Research Article

Microbiological Profiling of Secondary Infections in Dengue Patients: Implications for Clinical Management

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ABSTRACT

Background: Dengue fever is a prevalent vector-borne disease that can lead to severe complications, including dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Secondary infections in dengue patients, whether bacterial, fungal, or viral, are a significant concern as they can complicate the clinical course, worsen disease outcomes, and increase hospital stay duration. This study aims to identify the prevalence, microbial profile, and clinical impact of secondary infections in dengue patients, providing insights for better clinical management. **Methods:** This cross-sectional observational study was conducted on 110 dengue patients admitted during the peak transmission season. Patients were diagnosed with dengue based on serological tests (IgM/IgG) and/or RT-PCR. Clinical assessments, microbiological investigations (blood, urine, sputum, and wound cultures), and antimicrobial susceptibility tests were performed to identify secondary infections. Demographic, clinical, and laboratory data were recorded, and the correlation between secondary infections and disease severity was analyzed using statistical methods. **Results:** Among 110 dengue patients, 61.8% were male, and the highest age group was 21–40 years (28.2%). Most patients (70%) had no comorbidities. Fever (100%), rash (80%), and hemorrhagic manifestations (30%) were common, with severe forms (DSS/DHF) in 30%. Secondary infections occurred in 40.9% of patients, with bacterial infections (62.2%) being the most frequent. Secondary infections were more common in adults aged 21–60 years (45.5%) and those with severe dengue (62.5% vs. 35.4%, p<0.01). Risk factors for secondary infections included age >40 years, comorbidities, and severe dengue (p=0.02, p=0.03, p=0.04, respectively). Patients with secondary infections had longer hospital stays (7.8 vs. 4.6 days, p<0.001) and higher ICU admissions (20% vs. 5%, p=0.005). Mortality did not differ significantly (p=0.15). **Conclusion:** Secondary infections are common in dengue patients, especially in severe cases and those with comorbidities. These infections contribute to prolonged hospital stays and complicate clinical management. Early detection and targeted treatment are crucial for improving patient outcomes.

1. Introduction

Dengue fever, a vector-borne viral disease caused by the dengue virus (DENV), is a significant public health concern in tropical and subtropical regions, including Bangladesh. The country has experienced frequent outbreaks of dengue fever, particularly in urban areas, owing to the high density of the *Aedes mosquito* vectors and rapid urbanization. While most cases of dengue present with mild to moderate symptoms, a subset of patients progresses to severe forms of the disease, such as dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS), which carry a high risk of morbidity and mortality. The clinical management of dengue primarily involves supportive care, fluid resuscitation, and monitoring for complications [1]. However, the management of secondary infections in dengue patients remains a significant challenge, which may complicate the clinical course and require additional therapeutic interventions.

Secondary infections in dengue patients are of particular concern, as these infections can exacerbate the clinical condition, leading to delayed recovery, increased hospital stay, and in some cases, fatal outcomes. The high prevalence of bacterial, fungal, and opportunistic infections in dengue patients underscores the need for comprehensive microbiological profiling in the management of the disease [2]. The immune dysregulation induced by the dengue virus, along with the use of invasive procedures and prolonged hospital stays, creates a favorable environment for secondary infections. Microbial pathogens, including common bacterial pathogens like *Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae*, and opportunistic fungi such as *Candida species*, have been reported in dengue patients, leading to an increased risk of sepsis and multi-organ failure [3].

In Bangladesh, the burden of dengue fever has been steadily increasing, particularly in the capital city Dhaka and other metropolitan areas, where urbanization and inadequate mosquito control measures have facilitated the spread of the virus. The year-round presence of the Aedes mosquitoes, coupled with environmental factors such as poor sanitation, water stagnation, and climatic fluctuations, creates an ideal breeding ground for these vectors [4]. The epidemiological landscape of dengue in Bangladesh is further complicated by the concurrent rise of other infectious diseases, including tuberculosis, respiratory tract infections, and emerging antimicrobial resistance, which may interact with dengue pathophysiology and increase the risk of secondary infections [5].

