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RESEARCH ARTICLE

Dengue Fever Seroprevalence among Children Aged 0-5 Years at Paediatric University Hospital, Ouagadougou

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Abstract

Background: Dengue fever is a vector-borne disease that raises a major public health problem worldwide, particularly in Burkina Faso. The gold standard diagnosis is based on the research of viral RNA by reverse transcriptase polymerase chain reaction (RT-PCR) during the first days, or the presence of specific immunoglobulin M (IgM) by serological tests or the isolation of the virus. Burkina Faso reported a localized outbreak of dengue fever in 2016. This study aimed to evaluate dengue fever seroprevalence among children aged 0-5 years.

Methods: This was a descriptive cross-sectional study which covered the period from January 2016 to December 2019 and involved 621 suspected cases of children aged 0-5 years at the Charles de Gaulle University Paediatric Hospital in Ouagadougou, Burkina Faso from

Results: Of the suspected cases,189 were confirmed positive to dengue fever with a seroprevalence of 30.47%. Among positive cases, young children (1 to 29 months age group) were the most represented, with a sex ratio (M/F) of 1.15 in favor of males (53.44%) of dengue cases. Clinical symptoms were polymorphous. Fever (86.24%), algic syndrome (75.13%) and vomiting (46.03%) were the most frequent clinical manifestations. The majority of patients (28.57%) had positive IgG serology. The main biological feature was thrombocytopenia (26.50%), (*p=0.039*).

Conclusion: This study confirms the emergence of this disease in young children, as mentioned in previous studies. Improving the technical facilities in our hospitals, providing ongoing training for healthcare workers in the management of this disease and disseminating the national protocol for the management of dengue fever could improve the situation.

Keywords: Seroprevalence, Dengue Fever, Children, Burkina Fas.

Introduction

Dengue fever is a viral infection transmitted by the bite of Aedes mosquitoes. Symptoms can range from a mild febrile syndrome to a high, incapacitating fever with a rash, intense headaches, and muscle and joint pain. Dengue hemorrhagic fever is a potentially fatal complication, seen mainly in children. Treatment

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is symptomatic, as there is no specific antiviral treatment for this disease. However, since 2016, there has been a vaccine (Dengvaxia) against the dengue virus, which is not yet available in all the countries affected by this disease [1]. Dengue fever is rife in tropical and subtropical regions throughout the world. In recent years, global incidence has risen sharply, and geographical spread has increased, particularly in urban and peri-urban areas of Latin America, South-East Asia, the Western Pacific and Africa, making the disease a major public health concern (reference??). Around half the world's population is at risk. In recent years, cases of dengue fever have been reported in Europe, notably in Madeira in Portugal and in south-eastern France[1]. The incidence of dengue fever has risen dramatically in recent decades. The number of cases is underestimated, as the majority are asymptomatic or benign and self-treated. In addition, as with other febrile illnesses, many cases are misdiagnosed[2]. According to modelling estimates, 390 million dengue virus infections occur every year, 96 million of which manifest themselves clinically[3]. Dengue is thought to be the most widespread arbovirosis in the world, affecting around 3.9 billion people in 129 countries[4]. In Africa, little is known about the impact of the disease, but recent epidemics suggest that a large part of the continent could be at increased risk of transmission. The virus has been found to circulate in West Africa and in coastal areas of East Africa. Severe forms of the disease appear to be rarer. Some authors have suggested the possibility of genetic protection for Africans of African origin, based on the epidemic in Cuba in 1981, where Afro-Cubans appeared to be partly protected[5].

Burkina Faso reported a localized outbreak of dengue fever in 2016, with 1,061 probable cases, according to epidemiological data from the Department of Population Health Protection (DPSP). The first dengue epidemic is thought to have occurred in 1925[2]. Subsequently, a large number of cases were identified in the 1980s[6]. Burkina Faso is one of 34 African countries where cases of dengue fever have been reported since 2000[7]. Research carried out in 2003 among 191 blood donors and 492 pregnant women in a rural district (Nouna) and the capital (Ouagadougou) showed that between 26% and 39% of those surveyed had been in contact with the dengue virus. Another study carried out in 2004 among 3,000 children in Ouagadougou revealed that 22% of them had been in contact with a virus from the Flavivirus family, to which the dengue virus belongs[8]. Despite the fact that children are the most vulnerable, we have no data specific to this sub-population. With this in mind, the aim of this study is to examine the epidemiological profile of dengue fever at the CHUP-CDG in order to help improve the management of this disease in Burkina Faso.

2. Methods

2.1 Type and Study Setting

This study was carried out in the clinical and laboratory departments of the Charles de Gaulle University Paediatric Hospital (CHUP-CDG)in the city of Ouagadougou. It was a descriptive cross-sectional study that took place from January 2016 to December 2019.

