Original Article
DOI: https://doi.org/10.70749/ijbr.v3i4.1148

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://induspublishers.com/IJBR
ISSN: 2960-2793/ 2960-2807

Proteinuria in Adults with Severe Dengue Fever

Muhammad Awais[1], Inam Ullah Khan[1], Hanif Ullah Khan[1], Zakir Khan[1], Waheed Ullah[1], Almas Khan[1]

[1]Department of Medicine, Khyber Teaching Hospital (KTH), Peshawar, KP, Pakistan.

ARTICLE INFO

Keywords

Proteinuria, Severe Dengue, Renal Involvement, Pakistan, Biomarker.

Corresponding Author: Inam Ullah Khan,
Department of Medicine, Khyber Teaching Hospital (KTH), Peshawar, KP, Pakistan.
Email: Inam.83khan@gmail.com

Declaration

Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.

Conflict of Interest: No conflict of interest.

Funding: No funding received by the authors.

Article History

Received: 05-02-2025, Revised: 21-03-2025
Accepted: 08-04-2025, Published: 25-04-2025

ABSTRACT

Background: The mosquito-borne viral illness known as Dengue fever now threatens public health in Pakistan and other tropical nations. Profound cases of dengue frequently generate medical difficulties which transcend the bloodstream although renal damage is one of the main extra-hematological consequences. Renal injuries manifest first through proteinuria which experts now recognize as a warning sign of dengue disease among patients with severe manifestations. **Objective:** This research investigated how often proteinuria occurred among adult hospital patients who suffered severe dengue infection and examined the relationship between this condition and patient characteristics. **Methods:** Researchers from KTH Peshawar performed their study via a cross-sectional approach throughout six months. A research study included 100 patients within the age range of 18 to 60 years who experienced severe dengue without pre-existing renal, hepatic or cardiovascular medical conditions. The evaluation of proteinuria employed urine dipstick testing as the diagnostic method. The study analysis utilized SPSS v26 to process both clinical and demographic information. **Results:** In 56% of the patients, proteinuria was detected. The prevalence was the same across genders and age groups, without any significant differences. Nevertheless, proteinuria was significantly associated ($p = 0.02$) with a higher BMI (≥25). Proteinuria was also significantly related to elevated serum creatinine ($p < 0.01$) and suggests early renal involvement. **Conclusion:** Proteinuria is a common finding in adults with severe dengue fever, and could be a useful marker of renal impairment. Early detection of renal complications is facilitated by routine screening using dipstick analysis, especially in settings with high burden, which should ultimately lead to better patient outcome. Its prognostic implications need to be further explored through further longitudinal studies.

INTRODUCTION

Imran et al. (2022); Hushmandi et al. (2024) stated that Dengue fever is a major arboviral infection globally because of dengue virus transmission through Aedes mosquitoes in tropical and subtropical regions, including Pakistan. According to the World Health Organization (WHOR) there are about 390 million Dengue infections in the world yearly with 96 million people having symptoms ranging from mild fever up to severe dengue of which is dangerous (M. B. Khan et al., 2023). Severe dengue which previously called for dengue hemorrhagic fever or dengue shock syndrome (DHFS), combines plasma leakage (Leak syndrome) along with fluid in the organs, organ damage, severe bleeding and respiratory distress that usually affect the kidneys (Patel et al., 2024; Owais et al., 2023).

Renal involvement in dengue has garnered increasing attention over the past decade (Bushi et al., 2024; Wellekens, Betrains, De Munter, & Peetermans, 2022). One of the most common indicators of renal dysfunction is proteinuria, which is the abnormal excretion of protein in the urine and often serves as an early sign of glomerular or tubular injury (Zeng et al., 2024; Borg, Carlson, Søndergaard, & Persson, 2023). Proteinuria may be transient or persistent and has been observed in varying degrees among patients with dengue, particularly in severe cases (Tejo, Hamasaki, Menezes, & Ho, 2024; Ali, Gibreel, Suliman, Mohammed, & Nour, 2022). The pathogenesis of proteinuria in dengue is complex and multifactorial, involving immune-mediated damage, direct viral nephropathy, systemic inflammatory responses, hemoconcentration, and vascular leakage—all of which can affect renal microcirculation (Ray, Moudgil, & Sinha, 2022).