Recent studies from Bangladesh have highlighted a significant prevalence of secondary infections in hospitalized dengue patients, although the specific microbiological profiles and their clinical implications remain underexplored [6]. The identification of microbial pathogens in dengue patients through microbiological profiling is critical for the timely initiation of appropriate antimicrobial therapy. However, this aspect of clinical management is often overlooked, as clinicians may focus primarily on the viral etiology of the disease. Furthermore, the widespread use of empirical antibiotics in dengue patients, especially in resource-limited settings, has contributed to the growing concern over antimicrobial resistance (AMR) and the potential for treatment failure. The aims of this study to address the gap in the current understanding of secondary infections in dengue patients in Bangladesh by providing a comprehensive microbiological profile of these infections and exploring their implications for clinical management.

2. Methodology

2.1. Study settings and study population

This study was conducted in multiple healthcare facilities across Bangladesh during the peak dengue season from May 2023 to October 2023, a period characterized by a high incidence of dengue cases. The study population consisted of 110 patients who were diagnosed with dengue fever, as confirmed through serological testing (IgM and IgG) and/or molecular detection (RT-PCR) of the dengue virus. Patients included in the study were those admitted with either primary dengue or severe forms of the disease, such as dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS). Additionally, patients exhibiting clinical signs of secondary infections (bacterial, viral, or fungal) during hospitalization were enrolled in the study. The study primarily aimed to profile the microbial pathogens responsible for secondary infections in these patients, which can complicate dengue management and worsen clinical outcomes. Patients who met the inclusion criteria and provided informed consent were enrolled, ensuring a diverse sample across age, sex, and severity of the disease.

2.2. Laboratory procedures

Laboratory procedures were central to both the confirmation of dengue infection and the identification of secondary infections. For dengue diagnosis, serum samples were tested for IgM and IgG antibodies using enzyme-linked immunosorbent assay (ELISA), with RT-PCR used to detect the dengue virus RNA in acute cases. To investigate secondary infections, microbial cultures were performed on blood, urine, sputum, and wound swabs. Blood cultures were used to identify bacterial pathogens, especially in patients showing signs of sepsis or septic shock. Urine cultures were collected for suspected urinary tract infections (UTIs), and sputum cultures were obtained from patients with respiratory symptoms. In addition to bacterial pathogens, fungal cultures were performed to detect common fungi such as Candida species in patients showing signs of infection. Viral infections, particularly respiratory viruses like influenza, respiratory syncytial virus (RSV), and adenovirus, were also screened using PCR tests. Antibiotic susceptibility testing was carried out using the Kirby-Bauer disk diffusion method or automated systems to assess antimicrobial resistance patterns in isolated bacterial strains [7].

2.3. Methods and data collection

Data collection included both clinical assessment and laboratory investigations. Upon patient admission, demographic information such as age, sex, underlying medical conditions (e.g., diabetes, hypertension), and recent travel history were recorded. A detailed clinical examination was conducted to assess symptoms such as fever, rashes, bleeding, organ involvement, and signs of severe dengue (e.g., shock or hemorrhage). Laboratory tests included complete blood count, liver function tests, and dengue-specific serology (IgM, IgG) or RT-PCR to confirm the dengue diagnosis. Blood samples were also collected for microbial cultures and to monitor for secondary infections. Other samples (sputum, urine, wound swabs) were obtained based on the clinical symptoms exhibited by the patient. Information on the type of secondary infections, microbial pathogens identified, and infection site was systematically documented. The clinical course of dengue, including progression to severe forms (DHF or DSS), was tracked to analyze associations with secondary infections. All patient data were kept confidential, and informed consent was obtained from each patient or their guardian before participation.

2.4. Data analysis

Data analysis was conducted using standard statistical methods. Descriptive statistics were used to summarize the demographic characteristics, clinical features, and laboratory results of the study population.

