

Frequency of Category 1 and Category 2 Tuberculosis in District Kotli Azad Kashmir

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ABSTRACT

Objective: To estimate the frequency of Category 1 and 2 Tuberculosis in area of research.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted in District Kotli Azad Kashmir from January 2009 to December 2009.

Material and Methods: This study was conducted with a population of 750,000. Data was collected from all the eight national TB centres in the District Kotli. It included every patient registered there with the diagnosis of tuberculosis including pulmonary and extra pulmonary tuberculosis and sputum smear positive and negative patients. They were classified as category 1 and category 2 according to the standard definitions. Results were given in tabulated form.

Results: From a total of 752 patients, 579 (76.99%) were pulmonary and 173 (23%) were extra pulmonary. In pulmonary TB cases, 259 (44.78%) were sputum smear positive [235 (90.73%) of them were category 1 and 24 (9.24%) were category 2]. In 320 (55.26%) sputum smear negative patients, 300 (93.75%) were category 1 and 20 (6.25%) were category 2. All of the extra pulmonary TB cases were category 1 (100%). As a whole 708 (94.15%) were category 1 and 44 (5.85%) were category 2.

Conclusion: In our study frequency of category 2 patients was found to be relatively low. It indicates that the problem of drug resistant tuberculosis is probably low in the area. It also shows the effectiveness of local TB control programme.

Key words: Category 1 and category 2 tuberculosis; MDR tuberculosis; Azad Kashmir

INTRODUCTION

Tuberculosis (TB) is highly prevalent in Pakistan. Pakistan is included in top five countries with highest burden of the disease. It is second most common cause of death among the infectious diseases.¹ Treatment of TB poses a special problem especially for poor countries like Pakistan. Due to peculiar structure of mycobacterial cell wall, most of the common antibiotics are not effective. There are limited numbers of antibiotics which must be given in combination for a prolonged period of time. Although with treatment TB is a curable disease in almost all the cases of drug sensitive tuberculosis, but without treatment 50-65% of patients die within five years.² Treatment regimens are costly and prolonged and are associated with many side effects which makes the compliance difficult. So there are quite high chances that patients may leave the treatment before it is complete. Lack of health education compounds the problem further. This is dangerous because it leads to emergence of drug resistant tuberculosis which is very difficult to treat. A report from Delhi, India clearly demonstrated that primary resistance was responsible for only 1.4% cases

of MDR (Multi Drug Resistant) TB, the rest being due to improper treatment.³

TB is a highly contagious disease and can easily spread by droplet infection to the close contacts of the patient. All over the world approximately two billion people are infected but most of them are asymptomatic.⁴ There were approximately 8.7 million new cases of TB throughout the world during the year 2011.¹ Millennium Development Goal (MDG) target was set by WHO to stop the progression and reduce the incidence of tuberculosis epidemic by 2015 and to eliminate the TB as public health problem by 2050.¹ One of the best ways of preventing the disease is to detect and treat the patients as early as possible before they can transmit the infection to others. So the efficient and appropriate treatment of TB is essential. But achieving this goal is not easy because of the problems related to the treatment of TB mentioned earlier. In practice most of the patients may start the treatment but many of them default before the completion. Today we know that MDR TB is a man made problem because of improper treatment of tuberculous cases.⁵

In a study from India the incidence of MDR TB in Delhi was found to be 14%.³ These patients are very dangerous to the community and their treatment is

really challenging. The success rate for MDR TB was 60-80% and for XDR (Extensive Drug Resistance) TB 44-60%.⁵ They cannot be treated with routine anti TB regimens and need second line drugs which may be more expensive and cause more side effects.⁶ Although the treatment is possible with currently available drugs but the chances of treatment failure are high with a higher mortality.⁷

There are a number of factors responsible for development of drug resistant TB. One of the most important factors is the previous history of treatment with anti TB drugs.⁸ Considering the importance of this factor, TB cases have been divided into two groups as following:

Category 1: Newly diagnosed cases of tuberculosis who never received the anti TB treatment before. Chances for them to be drug resistant are quite minimal and they can be started on the routine standard treatment of TB i.e. 2(R, H, Z, E) and 4(R, H).

Category 2: Patients presenting with tuberculosis who have previously received anti TB treatment. These include treatment failure cases, relapsed cases or those who defaulted without completing the treatment and now returned after treatment interruption.⁹

Chances of category 2 patients to have drug resistant tuberculosis are so high that they are treated with special intensive anti TB regimens which include five drugs in first two months, four drugs for next one month and then three drugs for subsequent five months e.g. 2(S, R, H, Z, E), 1(R, H, Z, E) and 5(R, H, Z). Rise in incidence of drug resistant tuberculosis along with the pandemic of HIV and increased population movement are a big obstacle to the effective control of TB all over the world.¹⁰ Constant provision of funds to implement the regional and global action plans against tuberculosis are needed for control of MDR and XDR TB and it needs the committed political leadership which can understand and foresee the magnitude of the problem.¹⁰

