



# Breteau index as a potential warning tool for dengue outbreaks: a 14-year retrospective analysis in high-risk districts of Punjab-Pakistan

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## ABSTRACT

**Objective:** To evaluate the dengue fever burden across three high-risk districts: Lahore, Sheikhupura and Rawalpindi, over 14 years (2011-2024), and to assess the predictive validity of the Breteau Index (BI) for forecasting dengue outbreaks.

**Methods:** This retrospective ecological study utilized dengue surveillance data collected from 2011 to 2024 at the Institute of Public Health, Lahore. Laboratory-confirmed dengue cases from Lahore, Sheikhupura and Rawalpindi were analyzed to determine temporal trends. For BI validation, two Union Councils in Rawalpindi were selected by simple random sampling. The BI was calculated using entomological data from the preceding 10 days at 5-day intervals, with a threshold of >3 considered predictive of dengue transmission. Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated using laboratory-confirmed dengue cases as the reference standard.

**Results:** Lahore reported the highest dengue burden, with peak outbreaks in 2011 (16,984 cases) and 2021 (19,942 cases), while Rawalpindi showed a rising trend, reaching 6,606 cases in 2024. Sheikhupura consistently reported fewer cases. A weak negative correlation was observed between dengue cases and vector surveillance activities ( $r = -0.293$ ). In BI validity assessment, UC Dhoke Munshee showed high sensitivity (100%) and specificity (78.18%), with diagnostic accuracy of 84%, while UC Chak Jalal Din demonstrated high sensitivity (96%) but lower specificity (44.9%) and overall accuracy (62.16%).

**Conclusion:** Lahore remained the principal dengue hotspot, while Rawalpindi showed an increasing disease burden. BI demonstrated high sensitivity and negative predictive value, supporting its usefulness as an early warning tool for dengue surveillance.

**Keywords:** Dengue (MeSH); Public Health (MeSH); Disease Outbreaks (MeSH); Disease Vectors (MeSH); Mosquito Vectors (MeSH); Aedes (MeSH); Breteau Index (Non-MeSH); Pakistan (MeSH); Entomology (MeSH); Communicable Disease Control (MeSH); Population Surveillance (MeSH); Epidemiologic Monitoring (MeSH); Risk Assessment (MeSH).

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endemic and epidemic-prone disease, particularly affecting urban centers such as Lahore and Rawalpindi.<sup>4</sup> The first dengue outbreak was reported in 1994, caused by DENV-1 and DENV-2, resulting in thousands of cases.<sup>5</sup> The second dengue outbreak occurred in 2005 in Karachi (DENV-3) with increased DHF; since 2006, annual multi-serotype outbreaks have occurred, including major epidemics in Lahore (2011, >50,000 cases) and Khyber Pakhtunkhwa (2013D).

Multiple factors contribute to the spread of dengue fever in Pakistan. Outbreak prediction is challenging due to the complex interaction of climatic, ecological, and socio-demographic factors, along with limitations in surveillance systems and data integration.<sup>6</sup> The primary driver is the favorable climate, particularly during the monsoon season, when hot and humid conditions create an ideal environment for mosquito proliferation. High temperatures accelerate the breeding of *Aedes aegypti*, the most prevalent dengue-carrying mosquito in Pakistan, while also speeding up vector replication and maturation.<sup>7</sup> Unplanned urbanization further facilitates the spread of *Aedes aegypti* by creating abundant breeding grounds. Additional contributing factors include inadequate mosquito control, overpopulation, frequent travel, poor socioeconomic conditions and insufficient public health infrastructure and awareness.<sup>7-9</sup>

The Dengue Risk Alert Model (DRAM)

## INTRODUCTION

Dengue is a life-threatening viral disease that continues to emerge and re-emerge, predominantly affecting tropical and subtropical regions worldwide. Due to the high burden of dengue, it is a major public health concern in Pakistan.<sup>1</sup> Dengue fever is caused by the dengue virus (DENV), a single-stranded RNA Flavivirus (family Flaviviridae), with four distinct serotypes DENV-1 to DENV-4 further

divided into ten genotypes based on envelope gene variations.<sup>2</sup> Dengue is transmitted by *Aedes aegypti* and *Aedes albopictus* and presents as asymptomatic, mild-moderate fever, or severe forms like dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS).<sup>1,3</sup>

Dengue represents a major and growing global public health burden, with recurrent outbreaks in over 100 countries. In Pakistan, it remains an

is a digital surveillance and response system implemented for dengue control in Punjab. It integrates vector surveillance, geo-tagged field activities, and real-time data reporting through a centralized dashboard. The system supports early warning by generating alerts based on key indicators, including larval indices such as the Breteau Index (BI). In this study, DRAM served as the primary data source for entomological and epidemiological surveillance.

