

## ASSESSING THE TEMPORAL AND SPATIAL DISTRIBUTION OF DENGUE FEVER IN TEHSIL ADENZAI, DISTRICT DIR LOWER

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### ABSTRACT

*Tehsil Adenzai, District Dir Lower, and with the rate of prevalence also varying. This work here reports the highest prevalence at Chakdara at 58.95% which puts it at the top of the urgent list for increased testing and awareness campaigns. Ouch shares a similar rate at a prevalence of 43.02%, while moderate spread reports at Badwan and Gul Abad at 26.36%. Lower rates are found in Kharkani, Shiwa, and Asbnar, reflecting control measures are effective, or exposure is at the minimum. Gender-wise, Chakdara is predominant in females and in males for Ouch. Many of the children belong to the age group 0-15 years. This anomaly in the 46-60 age group calls for occupational or environmental factors. DHQ Chakdara has a prevalence rate of 72.2 percent since it is a referral hospital. Summarily, through locally tailored interventions among gender and age groups, sustaining surveillance, and engaging communities, this region would be made to control dengue.*

**Keywords:** Dengue Fever, Adenzai Dir Lower, Prevalence, Serotype.

### INTRODUCTION

Dengue virus is a flavivirus that is transferred by arthropods, primarily by Aedes mosquitoes. It is widespread throughout the tropical and subtropical regions of the world (Gubler and Clark, 1995). This virus-causing dengue fever comes in one of two forms, mild, flu-like, or severe circulatory disease. It is one of the major global public health problems. Implications are epidemics in the tropical and subtropical areas. The World Health Organization puts at about 100 million dengue infections yearly, and 250,000 to 500,000 of these advances into dengue hemorrhagic fever.

Dengue virus is a small RNA virus infecting both mosquitoes and human beings, which has become one of the major public health issues across Asia, Latin America, and Africa (Gubler, 1997). The disease normally goes through a milder stage of the disease, which characterizes high fever, rash, headache, and extreme pain in the muscles and joints. It is also referred to as dandy fever, Cuban fever, breakbone fever, or saddle fever. Recovery from infection leads to lifelong immunity against the serotype but only short-term immunity against reinfection with other serotypes (Halstead, 1988). Antibody-dependent enhancement is responsible for the fact

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that an infection may progress from dengue fever to dengue hemorrhagic fever, and on to dengue shock syndrome, largely in the heterospecific infections of various serotypes (Halstead, 1988).

Dengue virus is an enveloped, positive-stranded RNA virus of approximately 11 kilobases in size, with a single expressed polypeptide that subsequently cleaves into structural proteins - capsid [C], membrane [M], and envelope [E] - and seven non-structural proteins: NS1, NS2A, NS2B, NS3, NS4A, NS4B, NS5 (Chambers et al., 1990; Deubel et al., 1990). NS1 is a 50-kilodalton glycoprotein secreted from the surface of infected cells. It exists in secreted and non-secreted forms (Falconar et al., 1994). It is transmitted to humans through mosquito vectors, such as *Aedes aegypti* and *Aedes albopictus*, Chen and Wilson (2005). Primary infection produces partial immunity to all the serotypes, but cross-protection between serotypes is relatively weak. Secondary infections could result in more severe manifestations because of antibody-dependent enhancement. Other flavivirid diseases that are reemerging include yellow fever, Japanese encephalitis, West Nile encephalitis, and tick-borne encephalitis. These diseases exhibit antigenic relations, as evidenced by cross-neutralization tests with polyclonal antisera (Guzmán and Kouri, 1996). Fauci et al. have viewed fever, joint pain, headache, and rash as frequently occurring symptoms of dengue infection, besides thrombocytopenia which is a decrease in platelets. It has been believed that thrombocytopenia is an early indicator of severe disease (Fausi et al., 2008). In normal individuals, the platelet count ranges from 150 to  $450 \times 10^9$  per liter, but rapidly drops in dengue-related patients (George J.N., 2000).

The mechanism of pathogenesis of thrombocytopenia in dengue is still unknown. Dengue virus has been shown to cause suppression of the bone marrow and lower production of platelet synthesis that may give rise to thrombocytopenia (La Russa and Innis, 1995). The dengue virus is believed to react with the human platelet; thus, immunologic depletion of the platelet might be the reason for a high rate of thrombocytopenia in hemorrhagic patients suffering from the dengue (He et al., 1995). It is documented that dengue type 2 directly interacts with platelets, which results in thrombocytopenia (Chowdhury et al., 2008). In fact, it has been identified that severe forms of dengue disease are due to variations of the virus, its virulence, or dynamics involved within the immune response (Rico-Hesse et al., 1997). Dengue virus type 2 is bound poorly to platelets and can cause hemorrhage by non-Fc receptor pathways. Common neurological symptoms with severe cases include encephalopathy and motor weakness; this has been reported by researchers such as Misra et al. (2006) and Kumar et al. (2013).

