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Prevalence of Typhoid Fever in the Human Population of District Lower Dir, Khyber Pakhtunkhwa, Pakistan

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ABSTRACT

Background:

Typhoid fever, caused by *Salmonella typhi* (*S. typhi*), remains a major public health problem in the Asian sub-continent due to poor hygienic and sanitary conditions. This study aimed to determine the prevalence of typhoid fever in the human population of District Lower Dir, Pakistan.

Methods:

A total of 395 suspected cases were screened using the Typhidot test. Positive cases were further categorized based on the presence of IgM, IgG, or both antibodies. Data were analyzed by gender, age groups, and month-wise distribution.

Results:

Out of 395 cases, 204 tested positive, yielding an overall prevalence of 51.6%. The disease was more prevalent in females (54.4%) compared to males (45.6%). Among the positive cases, 141 (35.5%) were IgM positive, 14 (3.5%) were IgG positive, and 49 (12.4%) were positive for both IgM and IgG. The highest incidence (54.4%) was recorded in the 61–70 years age group. Month-wise analysis showed the maximum prevalence (100%) in August.

Conclusion:

Typhoid fever is highly prevalent in District Lower Dir, with variation by gender, age, and season. Further studies are recommended to determine antibiotic susceptibility patterns. Effective control programs, promotion of safe drinking water, hygienic food practices, and public awareness campaigns are essential to reduce the disease burden.

Keywords: Typhoid, IgM, IgG, Salmonella typhi, Kit, Diagnosis, Prevalence, Prevention, Dir Lower, Pakistan

INTRODUCTION

Typhoid fever is an acute, generalized infection of the reticulo-endothelial system, intestinal lymphoid tissues and gallbladder caused by Salmonella typhi (Burg *et al*., 2006). Typhoid fever is a communicable disease, found only in man and occurs due to systemic infection (Mushayabasa *et al*., 2013).

The occurrence of typhoid fever is a major threat globally with annual cases exceeds 20 million and approximately a quarter million deaths. The disease is mostly dominant in underdeveloped and developing countries where sanitation is poor, mainly in parts of South Asia (Crump *et al*., 2010). 200 years ago, one of the major causes of morbidity and mortality in the western world was typhoid fever or for that matter enteric fever (Khan *et al*., 1999). Typhoid fever continues to be a global health problem, especially in tropics and sub tropic (Behram *et al*., 2004). It is common in developing countries where it affects 12.5 million people each year. For instance, over 42,000 cases and 1,214 deaths were recorded in Congo between 2004 and 2005 (Marathe *et al*., 2012). Cases are more likely to be seen in areas like India, South and Central America, and Africa with rapid population growth, increased urbanization, and limited safe water, infrastructure, and health systems (Willke *et al*., 2002). Typhoid fever predominantly affects children and young adults and it is recognized as a major cause of morbidity globally with over 12.6 million cases worldwide, and an estimated 600000 deaths annually (Wasfy *et al*., 2000). Almost 80% of cases and deaths occur in Asia. The attack rate as high as 1100 cases per 100000 populations have been documented in developing countries (Ivanoff *et al*., 1994). The disease is endemic in Bangladesh with a recent record of the illness is estimated to be 390 cases per 100 000 persons (Naheed *et al*., 2008), while in Malaysia, it periodically gives an outbreak with annual incidence of 10.2 – 17.9 cases per 100 000 persons (Deris *et al*., 2010). In the USA, Europe, and other industrialized countries with clean water sources, typhoid fever is rare, but in 1 year, 1996–1997, in the USA there were 293 documented cases, of whom about 80% acquired their infections abroad (Ackers *et al*., 2000).

Typhoid fever is an enteric bacterial infection caused by Salmonella enterica serovar Typhi or Paratyphi A. Most cases are caused by Typhi, which is usually written S. Typhi (Ochiai *et al*., 2008). S. Typhi is more prevalent than S. Paratyphi A globally, with the best estimates predicting approximately 21 and 5 million new infections with each serovar per year, respectively (Buckle *et al*., 2012). Typhoid fever is a systemic infection caused by human-specific food and water-borne pathogens, such as Salmonella enterica subspecies, enterica serovar typhi (S. typhi) or by the related but less virulent Salmonella paratyphi A, B, and C, collectively called typhoidal Salmonella (Sattar *et al*., 2012). Typhoid fever is a systemic infection with the bacterium Salmonella enterica serotype typhi. This highly adapted, human-specific pathogen has evolved remarkable mechanisms for persistence in its host that help to ensure its survival and transmission. Typhoid fever was an important cause of illness and death in the overcrowded and unsanitary urban conditions of the United States and Europe in the 19th century (Osler *et al*., 1912). Salmonella typhi can survive in fresh, salty and brackish water for

several weeks and can multiply in milk products (EKESIOBI *et al*., 2017). S. Typhi is a motile Gram-negative facultative anaerobic rod-shaped bacterium that is closely related to Escherichia coli in the family Enterobacteriaceae (Todar *et al*., 2010). The bacterium is a Gram- negative bacillus which only infects humans (Chin *et al*., 2000). Salmonella's genus is Gram-negative, motile, non-sporing, non-capsulate bacilli which exist in nature primarily as parasites of the intestinal tract of man and other animals. Salmonella typhi and the paratyphoid bacilli are found only in the intestinal tract of man for whom they have a high degree of pathogenicity and in which they frequently cause invasive disease that causes symptoms which may vary from mild to severe and usually begin six to thirty days after exposure with gradual onset of a high fever after several days (Amah *et al*., 2013)

Once consumed, typhoid bacteria cross the epithelial layer of the intestinal wall. They are then quickly consumed by macrophages and transported to the aggregates of lymphoid tissue in the small intestine (Peyer's patches), where the immune function of the gut is most concentrated. The typhoid bacteria alter host cell signaling and function in such a way that host cells ultimately promote the survival and replication of S. typhi and S. paratyphi (Al Zubaidi *et al*., 2020). The incubation stage of a typhoid infection is characterized by the replication and transfer of S. typhi and S. paratyphi from the Peyer's patches in the gastrointestinal system, through the lymphatics, to the organs of the reticuloendothelial system including the lymph nodes, spleen, bone marrow and liver. Once in the gallbladder, S. typhi and S. paratyphi are secreted back into the gastrointestinal tract. the Peyer's patches respond with an intense inflammatory reaction, leading to congestion and clogging of the microcirculation and capillaries with release of lytic lysosomal enzymes and other inflammatory mediators (Ukwenya *et al*., 2011). These microorganisms colonize the small intestine, invade the gastrointestinal mucosa and then spread to the liver, spleen and bone marrow (Raffatellu *et al*., 2008). The severity of the infection depends on the initial infective dose, virulence and the host immune response (Tsolis *et al*., 1999).

