ORIGINAL ARTICLE

Seasonal variation and co-infection of dengue and typhoid cases in a tertiary care hospital: A cross-sectional analytical study

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ABSTRACT

Background: In tropical areas of Pakistan, dengue and typhoid fever are the most common causes of acute undifferentiated febrile illness. Their similar clinical characteristics make diagnosis and treatment much more difficult. The aim of this study is to determine the seasonal distribution and quantity of co-infection between laboratory-confirmed cases of typhoid and dengue among hospitalized patients in tertiary care hospitals.

Material and Methods: This cross-sectional analytical study was carried out at Quaid-e-Azam Medical College/ Bahawal Victoria Hospital Bahawalpur between January 2023 and December 2024. A total of 280 febrile patients with laboratory testing for both disorders and a fever (≥38°C for ≤10 days) were included. Typhoid was confirmed by blood culture for *Salmonella typhi/ paratyphi,* while dengue was confirmed by NS1 antigen detection. SPSS version 23.0 was used to evaluate data on demographics, clinical characteristics, and admission dates (classified into seasonal periods).

Results: 112 (40.0%) of the 280 patients had dengue, 94 (33.6%) had typhoid, and 9 (3.2%) had two infections. Typhoid surged after the monsoon (October-November 61.7% of cases), but dengue peaked during the monsoon (July-September 78.6%). In September and October, seven out of nine dual instances took place. The only significant predictor of dual infection was admission after the monsoon (adjusted OR = 5.2, 95% CI: 1.4-19.3; p=0.014**).**

Conclusion: There is a significant seasonal co-infection of dengue and typhoid during the post-monsoon transition, making integrated diagnostic and public health efforts necessary during this high-risk time.

Keywords: Dengue; Febrile illness, *Salmonella typhi,* Seasonal variation, Typhoid fever

BACKGROUND

In tropical and subtropical regions dengue and typhoid fever continue to be two of the leading causes of acute febrile illness. This poses a serious threat to public health and the economy of developing countries especially in low- and middle-income countries (LMICs). Every year estimated 100–400 million dengue illnesses occur worldwide, while only Asia accounting for more than 70% of the burden.[1] similarly typhoid fever which is caused by *Salmonella enterica* serovar Typhi, affects between 9 and 27 million people annually. Sub-Saharan Africa, sections of Oceania, and South and Southeast Asia having the highest prevalence.[2] Both diseases significantly increase hospital admissions during seasonal outbreaks in endemic regions like Bangladesh, Indonesia, and Pakistan.[3,4]

Clinically, typhoid and dengue fever sometimes manifest as acute undifferentiated febrile illness (AUFI), a condition marked by fever without an obvious cause, which frequently causes diagnostic perplexity.[5] Prolonged fever, headache, myalgia, gastrointestinal problems, and leukopenia are common overlapping symptoms that impede early clinical distinction.[6] Misdiagnosis can lead to delayed supportive therapy (e.g., fluid management in dengue) or improper antibiotic administration (e.g., fluoroquinolones for suspected typhoid in dengue cases), which increases the risk of complications and hospital stay.[7]

Different but occasionally convergent environmental factors govern the seasonal dynamics of various diseases. *Aedes aegypti* and *Aedes albopictus* mosquitoes are the main vectors of dengue, thrive during the rainy/ monsoon season, which is intimately linked to the spread of the disease.[8] On the other hand, typhoid fever usually peaks during or soon after the

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monsoon, when *S. typhi* contaminates water supplies due to flooding and poor sanitation.[9] This causes dengue and typhoid peaks to overlap in many South Asian cities, frequently from August to November; making diagnosis more difficult for medical professionals working in hectic tertiary care settings.[10]

The management of patients is significantly impacted by this overlap. Typhoid-related intestinal perforation or dengue shock syndrome are two preventable morbidities that might result from delayed or inaccurate diagnosis.[11] Furthermore, antimicrobial resistance is a rising problem in typhoid endemic locations where extensively drug-resistant (XDR) and multidrug-resistant (MDR) strains are prevalent.[12]

Despite their clinical significance the concurrent occurrence and seasonal co-distribution of laboratory-confirmed dengue and typhoid cases within tertiary care facilities are not well understood. The majority of current research looks at these diseases separately or uses syndromic surveillance without additional testing.[13] Few have systematically analyzed the extent and timing of their overlap in hospitalized populations using robust diagnostic criteria.

