PRESCRIBING PATTERN OF ANTI-TUBERCULAR DRUGS IN PRIMARY HEALTH CARE CENTRES

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ABSTRACT

Aim: Tuberculosis is an airborne, severe chronic infectious disease caused by mycobacterium tuberculosis. This study aims to analyse the prescribing pattern of Anti-tubercular drugs in primary health care centres to uplift the quality life in TB Patients. **Material and Methods:** An observational prospective study was conducted at Chikkabanavara and Hesaraghatta PHCs over three months with a sample size of 100 TB patients. **Results:** Among the 100 patients analysed in the study, 78% were male and 22% were female and majority of patients (49%) were between the age of 36-45years. Majority of the patients (91%) were new patients and had pulmonary TB (86%). Different drugs were prescribed which varied with age. 4FDC 3FDC (25%) was the most prescribed drug among adults, while 3FDC Ethambutol 100mg 2FDC was most prescribed among children (5-15years). The no. of doses prescribed varied with weight, patients who belong to 24- 35 kg (7%) weight category were mostly prescribed with 2 doses/day, 36- 49kg (47%) with 3 doses/day, 50- 64kg (36%) with 4 doses/day, 65-75kg with either 4 doses/day or 5 doses/day depending on the patient condition. **Conclusion:** This study provides valuable insights into the current landscape of TB treatment and tackles potential areas for improvement in rational drug prescription. It is crucial to continue monitoring and adapting TB treatment strategies to enhance the quality life and combat this infectious disease.

KEYWORDS: Tuberculosis (TB); Anti-tubercular drugs; Prescribing pattern; Drug regimen; FDC.

INTRODUCTION

According to WHO "Tuberculosis is an infectious disease that most often affects lungs and is caused by a type of bacteria. It spreads through the air when infected individuals spit, sneeze, or cough. It is an airborne transmissible illness claiming over millions of deaths annually.[1,2] It is a serious chronic infectious illness triggered by Mycobacterium tuberculosis that affects about one-third of the world's population, making it one of the top ten causes of death, with around 8 million people affected each year and 2 million dying as a result.[3,4,5] In the middle of the 19th century, Johann Lukas Schonlein came up with the word "TB," which refers to a disease that has been around for more than 15,000 years. In 1720, Benjimin Martin was the first to write about the viral origins of tuberculosis. Jean Antoine Villemin followed in 1865. Injections became a common treatment after Robert Koch identified tuberculosis in 1882 and termed it tuberculin in 1890.[6,7,8] The gram-positive, aerobic, rod-shaped bacterium that causes tuberculosis is called Mycobacterium tuberculosis. It is roughly 0.2 millimetres long and grows slowly. It produces vivid red rod-like formations when it reacts with Ziehl-Nelsen stain. Mycolic acid, which makes up the outer membrane, provides defence against the body's immunological reaction. Organelles inside the body supply energy for survival. The bacterium's pathogenicity is caused by a cord-like structure termed cord factor. Nearly 10,000 organisms/mL are needed over the three-to-nine-week incubation period to produce a positive sputum smear test result.[9] Around 10.6 million persons globally were predicted to have TB in 2021, with HIV-positive people accounting for 6.7% of cases. Africa, the Western Pacific, and South-East Asia had the largest proportion of cases. Sixty-seven percent of new TB cases were in the top three countries: India, the Philippines, and Indonesia. In 2021, more than two-thirds of all TB cases worldwide occurred in eight countries. In 2020, there were 8300 cases recorded in the US, and close to 13 million individuals had latent TB infection.[10] There are two primary forms of tuberculosis (TB): Extrapulmonary TB and Pulmonary TB. The primary symptoms of pulmonary tuberculosis are persistent coughing, exhaustion, irregular breath sounds, and appetite loss. Organs other than the lungs, including the pleura, lymph vessels, belly, genitourinary system, skin, joints, bones, even meninges, are affected by extrapulmonary tuberculosis. Frequent headaches, fever, and changes in mental status are among the symptoms. Back pain, paralysis of the lower extremities, and tuberculous arthritis are signs of skeletal tuberculosis. When a patient has a cough that lasts for two to three weeks or exhibits additional symptoms, the IDSA and CDC recommend probable tuberculosis. Tests include fluorescence microscopy and zinc, X-rays of the chest, CBNAAT, mucous culture, TRUENAT, FLLPA, SLLPA, along with skin tests for tuberculin.[11,12,13,14] As advised by the