Fig 1.1: Life cycle of Salmonella Bacterium

Symptoms can range from a mild course with fever associated to general malaise, abdominal manifestations, roseola, sweating, headache, anorexia, cough, weakness, sore throat, dizziness and muscle pain, to, in some cases, neuropsychiatric manifestations (Crump *et al*., 2010). Other findings include bradycardia, splenomegaly and hepatomegaly (Parry *et al*., 2011). S. typhi has the capacity to affect virtually every organ system; as a result, patients are vulnerable to a wide variety of complications. Intestinal perforation, occurring in 1–3% of cases, is associated with the highest mortality (Neil *et al*., 2012). Although both sexes are infected equally, some evidence suggests that males suffer significantly more intestinal perforations than females (Marchello *et al*., 2020). The most lethal complications of typhoid fever are intestinal bleeding and ileal perforations, both arising from necrosis of Peyer's patches in the terminal ileum (Akjun *et al*., 1995). Although altered liver function is found in many patients with enteric fever, clinically significant hepatitis, jaundice, and cholecystitis are relatively rare and may be associated with higher rates of adverse outcome, abdominal pain (usually in the right lower quadrant), tenderness, vomiting, sudden rise in pulse rate, hypotension, marked abdominal tenderness and guarding, and subsequent abdominal rigidity. A rising white blood cell count

with a left shift and free air on abdominal radiographs may be seen in such cases (Bergh *et al*., 1999).

Major risk factors of disease transmission are contaminated food, drinking water, miserable sanitation condition, close interaction with typhoid patients or carriers, education, flooding, personal hygiene and travelling to endemic region (Black *et al*., 1985). In addition, climatic condition such as, rainfall (Karkey *et al*., 2010) Hospital workers who do not follow the hospital's sterile procedures can be infected through the soiled linens of infected individuals. Similarly, the bacteria have been spread by personnel in pediatric wards, either on their hands or the soiled linens of infected individuals. Flies can infect or contaminate food (Den *et al*., 2003). Typhoid fever is a systemic infection caused by human-specific food and water-borne pathogens, such as Salmonella enterica subspecies, enterica serovar typhi (S. typhi) or by the related but less virulent Salmonella paratyphi A, B, and C, collectively called typhoidal Salmonella (Sattar *et al*., 2012). It is transmitted by the fecal–oral route through contaminated water and food (Mama *et al*.,2016) The hazard of disease is high in underdeveloped nations where typhoidal Salmonella is endemic and there is poor hygiene and sanitation and non-availability of safe sustenance and water (Gunn *et al*., 2014).

The absence of specific symptoms or signs makes the clinical diagnosis of typhoid difficult (Wain *et al*., 2001). In areas of endemic disease, a fever without evident cause that lasts more than one week should be considered typhoid until proved otherwise. Blood cultures are the standard diagnostic method; provided a large volume of blood is cultured (15 ml in adults), they are positive in 60 to 80 percent of patients with typhoid (Gilman *et al*., 1975). Culture of bone marrow is more sensitive. The result is positive in 80 to 95 percent of patients with typhoid, even patients who have been taking antibiotics for several days, regardless of the duration of illness (Hoffman *et al*., 1986). Blood cultures are less sensitive than bone marrow cultures because of the lower numbers of microorganisms in blood as compared with bone marrow (Wain *et al*.,2001). The sensitivity of blood culture is higher in the first week of the illness, is reduced by prior use of antibiotics, and increases with the volume of blood cultured and the ratio of blood to broth (Rubin *et al*., 1990). Cultures have also been made from the buffy coat of blood, streptokinase-treated blood clots, intestinal secretions (with the use of a duodenal string capsule), and skin snips of rose spots (Vallenas *et al*., 1985). The sensitivity of stool culture depends on the amount of feces cultured, and the positivity rate increases with the duration of the illness. Stool cultures are positive in 30 percent of patients with acute typhoid fever. For the detection of carriers, several samples should be examined because of the irregular nature of shedding. The role of Widal's test is controversial, because the sensitivity, specificity, and predictive values of this widely used test vary considerably among geographic areas. The test detects agglutinating antibodies to the O and H antigens of S. enterica serotype typhi (Lavine *et al*., 1982).

Unfortunately, S. enterica serotype typhi shares these antigens with other salmonella serotypes and shares cross-reacting epitopes with other Enterobacteriaceae (Clegg *et al*.,1994). Furthermore, patients with typhoid may mount no detectable antibody response or have no demonstrable rise in antibody titer. Despite this, some centers have found Widal's test helpful when it is used with locally determined cutoff points (Parry *et al*., 1999). A Vi agglutination

reaction has been used to screen for S. enterica serotype typhi carriers. Its reported sensitivity is 70 to 80 percent, with a specificity of 80 to 95 percent (Lanata *et al*.,1983). Newer serologic tests are being developed but do not yet perform well enough to ensure their widespread adoption (Bhutta *et al*.,1999). DNA probes and polymerase-chain-reaction protocols have been developed to detect S. enterica serotype typhi directly in the blood (Song *et al.,* 1993). The typhidot test is also used for the detection of Salmonella typhi IgM and IgG antibodies. It has undergone full scale globally due to clinical estimation of its diagnostic value (Ismail *et al*., 1991). In case of secondary infection, both IgM and IgG are detected (Bhutta *et al*., 1996).