Many studies in the past few years have emphasized the clinical relevance of proteinuria associated with dengue fever. A study in India found that nearly 15 in 20 patients with dengue with signs of severe disease had proteinuria indicating renal impairment more common than had been recognized. Additionally, proteinuria in

these patients has been associated with heightened risk of severe disease, intensive care admission and prolonged hospitalization (Nasir, Irfan, Asif, Khan, and Anwar, 2024; Costa, Chang, Costa, and Cunha, 2023). Despite these findings, knowledge on the prevalence, and clinical implications of proteinuria among dengue patients in Pakistan is scant.

Specifically, the implications of dengue-induced proteinuria are of paramount importance in countries with limited health resources and heavy burden of dengue outbreaks (San Martin et al., 2024). Early identification of renal complications such as proteinuria allows for timely interventions and monitoring strategies that may decrease morbidity and mortality (Kushner, Khunti, Cebrián, & Deed, 2024; Hamza & Burton, 2023). Dipstick testing for proteinuria is cheap, quick and noninvasive and is a readily applicable tool for the early detection of renal involvement among dengue (Kight, 2023).

During the past decade, dengue has become a recurrent outbreak in the Khyber Pakhtunkhwa province of Pakistan with the help of the Khyber Teaching Hospital (KTH), Peshawar, being a major tertiary facility for the dengue patients (J. Khan et al., 2022). But, none of the local studies tried to evaluate renal involvement, particularly proteinuria, in patients with severe dengue. Thus, the pattern of proteinuria and its demographic, clinical and biochemical correlates may have relevance to clinical practice and patient outcomes.

The study examines proteinuria occurrence in adult severe dengue fever patients who are admitted at the KTH Peshawar. This analysis investigates the relationship between proteinuria together with age, gender and BMI along with duration of fever, serum creatinine levels and other test results. This research assessment of proteinuria in this patient cohort will validate its predictive and standardization as a diagnostic practice for severe dengue treatment.

The rationale for focusing on adults aged 18 to 60 years lies in the differential disease presentation and renal physiology in pediatric and geriatric populations, which could confound the relationship between dengue and proteinuria. Additionally, excluding patients with comorbid conditions such as diabetes mellitus, chronic kidney disease, hypertension, and liver disease ensures that proteinuria observed in this cohort is likely attributable to dengue itself rather than pre-existing renal impairment. Such a focused inclusion criterion enhances the internal validity of the study.

In the context of a rapidly evolving arboviral epidemic and increasing reports of extra-hematologic complications, this study contributes to the growing body of literature that emphasizes the systemic nature of dengue infection. It reinforces the concept that dengue fever is not merely a hematologic or febrile illness but a multi-organ disease that can significantly impact renal function, even in individuals without underlying kidney disease.

To summarize, in high burden settings like Pakistan, this study compounds a largely ignored and critical complication of dengue fever - proteinuria, in exploring a potential solution to help clinicians manage such patients. Thus, it reaffirms the necessity of including renal monitoring in the therapeutic protocol for dengue case patients, particularly those with severe clinical features.

METHODOLOGY

This cross-sectional research took place at Khyber Teaching Hospital (KTH) Department of General Medicine in Peshawar. Studies started after the ethical review board approved the research synopsis and ran for six months.

The research included 100 participants as part of its sample. The researchers calculated their sample size through World Health Organization (WHO) sample size calculator at 95% confidence interval with a 7% margin of error and an expected proteinuria frequency of 85% in severe dengue cases based on previous study results. The research used consecutive sampling as a non-probability choice.

Healthcare workers treated adults who had severe dengue fever between the ages of 18 and 60 years from both genders. Participants with pre-existing renal disease and diabetes mellitus and hypertension and liver disease and heart failure were omitted from the study because these conditions could affect proteinuria measurements.

The study team received informed consent from patients who matched the study requirements. Medical professionals collected baseline demographic information from patients that included age, gender, body mass index (BMI), duration of symptoms and place of residence, education level, profession, and socioeconomic status through pre-designed patient research forms.

Medical and sterile procedures defined the clean-catch mid-stream method for obtaining urine samples. The urinary dipstick test (per manufacturer guidelines) assessed both protein presence and protein amount in each specimen right after collection. Researchers documented the presence of proteinuria for every individual after following the established definitions.