Since 2011, sporadic dengue and DHF cases have occurred in Pakistan, with control efforts reducing transmission, though underdeveloped areas remain disproportionately affected. Despite rising regional risk, the true disease burden and impact of preventive measures remain unclear. Entomological indices, particularly the BI, are widely used as proxy indicators of vector density and transmission risk, offering potential as early warning tools, although their predictive reliability varies by setting. This study evaluates the role of the BI in predicting dengue; although promising, its reliability is limited by weak correlation with adult mosquito density and variability in sampling, highlighting the need for local validation in Punjab. This necessity formed the primary rationale for conducting the present study with objectives to analyse the 14-year trend and burden of dengue cases across three high-risk districts (2011–2024) and a pilot validity assessment of the BI using 2024 data from two Union Councils in Rawalpindi.

## METHODS

This retrospective ecological study design was conducted at the Institute of Public Health, Lahore and ethical approval was obtained from the Institutional Review Board of the Institute of Public Health, Lahore (Reference #: 138/ERC/IPH, dated: November 15, 2025). The study covered the period from January 2011 to December 2024. High-risk districts were defined based on historical dengue burden, characterized by recurrent outbreaks and consistently higher numbers of laboratory-confirmed cases reported in the provincial surveillance system over

multiple years. For the 14-year trend analysis, all available laboratory-confirmed dengue case records from Lahore, Sheikhupura and Rawalpindi recorded in the official surveillance repository between January 2011 and December 2024 were included. For the BI validity assessment, available BI records and corresponding laboratory-confirmed dengue case data from the selected Union Councils during 2024 were used. Incomplete or inconsistent records, where present, were not considered in the validity analysis. The provincial data interface produced real-time information about the larvae prevention, detection, and cleaning activities. An alert-generating solution that looked at key variables like positive larvae presence, disease density was also developed to generate warnings proactively. The official dengue portal was being used actively through the deployment of thousands of Android phones; over a hundred thousand activities were reported every week, and the database had millions of entries on the Dengue Dashboard. For larval surveillance, the BI was calculated. The threshold for BI was  $>3$  at the Union Council level, which is used as an alert indicator, signaling potential occurrence of dengue cases within the next 1 to 4 weeks in that specific area (UC). To validate the predictive capability of BI for dengue cases, we selected two Union Councils randomly from Rawalpindi District that experienced epidemics in 2024. The simple random sampling technique was applied to the BI data of the year (2024) with an

interval of 5 days (The BI was calculated on every 5<sup>th</sup> day). The BI was computed using the previous 10-day data from the official dashboard, calculated according to the following formula.

Breteau Index (BI) =  $(\text{Number of positive containers} \div \text{Number of houses inspected}) \times 100$

In this study, BI was taken as the test variable, while laboratory-confirmed dengue cases were established as the gold standard. We employed simple random sampling with 5-day intervals to collect data throughout the year 2024. For validity assessment, BI values  $>3$  were considered test-positive and BI values  $\leq 3$  test-negative, while laboratory-confirmed dengue cases served as the reference standard. Based on these classifications, true-positive, false-positive, false-negative, and true-negative results were identified to calculate sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of the BI for predicting dengue cases.

Data were extracted in Microsoft Excel and analyzed in SPSS version 23. Descriptive statistics were used to summarize annual district-wise dengue case counts. For the validity assessment, BI was treated as the test variable and laboratory-confirmed dengue cases as the reference standard. Two-by-two contingency tables were constructed, and sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy were calculated. Where



Figure 1: Map of Province Punjab

correlation analysis was performed, the statistical test used and corresponding p-value were reported. The map below (Figure 1) highlights the districts of Lahore, Sheikhupura and Rawalpindi within Pakistan's Punjab province.<sup>9</sup>

