug resistance and genetic diversity of Plasmodium falciparum parasites from Tripura, Northeast India	Does not contain <i>pfdhps</i> or <i>pfdhfr</i> genotypes
	28303837	9. Prevalence of multiple drug-resistant Plasmodium falciparum malaria cases in Northeast India	missing information; did not understand the presentation of the results
	32280801	10. Comparative analysis of Plasmodium falciparum dihydrofolate-reductase gene sequences from different regions of India	Bioinformatics analysis of previously published genotypes
	NA	11. High-throughput genomic surveillance of plasmodium infections in India	Missing information
	27485211	12. Low prevalence of dihydrofolate	Only <i>P. vivax</i> data, no <i>P.</i>

S. No.	References	No. of samples	Sequencing method
1	Bharti et al. ¹	186	Sanger sequencing
2	Mishra et al. ²	384	Sanger sequencing
3	Rao et al. ³	16	Ion Torrent
4	Ozarkar et al. ⁴	63	Nanodrop 1000
5	Das et al. ⁵	180	Sanger sequencing
6	Mishra et al. ⁶	135	Sanger sequencing
7	Chakrabarti et al. ⁷	22	Not mentioned
8	Saksena et al. ⁸	1	Sanger sequencing
9	Das et al. ⁹	136	Not mentioned
10	Wedam et al. ¹⁰	112	Sanger sequencing
11	Rana et al. ¹¹	178	Sanger sequencing
12	Pathak et al. ¹²	179	Not mentioned
13	Prosser et al. ¹³	2	Sanger sequencing
14	Krishna et al. ¹⁴	308	Sanger sequencing
15	Kumar et al. ¹⁵	122	Sanger sequencing
16	Chatterjee et al. ¹⁶	51	Not mentioned
17	Mishra et al. ¹⁷	254	De novo NGS
18	Ashley et al. ¹⁸	1	Illumina sequencing
19	Das et al. ¹⁹	226	Sanger sequencing
20	Miraclin et al. ²⁰	42	Sanger sequencing
21	Patgiri et al. ²¹	71	Sanger sequencing
22	Unpublished study	371	Not mentioned

Supplementary Table 3: *pfk13* prevalence studies with sample size, and type of sequencing method used. nsSNP: Nonsynonymous Single Nucleotide Polymorphism.

References:

1. Bharti PK, Shukla MM, Ringwald P, Krishna S, Singh PP, Yadav A, Mishra S, Gahlot U, Malaiya JP, Kumar A, Prasad S, Baghel P, Singh M, Vadadi J, Singh MP, et al., 2016. Therapeutic efficacy of artemether–lumefantrine for the treatment of uncomplicated Plasmodium falciparum malaria from three highly malarious states in India. *Malar J* 15: 498
2. Mishra N, Prajapati SK, Kaitholia K, Bharti RS, Srivastava B, Phookan S, Anvikar AR, Dev V, Sonal GS, Dhariwal AC, White NJ, Valecha N., 2015. Surveillance of Artemisinin Resistance in Plasmodium falciparum in India Using the kelch13 Molecular Marker. *Antimicrob Agents Chemother* 59: 2548–2553
3. Rao PN, Uplekar S, Kayal S, Mallick PK, Bandyopadhyay N, Kale S, Singh OP, Mohanty A, Mohanty S, Wassmer SC, Carlton JM., 2016. A Method for Amplicon Deep Sequencing of Drug Resistance Genes in Plasmodium falciparum Clinical Isolates from India. *J Clin Microbiol* 54: 1500–1511
4. Ozarkar A, Kanyal A, Dass S, Deshpande P, Deobagkar D, Karmodiya K., 2021. Analysis of drug resistance marker genes of Plasmodium falciparum after implementation of artemisinin-based combination therapy in Pune district, India. *J Biosci* 46: 77