Multiplication of dengue virus is seen in the liver, and it leads to acute liver failure, jaundice, and bleeding disorders (An et al., 1999). Hemophagocytic syndrome is another serious complication in which there is hemophagocytosis in the bone marrow (Jain and Chaturvedi, 2010). Oxidative stress due to dengue infection results in severe outcomes such as dengue hemorrhagic fever (Soundravally et al., 2008).

The dengue virus can gain access to host cells through clathrin-mediated endocytosis but has recently also been demonstrated to use alternative entry pathways, such as caveolin- or lipid raft-dependent entry, dependent on serotype and target cell type (Acosta et al., 2008; Zybert et al., 2008). Entry of the virus is made possible by the viral E protein that inserts into the target membrane and mediates the fusion of the viral membrane with the host cell membrane (Zybert et al., 2008).

This study has data concerning the local dengue prevalence in this small area of the Khyber Pakhtunkhwa province and in the Malakand Division by Dir Lower, Pakistan. The basis for building these campaigns to contain the disease depends fundamentally on knowing the geographical factors, environmental factors, and the prevalence of the disease. The purpose of this research is to assess the prevalence of dengue in Tehsil Adenzai of Dir Lower. Analyze the trend of dengue virus gender and age-specific to target vulnerable groups and customize interventions.

## MATERIALS AND METHODS

### Dir Lower

Dir Lower is a district of Khyber Pakhtunkhwa, Pakistan. It possesses remarkable landscapes and holds cultural along with historical importance. These include the territories of Timergara, Chakdara, and Samar Bagh. Mountains, valleys, and rivers dominate the district terrain. The most noted among them includes the Panjkora

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River which also adds to its natural beauty. Many historical as well as cultural sites exist within Dir Lower, showing its many pasts.

## Laboratory-based sample collection

Sampling of patient reports was done from Tehsil Adenzai, District Dir Lower, from a laboratory setup during the years 2023-2024. Sampling was done between September 2023 and June 2024 when patients suffering from Dengue viral infections were reported.

## Selection of Health Care Facilities

Special to be chosen as the elected health care institutions, but out of them three have been particularly selected; these are THQ Chakdara, RHC Ouch, and CAT D Hospital Gul Abad. The facilities considered as health care have high diagnostic capacities and a huge volume of patients to incorporate and represent a diversity in various reports based on demographics of different conditions of illnesses or socio-economic statuses.

## Data Analysis

Sample collection was undertaken by the Centers for Disease Control at the District Dir Lower under the Department of Health concerning cases of Dengue viral infection.

## Patient Enrolment

The patients were willing volunteers for this study and consent was sought before they were enrolled for this research. This is an ethical procedure to respect people's autonomy, which in turn guarantees their confidentiality concerning contributing to this research.

## Serum Isolation and Antibody Preparation

After patients were recruited, serum samples were divided to be tested with Dengue-specific IgM and IgG antibodies. These antibodies are detected by ELISA kits to evaluate the incidence of the population against the Dengue virus.

## Proforma

All major portions of the necessary information relevant for the comprehensive data gathering included a set of particulars regarding the patients in question, their socio-economic and locality-based attributes, condition at home, and histories of dengue experiences and exposures. Much of it was incorporated and obtained effectively through the development of comprehensive proforma.

Data were also stratified by age, gender, Tehsil, and hospital, which allows for more complex statistical analysis. Patterns or trends observed may provide directions of dengue incidence in the Dir Lower, Tehsil Adenzai.

## RESULTS

The data on dengue screening among different localities indicated varying incidences and levels of infection that may also be dependent on the impacts or effectiveness of public health interventions. Chakdara leads with 58.95%, with 293 out of 558 screenings positive, which reveals that this locality has a major burden from dengue. Such high prevalence could be due to the density of the population, supposing greater, and it might be related to a better breeding condition of mosquitoes or because of lesser control measures. Just like in Ouch, high prevalence stands at 43.02%, with 77 positive cases from 179 screenings, meaning that this disease still is not under control in this region as well.