The vast majority of cases can be managed at home with oral antibiotics and close medical follow-up for complications or failure to respond to therapy However, patients with persistent vomiting, severe diarrhea, and abdominal distension may require hospitalization and parenteral antibiotic therapy. The general principles of management of typhoid include (1) general nursing and supportive care, (Renuka *et al*., 2005). Close attention must be given to adequate rest, hydration, and correction of fluid-electrolyte imbalance. Soft, easily digestible diet should be continued unless the patient has abdominal distension or ileus. This is especially important in children because inadequate nutrition and dietary restrictions can trigger acute malnutrition and increased risk of complications. Antipyretics (acetaminophen, 120–750 mg every 4 to 6 hours PO) should be administered as required, recognizing that despite clinical improvement, defervescence may take several days. Given the importance of overall clinical improvement, a composite typhoid morbidity score has been recommended for monitoring recovery in typhoid (Bhutta *et al*., 1994). Mortality rates in patients with typhoid fever who are not given specific chemotherapy can be as high as 26% (Van *et al*., 1999). although earlier work describes mortality rates of 10% or lower that were associated with careful management including strict adherence to a milk diet (Drigalski *et al*.,1994). The introduction of chloramphenicol (in 1948), ampicillin (1961), co-trimoxazole (1970s), and third-generation cephalosporins and fl uoroquinolones (1980s) reduced the mortality of typhoid fever considerably. However, multidrug-resistant strains14 that were resistant to all three first-line antimicrobial drugs emerged in the 1980s (Zaki *et al*., 2011).

Of the major risk factors for outbreaks of typhoid, contamination of water supplies with sewage is the most important. Therefore, a combination of central chlorination and domestic water purification is important during outbreaks. In endemic situations, consumption of street foods, especially ice cream and cut fruits, and lack of proper hand washing have been recognized as important risk factors (Hosoglo *et al*., 2006). The human-to-human spread of the organisms by the long-term carriers is also an important risk factor, and attempts should therefore be made to target food handlers and high-risk groups for S. typhi carriage screening. Once identified, long-term carriers must be counseled regarding the risk of disease transmission and given advice on hand washing and preventive strategies. Recent studies on community-based strategies for hand washing promotion indicate that these can be effective in reducing the problem on diarrheal diseases and acute respiratory infections (Curtis *et al*., 2003).

1.1 Aims and Objectives

The main aim and objectives of our study was following

- To find out the prevalence of typhoid fever among the general population of district Lower Dir, Pakistan.
- To determine the risk factors associated with typhoid fever.
- To outline the treatment and management options available for typhoid fever

Method and Materials

2.1 Study Area

The present study was carried out in District Lower Dir, (Malakand Division) Khyber Pakhtunkhwa, Pakistan. The area is bounded in the Hindukush range with in the area of 1583 square km. Its latitude is 35-10 to 35-16 degree and longitude 71-50 to 71-83 degree with an elevation of about 1200m to 2800m from sea level. Panjkora river flows in the middle of the valley across the district and divides the area into seven tehsils namely Timergara, Balambat, Lalqilla, Adenzai, Munda, Khall, and Samarbagh**.**

2.2 Study Design and Place

A descriptive epidemiological study was designed from July1, 2022 to May31, 2023. The laboratory work was performed at College as well as at different Laboratories of Timergara, District Lower Dir.

2.3 Collection of Data

The data were collected from all the patients who presented with common symptoms of typhoid at the different labs of seven tehsils namely Timergara, Balambat, Lalqilla, Adenzai, Munda, Khall, and Samarbagh District Lower Dir.

2.4 Blood Sampling

Blood samples were collected from both affected and normal members in 3ml EDTA tubes with the help of 5 ml syringe and stored the blood samples in room temperature.

2.5 Protocol of Typhtidot Test

The typhidot test is used for the detection of human antibodies IgM and IgG. The typhidot ICT kit consist of two wells. Specimen from typhoid suspected patients were taken and the samples were centrifuged to produce serum. Serum (20 µL) was poured using a micropipette on one well of the kit and also 1 µL of typhoid regent was poured into the other well of the kit. The test was recorded as negative if a single line was observed on examination but if a double line is observed the test is recorded as positive. e. The ICT kits used have high sensitivity; in which they are able to detect very minute levels of infectious agents thus limiting the occurrence of false negatives it is due to sensitivity.

Fig 2.1: Map of study Area District Dir (L)

