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'I'm fed up': experiences of prior anti-tuberculosis treatment in patients with drug-resistant tuberculosis and HIV

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SUMMARY

OBJECTIVES: To understand the impact of past experiences of anti-tuberculosis treatment among patients co-infected with the human immunodeficiency virus and multidrug-resistant tuberculosis (MDR-TB) on perceptions and attitudes towards treatment.

METHODS: Qualitative study using in-depth interviews with 12 HIV-MDR-TB co-infected patients in Mumbai, India.

RESULTS: Patients reported unnecessarily long pathways to care and fatigue with diagnostic and treatment procedures. In particular, they expressed concerns over the lack of efficacy of their current treatment regimen based on their experiences with anti-tuberculosis treatment regimens in the past.

CONCLUSION: Patients reported negative experiences with previous HIV and anti-tuberculosis treatment. Access to early diagnosis and rapid initiation of integrated care for HIV-MDR-TB co-infected patients, with a strong, patient-centered support system, could help to combat the low morale and lack of faith in treatment described in this group of patients.

KEY WORDS: human immunodeficiency virus; TB-HIV; multidrug-resistant tuberculosis; treatment adherence; qualitative study; India; operational research

TUBERCULOSIS (TB) is one of the main infectious diseases in the world today, with more than eight million cases and one million deaths reported annually.[1] Multidrug-resistant forms of TB (MDR-TB, defined as strains of *Mycobacterium tuberculosis* with in vitro resistance to at least isoniazid and rifampin)[2] are becoming an increasing global public health problem.[3] These strains have been associated with higher degrees of morbidity and mortality than pan-susceptible strains,[4,5] although acceptable outcomes can be achieved under certain conditions.[6] Such conditions require early diagnosis, timely access to appropriate treatment and regular treatment for a period of 18–24 months.[7]

Although access to diagnosis and treatment for MDR-TB is improving worldwide, significant gaps still need to be addressed.[8] The majority of patients do not have access to drug susceptibility testing (DST) at the time of TB diagnosis, and are thus started on empiric TB treatment.[9,10] While this treatment is successful in the majority of cases, substantial populations of individuals infected with drug-resistant strains of TB do not benefit from this empiric treatment.[11] In addition to suffering increased morbidity and mortality, as well as the possibility of recruiting additional resistance to TB during empiric treatment,[12] these individuals remain infectious.[13] For these reasons, multiple public health and advocacy groups have called for more timely diagnosis of and treatment for MDR-TB.[14,15]

The potential public health consequences of late diagnosis and treatment for MDR-TB have been described.[16–18] However, the impact of previous anti-tuberculosis treatment on patients' current experiences of MDR-TB treatment, especially among HIV co-infected patients, has not been reported. An understanding of the experiences of these patients is important, as such experiences may affect patient outcomes, particularly adherence to treatment.

The objective of this qualitative study is to explore the experiences of a group of co-infected MDR-TB-HIV patients who had received anti-tuberculosis treatment in the past, with a focus on understanding how such past experiences impact their current perceptions of treatment.

METHODS

Setting

The study took place at an out-patient MDR-TB treatment program supported by Médecins Sans Frontières (MSF) in the city of Mumbai, India. MSF

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began treating MDR-TB among HIV-infected patients in May 2007, and by April 2012 the cohort had registered a total of 120 patients. Patients received treatment through an ambulatory community-based program described elsewhere.[19] The data presented in this paper are drawn from a larger qualitative study conducted between April and October 2012 among patients with HIV and MDR-TB and their care givers.[20]

Participants

Thirty-three patients were actively receiving treatment at the time the study was conducted. Twelve of these patients were purposively selected to participate in the larger qualitative study described above, and data from these individuals are included in this subanalysis. Patient interviews were conducted in Hindi or Marathi and covered their experiences of help seeking prior to enrolment at the MSF clinic.

