



ORIGINAL RESEARCH ARTICLE

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Comparative prevalence of different types of viral hepatitis in the district Dera Ismail Khan, Khyber Pakhtunkhwa, Pakistan

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Abstract

Background: Viral hepatitis causes both liver inflammation and damage and is a serious health problem.

Methods: The indoor data of different types of hepatitis were collected from the official records of the administration of District Head Quarter Hospital Dera Ismail Khan for 2 years (2020–2021).

Results: A total of 1193 cases of viral hepatitis during the study period were found including viral hepatitis C accounted for 547 (45.9%) cases, followed by the co-infection of viral hepatitis A and E 367 (30.8%) cases, and viral hepatitis B 279 (23.4%) cases. March showed the highest prevalence of hepatitis (33.2%), followed by February (10.2%). The co-infection of hepatitis A and E showed a relatively higher prevalence in 6 months from May to November except September including a peak in June (76.5%) during the study period. While viral hepatitis B demonstrated a comparatively higher percentage prevalence in both February and September with a peak in February (68%), and viral hepatitis C is dominant in January, March, and December with a peak in March (83.8%).

Conclusion: All types of viral hepatitis showed variation in prevalence over months and monthly variation concerning peak prevalence exists among different types of hepatitis. Both viral hepatitis A and E demonstrated similar trend in relative prevalence in both 2020 and 2021. Nevertheless, viral hepatitis A and B showed monthly and seasonal variation in relatively prevalence in both years. The study help in adopting strategies for the prevention of viral hepatitis in the study area.

Keywords: Prevalence, Viral hepatitis, Dera Ismail Khan, Co-infection

Introduction

Viral hepatitis is a serious health problem globally. There are five main types of viral hepatitis including hepatitis A, B, C, D, and E [1–3]. All hepatitis viruses can cause acute hepatitis globally. Both hepatitis A virus (HAV) and hepatitis E virus (HEV) is transmitted through the fecal-oral route and sources of infection are contaminated water and food [2, 4, 5]. Both HAV and HEV are the most common causes of acute hepatitis in humans [6], and both are a serious public health concern in developing countries

[7] and have multiple modes of transmission [8] as well as zoonotic potentials globally [8, 9]. It is estimated that approximately 2 billion people are infected with HEV globally [8].

Hepatitis A, B, and C are the most common hepatitis. Hepatitis B virus (HBV) is one of the most important chronic infectious diseases globally, especially in developing countries [10]. Both viral hepatitis B and C are a major threat to public health [2], and can cause chronic hepatitis, and is spread by blood, vaginal secretions, or semen. Nevertheless, blood plays an important role in the transmission of both hepatitis B and C [11]. Hepatitis is among the leading causes of death ranked 7th globally [12] and is a growing concern in Asian countries.

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World Health Organization (WHO) ranked Pakistan 2nd because of having the high prevalence of chronic hepatitis globally [13]. Pakistan has a higher rate and wide prevalence of both hepatitis B and C, which led to end-stage liver diseases including hepatocellular carcinoma and cirrhosis in the country [14]. Pakistan has 10 million chronically infected hepatitis C virus (HCV) carriers [15].

HAV contributed 50 to 60% of cases of acute viral hepatitis in children in Pakistan [16, 17]. While Butt and Sharif [17] found that 20 to 22% of adults and 2.4% of children have acute hepatitis due to HEV. Both HAV and HAE mainly occurs as sporadic disease and are highly prevalent in Pakistan [4]. HAV generally is found in infants and young children, while, HEV is found comparatively more in older children and young adults [4, 18].

The present study is the first undertaken in Pakistan to determine the comparative monthly prevalence of the different types of viral hepatitis including the co-infection of HAV and HEV in the district Dera Ismail Khan.

Methods

Study area

The district of D.I.Khan is located in the south of province of Khyber Pakhtunkhwa (KP) in Pakistan and is bound on the east by the districts Bhakkar and Dera Ghazi Khan, on the southwest by a thin strip of the South Waziristan district, in the north by district Lakki Marwat, and in the northwest is by the district Tank [19]. The district has fertile alluvial plains along the river Indus River while lands farther from the river consist of clay soil cut by ravines from rainfall. It covered an area of 9334 km² and has a population of 1,625,088 according to Census-2017 [20].