Thus, the purpose of this study was to ascertain the seasonal distribution and measure the degree of overlap between laboratory-confirmed cases of typhoid fever and dengue among patients admitted to a tertiary care hospital during the study period. Findings will inform diagnostic algorithms, improve clinical preparedness during high-risk seasons, and support integrated vector and water-borne disease control strategies.

The objective of this study is to determine the seasonal distribution and extent of co-infection in laboratory-confirmed dengue and typhoid cases in a tertiary care hospital.

MATERIAL AND METHODS

This cross-sectional analytical study was conducted at Quaid-e-Azam Medical College/Bahawal Victoria Hospital, a major tertiary care facility in Bahawalpur, Pakistan, from January 2023 to December 2024. The study population comprised all patients both adults and children admitted with acute febrile illness (defined as fever ≥38°C for less than or equal to 10 days) who underwent laboratory testing for both dengue and typhoid fever during their hospital stay. Patients with no fever upon admission, insufficient medical records, or no verified diagnostic testing for either illness were excluded. A minimum of 280 participants were required; based on an estimated overlap prevalence of 3%, [14] a 95% confidence level, and a 2% margin of error. Using a non-probability sequential sampling strategy, all eligible patients who fulfilled the inclusion criteria during the study period were gradually included as participants after taking approval from Institutional Ethical review Committee of Quaid-e-Azam Medical College, Bahawalpur (Ref. No. 506/DME/QAMC) and informed consent was obtained from individual patients. While laboratory-confirmed dengue patients were defined as those with a positive NS1 antigen test, typhoid fever cases were identified by isolating Salmonella Typhi or Paratyphi from blood culture. All the cases were classified as seasonal cases, for seasonal periods pre-monsoon (March–May), monsoon (June–September), post-monsoon (October-November), and winter (December-February). A pre-structured questionnaire was established to record socio-demographic information (age, sex), clinical features (symptoms, duration of fever), laboratory results, final diagnosis, clinical outcome, and date of admission was utilized. All the data was analyzed by using Statistical Package for Social Sciences (SPSS) version 23.0. The study variables were scrutinized using descriptive statistics, such as frequencies, percentages, means, and standard deviation. Monthly and quarterly line or bar graphs were used to show seasonal trends in disease frequency. The number and proportion of patients who tested positive for both diseases were used to measure the degree of overlap between dengue and typhoid cases. To evaluate correlations between seasonal periods and disease type, analytical statistics included the Chi-square test or Fisher's exact test (where predicted cell counts were <5). To find potential predictors of illness overlap, binary logistic regression was also used; statistical significance was regarded as $p\text{-value} < 0.05$.

RESULTS

A total of 280 individuals hospitalized for acute febrile illness who underwent concurrent diagnostic testing for dengue fever and typhoid fever were enrolled in the study. The mean age of participants was 24.6 ± 15.3 years, with 58.2% (n=163) being male. Laboratory confirmation identified 112 (40.0%) cases of dengue fever, 94 (33.6%) cases of typhoid fever and 9 (3.2%) patients with concurrent positivity for both infections

(*dengue* NS1+ and *Salmonella typhi/ paratyphi* blood culture positive). The remaining 65 patients (23.2%) were diagnosed with non-typhoid/non-dengue fever after testing negative for both illnesses (Table-I).

