

Presence of dengue fever in semi-urban areas of two health districts in Burkina Faso



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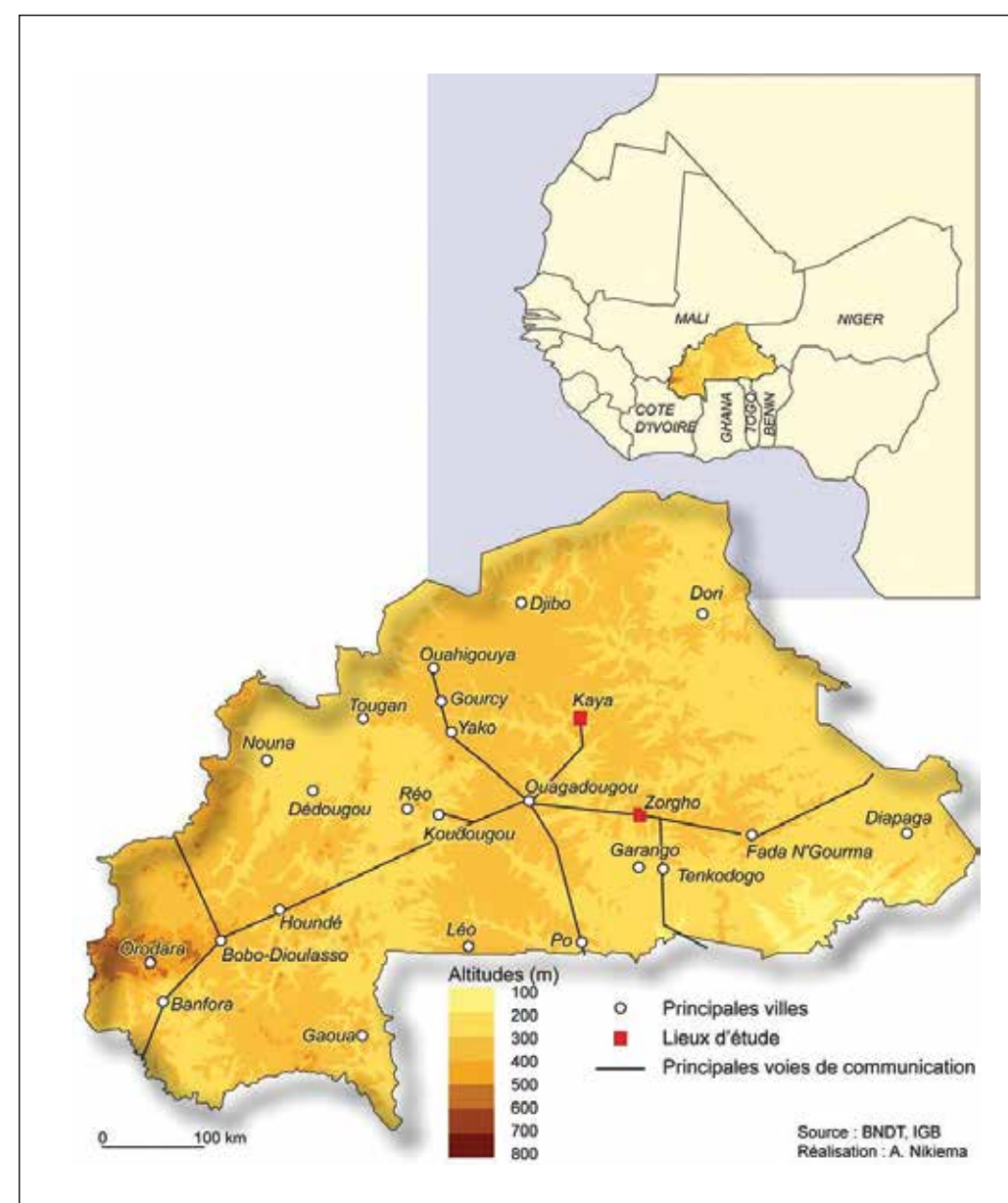
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BACKGROUND

- Dengue is a re-emerging infectious disease broadly distributed among tropical and subtropical countries and caused by any of the four-dengue serotypes (DENV 1-4).
- The global incidence of dengue has grown dramatically in recent decades. While dengue presence has been well known and broadly studied in South East Asia and Latin America, evidences about dengue in Africa remain very limited.
- In Burkina Faso, dengue has been neglected because febrile cases are systematically assumed as malaria cases. The last description of acute dengue cases date back from 1982, when DENV2 was documented.