Badwan and Gul Abad have an absolute number of smear examinations done much higher at 459 and 110, respectively, but prevalence rates are at much lower rates of 26.36%. It could be due to better management of patients or differences in socioenvironmental factors prevailing in those regions. The lowest prevalence rates

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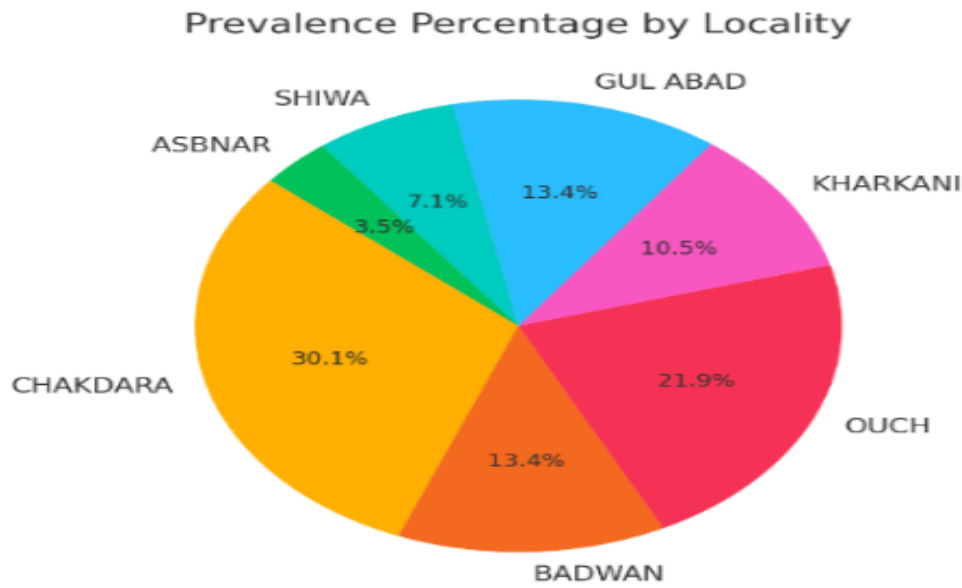
have been seen at Kharkani, Shiwa, and Asbnar with 20.63%, 13.89%, and 6.90% respectively due to effective vector control measures, lesser exposure towards breeding sites, and population size, respectively.

The above prevalence rates point out that there is a need for the adaptation of public health strategies and interventions in different localities towards effective management and reduction of dengue burden. A good data performance was developed, including essential details regarding name, gender, age, locality, socioeconomic status, home conditions, and cattle presence or absence. Samples of blood were taken from symptomatic persons for dengue symptoms that include fever, itchy skin, skin rashes, persistent headaches, bone pain, and vomiting. Such a detailed collection of data ensured proper intervention.

## **Tehsil Adenzai**

Data on dengue screening indicate that the prevalence rate is not evenly the case in all localities. The infection level varies and depends on the efficiency of public health intervention in different localities. CHACKDARA, it has the highest prevalence rate at 58.95%, with 293 positive cases out of 497 screenings. This is most likely to be indicative of a major dengue burden-at least partly due to the high population density, more favorable conditions for the mosquitoes' breeding, or less than adequate control measures. BADWAN has a prevalence rate of 26.36%, with 121 positive cases out of 459 screenings. In prevalence, it seems like environmental or socio-economic factors are controlling the spread of the disease and management is much stronger than in OUCH has a very high prevalence rate, 43.02%, and 77 confirmed positives out of 179 screenings. It gives an appearance of facing the same problems as that in CHACKDARA about control over dengue owing to friendly environmental conditions for larvae mosquitoes or gaps in public health interventions. KHARKANI has a prevalence rate of 20.63%, wherein 33 out of 160 screenings were positive cases. The reason for this comparatively lower prevalence is due to the effective vector control measures or a less dense population with other protective factors. GUL ABAD also offers a prevalence rate of 26.36% with 29 positive cases out of 110 screenings, reflecting a moderate prevalence rate that requires intervention management in dengue and its control measures. SHIWA has the lowest prevalence standing at 13.89%, with only 5 positive cases from 36 screenings. Low prevalence rates might imply effective control measures or less conducive conditions for mosquito breeding and dengue transmission. The lowest prevalence rate is recorded at ASBNAR standing at 6.90%, with 2 positive cases out of 29 screenings. This would therefore indicate that highly effective control measures are in place or minimal exposure to risk factors associated with dengue It gives an appearance of facing the same problems as that in CHACKDARA about control over dengue owing to friendly environmental conditions for larvae mosquitoes or gaps in public health interventions. KHARKANI has a prevalence rate of 20.63%, wherein 33 out of 160 screenings were positive cases. The reason for this comparatively lower prevalence is due to the effective vector control measures or a less dense population with other protective factors. GUL ABAD also offers a prevalence rate of 26.36% with 29 positive cases out of 110 screenings, reflecting a moderate prevalence rate that requires intervention management in dengue and its control measures. SHIWA has the lowest prevalence standing at 13.89%, with only 5 positive cases from 36 screenings. Low prevalence rates might imply effective control measures or less conducive conditions for mosquito breeding and dengue transmission. The lowest prevalence rate is recorded at ASBNAR standing at 6.90%, with 2 positive cases out of 29 screenings. This would therefore indicate that highly effective control measures are in place or minimal exposure to risk factors associated with dengue transmission.