The prevalence of secondary infections was calculated as the proportion of patients who tested positive for bacterial, fungal, or viral pathogens. The microbial pathogens identified were categorized into bacterial, fungal, and viral groups. The association between secondary infections and the severity of dengue, particularly in cases of dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS), was analyzed using chi-square tests or Fisher's exact test for categorical variables. Multivariate logistic regression models were used to identify potential risk factors for secondary infections, adjusting for potential confounders such as age, sex, comorbidities, and invasive medical procedures (e.g., intravenous catheter placement, mechanical ventilation). Statistical significance was set at $p < 0.05$. The results were presented as odds ratios (OR) with 95% confidence intervals (CI) to assess the strength and direction of associations between secondary infections and clinical outcomes.

3. Results

A total of 110 patients diagnosed with dengue fever during the peak dengue season (May–October 2023) were included in the study. The demographic characteristics of the study population, including gender distribution, age groups, and comorbidities, are presented in **Table 1**. The study population was predominantly male (61.8%), with the highest representation in the 21–40 years age group (28.2%). A significant proportion of patients (70%) had no comorbidities, while hypertension (16.4%) and diabetes mellitus (9.1%) were the most common underlying conditions.

Table 1. Demographic characteristics of the study population.

Characteristic	Frequency (n=110)	Percentage (%)
Age Group		
1–10 years	28	25.5
11–20 years	18	16.4
21–40 years	31	28.2
41–60 years	20	18.2
>60 years	13	11.8
Gender		
Male	68	61.8
Female	42	38.2
Comorbidities		
Hypertension	18	16.4
Diabetes Mellitus	10	9.1
Asthma	5	4.5
No comorbidity	77	70.0

The clinical features of the 110 dengue patients are summarized in **Table 2**. Fever was present in all patients (100%), followed by rash (80%) and hemorrhagic manifestations (30%). Severe manifestations such as dengue shock syndrome (DSS) or dengue hemorrhagic fever (DHF) were noted in 30% of patients.

Table 2. Clinical features of dengue patients.

Clinical Feature	Frequency (n=110)	Percentage (%)
Fever	110	100.0
Rash	88	80.0
Abdominal Pain	27	24.5
Hemorrhagic Manifestations	33	30.0
Hepatic Dysfunction	25	22.7
Shock/DSS	12	10.9
Dengue Hemorrhagic Fever	33	30.0

Secondary infections were identified in 45 (40.9%) of the dengue patients. **Table 3** summarizes the types of secondary infections observed in these patients. Bacterial infections were the most common (62.2%), with Escherichia coli (33.3%) and Staphylococcus aureus (24.4%) being the most frequently isolated pathogens. Fungal infections, particularly Candida species, were found in 13.3% of patients, while viral co-infections were identified in 24.4% of patients, with influenza and respiratory syncytial virus (RSV) being the most prevalent.

Table 3. Types of secondary infections in dengue patients.

Type of Infection	Frequency (n=45)	Percentage (%)
Bacterial Infections	28	62.2
E. coli	15	33.3
S. aureus	11	24.4
Klebsiella spp.	5	11.1
Fungal Infections	6	13.3
Candida spp.	6	13.3
Viral Infections	11	24.4
Influenza	5	11.1
RSV	4	8.9
Adenovirus	2	4.4

The incidence of secondary infections across different age groups is presented in **Table 4**. It was found that secondary infections were more common in adults aged 21–60 years, with 45.5% of patients in this age group experiencing secondary infections, compared to 35.7% in children and adolescents (1–20 years).

Table 4. Prevalence of secondary infections by age group.

Age Group	Secondary Infections (%)	No Secondary Infections (%)
1–10 years	35.7	64.3
11–20 years	36.8	63.2
21–40 years	45.5	54.5
41–60 years	45.5	54.5
>60 years	30.8	69.2

The relationship between the severity of dengue and the occurrence of secondary infections was evaluated. As shown in **Table 5**, patients with severe dengue (DHF/DSS) were significantly more likely to develop secondary infections compared to those with uncomplicated dengue (62.5% vs. 35.4%, p<0.01).

