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Ambulatory and Community Based Treatment of Multi Drug Resistant Tuberculosis: A Preliminary Report from Benue State, Nigeria

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ABSTRACT
Ambulatory and Community-based treatment for multidrug-resistant tuberculosis (MDR TB) has been practiced in other countries for several years with reports of successful outcomes. In Nigeria, it is a new concept that has not been evaluated in terms of feasibility and patients' acceptance. The study evaluated the performance and feasibility of ambulatory and community based treatment of multi drug resistant tuberculosis (MDRTB) in Benue state, Nigeria.
A retrospective cross sectional study of MDRTB patients in Benue State who were on ambulatory or community based treatment for at least 8 months was undertaken. A review of clinical records of the patients, reports of the monitoring officer and minutes of meetings of the consortium of experts on MDRTB were used. Data was analysed using the Statistical Package for Social Sciences (SPSS) version16. Qualitative was expressed as percentages while observations were documented. Forty (40) MDR TB patients were on treatment for least 8 months. There were 29(72.5%) males and 11(27.5%) females (M: F ratio 2.6:1) with a mean age of 39.2years (range19-65years).TB/ HIV co-infection rate was 27%. Twenty two (55%) out of the 40 patients had previous tuberculosis treatment with first line medications. The most common side effects were hearing loss (32.5%) and arthralgia (7.5%), while myalgia, dizziness and haematemesis were also present. Case holding was 95%, while 2(5%) patients were lost to follow up. Ambulatory and community based treatment of MDRTB is feasible. There are challenges of documentation, funding of treatment and related activities.
Keywords: *Ambulatory, Community, Multi drug resistant tuberculosis.*

INTRODUCTION

Tuberculosis (TB), a disease as old as mankind has remained an important cause of morbidity and mortality worldwide but more especially in the underdeveloped countries despite efforts at its control [1], [2]. The problem has been compounded by the advent of HIV infection that has led to the resurgence of tuberculosis in all countries including those that had earlier curtailed it. More recently, multi drug resistant TB (MDR-TB) and extensively drug resistant TB (XDR-TB) has further worsened the problem. MDR-TB, which is defined as TB resistant to at least Isoniazid and Rifampicin, the two most powerful anti-TB drugs, is a serious threat

to the fight against TB. The current estimated worldwide incidence of MDRTB is 620,000 cases annually with prevalence rate 2-3 times the incidence, mainly among the poor and middle class. In 2014, an estimated 190 000 people died of MDR-TB [1], [3]. Nigeria is classified as a high burden country for HIV, Tuberculosis and MDR-TB. The national prevalence rate for MDR-TB is 4.8% comprising 2.9% among the new and 14.3% among retreatment cases [4], [5]. This form of TB is now a major clinical and public health threat. It is 300 times more costly to manage; drugs are toxic and require to be taken for up to 20-24 months. Resource poor countries like Nigeria who depend mostly on donor funds are unable to provide enough treatment centres for MDR-TB [6], [7], [8].

In order to ensure that Drug Resistant TB (DR-TB) cases are promptly and appropriately treated, the National Tuberculosis and Leprosy Control Program (NTBLCP) in Nigeria like other national program in resource constrained nations adopted a mixed treatment delivery model in the year 2010 which includes two options for community based treatment. The first is ambulatory treatment in which, following successful initiation of intensive phase of treatment and discharge from an inpatient treatment centre, treatment is continued at the nearest DOT centre to the patient in the community for the remaining duration. The second option is the direct initiation of DR-TB treatment in the community which entails that MDR-TB patients are commenced on treatment at the nearest DOTS centre to their homes supported by the use of a treatment supporter. Both intensive and continuation phases of treatment are therefore provided in the community throughout their treatment period.

Benue State with an estimated population of 5.67million people in 2016 is one of the 36 states in Nigeria, located in the north central zone. The state has a high prevalence of HIV and TB [4]. Detection of mycobacterium tuberculosis (MTB) and Rifampicin resistance (which is a surrogate for MDR-TB) using Gene Xpert/RIF technology started in the state at one centre in 2012. By 2015, the state had eleven (11) Gene Xpert machines at different sites. However, Benue did not have inpatient treatment facilities. Therefore, prior to commencement of the ambulatory and community based treatment option, a large number of MDRTB patients diagnosed from the state were on the waiting list for inpatient treatment at the few available centres in Nigeria. The long waiting period lead to increased morbidity and mortality among these patients and high chance of spread of MDR-TB in the community.