MATERIALS AND METHODS

Study site: The study took place in Kaya and Zorgho, two semi-urban areas of the North Central and East-Central regions of Burkina Faso, respectively. Both municipalities are under a tropical climate with one rainy season between June to September, with a rainfall peak in August, and a dry season the rest of the year.



Study design and study population. To explore the presence of dengue, a cross sectional survey was nested into the third edition of an annual panel survey. The survey covered children under 10 in September 2013.

Selection criteria: All children who had fever (axillary temperature $\geq 37.8^\circ\text{C}$) at the moment of the survey or whom have reported presence of fever during the week previous to the survey were invited to participate.

Data and Sample collection: Socio-demographic data, health related status (including current symptoms), and information about health seeking behavior, were obtained through the administration of a structured questionnaire in the local language (Mooré) by trained surveyors. Blood samples of every eligible child (n = 263) were obtained through finger pricks during the survey.

Rapid Diagnostics Tests (RDT) used:

- SD BIOLINE Malaria Ag Pf/Pan (HRP-2 / pLDH)*.
- SD BIOLINE Dengue Duo (NS1Ag and IgG/IgM)*.

RT-PCR analysis:

Finger pricks blood samples were collected in filter paper from every child with positive dengue RDT and from every tenth with a negative result. This filter paper after dried were stored individually in a Ziploc bag in a dry cool place at 4–15°C and afterwards used for RT-PCR analysis at the microbiology laboratory at the Universidad del Valle. The DENV RNA was detected by a conventional DENV-1-4 nested RT-PCR protocol. The final PCR products were compared with the assay positive controls (CDC Reference DENV1-4 strains). To confirm the dengue specificity of the PCR products amplified from the samples, the PCR amplicons of the correct size were further sequenced.

Definition of febrile etiologies according to tests results:

MALARIA CASE	A positive result either for Malaria Ag,Pf or Pan with negative results for dengue RTD
DENGUE CASE	A positive NS1 RTD result; or either an IgM or IgG positive RTD with a qRT-PCR positive and negative result for malaria
PROBABLE DENGUE CASE	A positive IgM result; or a positive IgG with a positive IgM and negative result for malaria
POSSIBLE DENGUE AND MALARIA CO-INFECTION	A positive result for Malaria Ag,Pf/Pan and a positive result for either NS1 or IgM or IgG and presence of DENV in qRT-PCR
OTHER FLAVIVIRUS	A positive IgG with negative results for IgM, Malaria Ag,Pf/Pan and no presence of DENV in qRT-PCR
UNDIFFERENTIATED FEVER NON-MALARIA NON-DENGUE CASE	Negative results for malaria and dengue RDTs and no presence of DENV in qRT-PCR

Data management and analysis: All data were entered into PDAs and data analysis was performed with STATA 10 (Stata Corp).

Ethical considerations: Informed consents were obtained from the parent or legal guardians of participant children. The study protocol was reviewed and approved by the National Ethical Health Committee of Burkina Faso and the Institutional Review Board of CRCHUM.

SUMMARY

The global incidence of dengue has grown dramatically in recent decades. In Burkina Faso, the last description of acute cases was back in 1982. During an annual population-based survey in Kaya and Zorgho, two semi-urban areas, febrile individuals from 0-10 years old were evaluated for malaria and dengue virus (DENV). Rapid tests were performed and additional samples on filter paper were taken from every patient with a positive result and every tenth negative, to perform reverse transcription-polymerase chain reaction (RT-PCR) assays. From 259 children (150 in Kaya and 109 in Zorgho), 52.1% were positive for malaria and 6.9% for dengue while 45.2% remained undifferentiated. The RT-PCR results show the presence of DENV2 and DENV4. These findings reveal the presence of DENV in the country and the need to conduct research and actions on non-malaria febrile diseases in the region.

