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COMMON FACTORS INFLUENCING DISEASE RECURRENCE RELAPSE AND RE-INFECTION IN TREATED PATIENTS OF TUBERCULOSIS

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Abstract:

Background: *Tuberculosis is a potentially life-threatening, airborne bacterial infection that can be found worldwide. The treatment regimen is a lengthy one, but if you stick with it and take medications the way you should, you can beat the disease. Even with treatment, however, you can get tuberculosis infection again.*

Objective: *TB recurrence, relapse and re-infection are becoming more common every day in successfully treated patients of tuberculosis. This study aims to determine the common factors influencing T.B recurrence, relapse and re-infection.*

Methods: *This multi-center, cross-sectional study comprised of 200 patients (64.8% males and 35.2% females) chosen via simple random sampling and undergoing treatment for recurrent, relapsed or reinfection of tuberculosis at different T.B centers namely: Government T.B Sanatorium Kotri, Bhittai Hospital Hyderabad, Civil Hospital Hyderabad and Civil Hospital Mirpurkhas, from 1st December 2014 to 10th February 2015. Verbal informed consent was obtained before administering structured self-administered questionnaires. The data obtained was analyzed using SPSS v. 19.0 and Microsoft Excel 2013.*

Results: *The study shows that males are more prone (27.3%) to get a relapse within 2 years while females are less prone 15%. According to social economic status, there is 74.9% chance of low economic class for TB relapse, 19.6 % in case of middle class and 5.5% in case of high economic class. TB is 55.3% more common in those patients whose family members are suffering from same disease. Among cases of relapse within 5 years, 95.6% took medicine without supervision, 86.6% were supervised by the family and 84% by the health professional. Urban areas are less affected with TB relapse within 5 years than the rural areas. Non-smokers are more affected within 5 years while smokers are comparably less affected with TB.*

Conclusion:*My study concluded that secondary TB relapse cases gender variation , social economic status , medical monitoring , TB regimen coarse , family history, smoking all are the common factors which influence TB relapse within 5 years or above 5 years.*

Keywords: *Tuberculosis, Tuberculosis relapse, Tuberculosis Recurrence and Tuberculosis Recurrence.*

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INTRODUCTION:

Tuberculosis (TB) has arguably killed more human beings than any other disease throughout history. Into the 21st century it is still one of the leading infectious causes of death, killing at least 2 million people every year [1, 2]. In 1993, the World Health Organization (WHO) declared TB a global emergency and subsequently suggested treatment strategy to control TB. The aim was to detect and treat cases of sputum smear-positive TB in order to reduce further transmission and control the spread of the disease.

Several studies suggest that patients infected with drug-resistant strains of Mycobacterium tuberculosis do poorly when placed on standard short-course chemotherapy. End-of-treatment outcomes in patients infected with multidrug-resistant (MDR) TB, defined as resistance to at least isoniazid and rifampicin, are reported to be no better than in the pre-chemotherapy era [3–6]. However, data are more limited on the impact of initial drug resistance on rates of relapse following cure. High recurrence, which can be either relapse of the same infection or reinfection, has been reported among small numbers of successfully treated patients diagnosed with MDR TB or with rifampicin-resistant TB [7–11].

Recurrent tuberculosis (TB) poses significant threats, including drug resistance, to TB control programs. However, recurrence and its causes, particularly in our modern era, have not been well described for patients in our part of the world. It is seen in common clinical practice that adequately treated patients, let alone maltreated individuals, are still at high risk for recurrent disease. The proportion of recurrent tuberculosis cases attributable to relapse or reinfection and the risk factors associated with these different mechanisms are poorly understood.

Recurrence of tuberculosis (TB) can be due to a regrowth of the same strain of Mycobacterium tuberculosis that caused the previous TB episode, known as relapse, or reinfection through a different strain. The data reported suggests that recurrence rate is low in countries with a low TB incidence and mainly caused by relapse of a previously cured TB episode [12-14]. The recurrence rate in countries of high TB incidence is elevated and reinfection is the principal cause [15], especially in the presence of high prevalence of coexisting human immunodeficiency virus (HIV) [16]. Studies carried out in countries of medium incidence suggest that relapse more commonly causes recurrence, although the rate of reinfection could still play an important role [17, 18]. Therefore, the relative contribution of recurrent TB on the overall annual TB incidence and the influence of relapse or reinfection is likely to vary depending on epidemiological features of the area [12-19].