Hepatitis B vaccination status

Pentavalent vaccine protects a child from 5 life-threatening diseases, i.e., Diphtheria, Pertussis, Tetanus, Hepatitis B, and *Haemophilus influenzae* type b, and is orally administered to the children in three doses 1st dose aged 6 months, followed by 2nd dose aged 10 months, and 3rd dose aged 14 months in the district health centers.

Patient diagnosis and data collection

The present study is a retrospective study. Patients visited the District Head Quarter (DHQ) hospital D.I.Khan with symptoms of viral hepatitis A including Jaundice (yellow skin and eye), stomach pain, vomiting, fever, dark urine, and diarrhea are diagnosed through ALT (alanine aminotransferase) serological test, and hepatitis E with similar symptoms and also fatigue are diagnosed. Their serum samples were analysed for IgM (immunoglobulin M) anti-HAV and IgM anti-HEV or IgG (immunoglobulin G) anti-HAV or anti-HEV for the detection of HAV and HEV. While hepatitis B and C with the same

Table 1 Prevalence of different types of viral hepatitis in indoor patients in the District Dera Ismail Khan, Khyber Pakhtunkhwa, in 2020

Months	Hepatitis A and E	Hepatitis B	Hepatitis C	Total cases	Percentage
January	27	10	24	61	7.2
February	4	80	21	105	12.4
March	2	49	321	372	43.9
April	1	2	10	13	1.5
May	29	1	7	37	4.4
June	16	1	1	18	2.1
July	34	6	6	46	5.4
August	22	10	19	51	6.0
September	20	28	8	56	6.6
October	31	3	5	39	4.6
November	18	4	9	31	3.7
December	8	5	6	19	2.2
Total	212	199	437	848	100

forementioned symptoms were diagnosed to detect the type of virus in their blood samples by ICT (immuno-chromatographic technique) method and enzyme-linked immunosorbent assay (ELISA) kits and then confirmed by polymerized chain reaction (PCR) using specific primers. The indoor patient data was collected from the computer record of the admin of District Head Quarter (DHQ) hospital D.I.Khan. Serum samples were analyzed for IgM anti-HAV and IgM anti-HEV for the detection of HAV and HEV.

Limitation of the study

The present study is limited because it not included sex-wise and age-wise distribution of viral hepatitis in the study area.

Results

Statistical analysis

For Table 1, tests for the association between months and types of viral hepatitis were conducted which showed Pearson's chi-squared test ($\chi^2 = 654.54$, $df = 22$, p value < 0.0001) and Fisher's exact test p value = 0.0004998. Both tests are very significant, indicating there is an association between months and types of viral hepatitis.

For Table 2 tests for the association between months and types of viral hepatitis showed Pearson's chi-squared test ($\chi^2 = 61.814$, $df = 22$, p value < 0.0001) and Fisher's exact test p value = 0.0004998. Both tests

Table 2 Prevalence of different types of viral hepatitis in indoor patients in the District Dera Ismail Khan, Khyber Pakhtunkhwa, in 2021

Months	Hepatitis A and E	Hepatitis B	Hepatitis C	Total cases	Percentage
January	5	5	17	27	7.8
February	6	3	8	17	4.9
March	8	5	11	24	7.0
April	13	15	7	35	10.1
May	24	14	9	47	13.6
June	23	3	7	33	9.6
July	21	6	11	38	11.0
August	18	6	3	27	7.8
September	10	6	6	22	6.4
October	8	7	6	21	6.1
November	15	8	10	33	9.6
December	4	2	15	21	6.1
Total	155	80	110	345	-

Table 3 Prevalence of different types of viral hepatitis in indoor patients based on the pooled data in the District Dera Ismail Khan, Khyber Pakhtunkhwa, during 2020–2021

Months	Hepatitis A and E	Hepatitis B	Hepatitis C	Total cases	Percentage
January	32	15	41	88	7.4
February	10	83	29	122	10.2
March	10	54	332	396	33.2
April	14	17	17	48	4.0
May	53	15	16	84	7.0
June	39	4	8	51	4.3
July	55	12	17	84	7.0
August	40	16	22	78	6.5
September	30	34	14	78	6.5
October	39	10	11	60	5.0
November	33	12	19	64	5.4
December	12	7	21	40	3.4
Total	367	279	547	1193	-

are very significant, indicating there is an association between months and types of viral hepatitis.