RESULTS

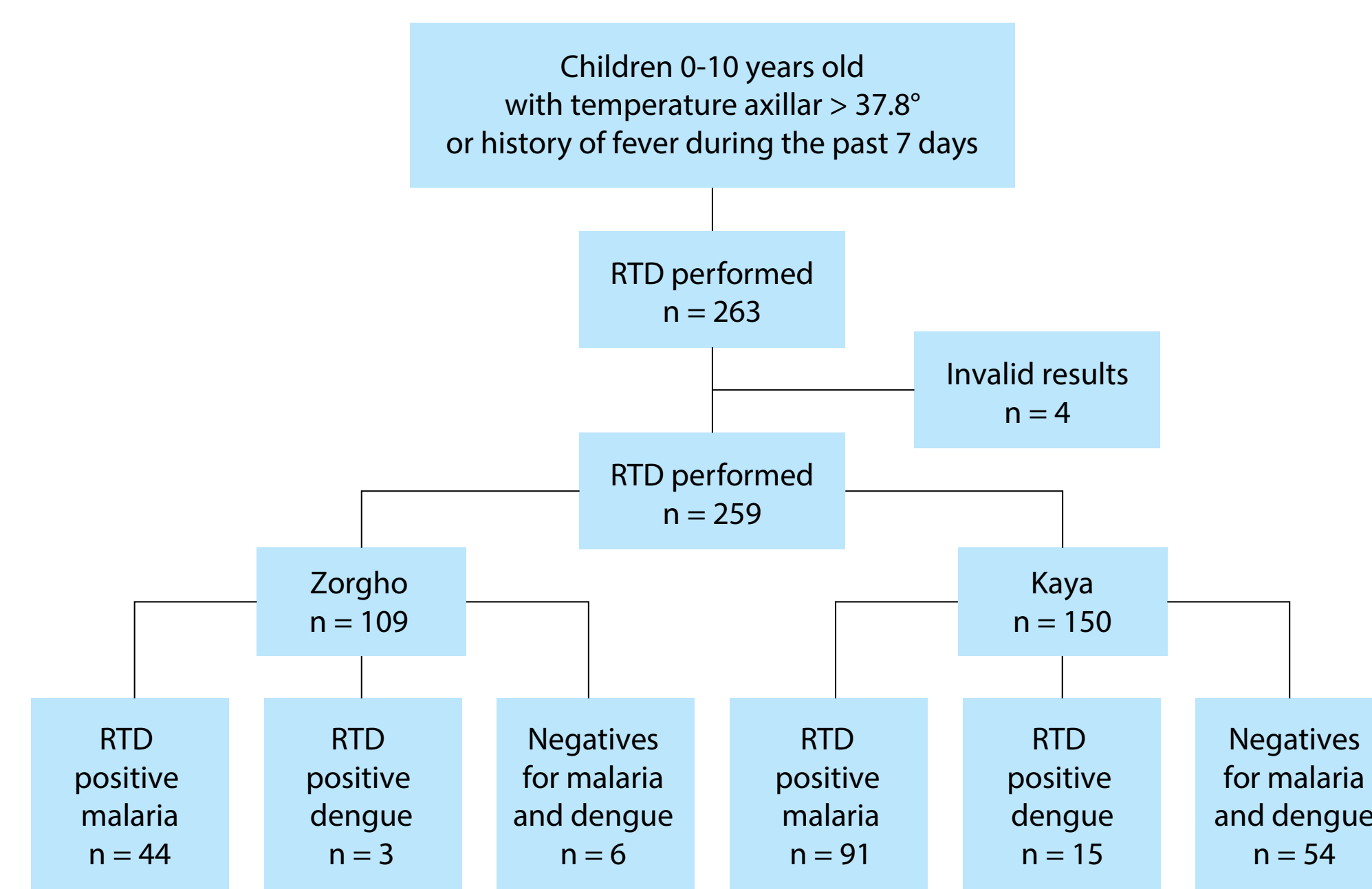


Figure 1. Flow chart of enrollment and classification

CHARACTERISTICS	ZORGHO		KAYA		TOTAL	
	N=109	(%)	N=150	(%)	N=259	(%)
SEX						
Female	50	45.9	56	37.3	106	40.9
AGE GROUP						
0–12 months	8	7.3	5	3.3	13	5.02
13–36 months	17	15.6	27	18	44	17
37–60 months	22	20.2	30	20	52	20.1
61–96 months	49	44.9	71	47.3	120	46.3
97–120 months	13	11.9	17	11.3	30	11.6

PRESENCE OF FEVER	ZORGHO		KAYA		TOTAL	
	N=109	(%)	N=150	(%)	N=259	(%)
Documented fever during the survey	67	61.5	128	85.3	195	75.3
Self-reported history of fever (last 2 weeks)	22	20.2	44	29.3	66	25.5

DURATION OF FEVER	ZORGHO		KAYA		TOTAL	
	N=109	(%)	N=150	(%)	N=259	(%)
< 7 days	22	100	42	95.5	64	97
> 7 days	0	0	2	4.5	2	3