2.2 Samples and Data Collection

This study included 621 patients aged between 0 and 5 years admitted to the CHUP-CDG whether hospitalized or not, for whom the inclusion criteria were met for the period of our study. All patients admitted to the CHUP-CDG and in whom a dengue diagnostic test was requested were included in this study; those whose personal details were correctly recorded in the register and patients whose dengue serology was carried out at the CHUP-CDG. Finally, patients for whom the results of biological parameters have been carried out, recorded and are available. Sampling was systematic and exhaustive, and only included patients who met the inclusion criteria. The data collection tools were essentially the patients' medical records, the data collection form and the medical analysis laboratory register. The variables included in this study were sociodemographic characteristics such as age, sex, place of birth and place of residence. There were also clinical parameters such as temperature, weight, blood pressure, pallor, respiratory distress, convulsions, pulse, vomiting, prostration, collapse, anemia, oedema, and diarrhea.

2.3 Biological Diagnostic

Finally, the biological variables included the dengue serological test (AgNS1, IgM, IgG),. the leucocyte count, the red blood cell count and the platelet count.

2.4 Data Analysis

Data was entered and analyzed on a computer using Microsoft Excel and then analyzed using Epi Info Version 7 software for descriptives statistics

2.5 Ethical Considerations

This protocol was submitted to the General Director

of the CHUP CDG for approval. The confidentiality of patients' personal data was preserved during data collection.

3. Results

Socio-demographic charactersitics of 621 subjects included in the study, 347 (55.9%) came from external structures and 274 (44.1%) from the CHUP-CDG. The average age of the patients was 27.2 months and age is between 1- 60 months. Also, 50% of the children were over 25 months old. The study population was predominantly represented by children aged 0 to 29 months (n=367), i.e. a frequency of 59.1%. The age group 30 to 60 months was 40.3%.