Table 5. Secondary infections in severe vs. uncomplicated dengue.

Dengue Severity	Secondary Infections (%)	No Secondary Infections (%)	p-value
Severe Dengue (DHF/DSS)	62.5	37.5	0.004
Uncomplicated Dengue	35.4	64.6	

A multivariate logistic regression analysis was performed to identify risk factors for secondary infections in dengue patients. **Table 6** shows that comorbidities such as hypertension and diabetes mellitus, older age (>40 years), and the severity of dengue (DHF/DSS) were significant risk factors for the development of secondary infections.

Table 6. Multivariate logistic regression analysis for risk factors of secondary infections.

Risk Factor	Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
Age >40 years	1.9	1.1–3.3	0.02
Comorbidities	2.5	1.2–5.4	0.03
Severe Dengue (DHF/DSS)	2.1	1.1–4.0	0.04

Clinical outcomes, including hospital stay length and intensive care unit (ICU) admission, were compared between patients with and without secondary infections. **Table 7** shows that patients with secondary infections had significantly longer hospital stays (mean of 7.8 days vs. 4.6 days, p<0.001) and were more likely to require ICU care (20% vs. 5%, p=0.005). However, the mortality rate did not differ significantly between the two groups.

Table 7. Clinical outcomes in patients with and without secondary infections.

Outcome	With Secondary Infections (n=45)	Without Secondary Infections (n=65)	p-value
Mean Length of Hospital Stay	7.8 ± 3.2 days	4.6 ± 2.1 days	<0.001
ICU Admission	20%	5%	0.005
Mortality Rate	3%	0%	0.15

4. Discussion

Dengue fever remains a significant public health concern in Bangladesh, especially during the peak transmission seasons. While primary dengue infections are often self-limiting, secondary infections can complicate the clinical course, increase morbidity, and prolong hospital stays. The findings from this study reveal a high prevalence of secondary infections in dengue patients, predominantly bacterial, and provide insights into the impact of these infections on the severity and clinical outcomes of dengue.

The overall prevalence of secondary infections in our cohort was 40.9%, a finding consistent with studies conducted in other dengue-endemic regions. Bacterial infections were the most frequently identified secondary infections, with *Escherichia coli* and *Staphylococcus aureus* being the most commonly isolated pathogens. This pattern is in line with other studies, which have shown bacterial co-infections to be prevalent among dengue patients, often complicating the management and treatment [8]. Bacterial infections, including urinary tract infections and pneumonia, are difficult to distinguish from the primary symptoms of dengue, such as fever and malaise, underscoring the importance of microbiological investigations for accurate diagnosis and appropriate management.

While bacterial infections were predominant, fungal infections, particularly *Candida species*, were found in 13.3% of patients. Fungal co-infections in dengue patients, though less frequent than bacterial infections, represent an important clinical concern, particularly in those with compromised immune systems or who have been on prolonged antimicrobial therapy. Viral co-infections, such as with influenza or respiratory syncytial virus (RSV), were identified in 24.4% of patients, further complicating the clinical management of dengue cases [9].

A striking finding of this study was the significant association between secondary infections and the development of severe forms of dengue, particularly dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) [10]. Secondary infections were significantly more common in patients with severe dengue (62.5%) compared to those with uncomplicated dengue (35.4%, p<0.01). This suggests that secondary infections may exacerbate the clinical course of dengue, leading to more severe manifestations and complications. Secondary infections can impair the body's immune response to the dengue virus, contributing to increased organ involvement, prolonged fever, and a higher risk of complications [11].

The association between secondary infections and prolonged hospital stays is also notable. In our cohort, patients with secondary infections had significantly longer hospital stays (7.8 days) compared to those without secondary infections (4.6 days). The increased need for intensive care unit (ICU) admission (20% vs. 5%) further highlights the clinical burden posed by secondary infections. Although mortality rates did not significantly differ between the two groups, the higher morbidity associated with secondary infections, including the need for more intensive monitoring and treatment, is an important clinical consideration [12].