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**Table 1 Prevalence in Tehsil Adenzai Localities, District Dir Lower Kpk. (2024)**

Localities	Total Screenings	Negative Cases	Positive Cases	Prevalence %
CHAKDARA	497	203	293	58.95%
BADWAN	459	228	121	26.36%
OUCH	179	102	77	43.02%
KHARKANI	160	126	33	20.63%
GUL ABAD	110	80	29	26.36%
SHIWA	36	30	5	13.89%
ASBNAR	29	26	2	6.90%
DHQ CHACKDARA	234	-	169	72.20%
Cat-D Hospitals	205	-	100	48.70%
HFCs- (RHCs, BHUs)	58	-	24	42.40%

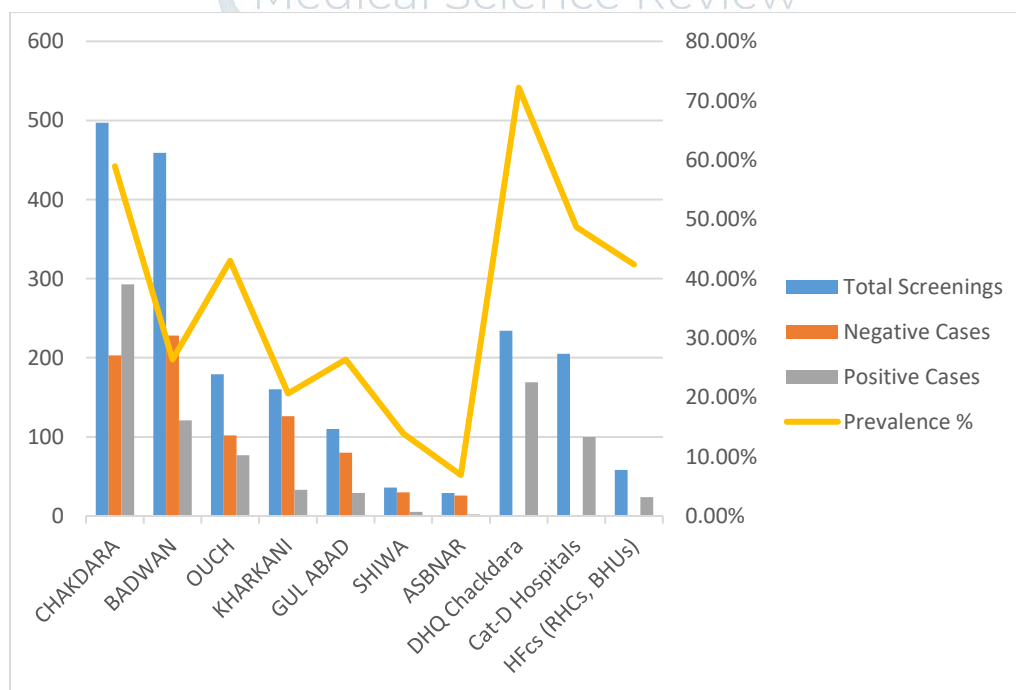
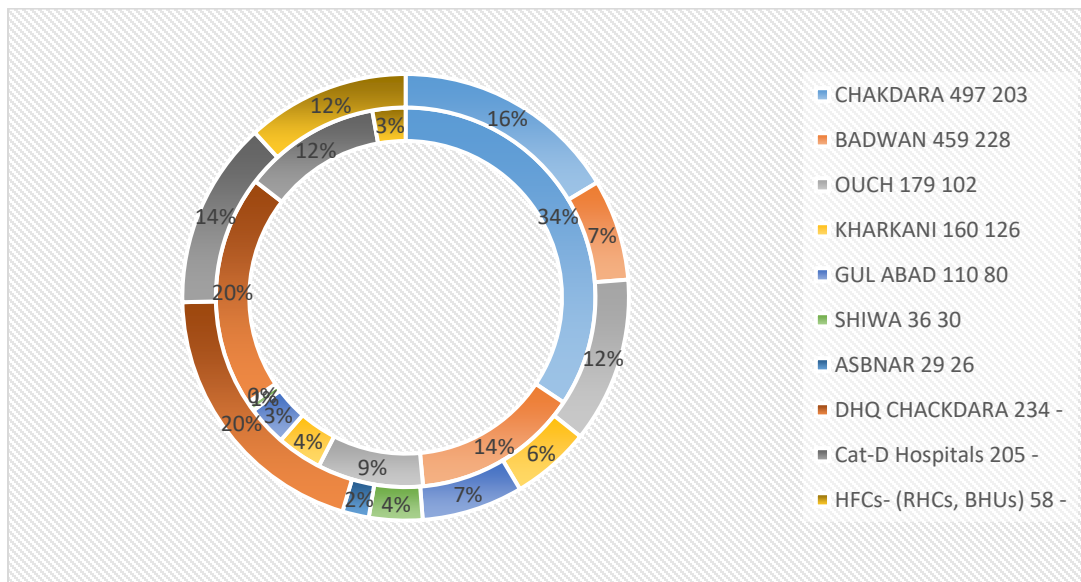
The general data presented reviews different levels of prevalence within different locations and health facilities of Tehsil Adenzai, District Dir Lower. For instance, Chakdara boasts the highest level of prevalence, recording 58.95%. Such a case necessitates more aggressive public health interventions, like intensified testing and campaigns to seek community awareness. The high prevalence rate could be due to the reasons of high population density or favorable conditions for mosquito breeding. On the contrary, places such as Badwan and Gul Abad which have registered the maximum number of total screenings depict a prevalence rate of 26.36% which once again reflects that preventive measures undertaken in these areas are relatively more effective. Some localities like Kharkani, Shiwa, and Asbnar have very low rates of prevalence, with Asbnar being the lowest at 6.90%; this could be because there is better control over vectors or lesser exposure to risk factors. The burden of dengue varies among healthcare units, as DHQ Chackdara depicts the highest prevalence at 72.20%, and may be accounted for the fact that it is a major referral center for patients with severe cases. Cat-D Hospitals and HFCs also bear a major load in the diagnosis and management of dengue patients with prevalence rates of 48.70% and 42.40% respectively. In this regard, the results presented can be said to mainly represent the need for a huge number of resources to be put into these health care centers regardless of their being in rural areas to capture the disease early in the system and consequently further treat it.