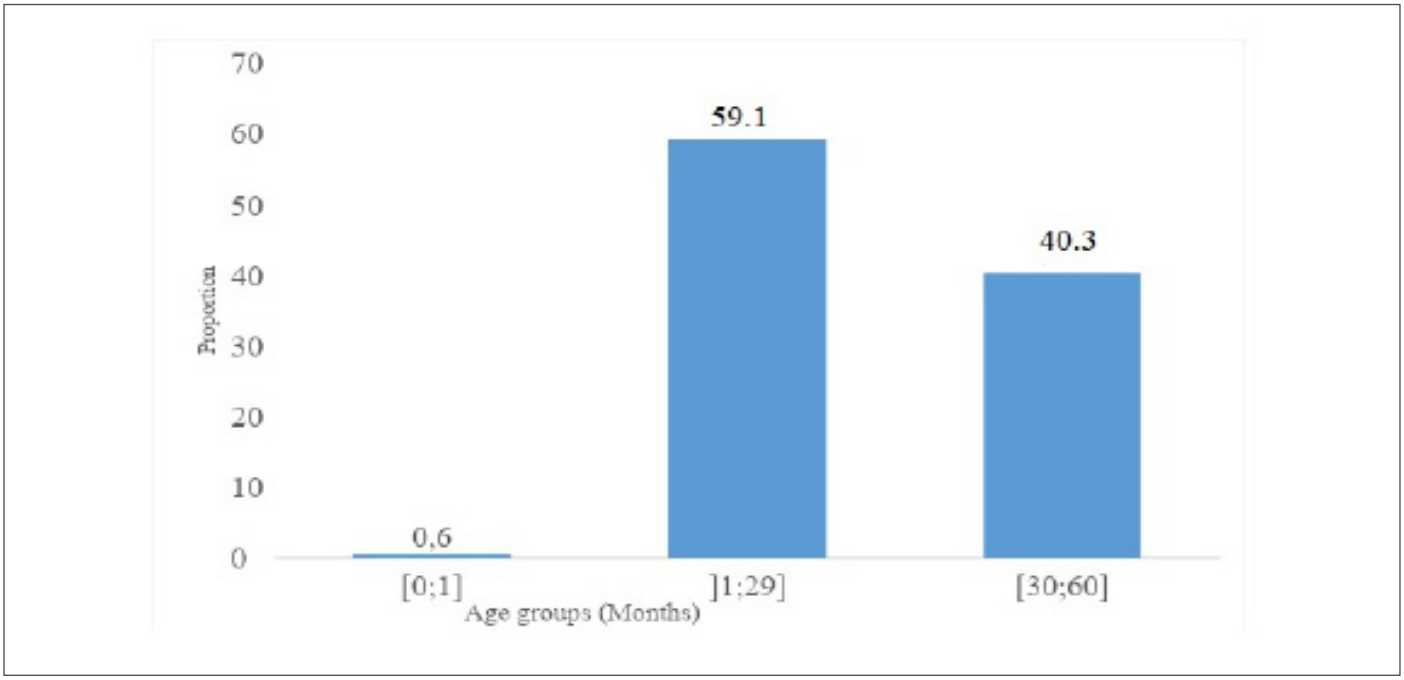

Figure 1. *Breakdown of study population by department of origin*

Males were the most represented (329/621) with a frequency of 53.1%. The sex ratio (M/F) was 1.13 in favour of men. During the study, patients from external facilities (EXT) represented more than half of the study population, i.e. 55.9%, compared with 44.1% from CHUP-CDG internal services (INT). Patients from the CHUP-CDG Infants and Infectious Diseases (IM) departments were few in number, with frequencies of 16.3% and 15.1% respectively. The Oncology (ONCO) and Surgical Emergencies departments had the lowest frequency, at 0.2%.

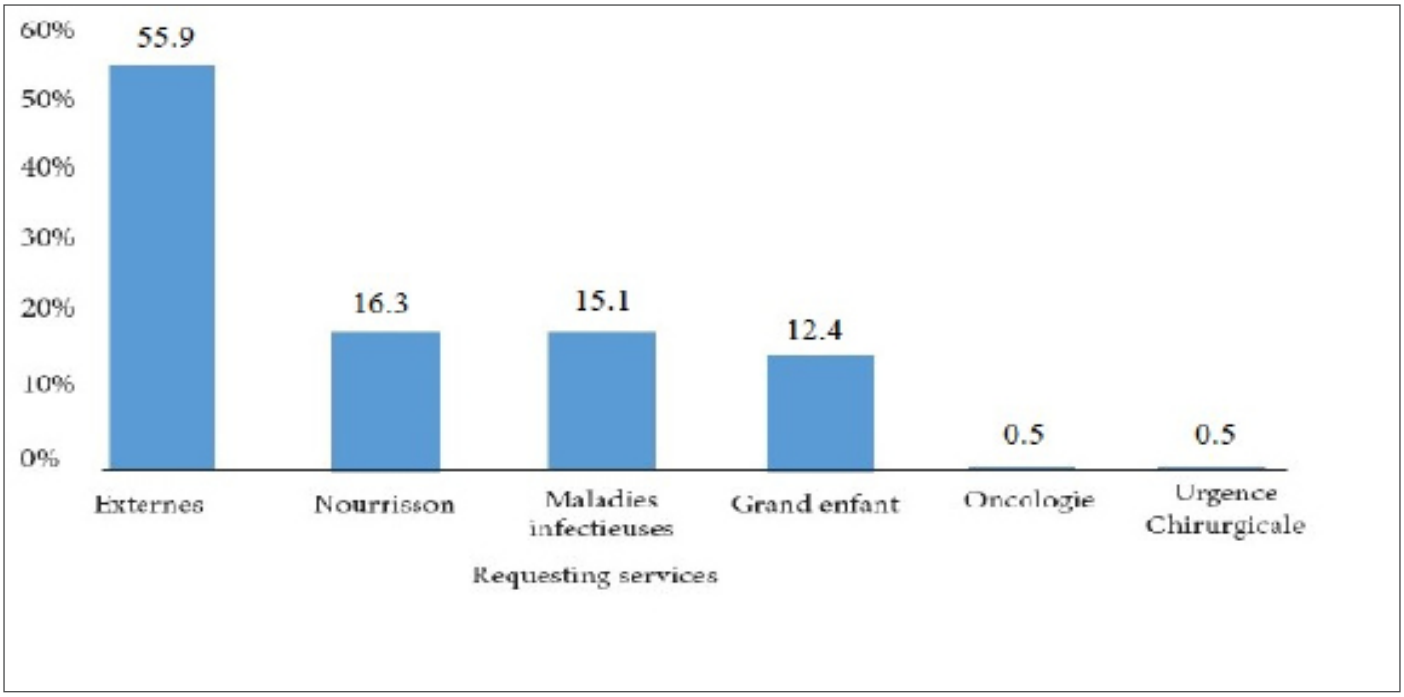

Figure 2. *Breakdown of study population by department of origin*

Dengue serology was positive in 189 cases (30.47 %). The following table shows the frequency of dengue cases in relation to the study population.

Table 1. *Frequency of dengue cases in relation to the study population*

Serology Dengue	Number	Frequency (%)
Negative	432	69.57
Positive	189	30.47
Total	621	100

The serological profile of children testing positive for dengue showed that 18% (34/189) had an acute infection (NS1+) of which 2.7% (5/189) had (NS1+/ IgM+) and 1.6% (3/189) (NS1+/ IgG+); 12.2% (23/189) had a secondary infection to dengue (NS1+IgM+IgG+). Past exposure to the virus (IgG+) accounted for 28.6% (54/189) of cases. A further 24.3% (46/189) had a late onset or recent secondary dengue infection (IgM+/ IgG). (Fig 13).

