Pediatric Uropathogens and their Antimicrobial Susceptibility Pattern: Experience from an Impoverished District of Karachi, Pakistan

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ABSTRACT

INTRODUCTION: Urinary tract infection (UTI) is the most common infection of the pediatric age group. Several factors linked to higher prevalence include poor personal hygiene, improper sanitation, lower socioeconomic status, and malnourishment. In addition to having a worse quality of life, the 1.8 million children who live in Karachi's Korangi district are routinely exposed to such factors.

OBJECTIVES: The study aims to evaluate the frequency of UTI and distribution of uropathogens along with their antimicrobial susceptibility pattern in patients presenting to a pediatric tertiary care center in the Korangi district of Karachi, Pakistan.

DESIGN: The study employed an observational cross-sectional design.

METHODS: The study was conducted at the Microbiology laboratory of Sindh Institute of Child Health and Neonatology, Karachi, Pakistan from 1st January to 15th August 2023. Urine samples of patients 1 to 16 years of age were collected via midstream clean catch method and of patients from birth up to 1 year were collected in urine collection bags. The samples were cultured on Cystine Lactose Electrolyte Deficient (CLED) agar and antibiotic susceptibility testing was performed using the Kirby-Bauer Disc Diffusion method.

RESULTS: A total of 457 urine samples were collected, of which 90 (19.7%) were positive for significant uropathogens. With a mean age of 4.6 years, majority of the culture-positive patients were female (n = 72; 80%). Enterobacterales were the most frequently isolated (n = 88; 95.6%), of which *Escherichia coli* was the most common (73.9%; n = 68). *Citrobacter* (n = 7; 7.6%), *Klebsiella* (n = 6; 6.5%), *Serratia* (n = 4; 4.3%), *Proteus* (n = 2; 2.2%), *Salmonella* (n = 2; 2.2%), and *Enterobacter* (n = 1; 1.1%) were among the other Enterobacterales isolated. Meropenem and imipenem were the most effective in isolates from Enterobacterales (n = 88) followed by amikacin (n = 84), ciprofloxacin (n = 75), and piperacillin-tazobactam (n = 70). Ceftriaxone and cefixime exhibited moderate susceptibility (n = 69 and 52) whereas, amoxicillin-clavulanate was the least susceptible (n = 3).

CONCLUSION: We report high frequency of UTI in our pediatric population with uropathogens and associated antimicrobial susceptibility pattern confirming to the existing trends of pediatric UTIs in Pakistan. In addition to valuable insights for treating patients under similar conditions, our study serves as a catalyst for further multi-center research in this area.

KEYWORDS: Pediatric population, urinary tract infection, uropathogens, antimicrobial resistance

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Introduction

Urinary tract infections (UTI) are the most common bacterial infections in pediatric population affecting 3% to 7.5% children each year.[1] Approximately 8% of children between the ages of 1 month and 11 years will have at least one episode of UTI.[2] Majority of pediatric UTIs are caused by Gram-negative coliform bacteria that enter and ascend the urinary tract, arising from fecal flora colonizing the perineum. Around 80% of pediatric UTIs are caused by the most prevalent uropathogen, *Escherichia coli (E. coli)*.[3] Within the pediatric demographic, age-related variations in prevalence are seen, with toddlers, young infants, and older adolescents experiencing the highest prevalence.[4] Some of the factors identified as significantly contributing to the increased risk of UTI include poor personal hygiene and the imposition of cultural habits. Also, some studies have pointed out the association of low education, low income, and overcrowding with higher risk and incidence of UTI.[5,6]

Furthermore, the development of antibiotic resistance in UTIs has posed a serious threat to global health and urological infection management strategies especially in developing countries where there is growing concern regarding available treatment options for UTIs.[7,8] Antibiotic resistance strains have rapidly emerged over the past decade due to the widespread and injudicious use of antibiotics in such countries.[9] Microorganisms have frequently become resistant to first-line antibiotics, indicating the need for second-line antibiotics, which are more costly, have a less favorable risk-benefit profile, are broad-spectrum, and may not be available locally.[10,11]

Korangi, the former satellite town converted district of Karachi that started as part of the ambitious "Greater Karachi Resettlement Plan," now faces frequent challenges in provision

of basic facilities for its residents.[12] From overcrowded infrastructure to suboptimal air quality, unsafe water channels, and improper sanitation, the district of approximately 2.5 million residents, encounters several difficulties in maintaining an acceptable quality of life. The pediatric age group accounts for almost 1.8 million of the total population of Korangi.[13] This study is thus important because it has the potential to help identify, assess, and detect common pediatric uropathogens and their antibiotic susceptibility profile in similar settings around the world. This information could help medical professionals create evidence-based treatment approaches and infection control strategies.