In 2014, the state commenced the ambulatory/community based treatment model based on the Nigerian National Guidelines for programmatic and clinical management of MDR-TB [7]. A consortium of experts drawn from the Benue State University teaching hospital, Federal Medical Centre (a tertiary health institutions in the State capital) and the State Ministry of Health comprising of a Chest physician, Public Health Expert/State TB and Leprosy control officer, Psychiatrist, Ear Nose and Throat specialist, Pharmacist, Laboratory Scientist, Administrative staff and a community based organization official/ Social worker was responsible for the program management. Enrolment and treatment of patients started in January 2014. These were patients transferred from inpatient treatment centres outside Benue state for ambulatory treatment or MDR-TB suspects tested at one of the Gene Xpert machine sites in the state in whom MTB with Rifampicin resistance was detected. The latter were evaluated for suitability for community based treatment by the clinicians including baseline audiometry according to the Nigerian national protocol. After collection of their sputum for culture and drugs sensitivity testing at any of the national laboratories, treatment was initiated in the community at a designated DOTS centre nearest to the patient's home. The recommended standard 20 months regimen was used for all patients [7]. Injectable medications were given by the health worker who also monitored daily drug swallowing along with the treatment supporter. Regular monitoring of patients was carried out based on the protocol recommended by the national guidelines. The monitoring officer

visited patients on treatment and DOTS centres regularly; and reported patients' complaints to relevant members of the consortium for necessary action. The consortium met every quarter of the year with emergency meetings held when necessary, to review progress and challenges encountered in the management of patients on treatment. Patients who had adverse reaction were reviewed by the relevant clinician. All patients with hearing impairments had audiometry to assess the severity of impairment for any interventions including drugs substitutions and provision of hearing aids.

This study evaluated the performance and feasibility of ambulatory and community based treatment of MDR-TB in Benue state so far, with a view to identifying the interim treatment outcomes and challenges.

METHODOLOGY

This was a retrospective cross-sectional study of MDR-TB patients on ambulatory and community based treatment in Benue State conducted in the month of July 2016. Medical records of patients, minutes of meetings of the consortium as well as reports of the monitoring officer over the period of January2014 to June 2016 were used.

Study population: These were patients who had been on ambulatory or community based treatment for at least 8months as at the time of the study.

Protocol: Records of all MDRTB patients who were on treatment for at least 8 months were reviewed. Information on Biodata, duration of treatment, HIV status, previous TB treatment, duration, outcomes and side effects of treatment were extracted and analysed using SPSS version16. Information from minutes of the consortium was also extracted and documented.

Definition of outcomes was based on the Nigerian national control program guidelines i.e. [7]

Cured - A DR-TB patient who completed treatment without evidence of failure and has three or more consecutive cultures taken at least 30 days apart that are negative after the intensive phase.

Completed treatment- A DR-TB patient who has completed treatment without evidence of failure but does not have three or more consecutive cultures taken at least 30 days apart which are negative after the intensive phase.

Treatment Failure - A DR-TB patient in whom treatment was terminated or need for permanent regimen change for at least two anti TB drugs because of

- Lack of conversion by the end of intensive phase or
- Bacteriological reversion in the continuation phase after conversion to negative or
- Evidence of additional acquired resistance to fluroquinolones or second-line injectable drugs or
- Adverse drug reaction

Loss to follow up- whose treatment was interrupted for 2 consecutive months or more,

Died – A TB patient who dies for any reason before starting or during the course of treatment.

Not evaluated- A DR-TB patient for whom no treatment outcome is assigned (this includes cases 'transferred out' to another treatment unit and where the treatment outcome is unknown to the reporting unit.

Treatment Success - The sum total of cured and treatment completed

Data analysis- Relevant data were extracted and analysed using SPSS version 16.0 Qualitative was expressed as percentages. A summary of observations from minutes of meetings was made and documented.

RESULTS

At the time of the study, 40 MDR TB patients had completed at least 8 months of treatment in their respective communities. There were 29 (72.5%) males and 11 females (27.5%) giving a male to female ratio of 2.6:1 with a mean age of 39.2years (range19-65years).HIV infection was found in 10 of 37 available HIV screening results giving a co-infection rate of 27%. A total of 22 (55%) out of the 40 patients had previous tuberculosis treatment with

first line medications. (TABLE 1) The most common side effects of drugs encountered were hearing loss (32.5%), and arthralgia (7.5%) while myalgia, dizziness, haematemesis occurred to a lesser extent. Of the 40 patients, 8(20%) had completed 20 months of treatment, 27(67.5%) were at various stages of continuation the phase (Ongoing). Loss to follow up (LTFU) and deaths accounted for 2(5%) and 3(7.5%) respectively. Case holding (made up of all patients except loss to follow ups) was 95 %. (TABLE 2)

Post treatment follow up sputum culture results were not available at the time of the study; therefore it was not possible to ascertain the status of cure for these patients. There was also an observed inadequacy of documentation of clinical, laboratory and radiological parameters in the patients' case notes. Extracts from minutes of the consortium and reports of the monitoring officer indicated that paucity of funds for monitoring activities, meetings and transport of specimens for culture and sensitivity testing was a challenge to success of the program.