## RESULTS

This study utilized dengue data obtained from the Provincial data interface for dengue, covering the period from 2011 to 2024 across three districts: Lahore, Sheikhupura and Rawalpindi. Lahore reported the highest number of confirmed cases, with a peak of 19,942 cases in 2021, followed by 16,984 cases in 2011. However, in 2024, Lahore recorded fewer cases compared to Rawalpindi. Rawalpindi's highest case count occurred in 2024, with 6,606 confirmed cases, followed by 6,298 cases in 2018. In contrast, Sheikhupura consistently reported fewer dengue cases than Lahore and Rawalpindi throughout the 2011-2024 periods. The lowest number of confirmed dengue cases in Lahore was reported in 2015. In contrast, Sheikhupura District recorded its minimum cases in 2011 and 2018, while Rawalpindi District had its lowest counts in 2011 and 2012 (Table I & Figure 2).

A weak negative correlation ( $r=-0.293$ ) was observed between confirmed dengue cases and indoor/outdoor surveillance activities, suggesting that increased survey efforts may contribute to better control of dengue cases.

The second objective of this study was to assess the validity of the BI in predicting confirmed dengue cases. Two Union Councils (UCs) in Rawalpindi District, i.e. Dhoke Munshee and Chak Jalal Din, were randomly selected for evaluation, both of which experienced dengue epidemics in 2024. In UC Dhoke Munshee, the BI demonstrated high sensitivity (100%) and NPV (100%), along with moderate specificity (78.18%), PPV (62.5%), and diagnostic accuracy (84%) when compared against confirmed dengue cases as the gold standard. Similarly, in UC Chak Jalal Din, the BI showed high sensitivity (96%) and NPV (95.65%), but lower specificity (44.9%), PPV (47.06%), and

diagnostic accuracy (62.16%) [Figure 4a, 4b & Table II].

**Table I: Comparison of confirmed dengue cases from 2011 to 2024 in high-risk districts (Lahore, Sheikhupura and Rawalpindi)**

| Year         | Lahore        | Sheikhupura  | Rawalpindi    | Annual Total  |
|--------------|---------------|--------------|---------------|---------------|
| 2011         | 16,984        | 0            | 0             | 16,984        |
| 2012         | 115           | 30           | 0             | 145           |
| 2013         | 1,316         | 78           | 914           | 2,308         |
| 2014         | 95            | 59           | 1,201         | 1,355         |
| 2015         | 6             | 6            | 269           | 281           |
| 2016         | 1,030         | 25           | 977           | 2,032         |
| 2017         | 73            | 7            | 334           | 414           |
| 2018         | 17            | 0            | 422           | 439           |
| 2019         | 766           | 24           | 6,298         | 7,088         |
| 2020         | 144           | 5            | 17            | 166           |
| 2021         | 19,942        | 363          | 2,509         | 22,814        |
| 2022         | 8,228         | 263          | 4,767         | 13,258        |
| 2023         | 6,555         | 239          | 2,631         | 9,425         |
| 2024         | 474           | 35           | 6,606         | 7,115         |
| <b>Total</b> | <b>55,745</b> | <b>1,134</b> | <b>26,945</b> | <b>83,824</b> |

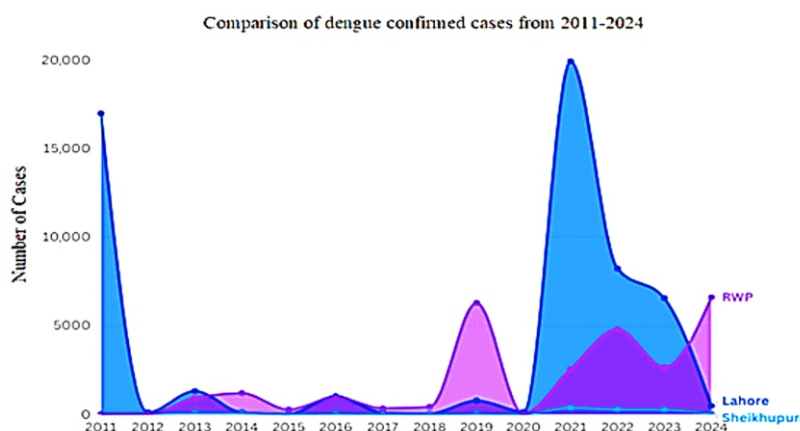


Figure 2: longitudinal analysis of dengue trends (2011-2024) in high-risk districts of Punjab, Pakistan