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Incidentally, data also reveal a trend related to gender, whereby Chakdara has a substantially higher prevalence among females (61.14%) compared with males (47.95%). Such cases require imperative targeted public health intervention which can consider various exposures and vulnerabilities with a perspective on gender.

Age-wise data show prevalence in the age group of 0-15 years to be very high, which also makes the age group vulnerable to the infection of dengue. These patterns of infections reflect the need for pertinent public health interventions regarding the age group to prevent infection with maximum effectiveness.

In addition, the prevalence rates differ from one locality to another and in some health facilities within Tehsil Adenzai. Thus, this calls for multiple types of approaches to be undertaken by enhanced surveillance activities, engagement with the community, as well as the distribution of resources to be able to effectively control dengue in the locality.



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## Interpretation

On conducting ANOVA for the incidence of Dengue in every Tehsil of the District Dir Lower, the finding revealed great variation with  $P < 0.05$  on percentage incidence at the varying levels of disease transmission and effectiveness of control measures. Apparently, diversities of public health strategies targeted to specific challenges and characters of every Tehsil have been brought forth. Areas like Chackdara and Ouch which are high prevalence areas need to be looked at immediately, whereas the areas reporting low prevalence rates—such as Kharkani and Asbnar—suggest effective control measures or less exposure to the risks of transmission. On the contrary, the hospital-wise distribution of Dengue patients in District Dir Lower does not signify any major gap in the patient ratios, as  $P > 0.05$ . This explains an equal distribution of health care and proper management of Dengue cases at all the health care facilities in the district. These results reflect that the healthcare facilities are well-balanced to manage the cases of Dengue. Therefore, this type of balanced facility provides uniform care without significant variations among hospitals. This statistical analysis gives valuable insight into the overall epidemiological patterns of Dengue in District Dir Lower. It puts forth targeted interventions based on local prevalence rates and points to a fairer distribution of healthcare resources for better control and a timely diminution of the impact of Dengue fever. The trends are said to be gender-specific and point toward age-wise vulnerabilities that inform strategic public health initiatives toward reducing disease transmission and protecting vulnerable populations. In the region, continued monitoring, social participation, and scientific research activities shall be important for applying long-term effective Dengue prevention and control measures.

## DISCUSSION

A total of nine countries experienced dengue hemorrhagic fever epidemics that had grown four-fold more by 1995 (Chaturvedi et al., 2005).