IBM SPSS version 26 served as the analytical tool for data processing. The study evaluated the distribution normality for age BMI and duration of complaints before reporting results as mean standard deviation or this use median interquartile range whenever distribution differed from normal. Data analysts displayed categorical variables through frequencies and percentages to present gender, place of residence, education, profession, socioeconomic status, and presence of proteinuria.

The researchers sectioned proteinuria results according to patient variables that included age combined with gender alongside BMI classifications and duration of symptoms. Post-stratification comparisons utilized the Chi-square test with Fisher's exact test as the alternative for appropriate situations. The analysis determined statistical significance when the p-value reached below 0.05.

RESULTS

One hundred patients who received a diagnosis of severe dengue fever selectively participated in the study. The patients in the cohort had a mean age of 36.8 years between the ages of 18 and 65 and a standard deviation of 12.4 years. Almost two-thirds of participants were male (n=62) and females made up the remaining percentage (n=38) of the study sample. The participants had an average body mass index value of 24.7 ± 3.8 kg/m².

The urine dipstick analysis demonstrated proteinuria in 56% of the 100 study population participants. A total of 44 patients (44%) showed negative results for proteinuria during tests. The high number of positive cases demonstrates kidney involvement should be considered a factor in severe dengue disease progression.

Table 1

Frequency of Proteinuria in Patients with Severe Dengue (n = 100)

Proteinuria Status	Frequency	Percentage (%)
Present	56	56%
Absent	44	44%

Proteinuria affected 56.5% of male patients and 55.3% of female patients respectively without any statistical difference. The comparison of the gender groups showed no significant difference (p = 0.91) regarding renal involvement thus indicating similar predisposition rates between male and female patients.

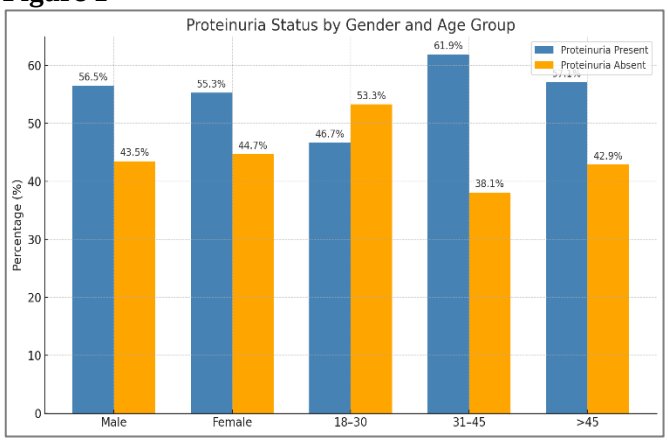
The research subjects received age-based categorization into three groups which included 18–30 years, 31–45 years, and >45 years. Among the patient groups evaluated for proteinuria, individuals between 31–45 years showed the most considerable rate at 61.9% yet the results failed to demonstrate significant variation between groups (p = 0.34).

Table 2

Association of Demographic Variables with Proteinuria

Variable	Category	Proteinuria Present (n=56)	Proteinuria Absent (n=44)	p-value
Gender	Male (n=62)	35 (56.5%)	27 (43.5%)	0.91
	Female (n=38)	21 (55.3%)	17 (44.7%)	
Age Group	18–30 (n=30)	14 (46.7%)	16 (53.3%)	0.34
	31–45 (n=42)	26 (61.9%)	16 (38.1%)	
	>45 (n=28)	16 (57.1%)	12 (42.9%)	

Figure 1



Proteinuria was most prevalent among patients with a BMI ≥25 (70%) and least common among those with BMI <18.5 (35%). This association was statistically significant (p = 0.02), indicating a potential link between higher BMI and renal impairment.

The average duration of fever before admission was 5.2 ± 1.8 days. Patients with proteinuria had a slightly longer fever duration (5.5 ± 1.6 days) than those without (4.9 ± 1.9 days), though this was not statistically significant (p = 0.09).

Serum creatinine levels were significantly higher in patients with proteinuria (1.34 ± 0.28 mg/dL) than in those without (1.08 ± 0.22 mg/dL), indicating renal dysfunction (p < 0.01).

