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ORIGINAL ARTICLE

Assessment of epidemiology of anti-tuberculosis drug resistance patterns and trends among known population

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ABSTRACT:

Background: In 2012, Mycobacterium tuberculosis (Mtb) infections were responsible for an estimated 1.4 million deaths worldwide, ranking second only to HIV among infectious causes of mortality. The present study was conducted for assessing epidemiology of anti-tuberculosis drug resistance patterns and trends among known population. **Materials & methods:**The study population included 100 cases who had received first-line anti-TB therapy for more than one month but remained smear positive and were subsequently started on retreatment regimens. Drug susceptibility testing was performed using the indirect proportion method on Löwenstein-Jensen medium. Standard laboratory procedures were followed to identify M. tuberculosis isolates and exclude non-tuberculous mycobacteria. Resistance was defined as ≥1% colony growth at the critical drug concentration for isoniazid, rifampicin, streptomycin, or ethambutol. Demographic and laboratory data were extracted from standardized records and analyzed with SPSS software. **Results:**The study population had a mean age of 43.8 years. Isoniazid resistance was most frequent (77%), followed by rifampicin (64%), streptomycin (61%), and ethambutol (59%). Single-drug resistance occurred in 25% of patients, mainly to streptomycin, while two-drug resistance was uncommon, with INH+STM being the most frequent pattern. Resistance to three or more drugs was substantial, especially INH+RIF+ETB+STM (33%). Overall, MDR-TB was identified in 41% of patients, highlighting its considerable clinical and public health significance. **Conclusion:**An upward trend in drug resistance has been noted in recent years, especially among retreatment cases. This underscores the need to strengthen advanced diagnostic facilities for early identification of MDR-TB and to expand second-line treatment centers, both to ensure timely management and to curb further transmission.

Key words: Anti-tuberculosis, Drug resistance

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INTRODUCTION

In 2012, Mycobacterium tuberculosis (Mtb) infections were responsible for an estimated 1.4 million deaths worldwide, ranking second only to HIV among infectious causes of mortality. Although intensified control strategies have contributed to a global reduction in tuberculosis incidence and related deaths, the prevalence of infections caused by drug-resistant strains continues to rise, posing a significant international health challenge.[1, 2]

Standard therapy for drug-susceptible Mtb typically consists of a four-drug regimen—rifampicin (RIF), ethambutol (EMB), pyrazinamide (PZA), and isoniazid (INH)—administered for two months, followed by an additional four months of treatment with RIF and INH (Lienhardt et al., 2012). Multidrug-resistant tuberculosis (MDR-TB) is defined by resistance to the two most potent first-line agents, RIF and INH. In 2011, approximately 60,000 MDR-TB cases were officially reported by WHO, though this figure is likely underestimated.[3- 5]Management of MDR-TB requires the use of second-line drugs such as fluoroquinolones (FQs), amikacin (AMK), kanamycin (KAN), and capreomycin (CAP). These agents are typically administered over a prolonged course of nearly 20 months, but their use is complicated by high toxicity, poor tolerability, and limited availability. Furthermore, about 95% of MDR-TB cases are classified as extensively drug-resistant tuberculosis (XDR-TB), characterized by additional resistance to at least one fluoroquinolone and one injectable agent (AMK, KAN, or CAP), leaving very few therapeutic alternatives.[6- 8]Hence; the present study was conducted for assessing epidemiology of anti-tuberculosis drug resistance patterns and trends among known population.

MATERIALS & METHODS

The present study was conducted for assessing the patterns of anti-TB drug resistance among previously treated patients. The study population included 100 cases who had received first-line anti-TB therapy for more than one month but remained smear positive and were subsequently started on retreatment regimens.Drug susceptibility testing was performed using the indirect proportion method on Löwenstein-Jensen medium. Standard laboratory procedures were followed to identify M. tuberculosis isolates and exclude non-tuberculous mycobacteria. Resistance was defined as ≥1% colony growth at the critical drug concentration for isoniazid, rifampicin, streptomycin, or ethambutol. Demographic and laboratory data were extracted from standardized records and analyzed with SPSS software. Resistance was categorized as primary (new cases) or secondary (retreatment cases), with MDR-TB defined as resistance to both isoniazid and rifampicin. Chi-square tests for trend were used to evaluate annual variations in resistance patterns.

RESULTS

The mean age of the study population was 43.8 years. Males comprised 66% of the patients, while females accounted for 34%. With respect to place of residence, a higher proportion (55%) came from rural areas compared to 45% from urban settings, indicating a modest rural predominance.Among the anti-tuberculosis drugs, isoniazid (INH) resistance was the most common (77%), followed by rifampicin (RIF, 64%), streptomycin (STM, 61%), and ethambutol (ETB, 59%). Single-drug resistance was observed in 25% of patients, predominantly against streptomycin (20%), while mono-resistance to INH and ETB was infrequent, and no mono-resistance to rifampicin was reported. Two-drug resistance was relatively rare, with INH+STM (5%) being the most frequent combination, whereas INH+RIF and INH+ETB were each seen in 1% of patients. Resistance involving three or more drugs was notable, with INH+RIF+ETB+STM (33%) being the most prevalent pattern, followed by INH+RIF+STM (10%) and INH+ETB+STM (4%). Importantly, multidrug-resistant tuberculosis (MDR-TB), defined as resistance to at least INH and RIF, was detected in 41% of the study population, reflecting a significant clinical and epidemiological burden.