It is clear that treatment of category 2 patients is very difficult due to obvious reasons. If these patients are not recognized at the onset and not started on appropriate treatment, chances of their cure are minimal. This is dangerous for themselves as well as for the community. Furthermore inappropriate treatment may lead to XDR TB which is extremely difficult to treat. Keeping in mind all these factors we have tried to determine the frequency of category 1 and category 2 patients in district Kotli Azad Kashmir, a remote area towards north of Pakistan. This will indirectly assess the problem of drug resistant tuberculosis in the area. It will also throw light on the success and effectiveness of TB control programme. The data may be used for proper planning and appropriately targeting the efforts and resources of anti TB control programmes. The data may also be helpful for further research to determine the actual incidence of drug resistant tuberculosis in category 2 patients by doing culture and sensitivity of their sputum samples.

MATERIALS AND METHODS

This was a cross sectional study conducted in District Kotli Azad Kashmir which is an area towards north of Pakistan with a population of 750, 000. Data was collected from all the eight national TB centres in the District Kotli. It included every patient registered there with the diagnosis of tuberculosis from January 2009 to December 2009. All the patients of tuberculosis including pulmonary TB, sputum smear positive and negative patients and extra pulmonary cases were classified as category 1 and category 2 according to the standard definitions mentioned earlier in the introduction. Results were given in tabulated form.

RESULTS

Total of 752 patients were registered as tuberculous during the study period. Among them 579 (76.99%) were pulmonary and 173 (23%) were extra pulmonary tuberculosis. In pulmonary TB cases, 259 (44.78%) were sputum smear positive of whom 235 (90.73%) were category 1 and 24 (9.24%) were category 2. In 320 (55.26%) sputum smear negative patients, 300 (93.75%) were category 1 and 20 (6.25%) were category 2. All of the extra pulmonary TB cases (100%) were category 1. As a whole from total of 752 patients, 708 (94.15%) were category 1 and 44 (5.85%) were category 2. (See Table 1 and Figure 1)

Table No.1: Category of TB cases in various types of tuberculosis

Type of tuberculosis		Category of cases		Total
		Category 1	Category 2	
Pulmonary	Sputum smear positive	235 (90.73%)	24 (9.24%)	259
	Sputum smear negative	300 (93.75%)	20 (6.25%)	320
Extra pulmonary		173 (100%)	0	173
Total		708 (94.15%)	44 (5.85%)	752

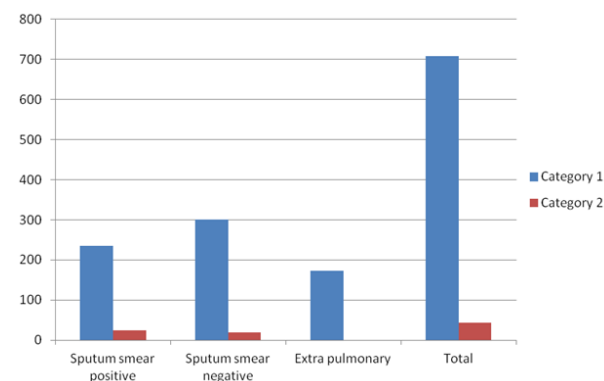


Figure No.1: Number of category 1 and category 2 cases in various types of tuberculosis

DISCUSSION

Tuberculosis is one of the oldest infectious diseases in the human history. Its treatment and control has always remained a challenge. With the development of anti TB drugs it was felt that the time of tuberculosis was over. But from the very beginning it was associated with multiple problems. We had only limited number of anti TB drugs. Streptomycin (S), Rifampicin (R), isoniazid (H), Pyrazinamide (Z) and Ethambutol (E) were the first line anti TB drugs. Most of the countries with highest disease burden were poor with very low economic resources to implement the proper TB control programmes and to provide complex and costly anti TB regimens. On top of that many of them were affected by political and social unrest, conflicts and corruption. Emergence of HIV epidemic in 1980s dramatically increased the incidence of TB throughout the world. Pakistan was amongst those with highest disease burden. WHO survey has indicated that incidence and prevalence of TB in Pakistan is 230 and 310 per hundred thousand respectively while the mortality is estimated to be 39/100,000.¹¹ With the consideration of poverty, poor socioeconomic conditions and lack of proper health facilities, it is extremely difficult to treat such an enormous number of patients adequately. Currently the world is facing another great problem in the control of TB i.e. the emergence of multi drug resistance (MDR) and extensive drug resistance (XDR) tuberculosis. MDR is defined as resistance against at least two drugs Rifampicin and Isoniazid, which are very important first line anti TB drugs. XDR is characterized by development of resistance, apart from rifampicin and INH, against one of the fluoroquinolones and one or more of the second line injectable drugs like Kanamycin, Capreomycin or Amikacin.^{5,2} This is a very dangerous development. Treatment of MDR and XDR TB is extremely difficult. It needs addition of more drugs including second line drugs which increases the cost and toxicity of the regimens.⁶ According to recommendations at least four drugs should be given to which mycobacterial isolates are sensitive. The drugs are chosen from five groups in a stepwise fashion on the basis of their efficacy, safety and cost.¹³ Previous treatment with second line drugs has increased the risk of resistance to these drugs leading to development of XDR TB.¹⁴ MDR TB is a major hurdle to TB control especially in certain areas of the world like some provinces of China and countries from former Soviet Union.^{15,16}