Given the present scenario of the district and with its notably large pediatric population, the occurrence of UTI is anticipated to be high posing significant challenges for the public health authorities. We, therefore, evaluated the frequency of UTI and distribution of uropathogens along with their antimicrobial susceptibility pattern in patients presenting to a pediatric tertiary care center in the Korangi district.

Materials and Methods

Study design and setting

This was an observational, cross-sectional study conducted on consecutively collected urine samples, at the Microbiology section of the Clinical laboratory of Sindh Institute of Child Health and Neonatology, Karachi, Pakistan from 1st January to 15th August 2023. Urine samples from patients 1 to 16 years of age were collected via midstream clean catch method in a sterile container pre-filled with *boric acid* (0.4 g). Whereas, urine samples of patients from birth up to 1 year i.e. neonates and infants were collected in urine collection bags and then transferred in sterile boric acid containers. All samples were transported to the laboratory immediately where they were further processed and in case of a processing delay, the samples were stored at 4°C.

Study population and patient criteria

The study population comprised pediatric patients regardless of gender and ethnicity admitted in the ward and intensive care unit as well as those who presented to the out-patient department. Inclusion criteria of the study included all urine samples that were collected from patients 0 to 16 years of age and with symptoms of UTI. All urine samples from patients above 16 years of age, without symptoms of UTI and those received after the timeframe of sample collection were excluded from the study. Patients who did not provide consent for participation were also excluded.

Sample size calculation

Sample size was calculated from the findings of a previous single center study determining the incidence patterns of uropathogens, their antimicrobial susceptibility pattern and risk factors for UTI among the general population of Pakistan, using the WHO sample size software.[14] We estimated that a minimum sample size of 432 urine samples would be needed to detect an expected UTI prevalence of 65.1%, keeping a 95% confidence interval and 4.5% margin of error, using the equation below,

$$n = \frac{Z^2 p(1-p)}{d^2} = \frac{(1.96)^2 \times 0.651 \times (1-0.651)}{(0.045)^2} = 432 \text{ urine samples}$$

where,
n = Sample size
$Z = Z$ statistic for a level of confidence ($Z = 1.96$ for a confidence level of 95%)
p = Expected prevalence or proportion
d = Precision

Urine culture and bacterial identification

The urine samples were cultured on Cystine Lactose Electrolyte Deficient (CLED) agar and incubated for 37°C for 48 hours, with plates examined every 24 hours for any bacterial growth. The appearance, morphology, size, and color of colonies were noted if any growth on the culture media was observed. A colony count of $>10^5$ cfu/mL was considered significant. Preliminary identification of the organisms was done on gram stain and different biochemical tests including catalase test, oxidase test, H_2S production, indole test, hanging drop motility test, urease test, citrate test, and Triple sugar iron (TSI) agar test etc. Identification was confirmed using the API® ID strips and *APIWEB*™ database (*bioMérieux*).

Antimicrobial susceptibility testing

Antibiotic susceptibility testing of the isolates was performed using the Kirby-Bauer Disc Diffusion method. A bacterial suspension of 0.5 McFarland was made from isolated colonies in phosphate buffered saline and the entire surface of a Mueller Hinton Agar (MHA) plate was inoculated from this suspension using a sterile swab. Then antibiotic discs for amoxicillin-clavulanate, amikacin, ceftriaxone, cefixime, ciprofloxacin, piperacillin-tazobactam, imipenem, and meropenem were placed on the inoculated plates after which they were incubated in ambient air at 37°C. After 24 hours the plates were examined for any zone of inhibition around the respective antibiotic discs. Interpretation of the zone diameters was done in accordance with the antimicrobial susceptibility breakpoints mentioned in the Clinical & Laboratory Standards Institute (CLSI) M100, in light of which the antibiotics were charaterized as sensitive, intermediate, or resistant.[15]