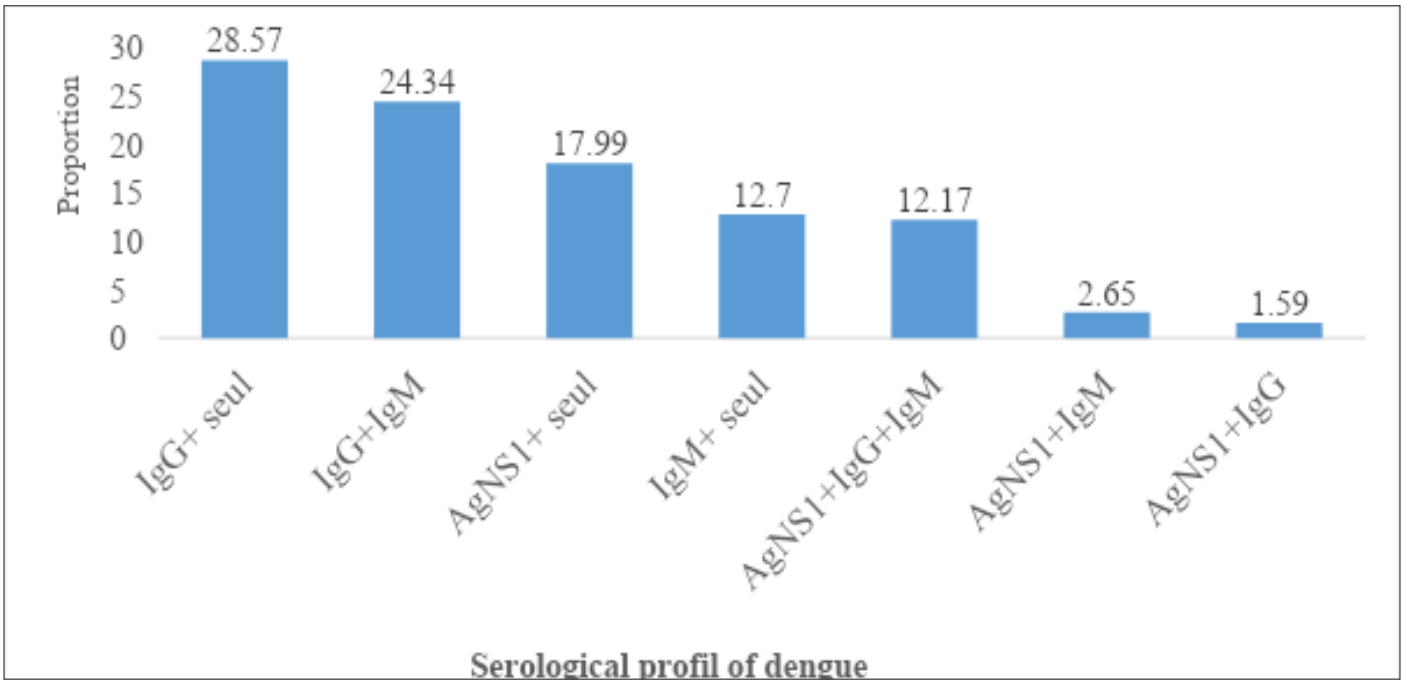

Figure 3. *Illustration of serological data for dengue-positive cases*

The mean age of positive dengue cases was 30.74 months, with extremes ranging from 2 to 60 months. The majority of positive cases were in the 1-30 month age group (n=100), representing a frequency of 52.91%. The 30-60 month age group accounted for 47.09%. The distribution of dengue cases by age group is shown in Table 2.

Table 2. Distribution of dengue cases by age group

Age groups (Months)	Dengue cases	Frequency (%)
] 0 ; 1]	0	0.0
] 1 ; 30]	100	52.9
] 30 ; 60]	89	47.1
Total	189	100

The male sex was the most represented, with 101 cases compared with 88 female cases, giving a sex ratio (M/F) of 1.15 in favor of men.

The serological profile of children testing positive for dengue showed that 18% (34/189) had an acute infection (NS1+) of which 2.7% (5/189) had (NS1+/ IgM+) and 1.6% (3/189) (NS1+/ IgG+); 12.2% (23/189) had a secondary infection to dengue (NS1+IgM+IgG+). Past exposure to the virus (IgG+) accounted for 28.6% (54/189) of cases. A further 24.3% (46/189) had a late onset or recent secondary dengue infection (IgM+/ IgG) (Fig 13).