**Table II: Validity of BI for prediction of confirmed dengue cases in UC Dhoke Munshi Rawalpindi and UC Chak Jalal Din Rawalpindi in the year 2024**

| UC=Dhoke Munshi |                 |    |       |    | UC=Chak Jalal Din |                 |    |       |    |
|-----------------|-----------------|----|-------|----|-------------------|-----------------|----|-------|----|
| Variable        | Confirmed Cases |    | Total |    | Variable          | Confirmed Cases |    | Total |    |
|                 | Yes             | No |       |    |                   | Yes             | No |       |    |
| BI              | >3              | 20 | 12    | 32 | BI                | >3              | 24 | 27    | 51 |
|                 | ≤3              | 0  | 43    | 43 |                   | ≤3              | 1  | 22    | 23 |
| Total           |                 | 20 | 55    | 75 | Total             |                 | 25 | 49    | 74 |

Sensitivity=100  
Specificity=78.18%  
PPV=62.5%  
NPV=100%  
Diagnostic Accuracy=84%

Sensitivity=96%  
Specificity=44.9%  
PPV=47.06%  
NPV=95.65%  
Diagnostic Accuracy=62.16%

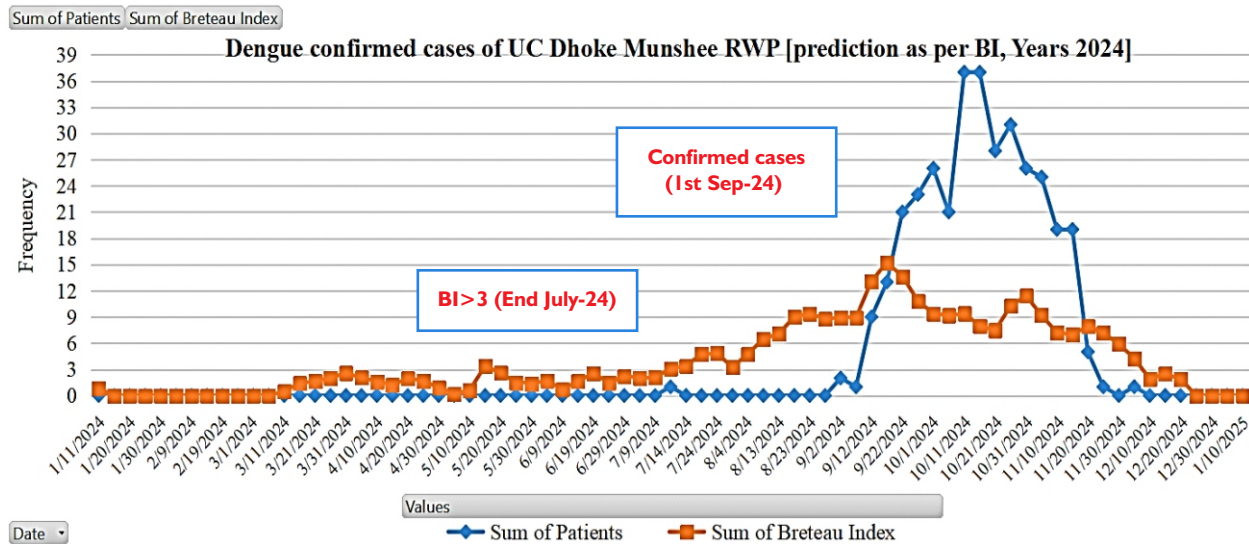


Figure 4a: Validity of Breteau Index for prediction of dengue confirmed from UC Dhoke Munshee Rawalpindi in year 2024