Table 1: Demographic data

Variable	Number	Percentage
Mean	43.8 years	
Males	66	66
Females	34	34
Rural residence	55	55
Urban residence	45	45

Table 2: Drug resistance pattern and trend

Variable	Pattern	Number	Percentage
Any drug resistance	INH	63	77
	RIF	52	64
	ETB	42	59
	STM	55	61
Single drug resistance	Mono INH	2	4
	Mono RIF	0	0
	Mono ETB	1	1
	Mono STM	16	20
Two drug resistance	INH+RIF	1	1
	INH+ETB	1	1
	INH+STM	3	5
	RIF+ETB	0	0
	RIF+STM	0	0
	ETB+STM	0	0
Three or more drugs	INH+RIF+ETB	1	1
	INH+RIF+STM	7	10
	INH+ETB+STM	2	4
	RIF+ETB+STM	0	0
	INH+RIF+ETB+STM	24	33
MDR-TB		41	41

INH = Isoniazid, RIF = Rifampicin, ETB= Ethabutol, STM = Streptomycin, MDR = Multi drug resistance (resistance at least INH and RIF).

DISCUSSION

Tuberculosis (TB) continues to be one of the leading infectious diseases worldwide, claiming millions of lives annually and representing a persistent public health challenge, particularly in developing nations. In recent years, the management of TB has become increasingly complicated due to the rising prevalence of drug-resistant Mycobacterium tuberculosis (MTB) strains, which has led to prolonged treatment regimens and unsatisfactory clinical outcomes. Among the spectrum of drug-resistant (DR) TB, multidrug-resistant tuberculosis (MDR-TB)—defined as resistance to at least isoniazid (INH) and rifampicin (RMP)—is recognized as one of the most difficult forms to treat. Despite its clinical significance, diagnostic coverage for MDR-TB remains limited; in most countries, fewer than 5% of newly diagnosed and previously treated TB patients undergo testing for

MDR. As a result, the number of confirmed MDR-TB cases in 2010 represented only about 16% of the total global estimates.[7- 10]

The study population had a mean age of 43.8 years, with males comprising two-thirds of the cases. A slight rural predominance was observed, with 55% of patients residing in rural areas.

Isoniazid resistance was most frequent (77%), followed by rifampicin (64%), streptomycin (61%), and ethambutol (59%). Single-drug resistance occurred in 25% of patients, mainly to streptomycin, while two-drug resistance was uncommon, with INH+STM being the most frequent pattern. Resistance to three or more drugs was substantial, especially INH+RIF+ETB+STM (33%). Overall, MDR-TB was identified in 41% of patients, highlighting its considerable clinical and public health significance.Zignol M et al analysed data on drug resistance among new and previously treated TB cases reported from 1997 to 2012. Data are collected in surveys of representative samples of TB patients or from surveillance systems based on diagnostic drug susceptibility testing.A total of 15.7% (95% confidence limits (CI): 9.5–21.9) of new and 45.3% (95%CI: 39.2–51.5) of previously treated TB cases are estimated to have MDR-TB in the Region. Extensively drug-resistant TB (MDR-TB and resistance to fluoroquinolones and second-line injectables; XDR-TB) had been reported by 38 of the 53 countries of the region (72%). The proportion of MDR-TB cases with XDR-TB is 11.4% (95%CI: 8.6–14.2). Between 1997 and 2012, population rates of MDR-TB declined in Estonia, Latvia and Germany and increased in the United Kingdom, Sweden and Tomsk Oblasts of the Russian Federation.Surveillance of drug resistance has been strengthened in the WHO European Region, which has the highest proportions of MDR-TB and XDR-TB ever reported globally.[11]A subsequent investigation[12], conducted demonstrated substantial genetic diversity among M. tuberculosis strains within the study population. Out of all isolates analyzed, 152 (40%) were grouped into clusters ranging in size from two to 21 isolates, while the remaining 60% were classified as unique. This relatively high level of strain diversity suggests that the likelihood of patients labeled as having acquired MDR-TB actually being re-infected with an identical pre-existing MDR strain is minimal. An earlier investigation conducted in 1999 reported pronounced genetic homogeneity when isolates were assessed by restriction fragment length polymorphism (RFLP).[13]Historically, mixed infections—where a single host harbors more than one strain of M. tuberculosis at the same time—were rarely detected, largely due to the limited sensitivity of earlier DNA fingerprinting methods.[14] With the advent of more advanced molecular tools, it has become evident that in high-incidence regions, sputum samples from TB patients often contain multiple distinct M. tuberculosis strains.[14, 15] Such mixed infections complicate interpretation, as patients may be erroneously classified as having acquired drug resistance when, in reality, they harbor a resistant strain alongside a susceptible one.[16] To address this challenge, newer genotyping technologies with greater discriminatory capacity have been developed,[17] including whole-genome sequencing of M. tuberculosis.[18, 19] Application of these advanced techniques offers the potential to more accurately distinguish between acquired resistance and re-infection, thereby clarifying several of the uncertainties highlighted in previous studies.

CONCLUSION

An upward trend in drug resistance has been noted in recent years, especially among retreatment cases. This underscores the need to strengthen advanced diagnostic facilities for early identification of MDR-TB and to expand second-line treatment centers, both to ensure timely management and to curb further transmission.

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