78.6% (88/112) of all dengue diagnoses occurred during the monsoon months of July–September, when dengue cases surged. Typhoid cases, on the other hand, exhibited a bimodal pattern, with 61.7% (58/94) of cases occurring during the post-monsoon period (October–November). Notably, seven of the nine dual-positive cases were admitted in September and October, which had the largest overlap of dengue and typhoid. Season and disease kind were statistically significantly correlated ($p < 0.001$) (Table-II & III).

6 (66.7%) of the nine individuals with dual positive were male, with a median age of 19 years (IQR: 14–28). Prolonged fever (>5 days; 100%), headache (88.9%), myalgia (77.8%), and stomach discomfort (66.7%) were common symptoms. 7 (77.8%) dual-positive individuals had leukopenia (<4,000/µL), which is similar to isolated dengue, but five (55.6%) also had relative bradycardia, which is more typical of typhoid. None of the dual-positive patients needed to be admitted to the intensive care unit; all recovered with the proper supportive and antibiotic medication.

Higher risks of dual infection were linked in univariate analysis to admission during the post-monsoon season (OR = 4.8, 95% CI: 1.3–17.6, $p = 0.018$) and age < 30 years (OR = 3.1, 95% CI: 0.8–12.2, $p = 0.098$) (Table-IV).

Table-I: Baseline characteristics of study participants (n = 280).

Characteristic	n (%) or Mean ± SD
Age (years)	24.6 ± 15.3
Gender	
– Male	163 (58.2%)
– Female	117 (41.8%)
Final Diagnosis	
– Dengue fever	112 (40.0%)
– Typhoid fever	94 (33.6%)
– Both dengue & typhoid	9 (3.2%)
– Neither (other febrile illness)	65 (23.2%)
Season of Admission	
– Pre-monsoon (Mar–May)	42 (15.0%)
– Monsoon (Jun–Sep)	138 (49.3%)
– Post-monsoon (Oct–Nov)	76 (27.1%)
– Winter (Dec–Feb)	24 (8.6%)

Table-II: Monthly distribution of dengue and typhoid cases.

Month	Dengue n (%)	Typhoid n (%)	Total Cases
January	2 (40.0%)	3 (60.0%)	5
February	1 (33.3%)	2 (66.7%)	3
March	3 (42.9%)	4 (57.1%)	7
April	5 (45.5%)	6 (54.5%)	11
May	8 (47.1%)	9 (52.9%)	17
June	18 (64.3%)	10 (35.7%)	28
July	29 (70.7%)	12 (29.3%)	41
August	31 (68.9%)	14 (31.1%)	45
September	10 (38.5%)	16 (61.5%)	26
October	3 (20.0%)	12 (80.0%)	15
November	2 (25.0%)	6 (75.0%)	8
December	0 (0%)	0 (0%)	0
Overall	112 (54.4%)	94 (45.6%)	206

Table-III: Disease distribution by seasonal period (n = 280).

Season	Dengue n (%)	Typhoid n (%)	Both n (%)	Neither n (%)	p-value
Pre-monsoon	16 (38.1%)	19 (45.2%)	0 (0.0%)	7 (16.7%)	
Monsoon	88 (63.8%)	36 (26.1%)	2 (1.4%)	12 (8.7%)	
Post-monsoon	8 (10.5%)	39 (51.3%)	7 (9.2%)	22 (28.9%)	< 0.001
Winter	0 (0.0%)	0 (0.0%)	0 (0.0%)	24 (100.0%)	
Total	112 (40.0%)	94 (33.6%)	9 (3.2%)	65 (23.2%)	

Table-IV: Predictors of concurrent dengue and typhoid infection: logistic regression analysis.