WHO, TB is managed using FDCs and anti-TB medications. Avoiding drug resistance and prescription errors, the 6-month regimen consists of an intense period with 4FDC containing HRZE, preceding a continuous phase via 3FDC carrying HRE.[1,15,16] TB treatment involves three categories: First-line, second-line, and newer-generation medications, such as isoniazid, rifampicin, ethambutol, pyrazinamide, streptomycin, ethionamide, protionamide, cycloserine, para-amino salicylic acid, and clofazimine.[17,18] To end tuberculosis, the Revised National Tuberculosis Control Programme (RNTCP) was launched in 1962. It offers assistance and oversight for all TB patients, guaranteeing appropriate treatment and case reporting throughout India. It was revamped in 1997 and 2020. All patients will receive high-quality anti-TB medications thanks to the initiative.[19] NSP 2020-25 was introduced as a result of the NSP-2017-25's failure to reach goals in 2020. The objective was to eradicate tuberculosis in India by means of a campaign, the creation of novel diagnostic instruments, and the execution of preventive initiatives. A web-enabled tool called the Nikshaya Portal keeps track of patient information, such as test results, comorbidities, treatment outcomes, and demographics. In order to lower incidence, lower mortality rates, and increase TB notification, the government's RNTCP, NTEP, and NSP programmes concentrate on ongoing patient surveillance, diagnosis, notification, and treatment.[20,21]

MATERIAL AND METHODS

The research was done at Chikkabanavara PHC and Hesaraghatta PHC in Bangalore, and the study centre was Mallige College of Pharmacy, Silvepura, Bangalore. A prospective observational study design was used, with a duration of three months. The population for the study was patients with tuberculosis (TB), and the sample size was 100 patients. Data were collected through patient treatment cards, patient consent forms, and Google Forms. The main sources of information were patient prescriptions and treatment cards. Inclusion criteria consisted of either male or female patients older than five years diagnosed with TB, and exclusion criteria included incomplete cases, complicated TB, and pregnant/lactating females. The process of study was conducted by a visit to PHCs and collection of patient treatment cards randomly following informed consent from patients and pharmacists. Moreover, hospital pharmacists were contacted to revise the data gathered. The data that were gathered were then analysed using different parameters which were in tandem with the purpose of the study. Statistical processing was done via MS Excel with results depicted by charts and graphs.

RESULTS

Demographic Characteristics and Participant profile

A total of 100 patients were involved in the study, and the demographic distribution of this population is as follows:

Gender distribution:

- Female: 22% (n=22)
- Male: 78% (n=78)

Age distribution:

- 5-15 years: 4% (n=4)
- 36-45 years: 25% (n=25)
- 76-85 years: 2% (n=2)

Weight distribution:

- 24-35Kg: 20% (n=9)
- 36-49Kg: 45% (n=44)
- 50-64Kg: 40% (n=39)
- 65-75Kg: 5% (n=5)

Types of TB Patients

Distribution of different types of patients according to age and gender

Distribution of different types of patients based on gender

- New: 91% (F=17, M=74)
- Previously treated: 6% (F=4, M=2)
- Recurrent: 3% (F=N/A, M=3)

Distribution of types of patients based on age

- New: 91% (36-45age group)
- Previously treated: 6% (36-45 age group)
- Recurrent: 3% (66-75 age group)

Drugs prescribed for different age groups

Drugs prescribed for 5-15years age group

- 3FDC Ethambutol 100mg 2FDC: 75% (n=3)
- 3FDC Ethambutol 800mg 3FDC 2FDC Ethambutol 800mg: 25% (1)

Drugs prescribed for 16-above years age group

- 4FDC Pyridoxine 50mg: 1% (n=1)

- 4FDC: 31% (n=28)

- 4FDC 3FDC: 49% (n=42)

- 4FDC Levofloxacin 500mg Ethambutol 800mg: 1% (n=1)