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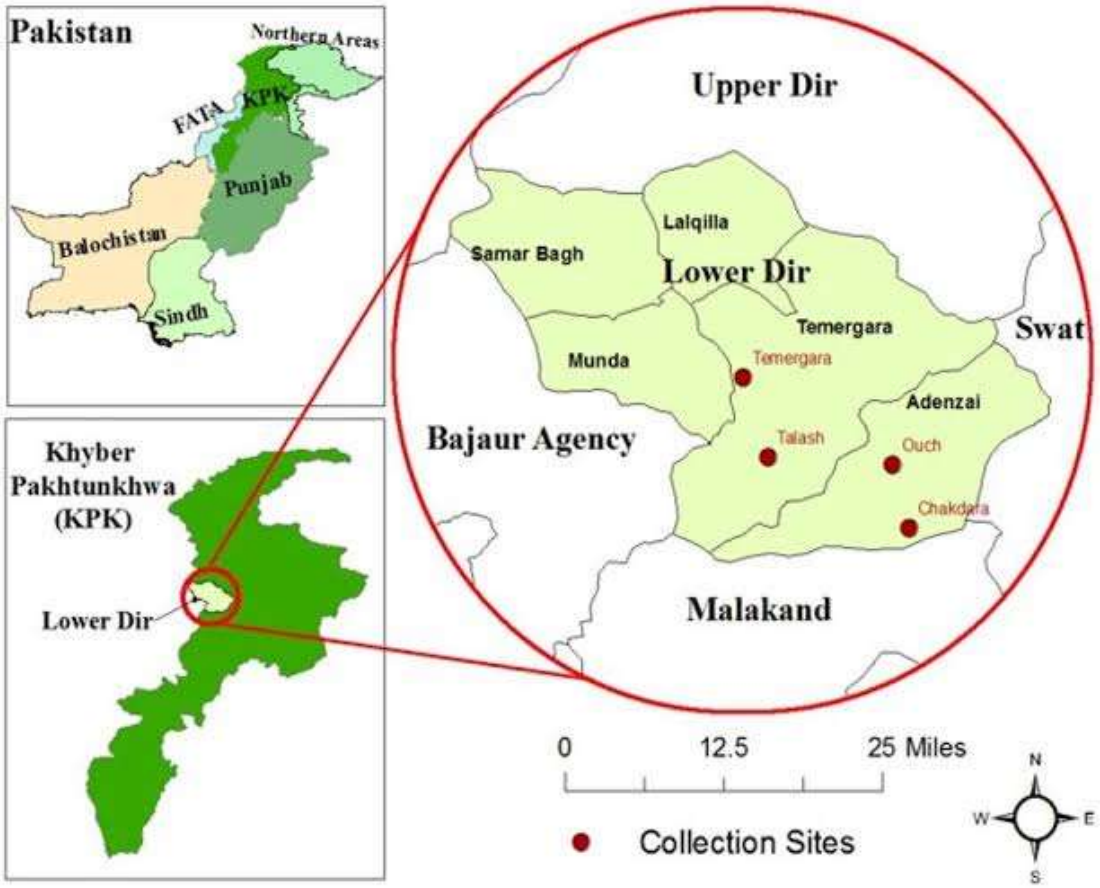


Demographic Information

The demographic information of all the suspected patients were recorded including date of entry, patients address, name, gender and age.

2.7 Study Limitation

Only typhidot test was performed for suspected cases, no other tests were performed like Widal test, polymerase chain reaction and culture test for the diagnosis of typhoid. Hence we could not determine the degree of resistance to typhoid fever in the study area.

The prevalence rate (%) was found using the following formula:

$$\text{Prevalence rate} = \frac{\text{Total no. of positive cases}}{\text{Total no. of diagnosed cases}} \times 100$$

2.8 Ethical Considerations

Before the commencement of the study, the research proposal was approved by the Board of Study (BoS), Department of Zoology, Government Post Graduate Degree College Timergara and further permission was granted by University of Malakand. Informed consents were

obtained from study participants and confidentiality was observed and maintained throughout the study.