Approximately 120 countries have endemic dengue virus transmission; that is, 2.5 billion people at risk, and between 70-500 million infections of which 2.1 million are clinically severe; 500,000 cases of dengue hemorrhagic fever require hospitalization, and 21,000 reported deaths annually (Dengue Fever World Health Organization Fact Sheet). Dengue is endemic in Pakistan with its usual peak incidence in the post-monsoon period (Jahan F 2011).

In children under 16 years of age, it was reported for the first time in Pakistan as an undifferentiated fever in the year 1985 (Akram et al., 1998). During 1995 in Hubb, Baluchistan 75 cases and 57 deaths were reported (Paul et al., 1998). 2003 - Dengue broke out in Haripur where 1000 cases were affected and 7 were reported dead, DEN 2 was the most prevalent serotype. The same year in Khushab 2500 cases were reported and 11 died. DEN 2 was present in 7 out of 17 cases that were serotyped. In 2004 only 25 cases were reported from Islamabad and Karachi. In 2005, 13 deaths were reported among 500 cases in Karachi.

In 2006, dengue was reported from Karachi, Sukkar, Nawabshah, Rawalpindi, and Islamabad with nearly 5400 cases and 55 deaths. (Tang et al 2008; Khan et al 2007) Co-circulation of the two serotypes DEN 2 and DEN 3 was documented in the 2006 outbreak (Khan et al 2008; Ahmed et al 2008). In 2007, Karachi, Hyderabad, Mirpur Khas, Lahore, Haripur, Rawalpindi, and Islamabad were affected by the killing of 24 people out of 2700 reported cases. In 2008, Lahore had taken 1800 positive cases with three dengue serotypes (DEN 2, 3 & 4) and a high frequency of dengue hemorrhagic fever. The Genotype of DEN 2 was subtype IV and subtype III of DEN 3 (Humayoun et al 2010; Humayoun et al 2010). A total of 570 cases were reported during the year 2009 and serotypes 2 and 3 dominated the situation (Fatima et al). In the year 2010, a total of 5000 positive cases were recorded. The study was conducted at Lahore, Sheikhpura, and Gujranwala on 320 patients. DEN 2 was the most prevalent followed by DEN virus type 1 (Mahmood et al 2012). The survey has revealed huge heterogeneity in the prevalence of dengue in different localities of District Dir Lower and reflects the different intensities of transmission, as well as the different effectiveness of control.

In areas of high prevalence, including Chackdara and Ouch, the prevalence rates were 58.95% and 43.02%, respectively. These areas require immediate attention because of their high population density or favorability for mosquito breeding and unabated effort at vector control. Localities like Kharkani and Asbnar have reported a lesser prevalence rate (20.63% and 6.90% respectively), which calls for better control measures or lesser

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predisposing environmental factors for mosquito breeding. The time-pressured, tailored public health responses focus can be on high-intensity surveillance and targeted interventions in those areas that report a high prevalence but keeping a watch on others in order not to let outbreaks occur. Other gender-related trends of dengue prevalence include the nuances in varying trends within localities within District Dir Lower. Such as, Chackdara and Badwan report a comparatively higher prevalence rate among females: 61.14% and 22.58% while males reported: 47.95% and 17.48% respectively. One might note differences here in the presence or absence of differing risk or susceptibility factors. Still, Ouch says more common in males as opposed to females, with males at 17.26%, and females at 7.25%. These differences would be required for building gender-sensitive public health interventions that will highlight various vulnerabilities and behaviors exposed in differing ways. Awareness improvement and preventive measure promotion with equal health care accessibilities among men and women. The apparent vulnerability pattern of different age groups may be seen in District Dir Lower.

The cases constituted a high percentage of children, and teenagers in the range 0-15 years constitute 77.27%; because of outdoor activities that promote immunity. On the contrary, adults, above the age of 46 -60 years, reflect the most marked increase in the rate of prevalence at a marked 42.7%. This will be highly influenced by factors related to occupation or lifestyle that promote increased exposure to mosquitoes. Programs such as vaccination in children and public health education for adults to reduce risk should be directed accordingly. Health facilities play a very influential role in dengue management throughout the Dir Lower district, with DHQ Chackdara being a significant referral point for severe cases.

The prevalence rate is 72.2%, meaning a lot is still to be done in terms of viable management strategies and adequate resources at hand. Cat-D hospitals and HFCs that constitute RHcs, BHUs, and CDs offer much toward early detection and management in smaller communities despite fewer screening activities being undertaken. Health capacity, equitable distribution of resources, health care providers, and the local authorities as well as the community are some of the essentials to be able to improve dengue management and control strategies in districts.