Statistical analysis

Data regarding patient's age, gender, and admission unit along with the isolated uropathogen and associated antimicrobial

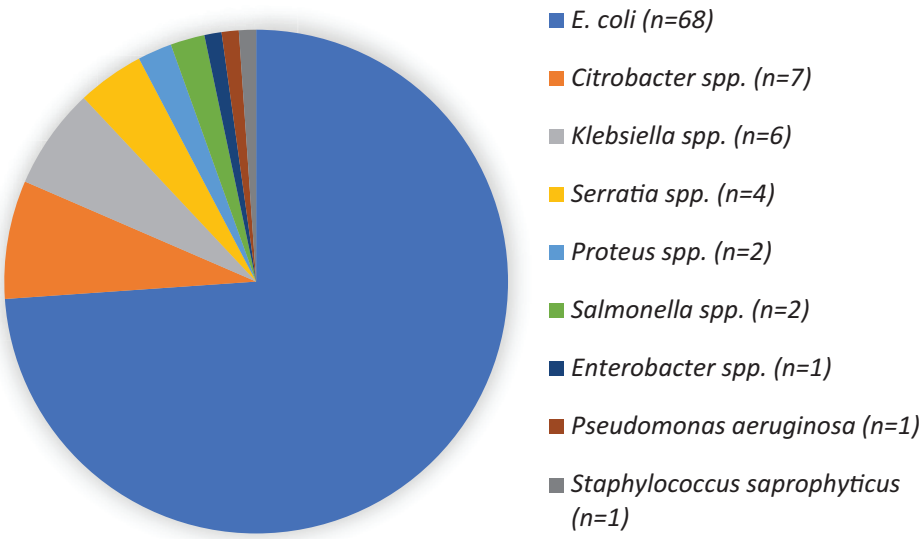

Figure 1. Distribution of pathogens among positive urine cultures (n = 90).

susceptibility pattern was entered in Microsoft Excel software (Microsoft Excel 2013 {15.0.5553.1000} 32-bit) for descriptive analysis. The analyzed data is presented in percentages and figures.

Results

A total of 457 urine samples were collected from patients between 1st January to 15th August 2023, of which 90 (19.7%) were positive for significant uropathogens. With a mean age of 4.6 years (IQR 6.8-2.2), majority of the culture-positive patients were female (n = 72; 80%). Most of these samples (n = 78; 86.7%) came from the out-patient department followed by the ward (n = 8; 8.9%) and intensive-care unit (n = 4; 4.4%).

Enterobacterales were the most commonly isolated uropathgens (n = 88; 95.6%), of which *E. coli* was identified in 73.9% (n = 68) of the total positive urine cultures. *Citrobacter spp.* (n = 7; 7.6%), *Klebsiella spp.* (n = 6; 6.5%), *Serratia spp.* (n = 4; 4.3%), *Proteus spp.* (n = 2; 2.2%), *Salmonella spp.* (n = 2; 2.2%), and *Enterobacter spp.* (n = 1; 1.1%) were among the other Enterobacterales isolated. *Pseudomonas aeruginosa* (n = 1; 1.1%) and *Staphylococcus saprophyticus* (n = 1; 1.1%) were identified in only 2 of the positive urine cultures. Distribution of pathogens among positive urine cultures is shown in Figure 1.

The antimicrobial susceptibility pattern of Enterobacterales revealed meropenem and imipenem to be sensitive in all the isolates (n = 88) followed by amikacin (n = 84), ciprofloxacin (n = 75), and piperacillin-tazobactam (n = 70). Ceftriaxone and cefixime exhibited moderate susceptibility (n = 69 and 52) among the isolates whereas, amoxicillin-clavulanate was the least susceptible (n = 3). Figure 2 shows the graphical representation of the antimicrobial susceptibility pattern of Enterobacterales isolated from urine cultures.