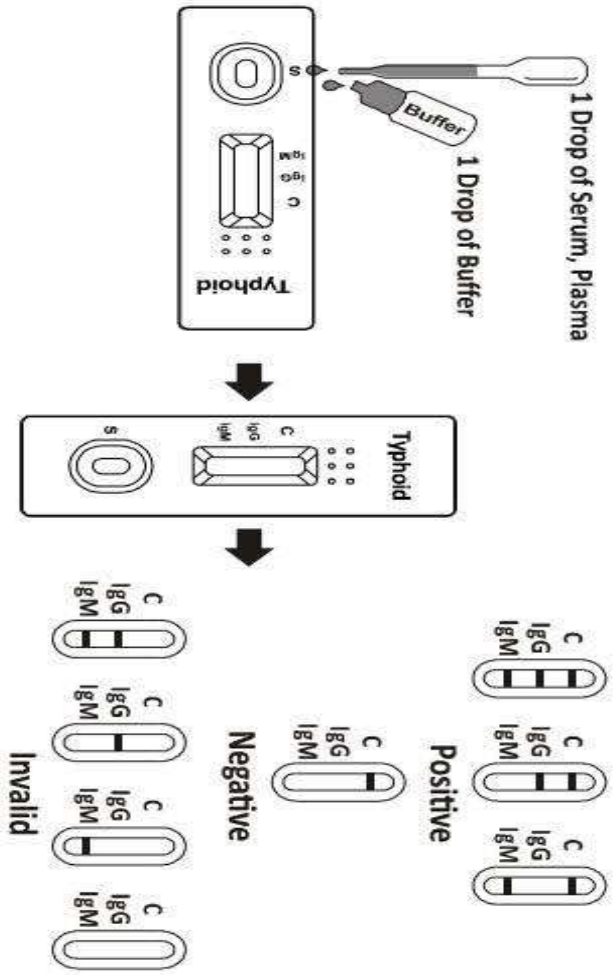


Fig 2.2: Kit method for Typhoid Fever

RESULTS

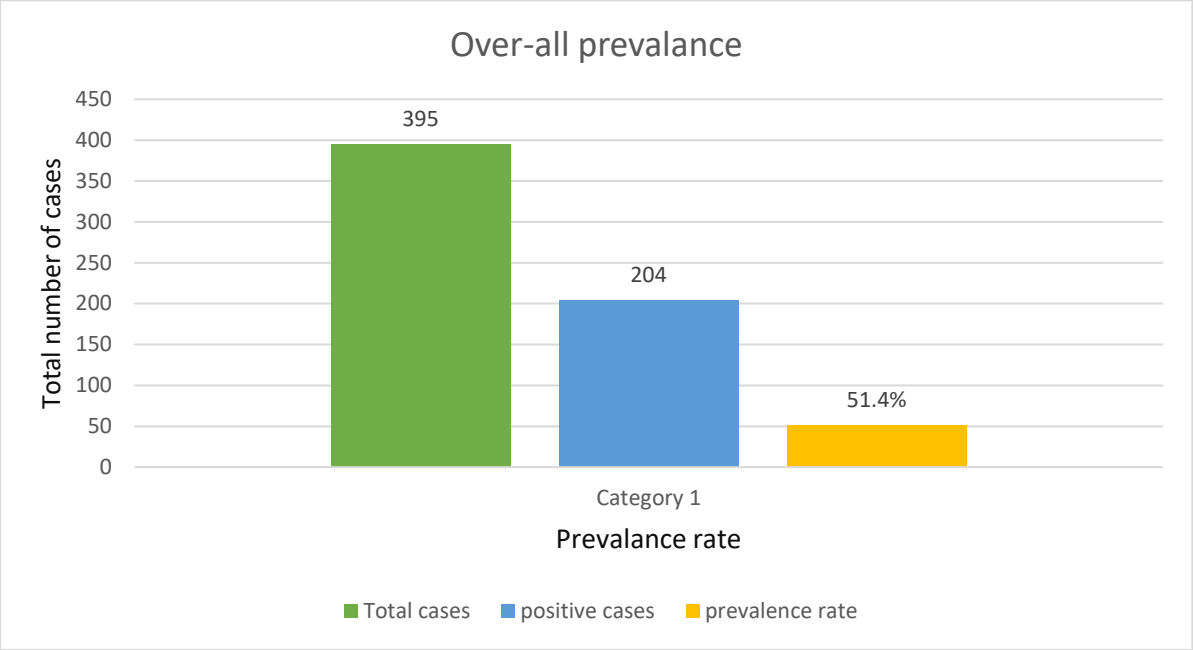
The present research study was conducted to diagnose the prevalence of typhoid fever in human population at Dir lower from July 2022 to May 2023.

A total of 395 cases were diagnosed, out of these 204 cases were found positive with overall prevalence rate of 51.6%. (table 3.1)

Table 3.1: The overall prevalence of Typhoid fever in Human population of District Dir Lower, Study conducted from July 2022 to May 2023

Total cases	Positive cases	Prevalence ratio
395	204	51.6%

Figure 3.1. Total prevalence of Typhoid fever in Human population of District Dir Lower,



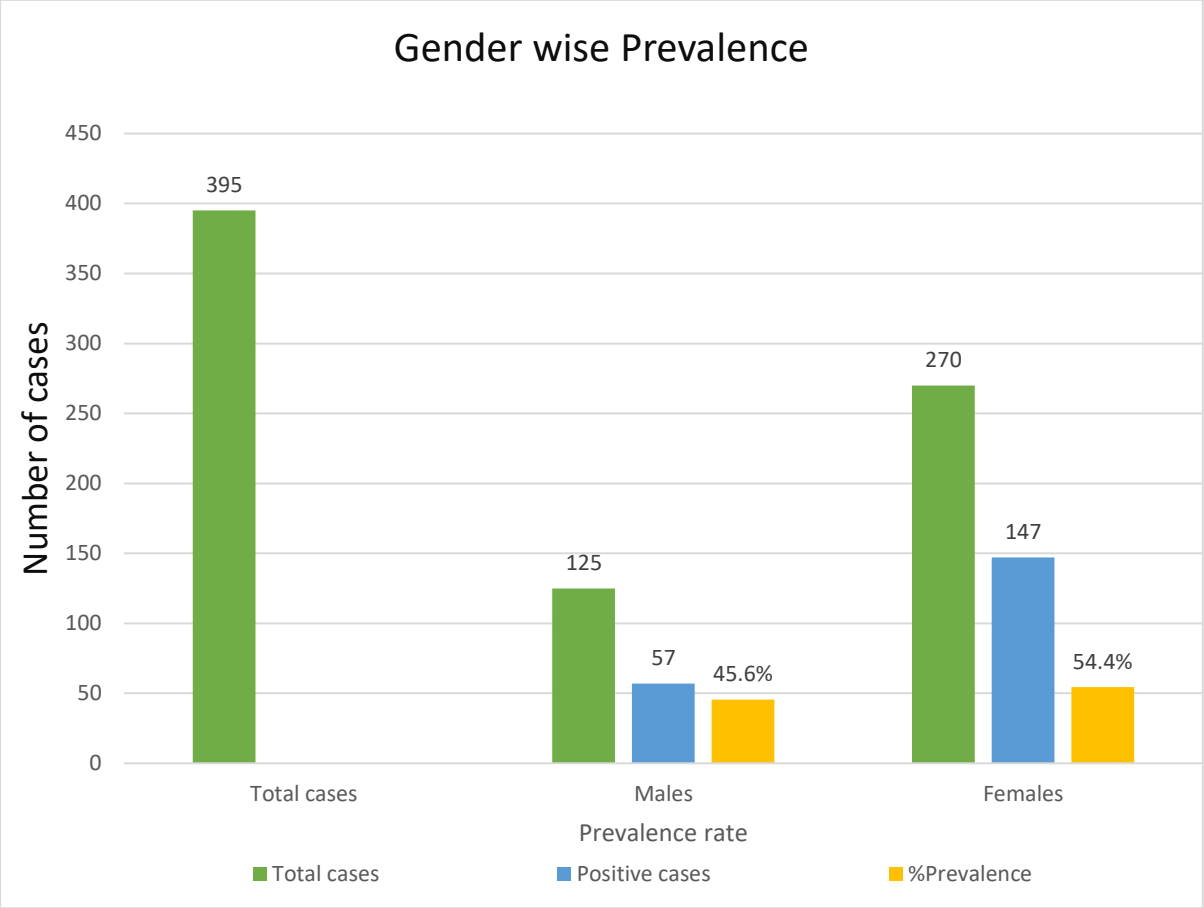
study conducted from July 2022 to May 2023

In present research study, the individuals were distributed on the basis of their gender. Gender wise prevalence rate of typhoid fever was reported. The total number of male individuals was 125; among which 57 were positive with prevalence rate of 45.6%. the female individuals were 270, among which 147 cases were positive with prevalence rate of 54.4%. (table3. 2)

Table 3.2: Gender wise prevalence of Typhoid fever in Human population of District Dir Lower, study conducted from July 2022 to May 2023

Gender	Total no. of cases	Positive cases	Prevalence ratio
Male	125	57	45.6%
Females	270	147	54.4%