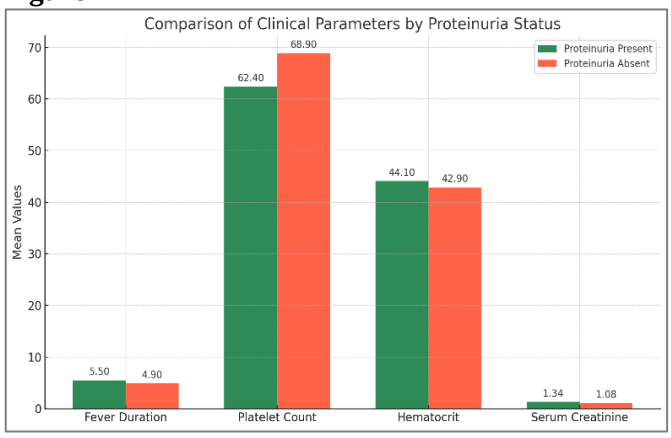
Table 3

Clinical Parameters in Patients With and Without Proteinuria

Parameter	Proteinuria Present (n=56)	Proteinuria Absent (n=44)	p-value
Fever Duration (days)	5.5 ± 1.6	4.9 ± 1.9	0.09
Platelet Count (×10⁹/L)	62.4 ± 21.5	68.9 ± 19.8	0.07
Hematocrit (%)	44.1 ± 3.7	42.9 ± 3.1	0.08
Serum Creatinine (mg/dL)	1.34 ± 0.28	1.08 ± 0.22	<0.01*

*Statistically significant at p < 0.05

Figure 2



Among patients with proteinuria, 42.9% also showed hematuria, and 19.6% required intensive care management. This suggests that proteinuria may correlate with increased disease severity and could serve as a prognostic marker, warranting further investigation in future studies.

DISCUSSION

This cross-sectional study was conducted to determine the frequency and associated demographic and clinical variables of proteinuria in patients diagnosed with severe dengue fever. The findings of this study suggest a significant burden of renal involvement in such patients, as evidenced by a 56% prevalence of proteinuria. This observation aligns with previous research indicating that renal dysfunction is a relatively common complication in severe dengue cases, warranting early recognition and monitoring for better clinical outcomes.

The high prevalence of proteinuria in our study reinforces the hypothesis that dengue virus infection, particularly in its severe form, has systemic effects extending beyond the classical hematological abnormalities and includes renal involvement. Dengue-associated kidney injury has been attributed to various mechanisms, such as direct viral nephropathy, immune complex deposition, rhabdomyolysis, hemolysis, and hypovolemia-related acute tubular necrosis. Although we did not perform histopathological assessments to confirm the exact etiology of proteinuria, the dipstick positivity suggests glomerular or tubular injury requiring attention during patient management.

The demographic breakdown showed a relatively balanced distribution of proteinuria between males (56.5%) and females (55.3%), indicating that gender does not play a significant role in the development of renal complications in the context of severe dengue. This is in agreement with earlier studies which have also found no consistent gender-based susceptibility to dengue-induced renal impairment. Similarly, age stratification did not yield statistically significant differences in the prevalence of proteinuria, although the highest frequency was observed in the 31–45 year age group. This suggests that working-age adults may be more likely to suffer from severe manifestations, possibly due to delayed healthcare-seeking behavior or increased exposure to mosquito vectors.

A noteworthy finding of this study is the statistically significant association between higher BMI and proteinuria ($p = 0.02$). Patients with a BMI ≥25 had a 70% prevalence of proteinuria compared to only 35% among underweight individuals. Obesity and overweight states are known to predispose individuals to altered renal hemodynamics and increased glomerular filtration pressures, which may exacerbate the renal effects of systemic infections such as dengue. Furthermore, adiposity has been linked to low-grade systemic inflammation, which may enhance vascular permeability—a known mechanism in severe dengue pathophysiology—contributing to renal endothelial damage.

Another key parameter analyzed was serum creatinine, which was significantly elevated in patients with proteinuria (1.34 ± 0.28 mg/dL vs. 1.08 ± 0.22 mg/dL, $p < 0.01$). This biochemical marker further supports the diagnosis of renal dysfunction and underscores the clinical significance of dipstick-positive proteinuria in severe dengue. The correlation between elevated creatinine and proteinuria emphasizes the need for routine renal function tests in hospitalized dengue patients to detect early renal involvement.