Discission

We reported high frequency of urine culture positivity (19.7%) in our pediatric patients. Our finding corroborates with several past studies conducted in Pakistan and internationally. A study from Hazara division, which is considered a comparatively lesser developed suburban region of the Khyber Pakhtunkhwa (KP) province, reported culture proven UTI in 375 out of 1000 pediatric patients with complaints related to UTI.[16,17] Moreover, a systemic review and meta-analysis of 26 cross-sectional and 8 case-control studies reporting UTI prevalence in malnourished children from around the world, revealed a 17% pooled prevalence of UTI.[18] The review discusses several general and specific factors leading to increased risk of UTI in malnourished children among which exposure to gut uropathogens in pre-toilet and toilet-training periods and the contributory role of malnourishment in diminished IgA response leading to a favorable milieu for uropathogens to cause disease.[18] In addition to these factors, Korangi district is also more likely to experience a high prevalence of UTI because of its densely populated residential areas, poor sanitation, and inadequate public infrastructure.[12]

These findings are in contrast with studies conducted in well-nourished regions of Pakistan and developed countries, which show relatively lower prevalence of UTI. According to a study from the Kohat district, a reasonably advanced region of KP province with well-developed mining and agricultural sector, the prevalence of UTIs were 11.6%.[19,20] Similarly, a multicenter study from Wales, UK reported laboratory confirmed UTI in approximately 6% of children out of 597 acutely unwell children who presented to 13 general practice centers.[21]

Most of our culture-positive patient population were females (80%). This is primarily due to the anatomy of the female genitourinary system, with a shorter urethral passage to

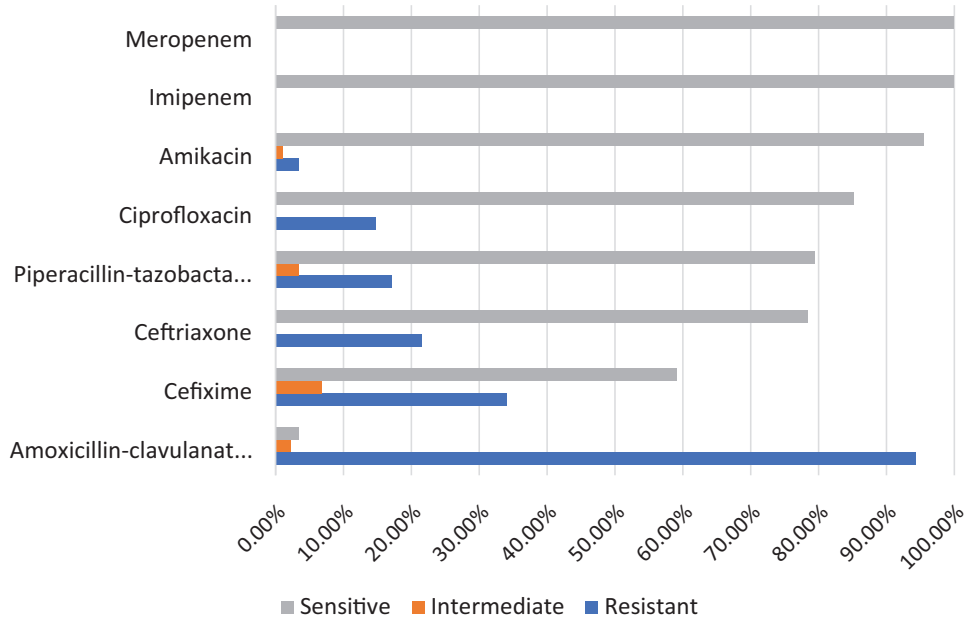

Figure 2. Antimicrobial susceptibility pattern of Enterobacterales isolated from urine cultures.

the perineum in comparison to males, making it easier for the uropathogens to enter the urinary bladder causing ascending infection. Also, wrong perineal hygiene practices in females such as incorrect washing and wiping that is back to forward, has also been identified as a potential risk factor for UTI.[5]

In our pediatric patient population, Enterobacterales, especially *E. coli*, accounted for 95.6% of the uropathogens. The role of *E. coli* in the pathogenesis of UTI has been studied and explained in detail. It possesses an array of virulence factors that play critical roles in UTI pathogenesis allowing it not only to ascend the urethral lumen and infect the urinary bladder but also increase the risk of bacteremia and sepsis by kidney colonization and host tissue damage. Some of the important virulence factors include flagella, pili, curli, non-pilus adhesins, lipopolysaccharide, polysaccharide capsule and outer membrane proteins. Furthermore, the expression of type 1 pili exhibits a remarkable "phase variation" mechanism, reversibly switching between on and off phases in response to environmental signals within the urinary tract such as acidic pH, further increasing the resilience of the organism to the host immune system.[22]