- 4FDC 3FDC Ethambutol 800mg Levofloxacin 250mg: 1% (n=1)

- 4FDC Ethambutol 800mg Levofloxacin 500: 1% (n=1)

- 4FDC Pyridoxine 50mg: 2% (n=2)

- 4FDC Pyridoxine 50mg 3FDC: 6% (n=6)

- Pyrazinamide 500mg Pyrazinamide 750mg 3FDC 4FDC: 1% (n=1)

- Pyrazinamide 750mg Pyrazinamide 500mg 3FDC CP 4FDC 3FDC CP: 3% (n=3)

- Pyridoxine 50mg: 1% (n=1)

- Pyridoxine 50mg 4FDC: 1% (n=1)

Number of doses prescribed as per weight

- 2dose/day: 24-35kg 7% (n=6)

- 3dose/day: 36-49kg 47% (n=43)

- 4dose/day: 50-64kg 42% (n=39)

Site of infection

Site of infection in different genders

- Extrapulmonary:14% (F=5, M=9)

- Pulmonary: 86% (F=16, M=69)

Drugs prescribed for different types of TB

For Extrapulmonary TB

- 4FDC 3FDC: 64% (n=9)

- 4FDC: 14% (n=2)

- 4FDC Ethambutol 800mg Levofloxacin 500: 7% (n=1)

- 4FDC Levofloxacin 500mg Ethambutol 800mg: 7% (n=1)

- 3FDC Ethambutol 800mg 3FDC 2FDC Ethambutol 800mg: 7% (n=1)

For Pulmonary TB

- 4FDC 3FDC:45% (n=37)

- 4FDC:33% (n=27)

- 4FDC Pyridoxine 50mg 3FDC:7% (n=6)

- 4FDC Pyridoxine 50mg:2% (n=2)

- 3FDC Ethambutol 100mg 2FDC:2% (n=2)

- 4FDC 3FDC Ethambutol 800mg Levofloxacin 250mg:1% (n=1)

- Pyrazinamide 500mg Pyrazinamide 750mg 3FDC 4FDC:1% (n=1)

- Pyrazinamide 750mg Pyrazinamide 500mg 3FDC CP 4FDC 3FDC CP: 4% (n=3)

- Pyridoxine 50mg: 1% (n=1)

- Pyridoxine 50mg 4FDC:1% (n=1)

DISCUSSION

The study aimed to analyse how anti-tubercular drugs are prescribed across different age groups, considering patient demographics such as age, gender, and weight-based dosage. It also assessed the rationality behind these prescriptions. A total of 100 patients were included in the study, with a male predominance of 78% and 22% female representation. Interestingly, the highest prevalence of TB was observed in individuals aged 36-45 years (25%), followed by 46-55 years (20%) and 26-35 years (15%), which differed from earlier reports. Among the patients, 91% were newly diagnosed cases, while 6% had undergone previous treatment, and 3% experienced recurrent infections.

This finding suggests that TB is more common among new patients, challenging previous studies. The prescribed drug combinations varied by age group, with children aged 5-15 years mostly receiving 3 FDC Ethambutol 100mg 2 FDC (75%). For adults, the most commonly prescribed regimen was a combination of 4 FDC and 3 FDC drugs (49%), followed by 4 FDC alone (31%), while other combinations were used less frequently. Dosing was weight-adjusted, with 75% being given medication twice a day, 47% three doses daily, and 36% four doses a day. Interestingly, pulmonary TB was much more common, occurring in 86% of patients, while 14% had extrapulmonary TB. Nonetheless, the cases of extrapulmonary TB seem to be slowly increasing.[22,23]

CONCLUSION

Our findings highlight the importance of tailoring treatment based on patient weight, with different dosing regimens for different weight categories. Our research provides valuable insights into the current landscape of TB treatment and offers potential areas for improvement in rational drug prescription. It is crucial to continue monitoring and adapting TB treatment strategies to enhance patient care and combat this infectious disease.

REFERENCES

1. Sotgiu G, Centis R, D'Ambrosio L, Migliori GB. Tuberculosis treatment and drug regimens. Cold Spring Harb Perspect Med, 2015; 5(5): a017822.

