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"A RETROSPECTIVE COHORT STUDY ON TREATMENT OUTCOME FOR MDR-TB UNDER DOT- PLUS PROGRAM"

Community Medicine

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ABSTRACT

BACKGROUND: Multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR- TB) are the major public health problem that threatens the progress in disease care and control worldwide. The treatment of MDR-TB with second line drug is prolonged, complex, and expensive, having high rate of mortality along with the considerable rate of adverse effects. But the treatment efficacy rates in MDR-TB are the key issue that cannot be ignored and this present study aims to evaluate the treatment outcomes and potential factors associated in patients with MDR-TB infections.

METHOD: - A retrospective cohort study was carried out among the enrolled in DOTS-Plus program with MDR-TB are 287 no. of patients from 2012 to 2018 in Tuberculosis department, Ashwini Rural Medical College Hospital and Research Centre Kumbhari, Solapur, Karnataka, India. The patients necessary information such as demographics, clinical parameters, if any previous TB treatment history and treatment outcomes to Cat IV anti-TB therapy, any interruptions in treatment, adverse drug reactions, culture conversion etc. were evaluated from the records.

RESULTS: Out of 287 patients, 32 (11.15%) had a successful cured after complete course of ATT). Remaining 153 patients had an unsuccessful outcome (death (27.53%), default (20.56%), failure or switched to Cat V (5.23%), and 75 patients (25.09%) are on treatment.

CONCLUSION:-The treatment success rate revealed that MDR TB patients has shown low treatment success rate. Patients still on treatment and High default treatment percentage had been observed, which could be the possible reason.

KEYWORDS

Multidrug-resistant Tuberculosis (MDR-TB), Extensively Drug-resistant Tuberculosis (XDR- TB), Second-line Drugs, Treatment Outcome.

INTRODUCTION

Multidrug-resistant tuberculosis (MDR-TB) is a type of TB that is resistant to at least the first line anti-TB drugs (Rifampicin and Isoniazid). MDR-TB results from either primary infection or may develop in the course of a patient's treatment [1]. MDR-TB patients respond poorly to short course chemotherapy and need to be treated intensively for up to 24 months with a regimen based on reserve anti-tuberculosis drugs [2]. The occurrence of MDR- TB is mainly attributable to human error, although genetic factors are believed to contribute to a certain extent [3]. The principal patient-related factor that predicts the occurrence of MDR-TB is non-adherence to treatment [4]. In 2014, globally, out of total TB cases, 5% were estimated to be MDR-TB, and the survival data show that an estimated 480,000 people developed MDR-TB and 190,000 patients had died as a result of MDR-TB (approximately 39.5 % died). And 123,000 patients with MDR-TB or Rifampicin resistant tuberculosis (RR-TB) were recorded, of whom about 75% lived in the European Region, India, South Africa or China [5]. In 2015, Globally, there was an estimated 480,000 new cases of MDR-TB and an additional 100,000 people with Rifampicin-resistant TB (RR-TB).[1] In 2016, an estimated 490,000 people worldwide developed MDR-TB, and an additional 110,000 people with Rifampicin-resistant TB were also newly eligible for MDR-TB treatment. Drug resistance surveillance data show that an estimated 240,000 people died from MDR/RR-TB in 2016. In spite of increased testing, the numbers of MDR/RR-TB cases detected in 2016 are 153,000.The countries with the largest numbers of MDR/RR-TB cases (47% of the global total) were China, India and the Russian Federation. It is estimated that about 6.2% of these cases were XDR-TB. As per WHO 2016 data, India has almost 80,000 registered which is among the highest in the world [1] Hence programmatic management of drug resistant TB (PMDT) services in 2007 for the management of MDR-TB was introduced. The major reasons for multidrug resistance (MDR) is mismanagement of TB treatment and person-to-person transmission leading to continues emerge and spread of infection. And the other factors are 1) Inappropriate or incorrect use of antimicrobial drugs, 2) using of ineffective formulations of drugs (such as use of single drugs, poor quality medicines or bad storage conditions), 3) premature treatment interruption,which can then be transmitted, especially in crowded areas very easily.