Data collection

Data were collected between May and September 2012. Informed consent was obtained from all participants before the interview. In-depth interviews were conducted with participating patients by an experienced qualitative researcher who was external to the program and spoke the three languages common to the patients interviewed (Hindi, Marathi, English). The majority of the interviews were recorded using a digital recorder, transcribed and translated into English. Notes were taken in cases where the respondents did not wish to be recorded and were expanded immediately afterwards.

Data analysis

A thematic analysis was performed to analyze the data in the study.[21] The data transcripts were read and reviewed manually by one of the medical anthropologists on the team (JF). First, the larger data set was read through to assess patient reports of previous treatment experiences. A number of themes were uncovered during this initial review, all of which were transcribed onto note cards with corresponding patient ID numbers and thematic codes. The second and third reviews were performed to further refine the themes, identify and code any subthemes, and group responses according to subtheme. A fourth review enabled verification of the subthemes that had emerged in previous reviews of the data. Finally, a second investigator (PI) reviewed the transcripts to enable cross-validation of the themes identified. Differences in interpretation were discussed and resolved by the two investigators.

Ethics

The study was approved by the Institutional Review Board of the Maharashtra Association of Anthropological Sciences – Centre for Health Research and Development, Pune, India. The MSF Ethics Review Board, Geneva, Switzerland, reviewed the protocol and advised on the study. Patients were given information about the purpose of the study and their role within it, and informed consent was obtained from them if they were available and willing to participate.

RESULTS

Patient characteristics

Of the 12 respondents, 8 were men, 3 were women and 1 was transgender (TG). All except one were between 35 and 55 years; the TG was 25 years old. Most of the respondents had completed only a few years of schooling; only one female respondent had 2 years of college education. Almost all the respondents were residents of Mumbai and its extended suburbs. One male respondent had completed treatment and one man and one woman were about to complete treatment at the time of interview. Of the remaining 9, 6 were in the intensive phase of treatment and 3 were in the continuation phase. The patients reported a median of 2.2 previous courses of anti-tuberculosis treatment, a median of 33 months of combined length of previous treatments and a median of 4.5 treatment institutions where the previous anti-tuberculosis treatment had been provided.

Thematic areas

Three main themes pertaining to previous experience of anti-tuberculosis treatment emerged from the data: 1) long pathways to care before the initiation of MDR-TB treatment, 2) diagnostic and treatment fatigue, and 3) lack of faith in treatment efficacy.

Long pathways before MDR-TB treatment initiation

All 12 patients described long and complicated pathways of care before being diagnosed and started on treatment for MDR-TB. Patients were sent from one public or private facility to another, made multiple visits to see the doctor and waited for long periods before they received treatment for MDR-TB. Similar experiences were also reported when receiving HIV treatment. This resulted in all of the patients going through one and often two courses of first-line anti-tuberculosis treatment before they were investigated for MDR-TB and reached MSF for their treatment. The experience of patient P06, a 41-year-old male who was sick for two and half years before receiving appropriate MDR-TB treatment, is typical of what was described by patients in the study:

> I had an ear infection and there was pus coming out of my ear. I had to go to K (municipal hospital) to get operated for that (. . .). That's when it was found that I have HIV (. . .). Then I had this back problem and I could not move my leg properly. The doctor said that this could be because of water in the spine (. . .) I was

> sent to the bone doctor. He was avoiding to do an operation and my condition worsened. For a year and a half, the doctors could not even tell me if I had TB. They could see the TB in the X-ray but not in the sputum. They would ask me to test the saliva all the time and I got fed up with that as there was nothing showing in that. They just kept testing the sputum and that was negative. It is only when they took the spinal fluid out that they found I had TB. So for 6 months I took [TB] pills from K. Then when they did an X-ray again the patch had increased. They said I have to start something called 'tack two' [referring to Cat 2 regimen]. So I started that and took it for 4 months but that made me worse. I could not sit or stand at all. They then removed the water from my back and they checked it at H (private hospital) and they found that I have MDR-TB and they asked me if I can take medicines from outside. I told them that I could not afford that so they sent me here to MSF. I could not even walk at the time (P06).