Drug resistance can develop in category 1 patients due to random genetic mutations in the mycobacteria but its frequency is very low. Exposure to anti TB drugs leads to selection pressure with predominant survival of drug resistant strains over susceptible strains. According to fourth report of global anti TB drug resistance, the prevalence of MDR TB in category 1 was 1.6% and in

category 2 it was 11.7%. During 2006 there were half a million MDR TB cases and 50% of them were in China and India.¹⁷ In 2008, 440,000 cases of MDR TB were found globally and it led to death of 150,000 patients. Among MDR TB, 5.4% were found to be XDR. All this is a man made problem which can be prevented by effective and prompt first line anti TB therapy of category 1 patients.¹⁸

A study from India found that prevalence of MDR TB was 20.4% among patients of category 2 pulmonary TB. Various other studies from India showed the prevalence of MDR TB to vary between 14 to 49% in patients who previously had received anti TB treatment. Such findings suggest that all category 2 patients should be screened for MDR TB. [9] On the other hand prevalence of MDR TB is low in category 1 pulmonary TB cases. A study from India showed the prevalence in such cases to be 1.1%. In various studies from India it varied between 0.14% to 5.3%.¹⁹ In a study from Gujarat state of India, MDR TB was found to be very low in category 1 patients (2.4%) but it was quite high in category 2 patients (17.4%). Among MDR cases there was very high resistance rate against Ofloxacin (24%) which can hamper the treatment and control of MDR TB.²⁰

It is of utmost importance to detect MDR and XDR TB cases early and start them on appropriate treatment. This can be done by high quality culture and sensitivity tests. But it is difficult and expensive. History of previous treatment with anti TB drugs is reliably associated with the risk of drug resistance and detection of category 2 patients can recognize those at risk of drug resistant tuberculosis. They can then be started on more intensive treatment regimens. In our study overall less than 10% patients were category 2. This is rather welcoming news because frequency of drug resistant TB is much higher in many parts of the world. Incidence of MDR tuberculosis in Delhi was 14% most which was due to improper previous treatment.³ According to WHO data from Pakistan, during 2012 frequency of MDR TB in retreatment cases was 32% while it was only 3.5% in newly diagnosed cases.²¹ More than 510,000 cases of MDR TB occur annually.²² According to a survey report from America, 20% of the isolates were MDR and 2% were XDR.²³

Treatment and control of MDR and XDR TB is cumbersome and its cost can be so high that it can drain all the money from the insufficient resources of the poor countries. It can destroy all our efforts for the control of TB globally.⁵ Stop-TB Drug-Resistance Programme was started to ensure optimal delivery of appropriate anti TB regimens. Its key components include strong political commitment, quality-assured drug susceptibility testing, reliable supply of good quality drugs, directly observed therapy settings, and strict monitoring of the individual treatment outcome and overall performance of the TB control programme.

[6] MDR TB is more common in poor and developing countries and more funds should be allocated for them to provide its quick and effective treatment. It is now possible through the Global Fund to Fight AIDS, TB, and Malaria, and the Green Light Committee for Access to Second-line Anti-tuberculosis Drugs.²⁴ To control tuberculosis it is essential to involve all the public and private practitioners and train them properly in the diagnosis and treatment.²⁵

In their study, Dr Mercedes C Becerra et al found that the households contacts of drug resistant tuberculosis patients, who developed active TB and who were tested for drug resistance, had very high frequency of MDR TB (90.9%).²⁶ According to these results, the chances of drug resistant TB in the household contacts of MDR and XDR TB patients are so high that if they are found to have active TB, they should be considered as category 2 patients and started on category 2 regimens although they may not have previous history of partial or complete anti TB treatment.

Low frequency of category 2 patients in our study indicates that the risk of MDR and XDR is probably low in the area. Further studies are needed to estimate the exact frequency of drug resistant tuberculosis in these category 2 patients. To minimize the risk of drug resistance we must implement all the preventive strategies like early diagnosis and treatment of category 1 patients, proper follow up and surveillance, inclusion and training of both private and public practitioners in the TB control programmes and efficient detection and appropriate treatment of category 2 cases. This needs a strong political will and constant supply of necessary funds.

CONCLUSION

MDR and XDR TB is an emerging problem throughout the world which can destroy all our efforts to control tuberculosis and eliminate it as a public health problem. Diagnosis of MDR and XDR TB needs costly investigations which are difficult to afford by a poor countries like Pakistan. Measuring the incidence of category 2 patients can give an indirect estimate of drug resistant TB. In our study frequency of category 2 patients was found to be relatively low. It indicates that problem of drug resistance is probably low in the area. It also shows the effectiveness of local TB control programme.

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