Table 3. Distribution of dengue cases by department of origin

Requesting services	Dengue Cases	Frequency (%)
Externes	96	50.8
Maladies infectieuses	44	23.3
Nourrissons	27	14.3
Grands enfants	22	11.6
Oncologie	0	0.0
Urgences chirurgicales	0	0.0
Total	189	100

At the end of this breakdown of dengue cases by department, the dynamics of dengue cases during the study should be given. Thus, the years 2017 and 2019 saw an increase in the seroprevalence of positive dengue cases compared with 2016 and 2018, when it was relatively declining. Periods of high endemicity occurred from August to December of each year, with peaks in October.

Figure 3 below shows the evolution of the number of dengue cases by month and year over the entire study period (January 2016 to December 2019)

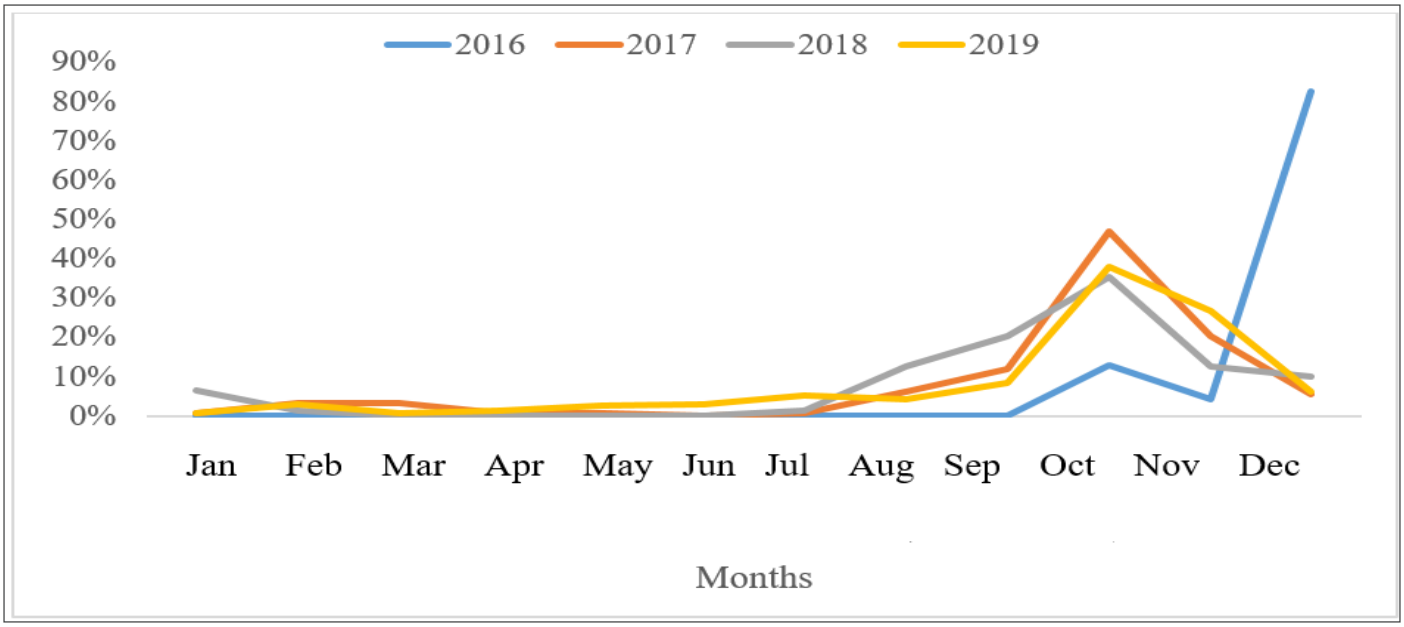

Figure 4. *Dynamic of dengue cases during the study period*

The clinical symptoms of dengue fever are polymorphous. Fever (91.5%; n=173), algic syndrome (75.1%; n=142) and vomiting (46.0%; n=87) were the most frequent clinical manifestations. Clinical symptomatology is summarized in Table IV.

Table 4. Distribution of patients according to clinical signs

Clinical symptoms	Number	Frequency (%)
Fever	163	86.2
Algesic syndrome	142	75.1
Vomitings	87	46.0
Asthenia	51	27
Convulsion	35	18.5
Chills	29	15.3
Jaundice	17	9.0
State of Shock	6	3.2

This clinical symptomatology is accompanied by biological disturbances. Biochemical data were recorded in 389 patients, 159 of whom were positive for dengue fever. Thus, 16.4% (26/159) had hyponatremia, 9.4% (15/159) were hypocalcemic and 24.5% (33/159) had metabolic acidosis.