Moreover, patients diagnosed in the private sector typically incurred significant expenses. Just over half of the patients described waiting for long periods of time before they were able to find the money or before finding a charity that could support their treatment. As few providers knew about the free MSF treatment for MDR-TB and second-/third-line antiretroviral therapy (ART), patients took time to reach MSF even after being diagnosed with MDR-TB. Several, like Patient P12, a 36-year-old woman who was sick for 3 years and saw at least six different practitioners before receiving her MDR-TB and HIV treatment, expressed feeling physically, financially and emotionally drained by the time they reached MSF:

> The doctor [at the public sector hospital] did not say it directly … he said it would be little expensive. I thought it will be a 1000 [rupees] or so but when I went to buy it I found out that it will be 12 000 or 14 000 per month and I would have to take it for at least 2 years. I did not have the capacity to spend that much. And I have lost courage and hope too. My sons too were not working at that time. It took long [2 months] to find out where I could get the support for cost of medications. (…) So first I looked around. At that time, 4–5 years had passed and [I thought] that another couple of months would not make much difference. If the condition of a person is so bad, the person is bedridden, what can this person do? (P12)

Diagnostic and treatment fatigue

The majority of the patients interviewed expressed being tired or 'fed up' with having to undertake several diagnostic tests and/or taking medications. Most of them had to undergo a battery of diagnostic tests by different providers before they would even be considered for MDR-TB treatment, including X-rays, blood tests and hearing tests. As some of these tests were not available at the same diagnostic centers, the majority of the patients reported having to make trips to several facilities. All of them noted the difficulty of undertaking multiple tests, especially when they were feeling physically unwell. The exhaustion reported by Patient P3, a 53-year-old man with HIV and MDR-TB, was commonly shared:

> There was confusion when the people at [Hospital A] made me run here and there. They got me tested for different things. They used to call me on different days for different tests. Sometimes they used to ask me to get the X-ray performed in 4 days and after 4 days get other tests done. Then they used to give me 15 days' time and told me to get the report. It used to take a lot of time. The area over there is very big. (P3)

Just over half of the patients interviewed (7/12) also reported fatigue over having to take medicines for long periods of time. Typically, these individuals had received at least two previous courses of anti-tuberculosis treatment, which consisted of two to four medications taken daily for a minimum of 6 months per treatment. HIV treatment consisted of three medications taken once or twice a day for life, along with at least one other tablet taken daily to prevent infection. Treatment for MDR-TB required taking five to six medications daily for 18–24 months, and most of the daily doses of each medication required two to three tablets each. At the time of the study, the patients were at different stages of MDR-TB treatment, which is often associated with severe side effects and daily injections. The large pill burden, the duration of their current treatments for HIV and MDR-TB and the long pathways described above left many of the patients tired, and at times angry. Patient P13, a 38-year-old male whose wife had died of HIV, described the frustration of most of the patients in the study:

> To speak about myself, I really think it is difficult to express. Taking so many tablets, going through so much pain, I am fed up. (P13)

Patient P09, a 25-year-old TG individual, echoed other patients when she voiced a sense not only of fatigue with treatment but with life in general:

> I used to feel that I take so many pills and an injection and do not eat well. I am not getting better. I would feel, what is the use of life like this? So I used to sit in a lot of tension. (P09)

Lack of faith in treatment efficacy

More than half of the patients interviewed (7/12) expressed concern that their current treatment might not work or they might not be cured of MDR-TB. Most of the patients in the study had received at least one course of treatment that did not cure them of TB (likely due to the fact that they had drug resistance from the start, but were empirically treated for pan-susceptible TB), and many of them had received two

previous courses of anti-tuberculosis treatment and were still suffering from the disease. It was common for such individuals to no longer believe that their TB could be cured. When this experience of not being cured was combined with the messages they received about HIV not being a 'curable disease', many patients expressed a general sense that even with medications they would not get better. The despair of such patients was articulated by patient P06, a 41-year-old male who underwent three courses of anti-tuberculosis treatment:

> I had all kinds of thoughts. I thought that I would never get better now. What the use of living like this was? I was sure that there is no way to get better with all this. I would think about suicide. I thought what was the use of taking so many medicines if there is no hope of a cure. (P06)