## CONCLUSION

The results of this integrated analysis on dengue prevalence rates, gender-specific trends, age-wise distribution, and the role of healthcare facilities can be really very useful in the public health intervention in District Dir Lower. Specific strategies are required to surpass differential prevalence rates among localities, gender disparities in exposure and impact and among age groups, and healthcare facilities capacity.

## Recommendations

**Focused Surveillance and Monitoring:** Orientation and installation of real-time surveillance systems to monitor dengue cases and the breeding ground of mosquitoes in all wards.

**Target Interventions:** Gender-sensitive, age-appropriate interventions with identified vulnerabilities and behavioral risk facilitators of dengue transmission.

**Community Mobilization:** Popular participation to participate in vector control activities, which would include clean-up campaigns besides education and action programs.

**Healthcare capacity building:** Training the health personnel, enhancing the diagnostic capacity, and having proper medicaments in all the tiers of the health institutions for enhancing the control of dengue.

**Policy Support:** Supporting policies that are oriented toward proper vector control, proper infrastructures of sanitation, and equal opportunity to have a share in healthcare measures meant to prevent dengue.

## Author Contributions:

Fawad Khan: Conceptualization, Data Collection, Methodology, Writing—Original Draft.

Faryal Syed: Data Analysis, Interpretation of Results, Writing—Review & Editing.



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Samina Yasmin: Investigation, Data Collection, Writing—Original Draft, Formal Analysis.  
Dr. Gul Zamin Khan: Supervision, Project Administration, Writing—Review & Editing.  
Dr. Muhammad Saad: Validation, Clinical Expertise, Review & Editing.  
Dr. Muhammad Anas: Investigation, Methodology, Data Collection, Writing—Original Draft.  
Ihsan Ullah: Data Collection, Statistical Analysis, Visualization, Writing—Original Draft.  
Inam Ullah: Conceptualization, Data Collection, Review & Editing.

## Conflict of Interest:

The authors declare that there are no conflicts of interest related to this study.

## REFERENCES

- Acosta, E. G., & Barten Schlager, R. (2008). The molecular mechanisms of dengue virus infection. *Future Virology*, 3(3), 211–220. <https://doi.org/10.2217/17460794.3.3.211>
- Ahmed, S., Ali, N., & Ashraf, S. (2008). Co-circulation of two serotypes of dengue virus in 2006 outbreak in Karachi. *Journal of Clinical Virology*, 43(2), 176-179. <https://doi.org/10.1016/j.jcv.2008.06.011>
- Akram, D. S., & Qureshi, H. (1998). Dengue Fever in Children: Karachi. *Infectious Diseases Journal of Pakistan*, 7, 15-16.
- Blok, J. (1985). Dengue viruses and epidemics. *The Lancet*, 2(8464), 858. [https://doi.org/10.1016/S0140-6736\(85\)90496-4](https://doi.org/10.1016/S0140-6736(85)90496-4)
- Chambers, T. J., Hahn, C. S., Galler, R., & Rice, C. M. (1990). Flavivirus genome organization, expression, and replication. *Annual Review of Microbiology*, 44(1), 649-688. <https://doi.org/10.1146/annurev.mi.44.100190.003245>
- Chaturvedi, U. C., Shrivastava, R., & Nagar, R. (2005). Dengue hemorrhagic fever: A global challenge. *Indian Journal of Medical Research*, 121(5), 635-652.
- Chen, L. H., & Wilson, M. E. (2005). Dengue and Chikungunya: A challenge for travelers. *Travel Medicine and Infectious Disease*, 3(4), 231-239. <https://doi.org/10.1016/j.tmaid.2005.06.006>
- Chowdhury, P., Bhattacharya, S., Roychowdhury, S., & Sengupta, S. (2008). Platelet disorder in dengue hemorrhagic fever. *Indian Pediatrics*, 45(1), 189-190.
- Deen, J. L., Harris, E., Wills, B., Balmaseda, A., Hammond, S. N., Rocha, C., ... & Rothman, A. L. (2006). The WHO dengue classification and case definitions: Time for a reassessment. *The Lancet*, 368(9530), 170-173. [https://doi.org/10.1016/S0140-6736\(06\)69006-5](https://doi.org/10.1016/S0140-6736(06)69006-5)
- Deubel, V., Kinney, R. M., & Trent, D. W. (1990). Nucleotide sequence and deduced amino acid sequence of the nonstructural proteins of dengue type 2 virus, Jamaica genotype. *Virology*, 176(2), 580-585. [https://doi.org/10.1016/0042-6822\(90\)90088-J](https://doi.org/10.1016/0042-6822(90)90088-J)
- Falconar, A. K., Young, P. R., & Miles, M. A. (1994). Biochemical and immunological characterization of a secreted form of the flavivirus nonstructural glycoprotein NS1 from dengue virus-infected mammalian cells. *Journal of General Virology*, 75(Pt 12), 3517-3525. <https://doi.org/10.1099/0022-1317-75-12-3517>
- Gibbons, R. V., & Vaughn, D. W. (2002). Dengue: An escalating problem. *BMJ*, 324(7353), 1563-1566. <https://doi.org/10.1136/bmj.324.7353.1563>
- George, J. N. (2000). Platelets. *The Lancet*, 355(9214), 1531-1539. [https://doi.org/10.1016/S0140-6736\(00\)02175-9](https://doi.org/10.1016/S0140-6736(00)02175-9)
- Gubler, D. J., & Clark, G. G. (1995). Dengue/dengue hemorrhagic fever: The emergence of a global health problem. *Emerging Infectious Diseases*, 1(2), 55-57. <https://doi.org/10.3201/eid0102.950205>
- Gubler, D. J. (1997). Dengue and dengue hemorrhagic fever: Its history and resurgence as a global public health problem. In Gubler, D. J., & Kuno, G. (Eds.), *Dengue and Dengue Hemorrhagic Fever* (pp. 1-22). CAB International.
- Guzmán, M. G., & Kouri, G. (1996). Advances in dengue diagnosis. *Clinical and Diagnostic Laboratory Immunology*, 3(6), 621-627. <https://doi.org/10.1128/cdli.3.6.621-627.1996>