According to the antimicrobial susceptibility pattern of Enterobacterales, meropenem, imipenem, amikacin, ciprofloxacin, and piperacillin-tazobactam were found to be the most effective antibiotics, while ceftriaxone, cefixime, and amoxicillin-clavulanate were relatively less effective. This pattern is in line with a number of research studies conducted in Pakistan in the past decade that showed Enterobacterales' increasing resistance to the cephalosporin and penicillin class of antibiotics.[14,23-25]

The rising antimicrobial resistance in Pakistan can be attributed to factors at various levels of the health care system. In situations where health regulatory bodies have failed to implement a strong framework for educating and overseeing the appropriate use of antibiotics, physicians are also responsible for the injudicious use of antibiotics. In addition, a general lack of patient education about antibiotic use and misuse has been connected to the issue, and self-medication is common. The issue can be greatly reduced with the support of strict government regulations, a code of conduct for physicians prescribing antibiotics, ethical marketing practices, and adherence to prescription ethics.[26]

Our study had a few limitations. Firstly, this was a single center study and similar studies are required from other pediatric health care centers in similar districts and neighborhoods all over Pakistan to fully grasp the frequency and characteristics of uropathogens in the country's pediatric population. Nonetheless, our study provides robust data from a tertiary care center located in the heart of the district which caters to a pediatric population of 1.8 million.[13] Secondly, data regarding whether the cases of UTI were acquired from the community or hospital was lacking. The information provided by our results reveal important insights regarding pediatric UTIs in our locality and the investigators aim to perform a long-term surveillance study in the future that will incorporate data regarding disease acquisition in addition to other variables.

Conclusion

We report high frequency of UTI in our pediatric population with uropathogens and associated antimicrobial susceptibility pattern confirming to the existing trends of pediatric UTIs in Pakistan. In addition to providing the physicians with valuable insights into treating patients under similar conditions, our study serves as a catalyst for further multi-center research in this area.

Declarations

Ethics Approval and Consent to Participate

The Ethical approval was obtained from the Institutional Review Board of the Sindh Institute of Child Health & Neonatology (IRB ID # SICHN/003/2023). This study was

conducted in accordance with the declaration of Helsinki. Informed consent was obtained from patients or their legally authorized guardians before being recruited into the study.

Consent for Publication

Not applicable.

Author Contributions

MK: Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Project Administration, Software, Supervision, Visualization & Writing—Original Draft. NS: Data Curation, Investigation, Project Administration, Resources & Supervision & Writing—Review and editing.

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Competing Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