Interestingly, although the mean duration of fever was slightly longer in the proteinuria group (5.5 days) compared to the non-proteinuria group (4.9 days), the difference was not statistically significant. Similarly, platelet count and hematocrit—key indicators in dengue severity—did not show a significant correlation with proteinuria. However, the trend toward lower platelet count and higher hematocrit among proteinuric patients may suggest an enhanced capillary leak and more severe intravascular depletion, indirectly affecting renal perfusion.

Proteinuria along with hematuria was found in 42.9% of patients while 19.6% needed intensive medical care. The study discovered proteinuria can serve as an indicator to estimate the severity of severe dengue infection. Close medical surveillance together with intensified supportive care may be needed for patients who present with proteinuria because these patients demonstrate increased susceptibility for serious complications and adverse clinical outcomes.

This study has several strengths, including the use of standardized dipstick testing for proteinuria and a focused inclusion criterion that minimized confounding factors by excluding patients with pre-existing renal, hepatic, or cardiovascular diseases. However, limitations must be acknowledged. The use of dipstick testing, while practical and cost-effective, is semi-quantitative and may be affected by hydration status, urine concentration, and other factors. Additionally, the study did not assess long-term renal outcomes, so the persistence or reversibility of proteinuria remains unclear. Future prospective studies incorporating 24-hour urine protein measurements, renal imaging, or even biopsy in selected cases could offer a more comprehensive understanding of the pathophysiology and clinical implications of dengue-associated renal involvement.

In summary, this study reports high prevalence of proteinuria among patients with severe dengue fever, and possible relationship to obesity and increased serum creatinine. Early renal impairment might be present as proteinuria, which may be a marker of increased disease

severity. Routine urine analysis during the clinical workup of the severe dengue patient may facilitate the early identification of patients at risk of complications and help improve patient outcomes by early intervention.

CONCLUSION

The prevalence of proteinuria (56%) among adults admitted with severe dengue fever at a tertiary care hospital in Pakistan is underlined in this study. The findings emphasize that renal involvement is a common, but frequently unrecognized, complication in critically ill dengue patients, and risk factors include raised serum creatinine and high BMI. Although it was not associated with gender or age, its presence may indicate early renal damage and its presence may be an independent predictor of increased clinical severity as indicated by ICU admission. Urine dipstick testing offered for the simplicity, affordability, and lack of invasiveness, warrant the incorporation of routine screening for proteinuria in dengue management protocols, in particular in resource constrained settings in order to facilitate patient monitoring and outcomes. Proteinuria beyond the acute phase of illness should be evaluated for its persistence and prognostic value, and early interventions based on its detection should be further explored to reduce the morbidity from dengue-associated renal complications.