DENGUE RAPID TEST	ZORGHO		KAYA		TOTAL	
	N=109	(%)	N=150	(%)	N=259	(%)
Any dengue RTD positive	3	2.7	15	10	18	6.9
NS1	0	0.0	2	1.3	2	0.8
IgM	2	1.8	5	3.3	7	2.7
IgG	3	2.7	13	8.7	16	6.2

MALARIA RAPID TEST	ZORGHO		KAYA		TOTAL	
	N=109	(%)	N=150	(%)	N=259	(%)
Any malaria RTD positive	44	40.4	91	60.7	135	52.1
Pf.	44	40.4	91	60.7	135	52.1
Pan.	16	14.7	46	30.7	62	23.9

ETIOLOGIES ACCORDING TO RTDS	ZORGHO		KAYA		TOTAL	
	N=109	(%)	N=150	(%)	N=259	(%)
Positive results dengue and malaria	1	0.9	10	6.6	11	4.3
Possible co-infection	0	0.0	4	2.7	4	1.5
Possible presence of other flavivirus	0	0.0	2	1.3	2	0.7
Undifferentiated Fever	63	57.8	54	36	117	45.2

Table 1. Study population characteristics¹

¹ Percentages may not sum to 100 because of rounding

From all children, 124 had positive RTD results for malaria, 18 for dengue and 117 were negative for both RTDs. Kaya had 65.3% (OR = 1.8, 95% CI = 1.1–3, P = 0.02) of all malaria positive results, 83.3% (OR = 3.9, 95% CI = 1.1–14.4, P = 0.02) of all dengue positive results. The majority of undifferentiated cases (i.e.: negative RTD results for malaria and dengue) were found in Zorgho with 53.8% (OR = 0.4, 95% CI = 0.2–0.7, P = 0.0005).

A total of 36 samples were collected in filter paper to be analyzed by RT-PCR, from which three were positive for DENV2 and one for DENV4. One of the individuals with DENV2 was from the 18 negative dengue RTD patients.

CHARACTERISTIC	MALARIA ¹ N=124				DENGUE ² = 18				UNDIFFERENTIATED=117			
	N	%	OR (IC95%)	P	N	%	OR (IC95%)	P	N	%	OR (IC95%)	P
Zorgho	43	34.7			3	16.7			63	53.8		
Kaya	81	65.3	1.8 (1.1-3)	0.02	15	83.3	3.9 (1.1-14.1)	0.024	54	46.2	0.4 (0.2-0.7)	0.0005

SEX	MALARIA				DENGUE				UNDIFFERENTIATED			
	N	%	OR (IC95%)	P	N	%	OR (IC95%)	P	N	%	OR (IC95%)	P
Female	52	41.9			4	22.2			50	42.7		
Male	72	58.1	0.9 (0.6-1.5)	0.75	14	77.8	2.6 (0.8-8.1)	0.095	67	57.3	0.9 (0.5-1.4)	0.6

AGE GROUP	MALARIA				DENGUE				UNDIFFERENTIATED			
	N	%	OR (IC95%)	P	N	%	OR (IC95%)	P	N	%	OR (IC95%)	P
0–12 months	0	0			0	0			13	11.1		
13–36 months	13	10.5			6	33.3			25	21.4		
37–60 months	27	21.8			5	27.8			20	17.1		
61–96 months	66	53.2			6	33.3			48	41		
97–120 months	18	14.5	1.6 (1.3-2.1)	0.000	1	5.6	0.7 (0.5-1.2)	0.19	11	9.4	0.6 (0.5-0.8)	0.0003

PRESENCE OF FEVER	ZORGHO		KAYA		TOTAL	
	N=109	(%)	N=150	(%)	N=259	(%)
Documented fever during the survey	96		128		195	
Self-reported history of fever (last 2 weeks)	40	1.9 (1.1-3.5)	44	0.016	66	0.025
Days of fever						
<1 day	5	12.5			5	22.7
1 to 7 days	34	85			16	72.7
>7days	1	2.5	1.7 (0.5-5.3)	0.389	1	4.5

Table 2. Socio demographic and clinical features of all individuals according to the fever etiologies

² Only positives result from either Malaria Pan or Malaria Pf rapid test.

³ Definite case and probable dengue case; see methods section.