Figure 3.2. Gender wise prevalence of Typhoid fever in Human population of District Dir Lower, study conducted from July 2022 to May 2023



The data was also distributed on the basis of presence of antibodies. Out of total positive case i-e 204; IgM was found in 141 with prevalence rate of 35.7%. IgG was found in 14 cases with prevalence rate of 3.5%. Similarly, in 49 positive cases both the IgM & IgG were found with prevalence rate of 12.4%. (table 3.3)

Table 3.3: Antibodies based Prevalence of Typhoid fever in Human population of District Dir Lower, study conducted from July 2022 to May 2023

Antibodies types	Positive cases	Prevalence ratio
IgM	141	35.50%
IgG	14	3.50%
IgM+IgG	49	12.40%

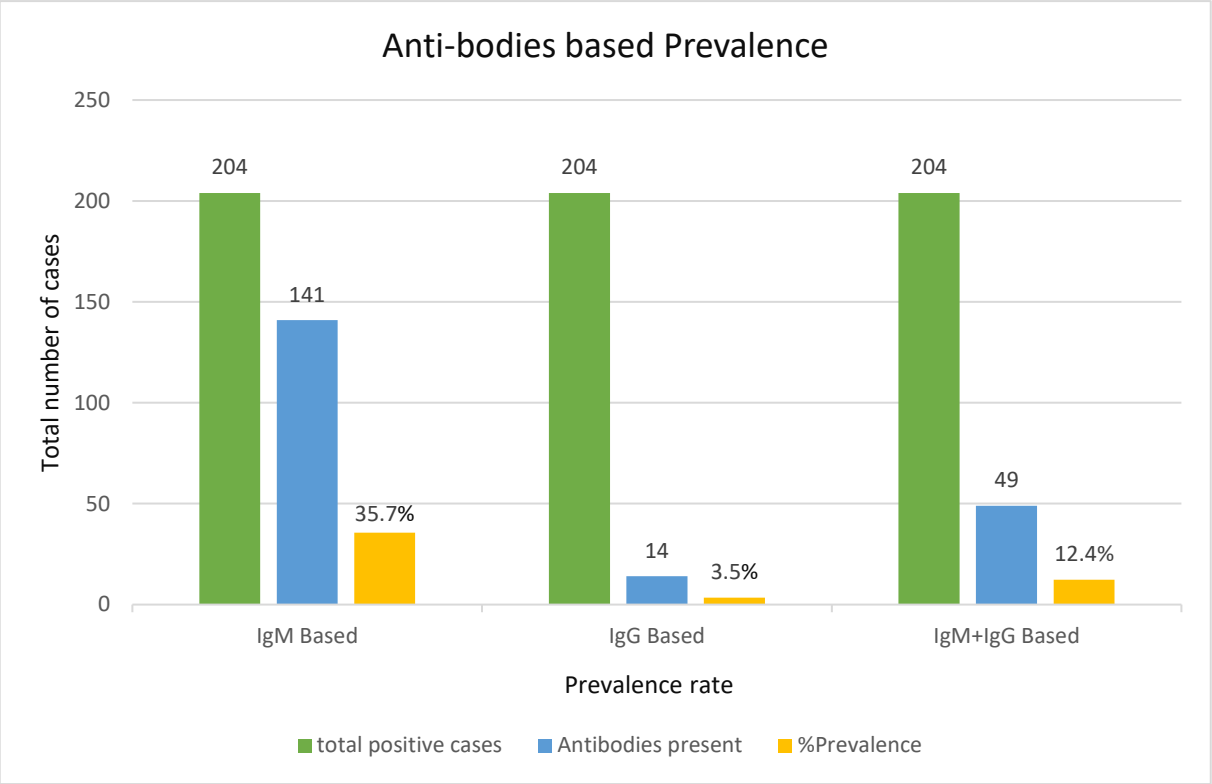


Figure 3.3. Antibodies based prevalence of Typhoid fever in Human population of District Dir Lower, study conducted from July 2022 to May 2023

Monthly cases of typhoid fever were also reported. The total cases were distributed month wise. In July 2022, a total of 7 cases were tested; among which 6 were positive with prevalence rate of 85%. Similarly, in august 2022, a total of 4 cases were tested; among which 4 were positive with prevalence rate of 100%. In September 2022, a total of 7 cases were tested; among which 1 were found positive with prevalence rate of 14.28%. in October 2022, a total of 9 cases were tested; among which 02 cases were found positive with prevalence rate of 22.22%. Similarly, in November 2022, a total of 86 cases were tested; among which 34 cases were found positive with prevalence rate of 39.53%. In December 2022, a total of 146 cases were tested; among which 93 cases were reported positive with prevalence rate of 63.69%. Similarly, in January 2023, a total of 60 cases were tested; among which only 24 cases were found positive with prevalence rate of 40%. In February 2023, 12 cases were reported; out of which 3 cases found positive with prevalence rate of 25%. In the month of March 2023, a total of 16 cases were tested; among which only 4 cases were found positive with prevalence rate of 25%. In the month of April 2023, a total of 32 cases were tested; among which 23 cases were found positive with prevalence rate of 71.87%. Similarly, in the month of May 2023, a total of 16 cases were tested; among which only 10 cases were found positive with prevalence rate of 62.5%. (table 3.4).