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REFERENCES

1. Alsaywid BS, Alyami FA, Alqarni N, et al. Urinary tract infection in children: a narrative review of clinical practice guidelines. *Urol Ann*. 2023;15:113-132.
2. Silva ACS, Oliveira EA, Mak RH. Urinary tract infection in pediatrics: an overview. *J Pediatr*. 2020;96:65-79.
3. Kaufman J, Temple-Smith M, Sanci L. Urinary tract infections in children: an overview of diagnosis and management. *BMJ Paediatr Open*. 2019;3:e000487.
4. Shaikh N, Morone NE, Bost JE, Farrell MH. Prevalence of urinary tract infection in childhood: a meta-analysis: a meta-analysis. *Pediatr Infect Dis J*. 2008;27:302-308.
5. Vyas S, Sharma P, Srivastava K, Nautiyal V, Shrotriya VP. Role of behavioural risk factors in symptoms related to UTI among nursing students. *J Clin Diagn Res*. 2015;9:LC15-LC18.
6. Jansåker F, Li X, Sundquist K. Sociodemographic factors and uncomplicated cystitis in women aged 15–50 years: a nationwide Swedish cohort registry study (1997–2018). *Lancet Reg Health Eur*. 2021;4:100108.
7. Li X, Fan H, Zi H, et al. Global and regional burden of bacterial antimicrobial resistance in urinary tract infections in 2019. *J Clin Med*. 2022;11:2817.
8. Shiralizadeh S, Taghizadeh S, Asgharzadeh M, et al. Urinary tract infections: raising problem in developing countries: Raising problem in developing countries. *Rev Med Microbiol*. 2018;29:159-165.
9. Alkhawaldeh R, Abu Farha R, Abu Hammour K, Alefishat E. Optimizing antimicrobial therapy in urinary tract infections: a focus on urine culture and sensitivity testing. *Front Pharmacol*. 2022;13:1058669.
10. Shakya S, Edwards J, Gupte HA, et al. High multidrug resistance in urinary tract infections in a tertiary hospital, Kathmandu, Nepal. *Public Health Action*. 2021;11:24-31.
11. Baral P, Neupane S, Marasini BP, Ghimire KR, Lekhak B, Shrestha B. High prevalence of multidrug resistance in bacterial uropathogens from Kathmandu, Nepal. *BMC Res Notes*. 2012;5:38.
12. Soomro TA, Department of Architecture & Planning, Dawood University of Engineering & Technology Karachi, et al. Planning failure of satellite town: a case study of korangi, Karachi-Pakistan. *Mehran Univ Res J Eng Technol*. 2018;37:209-222.
13. Pakistan bureau of statistics. Accessed March 6, 2024. https://www.pbs.gov.pk/census-2017-district-wise/results/096
14. Khatoon I, Khanam S, Azam A, Qadeer S, Naz S, Hassan NU. Incidence pattern, antibiotic susceptibility pattern and associated risk factors of bacterial uropathogens among general population of Pakistan. *Infect Drug Resist*. 2023;16:4995-5005.
15. Clinical & Laboratory Standards Institute M100. Accessed March 6, 2024. https://clsi.org/standards/products/microbiology/documents/m100/
16. Anis-ur-Rehman, Jahanzeb M, Siddiqui TS, Idris M. Frequency and clinical presentation of UTI among children of Hazara Division, Pakistan. *J Ayub Med Coll Abbottabad*. 2008;20:63-65.
17. Rahim N. Socio-economic impacts of CPEC on Hazara region: a suburban perspective. Accessed March 6, 2024. http://www.ashwinanokha.com/resources/2-Socio-Economic%20Impacts%20of%20CPEC%20on%20Hazara%20Region%20A%20Suburban%20Perspective.pdf
18. Uwaezuoke SN, Ndu IK, Eze IC. The prevalence and risk of urinary tract infection in malnourished children: a systematic review and meta-analysis. *BMC Pediatr*. 2019;19:261.
19. Ullah A. Prevalence of symptomatic urinary tract infections and antimicrobial susceptibility patterns of isolated uropathogens in kohat region of Pakistan. *MOJ Biol Med*. 2018;3:85-89.
20. District kohat.Accessed March 6, 2024. https://kpezdmc.org.pk/node/4535
21. O'Brien K, Edwards A, Hood K, Butler CC. Prevalence of urinary tract infection in acutely unwell children in general practice: a prospective study with systematic urine sampling. *Br J Gen Pract*. 2013;63:e156-e164.
22. Terlizzi ME, Gribaudo G, Maffei ME. UroPathogenic Escherichia coli (UPEC) infections: Virulence factors, bladder responses, antibiotic, and non-antibiotic antimicrobial strategies. *Front Microbiol*. 2017;8:1566.
23. Iqbal Z, Sheikh AS, Basheer A, et al. Antibiotic drug resistance pattern of uropathogens in pediatric patients in Pakistani population. *Antibiotics*. 2023;12:395.
24. Sohail M, Khurshid M, Saleem HGM, Javed H, Khan AA. Characteristics and antibiotic resistance of urinary tract pathogens isolated from Punjab, Pakistan. *Jundishapur J Microbiol*. 2015;8:e19272.
25. Bilal H, Khan MN, Rehman T, Hameed MF, Yang X. Antibiotic resistance in Pakistan: a systematic review of past decade. *BMC Infect Dis*. 2021;21:244.
26. Shaikh BT. Anti-microbial resistance in Pakistan: a public health issue. *J Ayub Med Coll Abbottabad*. 2017;29:184-185.