For Table 3, tests for the association between months and types of viral hepatitis showed Pearson's chi-squared test ($\chi^2 = 620.58$, $df = 22$, p value < 0.0001) and Fisher's exact test p value $= < 0.0001$. Both tests

are very significant, indicating there is an association between months and types of viral hepatitis.

Prevalence and comparison of different viral hepatitis in 2020

Out of a total of 848 cases recorded in the D.I.Khan (Table 1), Viral hepatitis C (VHC) contributed highest share of 437 (51.5%) cases, followed by the co-infection of viral hepatitis A (VHA) and viral hepatitis E (VHE) accounted for 212 (25%), and viral hepatitis B (VHB) 199 (23.5%) cases. Overall highest percentage prevalence of viral hepatitis was recorded in March (43.9%), followed by February 12.4% (Table 1), while April revealed lowest prevalence (1.5%). The co-infection of VHA and VHE contributed to the highest prevalence 16% (34 cases) in July, VHB highest 40.2% (80 cases) in February, and VHC highest 73.5% (321 cases) in March (Table 1).

The co-infection of VHA and VHE showed relatively higher percentage prevalence compared to VHB and VHC in January and during May–December except September: highest in June (88.9%), followed by October, 79.5% (Fig. 1). While VHB demonstrated relatively higher prevalence in February (76.2%), followed by September (50%) compared to the remaining types of hepatitis. Furthermore, VHC accounted for comparatively higher prevalence (86.3%) in March and April (76.9%) in D.I.Khan (Fig. 1).

Seasonal variation in the prevalence of different hepatitis are found in the D.I.Khan (Table 1 and Fig. 1). Overall the co-infection of VHA and VHE revealed a relatively higher prevalence in summer, autumn, and winter in the study area (Fig. 1). Similarly, VHB accounted for relatively higher prevalence both in late winter and late summer. While VHC resulted in comparatively higher prevalence in spring (Fig. 1).

Prevalence and comparison of different viral hepatitis in 2021

Out of a total of 345 cases recorded in the D.I.Khan (Table 2), the co-infection of VHA and VHE accounted largest share of 155 (44.9%) cases, followed by VHC 110 (31.9%) cases, and VHB 80 (23.2%) cases. Overall highest percentage prevalence of viral hepatitis was recorded in May (13.6%), followed by July 11%. While February revealed lowest prevalence (4.9%). The co-infection of VHA and VHE contributed to the highest prevalence 15.5% (24 cases) in May, VHB highest 18.8% (15 cases) in April, and VHC highest 15.5% (17 cases) in January (Table 2).

The co-infection of VHA and VHE showed relatively higher percentage prevalence compared to VHB and VHC from May through November and highest in June (69.7%), followed by August (66.7%) (Fig. 2). While

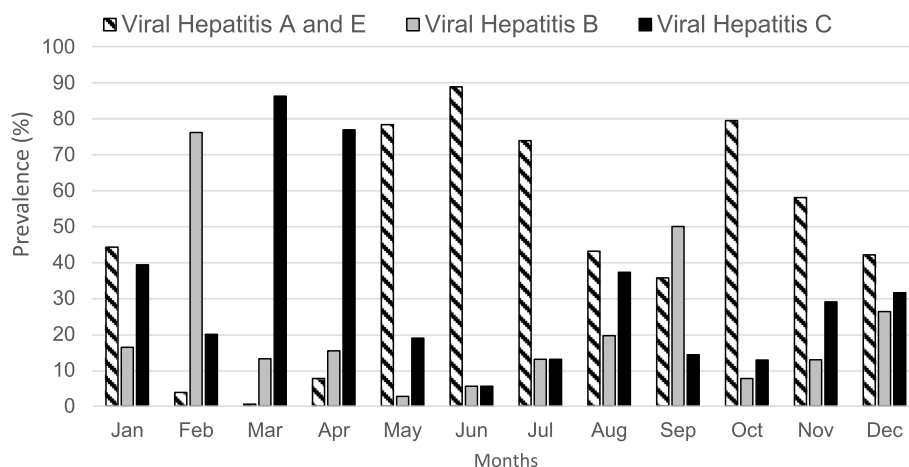


Fig. 1 Monthly comparative percentage prevalence of different types of viral hepatitis in the District Dera Ismail Khan, Khyber Pakhtunkhwa in 2020