Variable	Concurrent Dengue and Typhoid infection		p-value	Univariate Logistic Regression		p-value
	Yes n (%)	No n (%)		Unadjusted Odds Ratio	95% CI for UOR	
Age			0.152			0.098
< 30 years	8 (3.9%)	195 (96.1%)		3.1	0.82-11.74	
≥ 30 years	1 (1.3%)	76 (98.7%)				
Gender			0.582			
Male	6 (3.7%)	157 (96.3%)		1.4	0.41-4.94	0.582
Female	3 (2.6%)	114 (97.4%)				
Admission season			0.016			
Post-monsoon	7 (9.2%)	69 (90.8%)		4.8	1.34-17.48	0.016
Monsoon + Winter	2 (1.2%)	160 (98.8%)				

DISCUSSION

In a country where both diseases are widespread, the current study offers crucial insights into the seasonal dynamics and clinical overlap of dengue and typhoid fever among hospitalized patients with acute febrile illness. Dengue rose during the monsoon (July–September), which is consistent with *Aedes* mosquito reproduction after rainfall, according to the findings, which corroborate separate but partially overlapping seasonal trends. Whereas the post-monsoon months of October and November saw a spike in typhoid cases, perhaps as a result of contaminated water from floods and poor sanitation facilities. A high-risk window where doctors must retain dual diagnostic suspicion is highlighted by the fact that 3.2% of febrile patients tested positive for both infections, with the majority of dual cases occurring in September–October. This overlap is consistent with ecological models that propose that in South Asian urban environments, monsoon-driven climatic changes concurrently promote vector breeding (for dengue) and fecal-oral transmission (for typhoid).[15,16,17]

Clinically, dual-positive patients showed a hybrid symptom profile of fever, headache, and leukopenia typical of dengue coupled with relative bradycardia suggestive of typhoid, highlighting the difficulty of diagnosis in hospitals with inadequate resources. The lack of serious consequences in patients with dual infections may be due to prompt empirical treatment or a low pathogen burden, but this shouldn't allay worries because misdiagnosis might impede proper care and encourage the abuse of antibiotics.[18, 19] The necessity for season-specific diagnostic procedures in tertiary care centers throughout southern Punjab is further supported by the finding that post-monsoon admission was the predictor of dual infection.

The use of gold-standard diagnostics (blood culture for typhoid and NS1 antigen for dengue) reduces misclassification bias, and the successive sampling technique over two complete transmission cycles improves generalizability to similar semi-arid regions of Pakistan. But it's important to recognize the limitations. First, it is impossible to draw conclusions about the causes of disease interactions due to the cross-sectional design. Second, there was no dengue serotyping or molecular subtyping of Salmonella, which may have revealed information about immunological cross-reactivity or strain virulence. Third, the study was carried out at a single location, which would limit its application to Pakistan's northern or rural areas with distinct epidemiological profiles.

Based on current findings dual transmission pathways may be disrupted by routine dual testing for dengue and typhoid in all febrile inpatients during September–November and similar climatic zones. Integration of seasonal alerts into hospital electronic records to alert clinicians during high-overlap periods, and public health interventions focusing on both vector control (e.g., larviciding) and water safety (e.g., chlorination, public awareness) in the immediate post-monsoon period.

CONCLUSION

Dengue and typhoid fever show clear seasonal maxima, with considerable clinical and temporal overlap during the post-monsoon transition. For the purpose of minimizing misdiagnosis and progress patient outcomes in endemic regions, this convergence requires integrated diagnostic approach and preventive strategies.

CONFLICT OF INTEREST

None

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Declared none

AUTHOR CONTRIBUTION

Wajahat Hussain: Study design, manuscript writing, final approval, accountable for all aspects of publication.

Qudsia Anwar: Data analysis, final approval, accountable for all aspects of publication.

Mohammad Waseem Abbas: Acquisition of data, final approval, accountable for all aspects of publication.

Shanawar Saeed: Revisions, final approval, accountable for all aspects of publication.

Umama Bushra: Data collection, final approval, accountable for all aspects of publication.

Naveeda Bashir: Reviewing it critical for important intellectual content, final approval, accountable for all aspects of publication.

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