REFERENCES

1. Imran, M., Ye, J., Saleemi, M. K., Shaheen, I., Zohaib, A., Chen, Z., & Cao, S. (2022). Epidemiological trends of mosquito-borne viral diseases in Pakistan. *Animal Diseases*, *2*(1), 1-10. https://doi.org/10.1186/s44149-021-00034-4
2. Hushmandi, K., Saadat, S. H., Bokaie, S., Akbarein, H., Daneshi, S., Najafi, M., & Esfandiari, N. (2024). An Overview of Dengue Fever. *Archives of Advances in Biosciences*, *15*(1). https://doi.org/10.22037/aab.v15i1.44108
3. Khan, M. B., Yang, Z., Lin, C., Hsu, M., Urbina, A. N., Assavalapsakul, W., Wang, W., Chen, Y., & Wang, S. (2023). Dengue overview: An updated systemic review. *Journal of Infection and Public Health*, *16*(10), 1625-1642. https://doi.org/10.1016/j.jiph.2023.08.001
4. Patel, M. P., Oza, V. M., Tanna, H. B., Khadela, A. D., Bharadia, P. D., & Patel, J. K. (2024). Current perspectives in dengue hemorrhagic fever. *Rising Contagious Diseases*, 72-86. https://doi.org/10.1002/9781394188741.ch8
5. Owais, S. M., Ansar, F., Saqib, M., Wahid, K., Rashid, K., & Mumtaz, H. (2023). Unforeseen complications: A case of dengue shock syndrome presenting with multi-organ dysfunction in a subtropical region. *Tropical Medicine and Health*, *51*(1). https://doi.org/10.1186/s41182-023-00530-y
6. Bushi, G., Shabil, M., Padhi, B. K., Ahmed, M., Pandey, P., Satapathy, P., Rustagi, S., Pradhan, K. B., Al-qaim, Z. H., & Sah, R. (2023). Prevalence of acute kidney injury among dengue cases: A systematic review and meta-analysis. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, *118*(1), 1-11. https://doi.org/10.1093/trstmh/trad067
7. Wellekens, K., Betrains, A., De Munter, P., & Peetermans, W. (2020). Dengue: Current state one year before WHO 2010–2020 goals. *Acta Clinica Belgica*, *77*(2), 436-444. https://doi.org/10.1080/17843286.2020.1837576
8. Zeng, D., Wang, B., Xiao, Z., Wang, X., Tang, X., Yao, X., Wang, P., Li, M., Dai, Y., & Yu, X. (2024). Early diagnosis and treatment of kidney injury: A focus on urine protein. *International Journal of Molecular Sciences*, *25*(20), 11171. https://doi.org/10.3390/ijms252011171
9. Borg, R., Carlson, N., Søndergaard, J., & Persson, F. (2023). The growing challenge of chronic kidney disease: An overview of current knowledge. *International Journal of Nephrology*, *2023*, 1-8. https://doi.org/10.1155/2023/9609266
10. Tejo, A. M., Hamasaki, D. T., Menezes, L. M., & Ho, Y. (2024). Severe dengue in the intensive care unit. *Journal of Intensive Medicine*, *4*(1), 16-33. https://doi.org/10.1016/j.jointm.2023.07.007
11. Ali, S. A., Gibreel, M. O., Suliman, N. S., Mohammed, A. K., & Nour, B. Y. (2022). Prediction of acute renal failure in dengue fever patients. *Open Journal of Urology*, *12*(02), 99-106. https://doi.org/10.4236/oju.2022.122010
12. Ray, P. E., Moudgil, A., & Sinha, A. (2022). Viral infections and the kidney. *Pediatric Nephrology*, 707-733. https://doi.org/10.1007/978-3-030-52719-8_101
13. Nasir, M., Irfan, J., Asif, A. B., Khan, Q. U., & Anwar, H. (2024). Complexities of dengue fever: Pathogenesis, clinical features and

management strategies. *Discoveries*, *12*(2), e189. https://doi.org/10.15190/d.2024.8

14. Costa, C. H., Chang, K., Costa, D. L., & Cunha, F. V. (2023). From infection to death: An overview of the pathogenesis of visceral leishmaniasis. *Pathogens*, *12*(7), 969. https://doi.org/10.3390/pathogens12070969
15. Martin, Y. R., Silva, K. G., Dias, A. L., Soares, B. G., Julio, B. S., Cuba, J. A., Fagundes, N. S., & Oliveira, J. R. (2024). Cardiovascular complications associated with dengue virus infection. *Brazilian Journal of Health Review*, *7*(9), e75044. https://doi.org/10.34119/bjhrv7n9-219
16. Kushner, P., Khunti, K., Cebrián, A., & Deed, G. (2024). Early identification and management of chronic kidney disease: A narrative review of the crucial role of primary care practitioners. *Advances in Therapy*, *41*(10), 3757-3770. https://doi.org/10.1007/s12325-024-02957-z
17. Hamza, W., & Burton, J. O. (2023). Chronic kidney disease awareness and updates on the management of diabetic kidney disease. *Practical Diabetes*, *40*(3), 16-20. https://doi.org/10.1002/pdi.2454
18. Kight, E. C. (2023). *Advancements in Point-of-Care Diagnostic Assays for Non-Invasive Samples in Resource Constrained Settings* (Doctoral dissertation, Vanderbilt University). https://www.proquest.com/openview/3d26b932db8a1e2db3815f532fe679ee/1?cbl=18750&diss=y&pq-origsite=gscholar
19. Khan, J., Adil, M., Wang, G., Tsheten, T., Zhang, D., Pan, W., Khan, M. A., Rehman, I. U., Zheng, X., Wu, Z., & Wu, Y. (2022). A cross-sectional study to assess the epidemiological situation and associated risk factors of dengue fever; knowledge, attitudes, and practices about dengue prevention in Khyber Pakhtunkhwa province, Pakistan. *Frontiers in Public Health*, *10*. https://doi.org/10.3389/fpubh.2022.923277