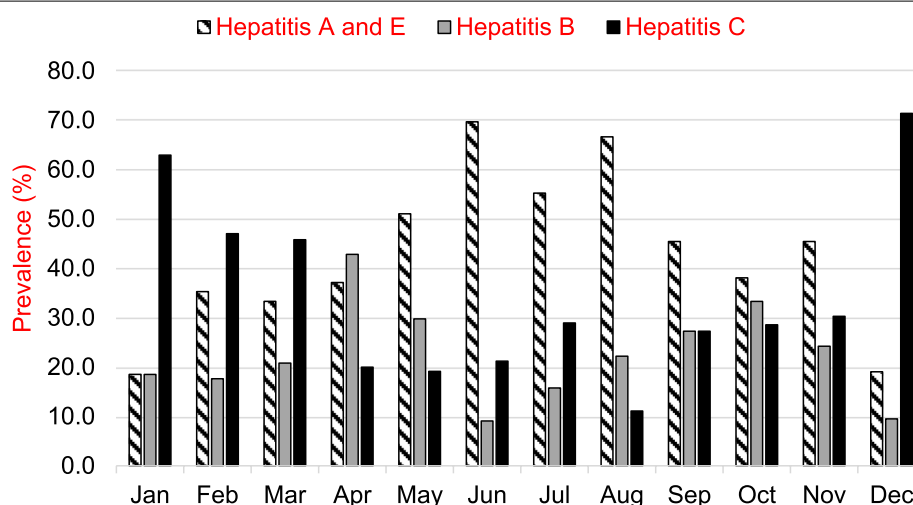


Fig. 2 Monthly comparative (relative) percentage prevalence of different types of viral hepatitis in indoor patients in the District Dera Ismail Khan in 2021

VHB demonstrated relatively higher prevalence only in April (42.9%) compared to the remaining types of hepatitis. Furthermore, VHC accounted for comparatively higher prevalence during January–March and in December with peak in December (71.4%) in D.I.Khan (Fig. 2).

Seasonal variation in the prevalence of different hepatitis exist in the D.I.Khan (Table 2 and Fig. 2). Overall, The co-infection of VHA and VHE revealed a relatively higher prevalence from early summer to late autumn (Fig. 2). Similarly, VHB accounted for relatively higher prevalence in late spring. While VHC resulted in comparatively higher prevalence in winter and early spring in the study area (Fig. 2).

Prevalence and comparison of different viral hepatitis based on pooled data during the study period (2020–2021)

Out of a total of 1193 cases recorded in the D.I.Khan during the study period, VHC showed highest prevalence of 547 (45.9%) cases, followed by the co-infection of VHA and VHE 367 (30.8%) cases, and VHB 279 (23.4%) cases (Table 3).

Overall highest percentage prevalence of viral hepatitis was recorded (33.2%) in March, followed by February 10.2% (Table 3), while December revealed lowest prevalence (3.4%). The co-infection of VHA and VHE contributed to the highest prevalence 15% (55 cases) in July, VHB highest 29.8% (83 cases) in February, and VHC highest 60.7% (332 cases) in March (Table 3).

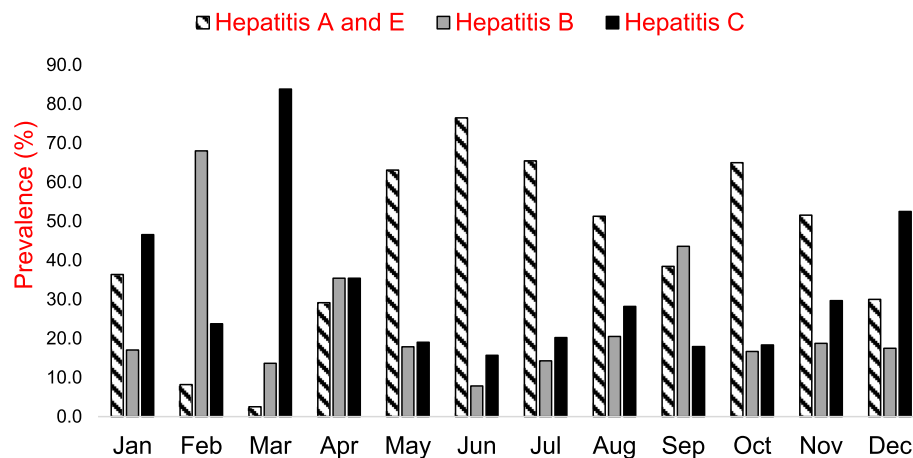


Fig. 3 Monthly comparative (relative) percentage prevalence of different types of viral hepatitis in indoor patients based on the pooled data in the District Dera Ismail Khan during 2020–2021