Several hematological parameters were noted. Thus, 35.2% (31/88) had thrombocytopenia. However, 18.2%

(16/88) of patients had thrombocytosis. Similarly, hematocrit was reduced in 93.8% (61/65) of patients. A further 6.2% (4/159) had normal hematocrit, and the mean hematocrit was 24.1%. Table V shows the various biological disturbances observed during the course of the dis

Table 5. Biological disturbances in dengue cases

Parameter	N	n	Frequency (%)
Anemia	88	62	70.5
Hemoconcentration	65	0	0
Hemodilution	65	61	93.8
Leukocytosis	88	16	18.2
Leukopenia	88	16	18.2
Lymphocytosis	78	7	9
Lymphopenia	78	26	33.3
Thrombocytosis	88	16	18.2
Thrombocytopenia	88	31	35.2
CRP	159	78	49.1
Sodium	159	26	16.4
Calcium	159	15	9.4
Bicarbonate	159	33	24.5

In addition to biological disturbances, it seems appropriate to give a univariate analysis of biological disturbances during dengue showed the results represented in the following Table VI:

Table 6. Results of the univariate analysis of biological disturbances during dengue fever

Parameter	Dengue (n=189)		P-value
	Number	Frequency (%)	
Anemia	62	32.8	0.189
Hemoconcentration	0	0	-
Hemodilution	61	32.2	0.728
Leukocytosis	16	8.5	0.407
Leucopenia	26	13.76	0.543
Lymphocytosis	7	3.7	0.909
Lymphopenia	26	13.8	0.124
Thrombocytosis	16	8.5	0.626
Thrombocytopena	31	16.4	0.039

Thrombocytopenia was a statistically significant biological disturbance in dengue fever(p=0.039). Certain comorbidities were also observed. In particular, malaria was the disease most frequently observed in the presence of dengue, accounting for 30.7% of cases (n=58). Table VII shows the distribution of patients according to the diseases associated with dengue.

Table 7. Distribution of patients according to co-infecting diseases

Co-infection	Number	Frequency (%)
Malaria	58	30.69
Viral hepatitis	16	8.47
HIV	4	2.12

Finally, we have also considered the evolutionary modalities. These were length of hospital stay and discharge patterns. Hospital stays ranged from 2 to 29 days, with an average of 8 days. Of the 189 confirmed cases of dengue fever, 91.5% (173/189) were cured and 2.1% (4/189) had an unknown outcome. Finally, 6.4% (12/189) had improved on discharge.

Moreover, all registered patients were 100% cured (185/185).

4. Discussion

According to socio-demographic characteristics, the most represented age bracket in this study was 1 to 29 months with 59.1% versus 40.3% among children aged 30 to 60 months in the study population; mean age was 27.2 months. The 1-29 months age group accounted for 52.9% and 47.1% of dengue-positive cases in children aged 30-60 months. Many authors corroborate this youthful trend in dengue cases. Kané et al. (2020) in Burkina Faso showed that infants were the most affected with 41.9%, with an average age of 4.8 years [9]. These data may be explained by the fact that severe dengue fever occurs predominantly at younger ages [10]. At birth, the newborn is protected against many viral attacks by maternal antibodies. In the case of dengue fever, maternal antibodies are protective against the circulating serotype in the first few months, then their neutralizing power diminishes and they may play a role in facilitating infection. According to the work of Suchat et al. (2001) in Thailand, dengue hemorrhagic fever accounted for 95% of cases in infants aged between 3 and 8 months [11]. This predominance may be linked to the nature of the hospital, which is pediatric and specializes in the care of children aged 0 to 15 years. The sampling technique included hospitalized and non-hospitalized patients who were able to pay the consultation fees. This is made possible by the fact that care for children aged 0 to 5 is free of charge, which is a priority of government policy in Burkina Faso. What's more, children of this age are highly mobile, and are likely to frequent damp areas that are breeding grounds for mosquitoes. This result corroborates that reported by most authors, notably Carlos et al. (2005) in a study of clinical signs and biological abnormalities between dengue fever and dengue hemorrhagic fever between 1999 and 2001 in the Philippines [12]. In, Kamath et al.(2006) in a study of complications and atypical clinical manifestations of severe forms of dengue haemorrhagic fever in children in southern India [13]; Witayathawornwong in 2001 in a comparative study of dengue haemorrhagic fever in infants and older children between 1997 and 1999 in Thailand reported a male predominance [14]. This could be explained by the fact that men are the most exposed, as they frequent humid areas that are mosquito habitats[15]. One hundred and eighty-nine (189) patients were declared probable cases at the end of the study. The outpatient department recorded the highest number of probable cases, i.e. 50.8% of the study population. This high proportion of outpatients can be explained by the fact that the outpatient department is one of the hospital's main points of entry. The same observation was made in a Malaysian study in 2010 involving both adults and children who reported outpatient distribution of severe dengue [16]. The prevalence of dengue virus infection varies considerably from month to month over the course of the year. The number of cases was on the rise during the period from July to November 2017, with a peak of 46.9% in October. These results are in line with those of Héma et al. (2016) in Burkina Faso in his work which focused on the molecular diagnosis of dengue cases in Ouagadougou which showed an increase in cases from August onwards with a peak in October[17]. Between 2001 and 2002, Monnin et al. (..) in Martinique, in a study carried out during a dengue epidemic in a pediatric ward, made the same observation[18]. A very significant reduction in the number of cases was noted between January and June. The seasonal periodicity of dengue fever could explain this trend. In fact, the rainy period from July to September coincides with the period when the cyclonic risk of Aedes is high, due to the high level of humidity. This would explain the high number of cases in October and November. Also, the further away we are from the rainy season, the less humidity and mosquitoes there are; and consequently, dengue transmission is reduced. This could explain the drop in the number of cases during the dry season between February and June. It is therefore essential to implement a policy of prevention, such as the elimination of mosquito breeding grounds, and the use of insecticides such as indoor spraying and outdoor fogging. In addition, preventive measures can be taken at individual level, such as applying repellent products, wearing light-colored clothing with long sleeves and using insecticide-impregnated mosquito nets. This reduces the transmission of infectious agents such as the dengue virus.