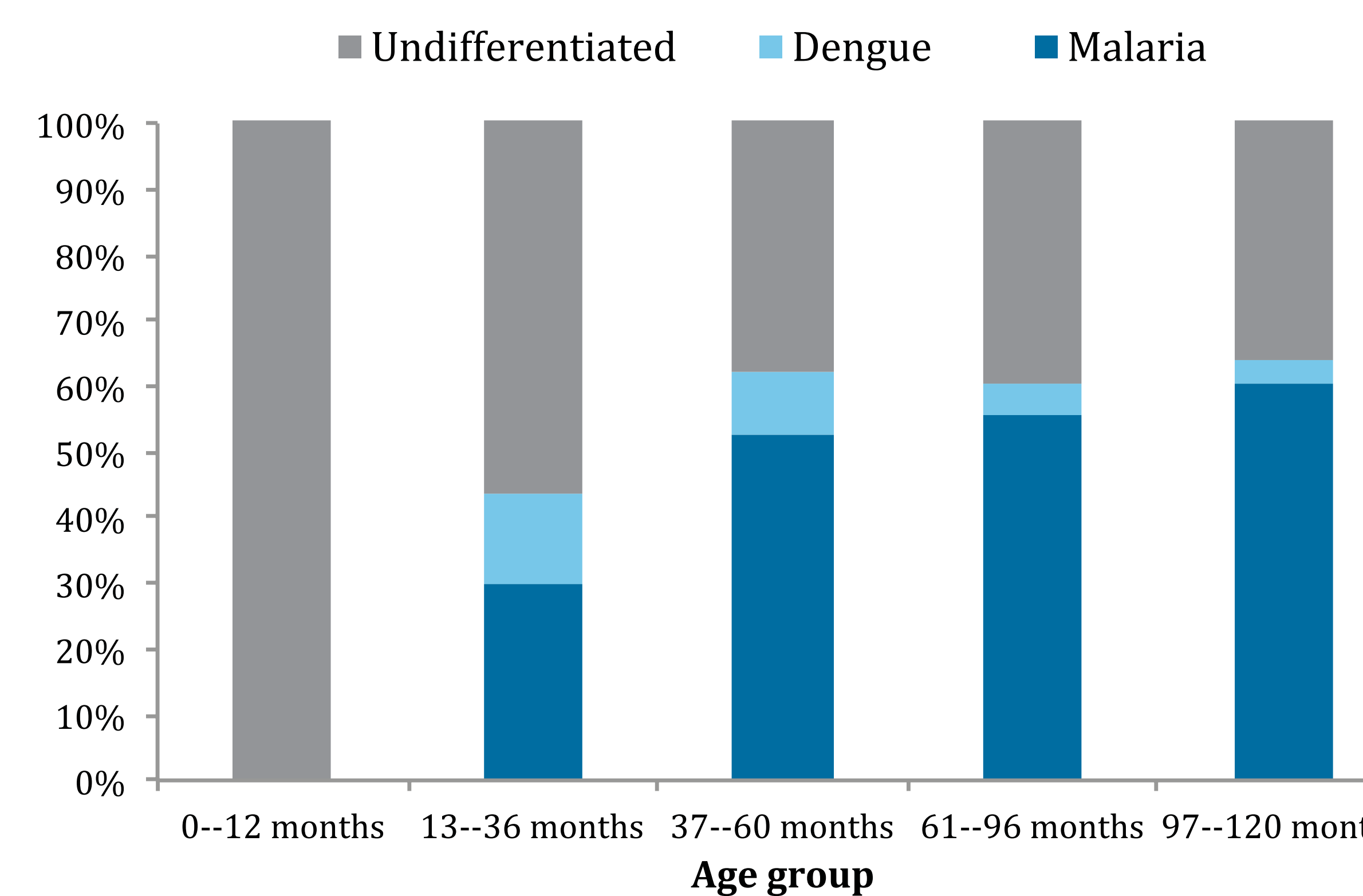


Figure 2. Distribution of febrile etiologies across age group (n = 259)