The co-infection of VHA and VHE showed relatively higher percentage prevalence compared to VHB and VHC from May to November except September with peak in June (76.5%), followed by July, 65.5% (Fig. 3). While VHB resulted in relatively higher prevalence in February (68%) and September (43.6%). Furthermore, VHC contributed comparatively higher prevalence (83.8%) in March, December (52.5%), and January (46.6%) compared to the remaining types of hepatitis in D.I.Khan (Fig. 3).

Seasonal variation occur in the prevalence of different hepatitis in the D.I.Khan (Table 3 and Fig. 3). The co-infection of VHA and VHE revealed a relatively higher prevalence mostly from early summer to late autumn in the study area. Similarly, VHB demonstrated relatively higher prevalence both in late summer and late winter. While VHC resulted in comparatively higher prevalence in winter and early spring (Fig. 3).

Discussion

Although sufficient literature on the prevalence of viral hepatitis in Pakistan is available. Yet, previous studies on the monthly prevalence of viral hepatitis in Pakistan are scarce while literature on the prevalence of co-infection of viral hepatitis A and E in Khyber Pakhtunkhwa is not available.

The overall higher prevalence rate of VHC compared to VHB in both 2020 (Table 1) and 2021 (Table 2) was supported by the Irfan et al. [13] who found out of 4270 positive samples of blood collected at the Pakistan Institute of Medical Sciences (PIMS), Islamabad in 2014 including 3427 (12.1%) samples were found positive for HCV antibodies, while 843 (7.5%) were positive for HBV antigen. However, Khattak et al. [21] determined

hepatitis B was dominant over C in D.I.Khan, as he found out of 349 cases of hepatitis, 248 (71.1%) were VHB and 101 (28.9%) were VHC in the District D.I.Khan during 2008–2009, and also concluded hepatitis B and C are common in this region and males have a higher prevalence of hepatitis than females. Furthermore, Mashud et al. [22] also found hepatitis B was dominant over C in D.I.Khan, and determined out of 60 patients, 28 (46.67%) were HBV+, and 8 (13.33%) were HCV+ in D.I.Khan in 2002.

Najib et al. [23] described 300 internally displaced persons (IDPs) from South Waziristan screened in different health centers of D.I.Khan for HBV and HCV found males suffered more from hepatitis than females and found HBV higher [prevalence compared to HCV. Khan [2] found both VHB and males contributed $\geq 70\%$ share of the overall prevalence of hepatitis B and C in the District Bannu. HBV demonstrated a higher prevalence than HCV in males (except August) and in females (except August and November). Khan [2] also found HBV is dominant in all age groups. Nevertheless, the present study concluded that HCV showed a higher prevalence than HBV in all months except both February and September, and equal to HBV in April (Fig. 3).

Overall HCV has a higher prevalence compared to an HBV in D.I.Khan in the present study in contrast to the previous studies both in D.I.Khan and Bannu. The change in trends of prevalence of HCV as dominant over HBV in D.I.Khan now may be because of more influx of the people migrated particularly from South Waziristan during the previous decade and settled permanently in D.I.Khan and who are not early vaccinated against HCV contributed to the increased prevalence of HCV than HBV during 2021–2022 in the district.

Overall the higher prevalence of co-infection of HAV and HEV during mostly May through November was because of the increase in population of flies, increase in contaminated water and unhygienic conditions, and lack of sanitation prevailed in D.I.Khan during summer and autumn. The cross contamination of drinking water with the sewage is one of the major problem in D.I.Khan and is main source of transmission of hepatitis E in the study area. As pointed out by Wang and Li [5] that poor sanitary conditions are the main cause of both HAV and HEV which are the leading causes of acute viral hepatitis in developing countries and remain a significant public health concern. Likewise, in Pakistan, the unhygienic conditions and poor sanitation lead to 90% of children being infected with hepatitis A of < 10 years of age [17, 24–27]. Hepatitis E in Pakistan has occurred as outbreaks and sporadic cases associated with contaminated water supply [28, 29].