In this study, the clinical signs found were fever (86.24%), asthenia, algic syndrome, vomiting, convulsions and jaundice. These results are supported by those of Monnè et al. (2017), who in a study of dengue fever in Ouagadougou reported 84.2% fever, 67.1% algic syndrome and 44.3% vomiting [19]. This is also the case for Aug et al [20] who reported in Bangkok in 2006 (100% fever, 70% headache, nausea/vomiting 70.30%). Faye et al. in Senegal in 2009 reported 100% fever, 51% headache and 60% myalgia [21]. These signs are classically found in the clinical manifestations of dengue fever. NS1 antigen is the serological marker of acute dengue virus

infection. In our series, it was detected in 18% of cases. Our data differ from those of Mishra et al, who found AgNS1 in 23.1%, and also from those of Soma in Burkina Faso, who found it in 87.5% [22]. Early diagnosis of dengue fever is based on the detection of AgNS1. This protein is secreted during infection by all serotypes, but does not differentiate between them. It is found at high levels in serum, varying between 0.04 and 2 µg/ml between day 0 and day 5, and disappears around day10[23]. During this phase, the patient is a reservoir of virus for mosquitoes. This frequency is relatively lower than that found by Ridde et al. in their work on children in Zorgho and Kaya, where 83% of cases were positive for AgNS1[24]. In addition, type M immunoglobulins (IgM) were positive in 12.17% of cases, and IgG in 28.57%. These results are relatively close to those of Soma, who reported 12.5% for IgM in patients and 26.79% for IgG[22]. The high frequency of IgG (28.57%) found in this study could be explained by the fact that the SD BIOLINE Dengue Duo® test was performed late after the onset of clinical signs, hence the presence of IgG, which appears and persists for a long time in the body. This would suggest that the presence of IgG is evidence of secondary dengue fever, or an old malaria infection with a clinical picture identical to that of dengue fever. Thrombocytopenia was found in 16.8% of patients. These data fall short of those of Kamath SR in India, who reported that 100% of patients had thrombocytopenia with a platelet count < 100,000/µL[25]. We reported significant thrombocytopenia ($p = 0.039$) in dengue cases, as did Ali et al[26]. A study by Praveen in India reported a correlation between thrombocytopenia and the onset of severe dengue fever[27]. In the literature, thrombocytopenia is classic and forms part of the definition of dengue hemorrhagic fever [28]. The mechanism of thrombocytosis is linked to phagocytosis of platelets by macrophages, particularly in severe forms of the disease. This property of DENV may explain platelet consumption and the link between thrombocytopenia, viral load and clinical severity. Moreover, the mechanism of thrombocytopenia is not only peripheral but also central [29]. The mean hematocrit was 24.1%, with extremes ranging from 7.4% to 45.3%. In our study, hematocrit was below normal in 61 patients (32.2%). This result could be explained, on the one hand, by multiple infusions with physiological saline, exacerbating the anemia; on the other hand, by anemia resulting from an unbalanced diet with a significant vitamin B12 or B9 deficiency, or by a bone marrow disorder (in aplastic anemia, blood cell production is greatly reduced) [30]. We observed an increase in hematocrit in one patient (0.5%). Elevated hematocrit levels are a sign of hemoconcentration and a predictive parameter for severe forms of dengue fever [31]. The hematocrit level cannot justify hospitalization of a patient on the basis of a single assay, but it does guide therapy, as recommended by the WHO. In fact, a 25% increase in hematocrit over several determinations is considered a factor in the occurrence of severe dengue fever[32]. These findings demonstrate the importance of repeated biological monitoring of patients by the attending physician. The fact that this is so rarely carried out reflects the lack of knowledge of the mechanism of dengue fever among health workers, and the importance of testing for this parameter in the management of severe dengue fever [32, 33]. Anemia was found in 32.8% of patients, and the mean hemoglobin level was 7.8g/dL. This result is similar to those of other authors such as Arundhati et al. in Mumbai; and Murali et al. who reported a mean hemoglobin level of between 9.9 g and 11.2g/dL in patients with dengue fever[34, 35]. Co-infections and repeated hemorrhages could explain these data. In our series, 16 patients (8.5%) had hyperleukocytosis, 45 patients (57.7%) had normal leukocyte counts and 26 patients (13.8%) had leukopenia. The mean leukocyte count was 11410/µL. Leukopenia is a constant feature of dengue fever. It initially consists of lymphopenia, followed by neutropenia[29]. A drop in bicarbonates was noted in 24.5% of dengue cases in this study. This result is significantly higher than that of Vachvanichsanong et al. who found 14%[36]. These low HCO_3 values could be explained, on the one hand, by digestive losses (nausea, vomiting) and, on the other, by renal impairment in some of the patients. Hyponatremia was found in 16.6% of dengue cases. These results are low compared with those of Ilboudo; Vachvanichsanong et al. who noted 23.1% and 46.7% hyponatremia[30, 36]. The overall mean calcium value was 2.3 mmol/L. Hypercalcemia was found in 9.4% of patients. These results are well below the 45% of hypocalcemic patients reported by Dibri during dengue fever [7]. Hypercalcemia could be explained by excess calcium, which remains an important parameter for avoiding cardiac complications[37]. This result exceeds that of Héma, who noted a proportion of 25.5% [17]. In contrast, Tamalepko's series from Ouagadougou found 42.9% co-infection, with a case-fatality rate of 75% [38]. This proportion can be explained by the fact that Burkina Faso lies in an area of high malaria endemicity. It is also explained by the same mode of occurrence of this disease, namely