Table 1. Characteristics of Patients

Age (years)	39.2±11.0 (Range16-65)
Age groups (years):	N^{o} (%)
<= 29	7 (17.5)
30 – 39	15(37.5)
40 – 49	12(30.0)
50+	6(15.0)
Gender:	N^{o} (%)
Male	29(72.5)
Female	11(27.5%)
HIV status:	N^{o} (%)
Positive	10(25.0)
Negative	27(67.5)
N/A	3(7.5)
Previous TB treatment:	N^{o} (%)
Yes	22(55.0)
No	14(35.0)
N/A	4(10.0)

Table 2: Adverse Drug Reaction and Treatment Outcomes

Adverse reactions:	N^{o} (%)
Hearing loss	13(32.5)
Dizziness	1(2.5)
Arthralgia	3(7.5)
Myalgia,	1(2.5)
Haematemesis	1(2.5)
Nil	21(52.5)
Treatment Outcomes:	N^{o} (%)
Unassessed (Ongoing)	27(67.5)
Died	3(7.5)
LTFU	2(5.0)
Completed	8(20.0)
Case holding	38(95%)

DISCUSSION

This study evaluated 40 patients that were on ambulatory and community based treatment for at least 8 months. The program achieved 95.0% case holding with only 5% lost to follow up. This indicates that community based treatment is feasible, practicable and acceptable to patients. This is similar to findings by Shina et al (2004) in Peru who reported successful treatment of MDR-TB in the community with low default rates [2] .Waheed et al (2011) in Pakistan and Moyo et al (2015) in South Africa however reported high loss to follow-ups of 47.2% and 30.0% respectively in their studies [6], [9]. This difference from the Pakistani and South African studies could be from the differences in patient selection, our study included carefully selected suitable patients of small sample size. We are of the opinion that careful patient selection and adequate counselling could lead to better adherence. This seems to be the implication of earlier reports by Cavanaugh et al (2016) in Bangladesh and Medicines Sans Frontiers (2012) in Uganda who independently reported high acceptability and patients' preference for community based treatment [8]. [10]. Moreover, large scale Meta analysis of several studies did report superior cure rates or no significant differences in outcomes between community and hospital based treatments [11], [12], [13], [14]. Although our review did not include a detailed study of earlier concerns about outpatient treatment

in respect of the need to monitor complex drug regimens and limit disease spread within the community, our observation was that, it did not impair adherence to treatment by patients. This tends to agree with findings in other studies [6], [8], [13]. Similarly fears about spread of MDRTB in the community appear to be insignificant considering that such patients are already living in the communities and could even spread more MDRTB if not started on treatment [6], [8], [13]. This form of treatment also offers the advantage of reduced socioeconomic costs as well as emotional support by patients' relations and friends at home [6], [8].

Hearing loss was the major adverse reaction. This is similar to reports from Bangladesh, Peru, South Africa and others where incidence of hearing loss ranged from 10-30% [10], [14], [15].Most of the regimens used contain highly ototoxic medications such as Amikacin and Kanamycin. Arthralgia, gastrointestinal symptoms, and musculoskeletal pains were few or absent in our study unlike the others. This may be due to under reporting of adverse effects by patients or poor documentation. In the study by Cavanaugh et al in Bangladesh, adverse effects were grossly under documented compared to findings from direct interviews with the patients. It also found as in our study that most side effects can be successfully monitored and treated at home [10].

The proportion of patients that failed first line treatment was relatively high (55%) among the enrolled DR-TB patients. This agrees with other findings that MDR-TB is driven by failure of effective National programmes [1], [6]. In Nigeria stock out of medications was rampant until recently with the possible consequence of patients interrupting their treatment or being exposed to substandard drugs, inadequate dosage and duration of therapy outside the National TB program. Some patients may interrupt or even abandon their treatment as soon as improvement occurs. [16]

We observed from program reports that there was paucity of funds for activities related to treatment such as regular monitoring. Since the program is donor dependent, delayed release of funding to an extent also led to delay in implementation of scheduled activities.

CONCLUSION

Ambulatory and community based treatment of MDR-TB is feasible and acceptable to patients in Benue State. However, documentation in patients' case notes was deficient and there is challenge of funding of treatment and related activities. Hearing loss is a major adverse drug effect of treatment.

RECOMMENDATIONS

Ambulatory and Community based treatment should be scaled up in Nigeria. The DOTS program should be strengthened to reduce prevalence of MDR-TB. Funding needs of the program should be met promptly. There should be improved documentation in patients' notes. Less ototoxic drugs need to be employed in the treatment of patients.

LIMITATIONS

The study was retrospective with a small sample size. A prospective study with larger sample size is needed to confirm these findings.

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