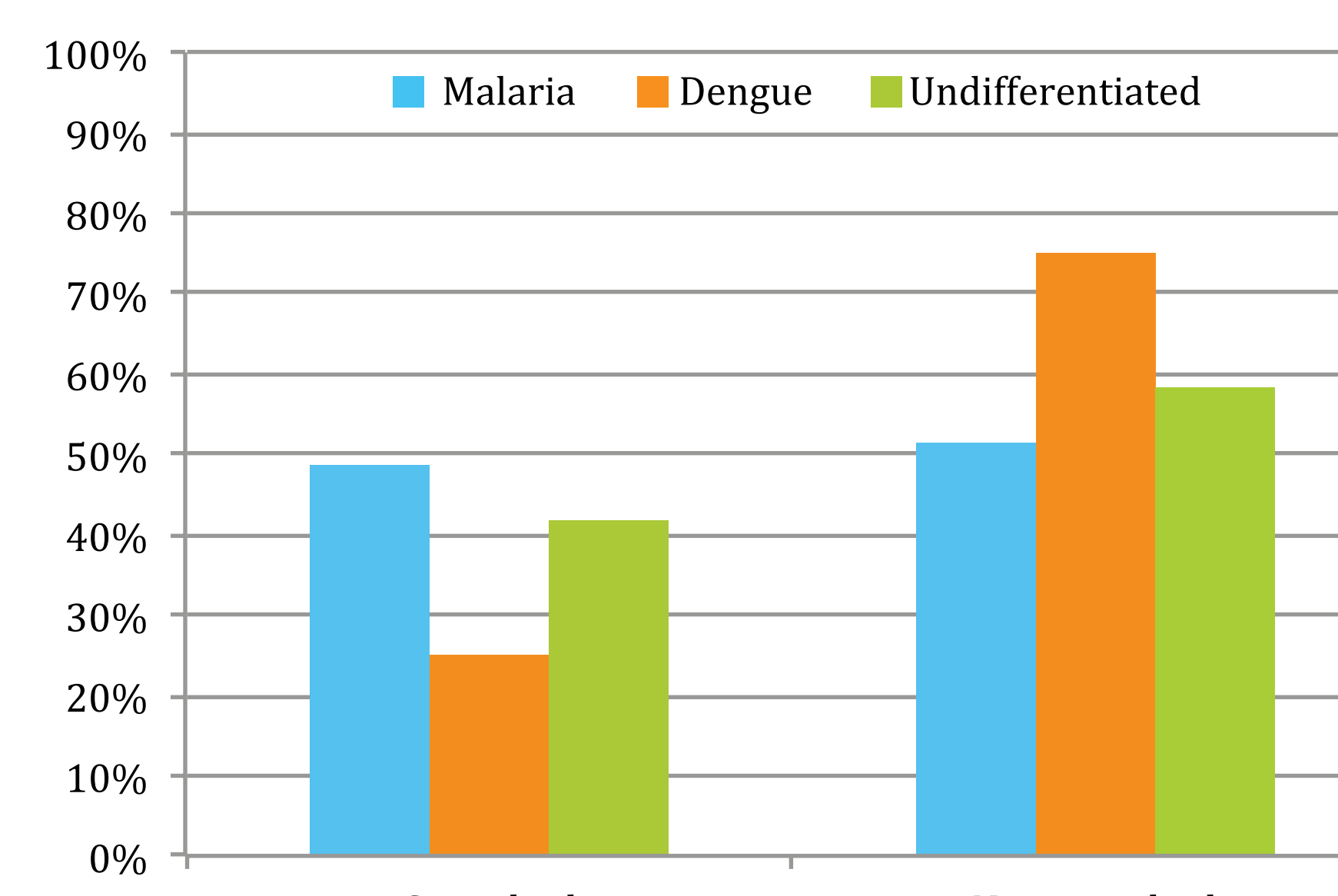


Figure 3. Health seeking behavior of individuals according to the fever etiologies (n = 63)

LIMITATIONS

Contextual limitations such as local temperature, distance to health care centers, and the lack of some laboratories facilities made difficult the use of other type of tests (i.e., IgG Indirect ELISA for serological prevalence or IgM/IgG capture for acute cases). Therefore, the combination of TDR and filter papers was a practical methodology to explore dengue presence.

CONCLUSIONS

- Thirty years after its last report, dengue presence has been documented in febrile children, from semi-urban areas of Burkina Faso in 2013. Thus, allowing the possibility to consider DENV as one of the causes for non-malaria febrile diseases in the country.
- This is the first time DENV4 has been documented in the region and the first time that more than one serotype is reported simultaneously in Burkina Faso.
- These findings reveal the need to conduct research and actions on non-malaria diseases in the region.

PUBLIC HEALTH IMPLICATIONS

- Need of an improved diagnosis for febrile patients, especially children under 5 years old.
- Improved vector control and training to the health staff

ACKNOWLEDGMENTS

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KEY REFERENCES

1. Ridde V, Carabali M, Ly A, et al. (2014) The Need for More Research and Public Health Interventions on Dengue Fever in Burkina Faso. PLoS Negl Trop Dis 8(6): e2859. doi:10.1371/journal.pntd.0002859
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