5. Das S, Kar A, Manna S, Mandal S, Mandal S, Das S, Saha B, Hati AK., 2021. Artemisinin combination therapy fails even in the absence of *Plasmodium falciparum* kelch13 gene polymorphism in Central India. *Sci Rep* 11: 9946
6. Mishra S, Bharti PK, Shukla MM, Ali NA, Kashyotia SS, Kumar A, Dhariwal AC, Singh N., 2017. Clinical and molecular monitoring of *Plasmodium falciparum* resistance to antimalarial drug (artesunate+sulphadoxine-pyrimethamine) in two highly malarious district of Madhya Pradesh, Central India from 2012–2014. *Pathogens and Global Health* 111: 186–194
7. Chakrabarti R, White J, Babar PH, Kumar S, Mudeppa DG, Mascarenhas A, Pereira L, Dash R, Maki JN, Sharma A, Gogoi K, Sarma DK, Pal Bhowmick I, Manoharan SK, Gomes E, et al., 2019. Decreased *In Vitro* Artemisinin Sensitivity of *Plasmodium falciparum* across India. *Antimicrob Agents Chemother* 63: e00101-19
8. Saksena R, Matlani M, Singh V, Kumar A, Anveshi A, Kumar D, Gai ND., 2017. Early treatment failure in concurrent dengue and mixed malaria species infection with suspected resistance to artemisinin combination therapy from a tertiary care center in Delhi: a case report. *Int Med Case Rep J* 10: 289–294
9. Das S, Saha B, Hati AK, Roy S., 2018. Evidence of Artemisinin-Resistant *Plasmodium falciparum* Malaria in Eastern India. *New England Journal of Medicine* 379: 1962–1964
10. Wedam J, Tacoli C, Gai PP, Siegert K, Kulkarni SS, Rasalkar R, Boloor A, Jain A, Mahabala C, Baliga S, Shenoy D, Devi R, Gai P, Mockenhaupt FP., 2018. Molecular Evidence for *Plasmodium falciparum* Resistance to Sulfadoxine–Pyrimethamine but Absence of K13 Mutations in Mangaluru, Southwestern India. *The American Journal of Tropical Medicine and Hygiene* 99: 1508–1510
11. Rana R, Ranjit M, Bal M, Khuntia HK, Pati S, Krishna S, Das A., 2020. Sequence Analysis of the *K13* -Propeller Gene in Artemisinin Challenging *Plasmodium falciparum* Isolates from Malaria Endemic Areas of Odisha, India: A Molecular Surveillance Study. *BioMed Research International* 2020: 1–6
12. Pathak A, Mårtensson A, Gawariker S, Sharma A, Diwan V, Purohit M, Ursing J., 2020. Stable high frequencies of sulfadoxine–pyrimethamine resistance associated mutations and absence of K13 mutations in *Plasmodium falciparum* 3 and 4 years after the introduction of artesunate plus sulfadoxine–pyrimethamine in Ujjain, Madhya Pradesh, India. *Malar J* 19: 290
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3	Patel et al. ³	163	Sanger sequencing
4	Mishra et al. ⁴	155	Not mentioned
5	Sarmah et al. ⁵	75	Sanger sequencing
6	Das et al. ⁶	176	Sanger sequencing
7	Kumar et al. ⁷	185	Sanger sequencing
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9	Das Sutar et al. ⁹	201	Not mentioned
10	Das et al. ¹⁰	90	Enzymatic digestion
11	Mishra et al. ¹¹	<i>pf dhps</i> :327, <i>pf dhfr</i> :292	Not mentioned
12	Das et al. ¹²	180	Sanger sequencing
13	Sharma et al. ¹³	55	Sanger sequencing
14	Sharma et al. ¹⁴	58	Not mentioned
15	Pathak et al. ¹⁵	<i>pf dhps</i> :105, <i>pf dhfr</i> :104	Not mentioned
16	Pathak et al. ¹⁶	<i>pf dhps</i> :77, <i>pf dhfr</i> :78	de novo NGS
17	Wedam et al. ¹⁷	107	Not mentioned
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20	Mishra et al. ²⁰	<i>pf dhps</i> :216, <i>pf dhfr</i> :232	Sanger sequencing
21	Mohapatra et al. ²¹	<i>pf dhps</i> :173, <i>pf dhfr</i> :168	PCR-RFLP
22	Rao et al. ²²	16	Ion torrent
23	Ozarkar et al. ²³	63	Nanodrop 1000
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25	Tyagi et al. ²⁵	<i>pf dhfr</i> :39	Sanger sequencing
26	Srivastava et al. ²⁶	<i>pf dhps</i> :88, <i>pf dhfr</i> :136	Mutation specific PCR assays
27	Das et al. ²⁷	<i>pf dhps</i> :127	Sanger sequencing
28	Sharma et al. ²⁸	217	Sanger sequencing
29	Ganguly et al. ²⁹	<i>pf dhps</i> :26, <i>pf dhfr</i> :24	Sanger sequencing
30	Kumar et al. ³⁰	<i>pf dhps</i> :121, <i>pf dhfr</i> :122	Sanger sequencing
31	Unpublished	<i>pf dhps</i> :401, <i>pf dhfr</i> :392	Not mentioned

Supplementray Table 4: *pf dhps*/*pf dhfr* prevalence studies with sample size, and type of sequencing method used. nsSNP: Non synonymous Single Nucleotide Polymorphism.

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