Table 3.4: Month wise prevalence of Typhoid fever in Human population of District Dir Lower, study conducted from July 2022 to May 2023

Months	Total cases	Positive cases	Prevalence ratio

July 2022	07	06	85%
Aug 2022	04	04	100%
Sept 2022	07	01	14.28%
Oct 2022	09	02	22.22%
Nov 2022	86	34	39.53%
Dec 2022	146	93	63.69%
January 2023	60	24	40%
Feb 2023	12	3	25%
March 2023	16	04	25%
April 2023	32	23	71.87%
May 2023	16	10	62.5%

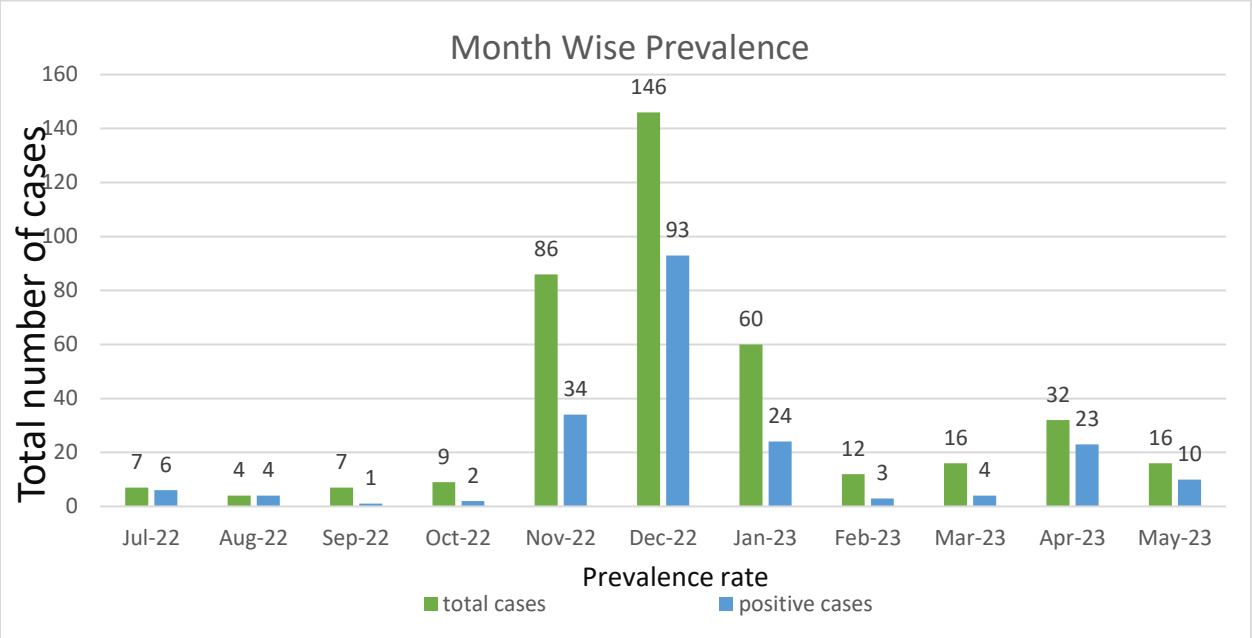
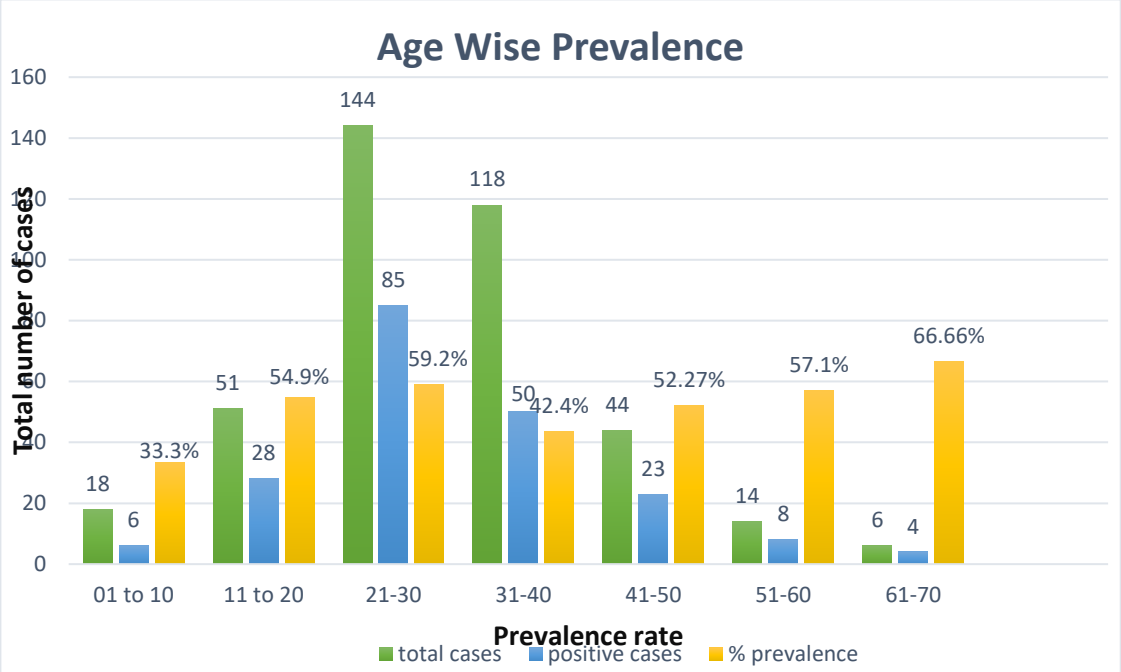


Figure 3.4. Month wise prevalence of Typhoid fever in Human population of District Dir Lower, study conducted from July 2022 to May 2023

People were divided into different age groups; 1-10, 11-20, 21-30, 31-40, 41-50, 51-60, 61-70 years. The results were analyzed on the basis of their age groups. From 1-10 years the total number of cases was 18, out of which 6 were diagnosed positive with prevalence rate of 33.3%. Similarly, from the age group of 11-20, a total number of 51 cases were tested; among which 28 cases were found positive with prevalence rate of 54.9%. From 21-30 years the total number of tested cases was 144, out of which 85 cases were found positive with prevalence rate of 59.2%. Similarly, from the age group of 31-40, a total number of 118 cases were tested; among

which only 50 cases were found positive with prevalence rate of 42.4%. From the age group



of 41-50, only 44 cases were diagnosed; out of which 23 cases were found positive with prevalence rate of 52.27%. From 51-60 years, a total of 14 cases were tested; among which only 8 cases were reported positive with prevalence rate of 57.1%. Similarly, from the age group of 61-70 a total number of 06 cases were diagnosed; out of which only 04 cases were reported positive with prevalence rate of 66.66%. (table 3.5).