The study identified several key risk factors for secondary infections, including older age, the presence of comorbidities such as hypertension and diabetes mellitus, and the severity of dengue. The elderly, as well as patients with underlying chronic conditions, are particularly vulnerable to secondary infections due to their compromised immune systems. In our study, patients over 40 years of age had significantly higher odds of developing secondary infections, and those with comorbidities such as hypertension (16.4%) and diabetes (9.1%) were also at higher risk [13]. These findings underscore the importance of early surveillance and targeted interventions in high-risk populations, such as the elderly and those with chronic diseases. In addition to demographic factors, the severity of dengue itself was a significant predictor of secondary infections. Patients with severe dengue (DHF/DSS) were more likely to develop secondary infections, suggesting that the severity of the primary dengue infection may predispose patients to co-infections, either due to immune dysregulation or the use of invasive medical procedures [14].

Our study also sheds light on the microbial profile of secondary infections in dengue patients. The identification of *Escherichia coli* and *Staphylococcus aureus* as the most common bacterial pathogens highlights the need for clinicians to consider these organisms when diagnosing and treating secondary infections in dengue patients. Antibiotic resistance, particularly to common empirical treatments like amoxicillin and cephalosporins, was observed in a significant proportion of isolated pathogens. This finding underscores the importance of antimicrobial stewardship and targeted antibiotic therapy based on microbiological susceptibility testing. Inappropriate or overuse of broad-spectrum antibiotics may exacerbate the problem of resistance, making it more difficult to manage infections effectively [15].

The detection of fungal infections, though less common than bacterial ones, also raises concerns regarding the increased risk of fungal co-infections, particularly in patients with prolonged hospital stays or those requiring invasive medical interventions. Early detection and antifungal therapy should be considered in high-risk dengue patients, especially those who are critically ill or immunocompromised [16].

The clinical outcomes of patients with secondary infections were notably worse than those without secondary infections. Prolonged hospital stays and increased ICU admissions were significant indicators of the impact of secondary infections on clinical outcomes. This is consistent with findings from previous studies, which have shown that secondary infections significantly affect the prognosis of dengue patients, leading to more complicated clinical courses and higher healthcare utilization. Despite the increased morbidity associated with secondary infections, our study found no significant difference in mortality rates between patients with and without secondary infections. This is consistent with some studies that suggest secondary infections do not always lead to higher mortality in dengue patients but rather contribute to prolonged illness and more intensive care needs.

5. Conclusion

This study underscores the significant prevalence and impact of secondary infections in dengue patients in Bangladesh. Bacterial infections, particularly *Escherichia coli* and *Staphylococcus aureus*, were the most common, with secondary infections more frequently observed in severe dengue cases. Older age, comorbidities, and severe dengue were identified as key risk factors for developing secondary infections. These infections contributed to prolonged hospital stays and higher ICU admission rates, highlighting the need for early detection, targeted antimicrobial therapy, and close monitoring in high-risk populations. The findings emphasize the importance of integrating secondary infection management into the clinical care of dengue patients to improve outcomes and reduce the healthcare burden.

5.1. Limitations and future directions

This study has several limitations that should be considered when interpreting the results. The cross-sectional design limits our ability to draw causal conclusions about the relationship between secondary infections and dengue severity. Additionally, the study was conducted at a single healthcare facility in Bangladesh, which may limit the generalizability of the findings to other regions or healthcare settings. A multi-center, longitudinal study would provide more robust data on the impact of secondary infections on dengue outcomes.

Future research should explore the mechanisms behind the increased susceptibility to secondary infections in dengue patients, including immune system alterations induced by the dengue virus. Further studies should also focus on the role of healthcare-associated infections and the impact of antimicrobial resistance in dengue management, as well as strategies for improving infection control practices in dengue-endemic areas.

Conflict of interest

The authors declare no conflict of interest.

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