Even the Treatment options are limited and expensive, recommended medicines may not always available easily, and patients experience many adverse effects from the drugs and co-infection of HIV makes difficult to treat MDR-TB. DOTS-Plus program follows a standardized regimen of treatment (labelled as Cat IV) which has shown feasibility and effectiveness with 61% successful outcome in MDR-TB in resource limited countries. However, in real life conditions, the picture is dismal with WHO reporting a treatment success rate of only 46% in India.[1]

Regular surveillance of the program highlighting both its success and failure is important to find weak areas which need intervention for better program outcome. Hence, the present study was undertaken to assess different treatment outcome among MDR-TB patients being treated under programmatic conditions.

METHOD AND METHODOLOGY:-

It is a retrospective study conducted at Tuberculosis department, Ashwini Rural Medical College Hospital, Solapur, Karnataka, India, were subjects registered and followed up from 2012 to 2018 at the above-mentioned DOTS plus site and initiated on Cat IV regimen of RNTCP. Informed consent was not taken as whole data was retrieved from the medical records of the patients who had already completed treatment or had some specific outcome. The diagnosis of MDR-TB was done at RNTCP accredited Intermediate Reference laboratory using cartridge based nucleic acid amplification test (CBNAAT) according to the standard guidelines.[5] Basic demographic and clinical profile including patients lifestyle, associated disorder (HIV Status etc), history of previous anti-tuberculosis treatment (ATT), routing investigations done as a part of pre-treatment evaluation were extracted from the medical record available at the Hospital. Further details on the current course of Cat IV ATT particularly such as any interruption in the treatment, adverse drug reactions, time of culture conversion, final outcome, weight gain etc. were also retrieved. Different outcomes to Cat IV treatment such as, cure, treatment default, treatment completed death and treatment failure were defined as per RNTCP-PMDT guidelines. [5] For Statistical analysis, successful outcome was represented by cure and completion of treatment and adverse outcome in previous ATT regimens was labelled in the event of default or failure in any of the previous anti-TB therapy. And these different quantitative outcomes are represented and summarized as mean+ SD and qualitative percentages.

RESULTS

Total 287 patients had registered over a period of 6 years under DOTS-Plus program in Ashwini Rural Medical College Hospital,. Majority of the patients comprised of young to middle aged subjects (i.e. 36.2±14.1) with low body mass index. Percentage of male subject is more when compared to that of female subjects (66.2%, 33.8% respectively). Among the total subjects 13% were HIV positive patients and the number is more with male compared to that of female (77.14%, 8.57% respectively) (Table 1)

TABLE: 1 Demographic and clinical characteristics of MDR-TB patients enrolled in DOTS-Plus program with Navodaya Medical College from 2012-2018

Demographic and clinical characteristics of MDR-TB patients	
Variables	**Demographic values**
Female	33.8
Male	66.2
Age (years)	36.2+14.1
Weight (kg)	42.3+10.4
Total Positive HIV among MRD TB	13.0
Positive Female HIV	8.57
Positive male HIV	77.14

Category of MDR-TB Among the study subjects, high proportion of them are previously treated for TB (34.49%), followed by relapse and newly cases (15.68%, 12.54% respectively) and (6.97%) of patients were enrolled after failure of re-treatment, while (10.10%) of them were after default (Figure 1)

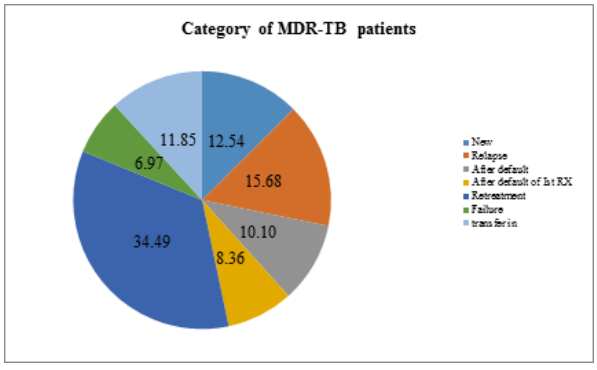

FIGURE 1: Percentage of different categories of MDR-TB patients enrolled in this programme.