the notion of a vector, the hematophagous mosquito. Pending studies to establish the mechanisms behind the severity of this association, RDTs and thick blood tests should be made available and accessible in all health centers in Burkina Faso, for early detection of these two diseases, whose association can sometimes prove highly morbid. The duration of hospitalization ranged from 2 to 29 days, with an average length of stay of 8 days. This result is slightly higher than that of Faye et al. who recorded an average length of stay of 6 days in Senegal, in contrast to Tamelepko who reported an average length of stay of 4.6 days [38,39]. This duration reflects the favorable evolution of the disease, especially when it is managed early. Analysis of patient outcome showed that most patients were cured (n=185; 100%). The absence of lethality observed in our study differs from those reported by Diallo et al. 4.1%; Monné with 2.9% deaths in Burkina Faso [19]; and Mariko in Mali with 3.7% [40]. However, Bouldouyre in New Caledonia reported a considerably higher rate at 41.7% [41].

5. Limitations of this Study

The present study had its limitations. Of the 704 dengue cases notified, 621 had usable data. Also, of the 621 cases with usable results, several pieces of information were missing. It couldbe linked to a heavy workload for health workers, or to a lack of cooperation from patients

6. Conclusion

This study confirmed the presence of dengue infection in our context, noted the predominance of the recovery phase, and highlighted cases of co-infection. This work suggests the need for rigorous epidemiological and entomological surveillance, with appropriate patient management. Dengue does not have a specific clinical picture, and paraclinical examinations must be used to clarify the diagnosis. The disease can progress to a severe form within a few dozen hours, requiring immediate intensive care. This is why children must be seen again if there is the slightest doubt.

Moreover, the exponential spread of dengue fever in recent decades has raised the question of the role played by global warming. As with malaria, prevention requires vector control. Raising awareness among the general public and primary healthcare workers, and making diagnostic kits available, will help reduce the frequency of dengue fever in the years to come, and prevent severe forms of the disease

7. Conflict of Interest

The authors declare that they have no conflict of interest in the publication of these data.

8. Acknowledgements

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8.1 Authors' Role

Conceptualization: KD , SM , OTR

Data curation: KD ; DU

Formal analysis: KD, DU, SM

Investigation: KD , TM , OO

Resources: OTR, SM

Supervision: KD, OTR, SM

Validation: OTR, SM, KD

Visualization: KD, ZAA, OO, KDS, CTR, ZS, ST, SST, SLO, OHG, OTR, SM

Writing ± original draft: KD, DU, SM

Writing ± review & editing: KD, DU, OTR, SM, OHG, OO

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