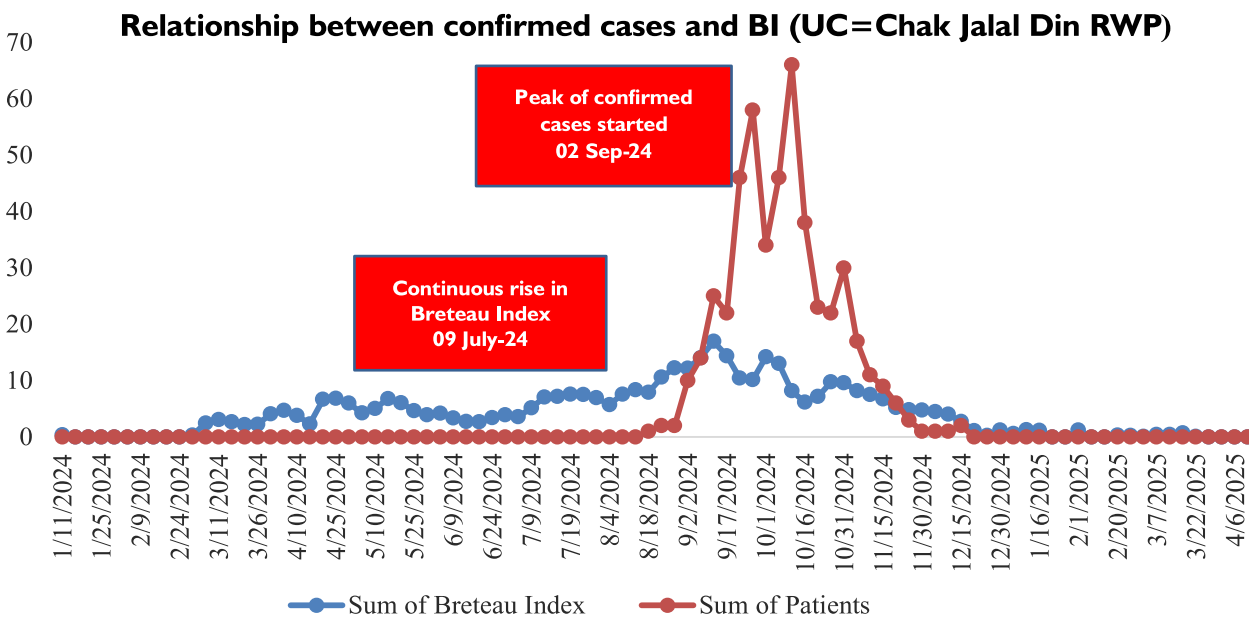


Figure 4b: Validity of BI for prediction of dengue confirmed from UC Chak Jalal Din Rawalpindi in year 2024

## DISCUSSION

This study analyzed dengue data from 2011-2024 in Lahore, Rawalpindi, and Sheikhupura. Lahore reported the highest dengue burden with 19,942 cases in 2021, while Rawalpindi recorded 6,606 cases in 2024, the highest in its district history, whereas Sheikhupura consistently showed lower case counts. A weak negative correlation ( $r = -0.293$ ) was observed

between dengue cases and surveillance activities, suggesting improved surveillance may reduce transmission. BI showed high sensitivity and NPV in Dhoke Munshee (100%, 100%) and Chak Jalal Din (96%, 95.65%), indicating good potential for early dengue outbreak prediction.

A local study conducted by Mukhtar MU, et al.,<sup>10</sup> in Sheikhupura District tested 333 samples, of which 120 were

positive for DENV, yielding an overall prevalence rate of 36%. Among the confirmed cases, the majority (55%;  $n = 66$ ) were reported in 2014, followed by 27.5% ( $n = 33$ ) in 2016, 10% ( $n = 12$ ) in 2015, and 7.5% ( $n = 9$ ) in 2017. The study revealed a higher infection rate in males (68.3%;  $n = 82$ ) compared to females (31.7%;  $n = 38$ ), with 61% ( $n = 74$ ) of patients falling within the 11–30-year age group. Notably, the peak prevalence of infection (94.2%;

n=113) occurred after the rainy season.<sup>10</sup>

Dengue is caused by four distinct virus serotypes: DEN-1, DEN-2, DEN-3, and DEN-4.<sup>11</sup> During this outbreak, a total of 322 blood samples were analyzed. DEN-2 emerged as the most common serotype, detected in 126 cases (39%), followed by DEN-3 in 96 cases (30%), DEN-4 in 58 cases (18%), and DEN-1 in 42 cases (13%). In the outbreaks reported by Pakistan previously, it was observed that DEN-2 was the prominent serotype. In 2008 and 2009, outbreaks of DEN 2 to 4 and DEN 2,3 were the prominent serotypes, respectively.<sup>12</sup> Similarly, dengue case data from the Sheikhpura and Gujranwala districts showed that DEN-2 was the most prevalent serotype, followed by DEN-1.<sup>13</sup>