2. Ledesma JR, Ma J, et al. Global, regional, and national sex differences in the global burden of tuberculosis by HIV status, 1990-2019: results from the Global Burden of Disease Study 2019. Lancet Infect Dis, 2022; 22(2): 222-41.

3. Qiu B, Wu Z, et al. Risk factors for types of recurrent tuberculosis (reactivation versus reinfection): A global systematic review and meta-analysis. Int J Infect Dis, 2022; 116(2): 14-20.

4. Pai M, et al. Tuberculosis. Nat Rev Dis Primers, 2016; 6(1): 1-23.

5. Kumar SV, et al. A systematic review of different types of tuberculosis. Eur Rev Med Pharmacol Sci, 2010; 14(10): 831-43.

6. Dutta SS. History of tuberculosis. News Med Life Sci, [Internet]. Available at: https://www.newsmedical.net/health/History-of-Tuberculosis.aspx.

7. Barberis I, Bragazzi NL, Galluzzo L, Martini M. The history of tuberculosis: from the first historical records to the isolation of Koch's bacillus. J Prev Med Hyg, 2017; 58(1): E9.

8. Daniel TM, Bates JH, Downes KA. History of tuberculosis. In: Tuberculosis: pathogenesis, protection, and control. Respir Med, 1994; 13(1): 13-24.

9. Talbot EA, Raffa BJ. Mycobacterium tuberculosis. In: Molecular medical microbiology. Acad Press, 2015; 1637-53.

10. Centers for Disease Control and Prevention. Data and statistics. [Internet]. Available at: https://www.cdc.gov/tb/statistics/default.htm?s_cid=qr2022.

11. Dzodanu EG, Afrifa J, Acheampong DO, Dadzie I. Diagnostic yield of fluorescence and Ziehl-Neelsen staining techniques in the diagnosis of pulmonary tuberculosis: A comparative study in a district health facility. Tuberc Res Treat, 2019; 2019(1): 1-8.

12. Gill CM, Dolan L, Piggott LM, McLaughlin AM. New developments in tuberculosis diagnosis and treatment. Breathe, 2022; 18(1): 210149.

13. Sahana KS, Prabhu AS, Saldanha PR. Usage of cartridge-based nucleic acid amplification test (CB-NAAT/GeneXpert) as a diagnostic modality for pediatric tuberculosis: Case series from Mangalore, South India. J Clin Tuberc Other Mycobact Dis, 2018; 11(1): 7-9.

14. Shanmugasundaram D, et al. Impact and operational feasibility of TrueNat MTB/Rif under India's RNTCP. Public Health Action, 2020; 10(3): 87-91.

15. World Health Organization. WHO operational handbook on tuberculosis: Module 4: Drug-susceptible tuberculosis treatment, 2022; 18-24.

16. World Health Organization. WHO operational handbook on tuberculosis: Module 4: Drug-resistant tuberculosis treatment, 2022; 34-9.

17. O'Connor C, Brady MF. Isoniazid. In: StatPearls. Treasure Island (FL): StatPearls Publishing, 2022; 02-6.

18. Suresh AB, Rosani A, Wadhwa R. Rifampin. In: StatPearls. Treasure Island (FL): StatPearls Publishing, 2022; 85-91.

19. Ministry of Health and Family Welfare, India. Treatment of tuberculosis. [Internet]. Available at: https://tbcindia.gov.in/WriteReadData/1892s/8337437943TOG.

20. Khanna A, Saha R, Ahmad N. National TB elimination programme - what has changed. Indian J Med Microbiol, 2022; 40(4): 567-72.

21. National Tuberculosis Elimination Program (NTEP). NTEP paediatric TB guidelines. [Internet]. Available at: https://ntep.in/node/495.

22. Banta JE, et al. Pulmonary vs. extra-pulmonary tuberculosis hospitalizations in the US (1998-2014). J Infect Public Health, 2020; 13(1): 131-9.

23. Hemalatha VS, Thaliath ZX, Somson HT. Comparison of pulmonary tuberculosis and extra-pulmonary tuberculosis in a tertiary care setting. Int J Acad Med Pharm, 2023; 5(1): 225-28.