Table 3.5: Age wise prevalence of Typhoid fever in Human population of District Dir Lower, study conducted from July 2022 to May 2023

Ages	Total cases	Positive cases	Prevalence ratio
1-10	18	6	33.3%
11-20	51	28	54.9%
21-30	144	85	59.02%
31-40	118	50	42.4%
41-50	44	23	52.27%
51-60	14	08	57.01%
61-70	06	04	66.66%

Figure 3.5. Age wise prevalence of Typhoid fever in Human population of District Dir Lower, study conducted from July 2022 to May 2023

During the present research study, a questionnaire too was designed. As per data obtained through questionnaire 72% of diagnosed individuals knew about sign and symptoms of typhoid fever. Approximately 48% were aware of control and prevention. Peoples were asked about types of drinking water, 36% of the studied cases drink boiled water, 15% drink chemically treated water while 69% drink untreated water. 42% people knew about transmission of disease.

DISCUSSION

Pakistan is a low income country; where the ratio of infectious diseases is high compared to developed countries. Similarly, typhoid is one of the most significant health issues. The present study was undertaken to determine the prevalence of typhoid fever in human population of district Lower Dir, Khyber Pakhtunkhwa, Pakistan. In present study, the overall prevalence of typhoid fever among the suspected cases was found high (51.6%). The study carried out by *Joshua et al* (2017) shows an overall infection rate of 75.20%, a high prevalence of typhoid fever among Bingham University students, which is contrast to our overall prevalence (51.6%). These differences may be due to variations in climatic condition as well as diagnostic methods used. The study conducted by *Hussain et al* (2017) shows an overall of typhoid fever among the local population of district Dir Lower was found 37.26%, which is less than present study prevalence (52.17%) among district Dir Lower. This contrast may be due unhygienic conditions, environmental conditions and diagnostic method used. The study carried out by *Njoya et al (*2021) shows the prevalence of typhoid fever was 30.1% at the Saint Elisabeth General Hospital Shisong, Bui Division, Cameroon, which is contrast to our prevalence (51.6%). These variations may be due to different cultural values of the studied communities.

In present study the disease ratio was recorded high among the females (54.4%) as compared to males (45.6%). A study conducted by *Ayub et al* (2015) at Islamabad reported high ratio (60.32%) of disease in females, which is contrast to present study. This variation may be due to variant environmental conditions. Another study carried out by *Sharma et al* (2013) at Lakhimpur District of Assam (India) recorded that 52.3% female patients were found positive through Widal test, while in present research study the prevalence ratio is 54.4 %. These approximate similar values may be due to same immune system of the study population.

The data was also distributed on the basis of presence of antibodies. Out of 204 positive cases, IgM was found in 141 with prevalence rate of 35.7%, IgG was found in 14 cases with prevalence rate 3.5%. Similarly, 49 positive cases both the IgM and IgG were found with prevalence rate of 12.4%. The study done by *Cinthujah et al* (2014) shows that among the total positive cases, IgM was found in 4861 cases with prevalence rate 25%, IgG was found in 318 cases with prevalence rate of 1.63%. Similarly, in 12503 positive cases both the IgM and IgG were found with prevalence rate of 64.34%. It is completely contrast to our study, because of variant environmental conditions and some other factors during tests. According to study conducted by *Hussain et al* (2019) in district Dir Lower, among the total positive cases,353 were found IgM antibodies with prevalence rate 88.03%, IgG was found in 48 cases with prevalence rate 11.97%. It is contrast to our current study, in which out of 202 positive cases, IgM was found 139 with prevalence rate of 39.19%, IgG was found in 14 cases with prevalence rate 2.60%. This contrast may be due to environmental conditions during tests and some other factors.

In present study the disease progression is recorded high (100%) in August 2022, while found low (14.28%) in September 2022. A study carried out by *Soomro et al* (2014) recorded maximum number of cases (61.51%) in March, which is contrast to present study. This difference may be due to climatic factors. Another study showed high occurrence (73.66%) of disease in October while low frequency (21.66%) was observed in January *Sharma et al* (2013), which is different to present study in which maximum cases (100%) were recorded in August 2022, while less number of cases (14.28%) was found in September. Again these variations may be due to environmental conditions. The study was carried out by *Ganesh et al* (2010) in South India Channai, the incidence rate of disease was increasing from January to April (64%) but in present study the disease was reported high (100%) in August and February. So when we compare present result to this study, it is contrast to present study. The reason is that the rainfall in April was high in Ethiopia.

Age is one of the most important factors in epidemiology of disease. On the basis of age-wise occurrence the high number of cases (66.66%) was noted in the age group 61–70 years. The higher incidence rates (69%) were reported of typhoid fever in age group of 21–30 years; this is in agreement with the report of *Farooq et al* (2009). The results of the study conducted by *Chalya et al* (2012) revealed that high number of cases (60%) was found in age group of 10-20 years and then 20-30 years. In present study the high number of cases (59.02%) was found in age group of 21-30 years. These differences may be due to variation of immune systems of the age groups. In present study the lowest prevalence rate i-e 33.3% was found in age groups of 01-10. According to study conducted by *Eba et al* (2019) the lowest prevalence rate i-e 50.4% was found in age group of 28-37. These variations may be due to different immune systems and serological techniques.

CONCLUSIONS

From the current research it was concluded that the disease was prevalent in Lower Dir (Pakistan). The disease actively affected the most economically and productive age group of 61-70 years and the disease was high in female patients. Further studies to determine the disease occurrence and antibiotic susceptibility pattern are recommended. There is an urgent need for the health authority and government to launch an effective program for the eradication of the disease while public awareness and education about safe drinking water and food should be promoted to facilitate control of the disease.

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