Lack of faith in treatment efficacy also stemmed from the fact that many patients perceived that previous treatments as well as the current regimen made them feel more ill, rather than providing relief or curing them. Again, patient P06 described this very clearly:

> It was not a good time as I took the pills and kept going there all the time. There were no visible signs of any benefit at the time. It was more problematic – it worsened my condition. (P06)

While many patients were concerned about the lack of efficacy of their treatment based on their own experiences, some of them also reported that they were told by care givers that treatment would not work for them. According to many patients, doctors, nurses, and treatment supporters had doubts about the treatment the patients were receiving and expressed this doubt either directly in conversation with the patient or with other staff in front of the patients. Patient P08 was a 35-year-old man who was sick for almost 2 years before he was started on MDR-TB and HIV treatment. His lack of faith in treatment came from what he heard from providers:

> So here, doctors, sisters [nurses] would all say: 'what is happening? ... the medicines are not affecting you ... the medicines should work in a month or two. (P08)

For some patients, the loss of faith in their medications was mitigated by family support and, more generally, by having a strong social support system. Thus, while they themselves reported having little faith in the power of treatment to make them well, they were encouraged by friends and family around them. The positive experiences of such individuals are reflected in the words of Patient P02, a 40-year-old man living with his wife and extended family:

> I do not think what will happen to me? What will happen tomorrow? I feel I will deal with whatever comes my way. I never have tension. [English word used]. I believe that whatever has happened has happened and I have to live with it ... The best part is that I have a lot of support from my family, my wife, and my parents (P02).

DISCUSSION

To our knowledge, this is the first qualitative study of an Indian cohort of HIV-MDR-TB co-infected patients providing insight on how patients' experiences with previous anti-tuberculosis treatment might affect their current treatment experiences.

This study reveals some disturbing themes in a population of patients undergoing treatment for MDR-TB and HIV in Mumbai. All of the patients interviewed in the study reported unnecessarily long pathways to care, and the majority reported a high level of fatigue related to both diagnosis and treatment. This feeling may be associated with an increased risk for loss to follow-up from treatment and care, especially given the pill burden and duration of current treatment for MDR-TB.[22,23] Studies on other diseases, including HIV, asthma and hypertension, show a clear association between delays in accessing care and poor treatment outcomes as well as a sense of exhaustion with treatment and poor treatment outcomes.[24–26] Of note, the pathways to care among co-infected patients were usually longer than those infected with HIV or MDR-TB alone, as care for TB and HIV is not integrated in most programmes in India.

The majority of the patients in this study also expressed a loss of faith in the efficacy of their current treatment regimen based on their previous treatment experiences. This loss of faith may directly affect adherence to a long and difficult treatment regimen such as the one used for MDR-TB.[27] Perceived lack of efficacy has been noted to be linked with poor outcomes of a number of diseases,[28] and studies conducted among persons with HIV have found that a perceived lack of treatment efficacy was one of the primary reasons why people discontinued ART.[29]

There are a number of public health implications from this study. First, the findings suggest the need to reduce time to diagnosis and initiate appropriate treatment for MDR-TB to restore patients' and family members' faith in treatment efficacy and reduce the risk of treatment fatigue. Second, our findings suggest that in Mumbai, as in other settings with a high burden of drug-resistant TB, patients continue to be treated with empiric first-line anti-tuberculosis treatment without performing systematic DST, mainly due to limited resources. This may result in a population of patients being subjected to

ineffective treatment,[30,31] with attendant medical consequences.[31,32] Increased access to DST in these settings is required to address these concerns.

Third, the study also reveals diagnostic/treatment fatigue and loss of faith in treatment efficacy that could affect adherence to treatment and adversely affect MDR-TB treatment outcomes, as has been reported in pan-susceptible TB.[33] The introduction of rapid molecular methods for diagnosis of MDR-TB could accelerate the initial diagnosis of MDR-TB.[34]

Along with improved diagnostics is the need for rapid initiation of appropriate MDR-TB treatment, as recent studies have shown that a substantial proportion of patients diagnosed with MDR-TB never initiated treatment.[35] Given the challenging current treatment options we offer to patients, a strong psychosocial component should be part of every MDR-TB treatment program, and patients and their families should be supported throughout their efforts to be diagnosed, initiate treatment and successfully complete treatment.