Muneer [30] recorded HAV and HEV positive patients who were 60% and 20%, respectively in 5 major cities in Sindh (Pakistan), and also concluded young children of aged 2 m ≤ 10 years were the most affected population due to poor sanitary conditions and children of this age are comparatively more vulnerable to the disease. The variability in the peak prevalence of different hepatitis viruses in the different regions was described by Qureshi et al. [31] and Khan [2] because of differences in age, sex, and race-specific rates among different regions. Joon et al. [32] supported the present finding and found co-infection of HAV and HEV were dominant towards the end of monsoons and at beginning of winters, i.e., from June to November, and a peak in HEV was also noted in the beginning of rainy season (June) strongly supported similar HEV peak in June in the present study.

The sudden rise in the prevalence of hepatitis B in February and C in March (Table 1 and Fig. 1) may be because people who are not vaccinated against the viral hepatitis travel from Waziristan to plain areas including D.I.Khan in early winter (December) to pass their winter and go back in early summer (May). The people migrated and settled in the D.I.Khan permanently mainly from South Waziristan who are not been vaccinated against hepatitis before making the D.I.Khan more densely populated, contributed to the sanitation problems and unhygienic conditions in the area, resulted in the increase in the hepatitis in the area and thus contributed to the D.I.Khan in Pakistan as he most highest rate of hepatitis. As Benjamini and Hochberg [33] pointed a large number of newborns do not get vaccinated resulting in many children being exposed to these diseases.

Conclusions

Overall, VHC accounted for 45.9% prevalence. The co-infection of VHA and VHE (30.8%), and VHB (23.4%) in the study area, with peak prevalence of viral hepatitis in March (33.2%) followed by February (10.2%). Monthly variation concerning relative and peak prevalence exists among different types of hepatitis studied: Overall co-infection of HAV and HEV revealed relatively higher prevalence mostly during May–November. HBV is relatively dominant in February and September. While HCV is comparatively dominant in January, March, and December. Both VHA and VHE demonstrated relatively higher prevalence mostly during May to December in both 2020 and 2021. Nevertheless, VHB and VHC showed monthly and seasonal variation in relatively prevalence and in peak prevalence of hepatitis in both years. VHB are relatively more prevalent in February and September in 2020, than in April 2021. While, VHC are relatively more prevalent in both March and April in 2020, and has relatively higher prevalence in January to March (2021) and in December in 2021.

What is already known?

- Age-wise, sex-wise, and monthly prevalence of viral hepatitis in Pakistan.

What is new in this study?

- Month-wise prevalence of hepatitis B and C in Dera Ismail Khan.
- Monthly prevalence of hepatitis A and E in Dera Ismail Khan as well as in Khyber Pakhtunkhwa.
- Comparative prevalence of hepatitis A, B, C, and E in Pakistan.

What are the future clinical and research implications of the study findings?

- To know the seasonality of different types of hepatitis in the study area.
- To devise strategies to control both types of hepatitis A and E in the study area.
- To determine factors responsible for viral hepatitis A and E in the study area.

Abbreviations

HAV: Hepatitis A Virus; HBV: Hepatitis B Virus; HCV: Hepatitis C Virus; HEV: Hepatitis E Virus; D.I.Khan: Dera Ismail Khan; ALT: Alanine aminotransferase; IgM: Immunoglobulin M; IgG: Immunoglobulin G; ICT: Immunochromatographic technique; ELISA: Enzyme-linked immunosorbent assay; PCR: Polymerized chain reaction; DHQ: District Head Quarter; VHA: Viral hepatitis A; VHB: Viral

hepatitis B; VHC: Viral hepatitis C; VHE: Viral hepatitis E; PIMS: Pakistan Institute of Medical Sciences.

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Author's contributions

I am the sole author of the manuscript and participated sufficiently in the design of this work, collecting data, management of data, and interpretation of data. The author read and approved the final manuscript.

Author's information

I am Dr. Muhammad Ashraf Khan with Ph.D. in Environmental Sciences, serving as a regular employee in the Elementary and Secondary Education Department, Khyber Pakhtunkhwa, Pakistan.

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Availability of data and materials

Data is available in the tables in the manuscript.

Declarations

Ethics approval and consent to participate

The study was approved by the medical director and head of the ethics committee of DHQ hospital D.I.Khan. I willingly participated in the study.

Consent for publication

Not applicable.

Competing interests

The author declares no competing interests.

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