# The Research of Medical Science Review

- Halstead, S. B. (1988). Pathogenesis of dengue: Challenges to molecular biology. *Science*, 239(4839), 476–481. <https://doi.org/10.1126/science.239.4839.476>
- He, Q., Yao, F., & Huo, Y. (1995). Dengue virus infection on human platelets. *Journal of Infectious Diseases*, 172(2), 435-438. <https://doi.org/10.1093/infdis/172.2.435>
- Jain, D., & Chaturvedi, U. C. (2010). Dengue in infants: What is known. *Pediatrics and International Child Health*, 30(4), 271-278. <https://doi.org/10.1179/146532810X12858955921364>
- Khan, E., Kisat, M., Khan, N., Nasir, A., Ayub, S., & Hasan, R. (2007). Demographic and clinical features of dengue fever in Pakistan from 2003–2007: A retrospective cross-sectional study. *PLoS ONE*, 5(9), e12505. <https://doi.org/10.1371/journal.pone.0012505>
- Kumar, S. S., Pandit, V., & Patil, M. M. (2013). Dengue-associated hypokalemic paralysis. *Journal of the Association of Physicians of India*, 61(5), 375-376.
- La Russa, V. F., & Innis, B. L. (1995). Mechanisms of dengue virus-induced bone marrow suppression. *Bailliere's Clinical Hematology*, 8(1), 249-270. [https://doi.org/10.1016/S0950-3536\(05\)80254-1](https://doi.org/10.1016/S0950-3536(05)80254-1)
- Mahmood, B., Nasir, M., & Sadiq, A. (2012). Dengue fever in Lahore: Epidemiology, clinical and laboratory findings during the 2011 epidemic. *Journal of the College of Physicians and Surgeons Pakistan*, 22(1), 22-26.
- Misra, U. K., & Kalita, J. (2006). Dengue virus-induced neurological disorders: The Indian perspective. *Neurology India*, 54(3), 245-251. <https://doi.org/10.4103/0028-3886.27150>
- Rico-Hesse, R., Harrison, L. M., Salas, R. A., Tovar, D., Nisalak, A., Ramos, C., ... & Boshell, J. (1997). Origins of dengue type 2 viruses associated with increased pathogenicity in the Americas. *Virology*, 230(2), 244-251. <https://doi.org/10.1006/viro.1997.8494>
- Soundravally, R., Hoti, S. L., Patil, S. A., & Bhatia, A. (2008). Oxidative stress in severe dengue infection: Association of thrombocytopenia with lipid peroxidation. *Platelets*, 19(6), 447-454. <https://doi.org/10.1080/09537100802127087>
- Tang, J. W., Khanani, M. R., & Meltem, T. (2008). The emergence of dengue in Pakistan. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 102(8), 811-814. <https://doi.org/10.1016/j.trstmh.2008.04.022>
- Wang, W. K., Chao, D. Y., & Lin, S. R. (2000). Analysis of dengue virus infection in mosquitoes, humans, and tissue culture using quantitative reverse transcriptase real-time PCR. *Journal of Clinical Microbiology*, 38(8), 3306-3313. <https://doi.org/10.1128/JCM.38.8.3306-3313.2000>
- World Health Organization. (2009). \*Dengue: Guidelines.