A study by Aryaprema VS, et al., also showed their finding in favor of our study results. The author reported strong performance, with areas under the ROC curves exceeding 80%, sensitivity over 75%, and specificity above 70% for threshold values with defined lag periods. This study highlights the importance of reporting of BI in outbreaks. The results highlight the importance of systematically planned routine vector larval surveillance within dengue control programs, as it enables reliable outbreak predictions and provides an adequate lead time for early preparedness and response.<sup>14</sup> The difference in specificity (78.18% in UC Dhoke Munshee vs. 44.9% in UC Chak Jalal Din) likely reflects local heterogeneity in population density, housing structure, larval habitat diversity and field data quality between the two UCs. UC Chak Jalal Din's lower specificity suggests a higher rate of false positives i.e., BI exceeded the threshold even in the absence of confirmed cases, which may reflect environmental factors that elevate larval indices without necessarily translating to human transmission.

Multiple studies indicate that well-calibrated threshold values for entomological indices can effectively reflect disease vector population dynamics in specific endemic regions. These thresholds provide reliable and actionable predictions for impending

dengue outbreaks.<sup>14-17</sup>

The DRAM is recognized as a promising digital surveillance and response platform; however, it has not yet been fully operationalized within an integrated predictive framework. We recommend its systematic implementation and scale-up at provincial and national levels to enhance real-time surveillance, strengthen early warning capacity, and support timely, evidence-based dengue control interventions.

On the findings of this study, it is suggested that a robust reporting mechanism results in effective findings; secondly, larvicidal activities (Indoor/Outdoor) survey should be enhanced. The role of BI should not be neglected; proper reporting and in response action must be performed timely manner. The study provided valuable data; however, it did not adjust for key climatic drivers such as temperature, rainfall, and humidity. Therefore, the association between BI and dengue cases should be interpreted cautiously, and future studies should incorporate these variables to improve predictive validity. Lastly, health education strategies to increase awareness of dengue disease should be done so that the efforts are not only by the government but also from communities are done to control this disease.

## CONCLUSION

This study demonstrates distinct temporal and spatial variation in dengue burden across Lahore, Rawalpindi, and Sheikhpura from 2011 to 2024. Lahore experienced major outbreaks in 2011 and 2021, while Rawalpindi showed a rising trend and reported the highest number of cases in 2024. Sheikhpura consistently exhibited a lower disease burden throughout the study period.

The Breteau Index showed high sensitivity and negative predictive value, indicating its usefulness as an early warning indicator for dengue risk. However, the observed variability in specificity across settings suggests that BI should be interpreted cautiously and used in conjunction with other epidemiological and environmental indicators rather than as a standalone

predictive tool.

## REFERENCES

1. Zohra T, Din M, Ikram A, Bashir A, Jahangir H, Baloch IS, et al. Demographic and clinical features of dengue fever infection in Pakistan: a cross-sectional epidemiological study. *Trop Dis Travel Med Vaccines* 2024;10(1):11. <https://doi.org/10.1186/s40794-024-00221-4>
2. Haroon M, J Hasnain, Faisal S, Ali N, Kamran M, Ullah F. Dengue outbreak in Peshawar: clinical features and laboratory markers of dengue virus infection. *J Infect Public Health* 2019;12(2):258-62. <https://doi.org/10.1016/j.jiph.2018.10.138>
3. Atique S, Abdul SS, Hss CY, Chuang TW. Meteorological influences on dengue transmission in Pakistan. *Asian Pac J Trop Med* 2016;9(10):954-61. <https://doi.org/10.1016/j.apjtm.2016.07.033>
4. Rasheed SB, RK Butlin, M. Boots. A review of dengue as an emerging disease in Pakistan. *Public Health* 2013;127(1):11-7. <https://doi.org/10.1016/j.puhe.2012.09.006>
5. Yang X, Quam MBM, Zhang T, Sang S. Global burden for dengue and the evolving pattern in the past 30 years. *J Travel Med* 2021;28(8):taab146. <https://doi.org/10.1093/jtm/taab146>
6. Abi R, Adetunji O. AI-enhanced health informatics frameworks for predicting infectious disease outbreak dynamics using climate, mobility, and population immunization data integration. *Int J Med Sci* 2023;5(1):21-31. <https://doi.org/10.33545/26648881.2023.v5.i1a.69>
7. Younas M, Aziz MA, Afzal RK, Hamid Iqbal, Hussain M, Mir RS. Effectiveness of comprehensive campaign for dengue control in southern punjab, Pakistan-an experience of 2 years. *Pak Armed Forces Med J* 2021;71(6):2121-5. <https://doi.org/10.51253/pafmj.v71i6.6072>
8. Tahir U, Khan UH, Zubair MS,