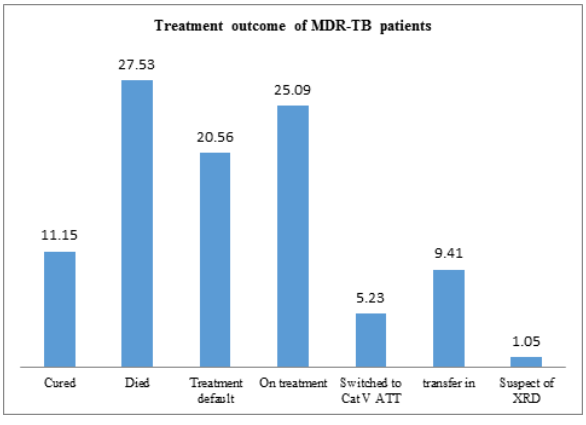

FIGURE 2: Treatment outcome among MDR-TB patients.

Treatment outcome

TABLE: 2 Treatment outcomes of MDR-TB patients among the study population

Treatment outcome of MDR-TB patients	Percentage
Cured	32 (11.15%)
Died	79 (27.53%)
Treatment default	59 (20.56%)
On treatment	75 (25.09%)
Switched to Cat V ATT	15 (5.23%)
transfer in	27 (9.41%)
Suspect of XRD	3 (1.05%)

Out of 287 patients, 32 (11.15%) had a successful cured after complete course of ATT). Remaining 153 patients had an unsuccessful outcome (death (27.53%), default (20.56%), failure or switched to Cat V (5.23%) (Table: 2).

DISCUSSION

The present study was conducted to evaluate six years of retrospective treatment outcome and survival status data among MDR TB patients under DOT plus program, where the patients had received a standardized regimen comprising of six medicines for first 6-9 months and four drugs for next 18 months as a part of continuation treatment. The prevalence and effective outcome was significant in clinical parameters among different outcome groups. In this present study treatment success (cured completely) rate is 11.15% and during the follow-ups 153 patients had shown unsuccessful outcome (i.e. death (27.53%), default (20.56%), failure or switched to Cat-V (5.23%). The rate of success at the end of this study is low than a study conducted in St. Piter hospital (Ethiopia), South Africa and Lithuania [6-8] where a probability of 75-78% was reported. Incidence of mortality noted above is slightly high i.e 27.53%, to that of St. Piter TB referral hospital which was 13.3 patients per 100 person year of observation [6]. However in this study a significant proportion (25.09%) of patients are still on treatment and death may be possible at the later part of the treatment. Most researchers reported that poor outcome of MDR TB treatment is highly contributed by prevalence of HIV co-infection [6]. We have discovered the same relation in which the hazard of death in HIV positive individuals was 3 times higher than negatives. This is in line with most recent national and international studies [6]. This is because during HIV infection the prevalence of co-infection, the probability of drug interaction and side effects and overall compliance will decrease which further increase the hazard of mortality. Our study had achieved a treatment success rate of 11.15% which is very less compared with the recently published meta-analysis. [13-15] In our study treatment, 27.53% of patients in our cohort died during the course of treatment, this figure is almost on the same range to those quoted in the previous 2 Indian studies (19.3% and 30.4%) but is higher than the results of recent 2 meta-analysis (11% and 12.6%).[13,14] Our study showed a treatment default rate of 20.56% which is almost similar to 21%4 and 23%3 as achieved in previous Indian studies. [13,14] Treatment default rate is an important parameter to judge performance of the program, as it not only improves treatment outcome abut also prevents further spread of MDR-TB strain in the community. However, there were few limitations in our study. It was a single centre observational study in which the data was retrieved from the medical record. Information on certain parameters like alcohol abuse, smoking, adverse drug reactions were missing for the patients.

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