Some limitations to this study need to be acknowledged. As the analysis draws on a larger qualitative study that did not have treatment experience as the main focus, some experiences may have been underreported. We were also not able to probe into some topics, as would be the case in the primary study. However, the themes that were revealed were quite clear and consistent. The study was limited to a specific context (i.e., a group of patients being treated at an MSF clinic) and reported on co-infected patients only; their experiences may therefore not be representative of the wider, global cohort of MDR-TB patients. However, we believe that the data reflect diversity in experiences and views. A strength of this methodology is that it can uncover aspects of patient experiences that may not be revealed in more structured and quantitative studies, and also allows the description of the context in which these experiences occur. Variations in context should, however, be considered before generalizing these results to other settings

In conclusion, this qualitative study revealed a significant burden of suffering among HIV-MDR-TB co-infected patients in Mumbai. Long delays in diagnosis and treatment and previous experience of substandard treatment had led to profound physical and mental fatigue among the patients and a sense of hopelessness regarding their recovery. There is a clear need to examine the treatment-seeking pathways of patients with MDR-TB and HIV and to identify the critical points at which delays are incurred and patients' time, money and energy are expended at severe cost to themselves and their families.

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RESUME

OBJECTIFS : Comprendre l'impact de l'expérience d'un traitement passé de la tuberculose (TB) chez des patients co-infectés par le virus de l'immunodéficience humaine (VIH) et une TB multirésistante (TB-MDR), sur leurs perceptions et attitudes vis-à-vis du traitement.

MÉTHODES : Etude qualitative basée sur des entretiens approfondis avec 12 patients co-infectés par le VIH et une TB-MDR à Mumbai, Inde.

RÉSULTATS : Les patients se sont plaints d'un cheminement inutilement long vers le traitement et d'une fatigue très importante liée aux procédures de diagnostic et de traitement. Ils se sont montrés particulièrement préoccupés par l'inefficacité potentielle de leur protocole de traitement actuel en fonction de leur expérience des protocoles de traitement du passé.

CONCLUSION : Les patients ont rapporté des expériences négatives de leurs précédents traitements du VIH et de la TB. L'accès à un diagnostic précoce et une mise en route rapide d'un traitement intégré du VIH et de la TB-MDR des patients co-infectés, couplée à un système de soutien solide, centré sur le patient, pourrait contribuer à lutter contre la baisse de moral et le manque de confiance dans le traitement évoqués par ce groupe de patients.

RESUMEN

OBJETIVOS: Comprender la repercusión de las experiencias anteriores con el tratamiento antituberculoso en personas que padecen coinfección por el virus de la inmunodeficiencia humana (VIH) y tuberculosis multidrogorresistente (TB-MDR) y evaluar las percepciones y actitudes de los pacientes frente al tratamiento.

MÉTODOS: Se llevó a cabo un estudio cualitativo mediante entrevistas en profundidad a 12 pacientes que presentaban coinfección por el VIH y TB-MDR en Mumbai, en la India.

RESULTADOS: Los pacientes refirieron mecanismos innecesariamente prolongados hasta la obtención de atención sanitaria y una gran fatiga con los procedimientos diagnósticos y terapéuticos. Expresaron sobre todo preocupación con la falta de eficacia de su tratamiento actual, dadas sus experiencias con regímenes antituberculosos recibidos en el pasado.

CONCLUSIÓN: Los pacientes notificaron experiencias negativas con los tratamientos previos contra el VIH y la TB. Lograr el acceso al diagnóstico precoz y comenzar prontamente una atención integrada de la infección por el VIH y la TB-MDR en los pacientes coinfectados, mediante un sistema de apoyo eficaz centrado en el paciente, podría contribuir a combatir la desmoralización y la falta de confianza en el tratamiento recetado a este grupo de personas.