- Mustafa B. Wolbachia pipientis: A potential candidate for combating and eradicating dengue epidemics in Pakistan. *Asian Pac J Trop Med* 2015;8(12):989-98. <https://doi.org/10.1016/j.apjtm.2015.11.012>
9. Yousaf MZ, Siddique A, Ashfaq UA, Ali M. Scenario of dengue infection & its control in Pakistan: An update and way forward. *Asian Pac J Trop Med* 2018;11(1):15-23. <https://doi.org/10.4103/1995-7645.223529>
  10. Mukhtar MU, Mukhtar M, Iqbal N, Nawaz Z, Bhatti A, Haq F, et al. The emergence of Dengue Fever in Sheikhupura, Pakistan: its seroprevalence and risk factors assessment during 2014-2017. *J Infect Dev Ctries* 2021;15(09):1351-5. <https://doi.org/10.3855/jidc.13976>
  11. World Health Organization (WHO). Tuberculosis fact sheet. [Accessed on: May 25, 2026]. Available from URL: <https://www.who.int/news-room/fact-sheets/detail/tuberculosis>
  12. Humayoun MA, Waseem T, Jawa AA, Hashmi MS, Akram J. Multiple dengue serotypes and high frequency of dengue hemorrhagic fever at two tertiary care hospitals in Lahore during the 2008 dengue virus outbreak in Punjab, Pakistan. *Int J Infect Dis* 2010;14(Suppl 3):e54-9. <https://doi.org/10.1016/j.ijid.2009.10.008>
  13. Fatima Z, Idrees M, Bajwa M, Tahir Z, Ullah Q, Zia M, et al. Serotype and genotype analysis of dengue virus by sequencing followed by phylogenetic analysis using samples from three mini outbreaks-2007-2009 in Pakistan. *BMC Microbiol* 2011;11:200. <https://doi.org/10.1186/1471-2180-11-200>
  14. Aryaprema VS, Xue RD. Breteau index as a promising early warning signal for dengue fever outbreaks in the Colombo District, Sri Lanka. *Acta Trop* 2019;199:105155. <https://doi.org/10.1016/j.actatropica.2019.105155>
  15. Udayanga L, Gunathilaka N, Iqbal MCM, Najim MMM, Pahalagedara K, Abeyewickreme W. Empirical optimization of risk thresholds for dengue: an approach towards entomological management of Aedes mosquitoes based on larval indices in the Kandy District of Sri Lanka. *Parasit Vectors* 2018;11(1):368. <https://doi.org/10.1186/s13071-018-2961-y>
  16. Udayanga L, Aryaprema S, Gunathilaka N, Iqbal MCM, Fernando T, Abeyewickreme W. Larval indices of vector mosquitoes as predictors of dengue epidemics: an approach to manage dengue outbreaks based on entomological parameters in the districts of Colombo and Kandy, Sri Lanka. *Biomed Res Int* 2020;2020(1):6386952. <https://doi.org/10.1155/2020/6386952>
  17. Wijegunawardana NDAD, Gunawardene YINS, Chandrasena TGAN, Dassanayake RS, Udayanga NWBAL, Abeyewickreme W. Evaluation of the effects of Aedes Vector indices and climatic factors on Dengue incidence in Gampaha District, Sri Lanka. *Biomed Res Int* 2019;2019:2950216. <https://doi.org/10.1155/2019/2950216>

## AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

**SA:** Conception and study design, critical review, approval of the final version to be published

**MUM & MAM:** Study design, acquisition of data, drafting the manuscript, approval of the final version to be published

**MUF:** Acquisition, analysis and interpretation of data, drafting the manuscript, critical review, approval of the final version to be published

*Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.*

## CONFLICT OF INTEREST

Authors declared no conflict of interest, whether financial or otherwise, that could influence the integrity, objectivity, or validity of their research work.

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## DATA SHARING STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.



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