Information about the epidemiological characteristics of recurrent TB is an important issue for public health programs to ensure appropriate health control strategies [20]. Moreover, recurrence rates can be used to assess the effectiveness of TB control programs. This study aims to determine the common factors influencing T.B recurrence, relapse and re-infection.

METHODOLOGY:

This multi-center, cross-sectional study comprised of 200 patients (64.8% males and 35.2% females), histo-pathologically diagnosed prior to inclusion, chosen via simple random sampling and undergoing treatment for recurrent, relapsed or reinfection of tuberculosis at different T.B centers namely: Government T.B Sanatorium Kotri, Bhittai Hospital Hyderabad, Civil Hospital Hyderabad and Civil Hospital Mirpurkhas, from 1st December 2014 to 10th February 2015. Verbal informed consent was obtained before administering structured self-administered questionnaires. Information was also obtained from the respective authorities of the health facilities. The data obtained was analyzed using SPSS v. 19.0 and Microsoft Excel 2013.

RESULTS:

The study shows that males are more prone (27.3%) to get a relapse within 2 years while females are less prone 15%. However, as the years progress, the scenario shifts and the propensity of encountering relapsed, recurrent or re-infected rate of tuberculosis is more inclined towards the fairer sex. Figure 1 below explains the phenomenon to a greater depth.

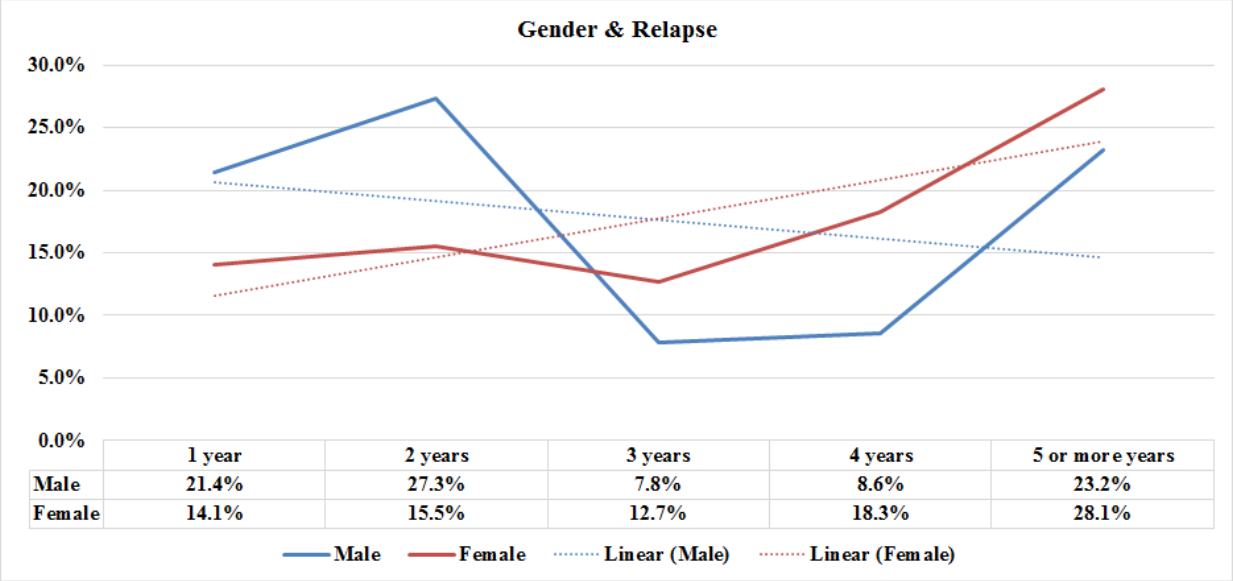

Fig 1: The relationship between gender and TB relapse, recurrence and re-infection are clear. In the initial years immediately following successful treatment show a greater predisposition for males and a lesser predisposition towards relapse, recurrence and reinfection for females. However, with the time the opposite trend appears in the sample.

According to social economic status, there is 74.9% chance of for patients belonging to the low economic class to encounter a TB relapse, 19.6 % in case of patients belonging to the middle class and 5.5% in case of patients falling in the high economic class. The trends however varied considerably with time. The details can are depicted in the figure 2 below.

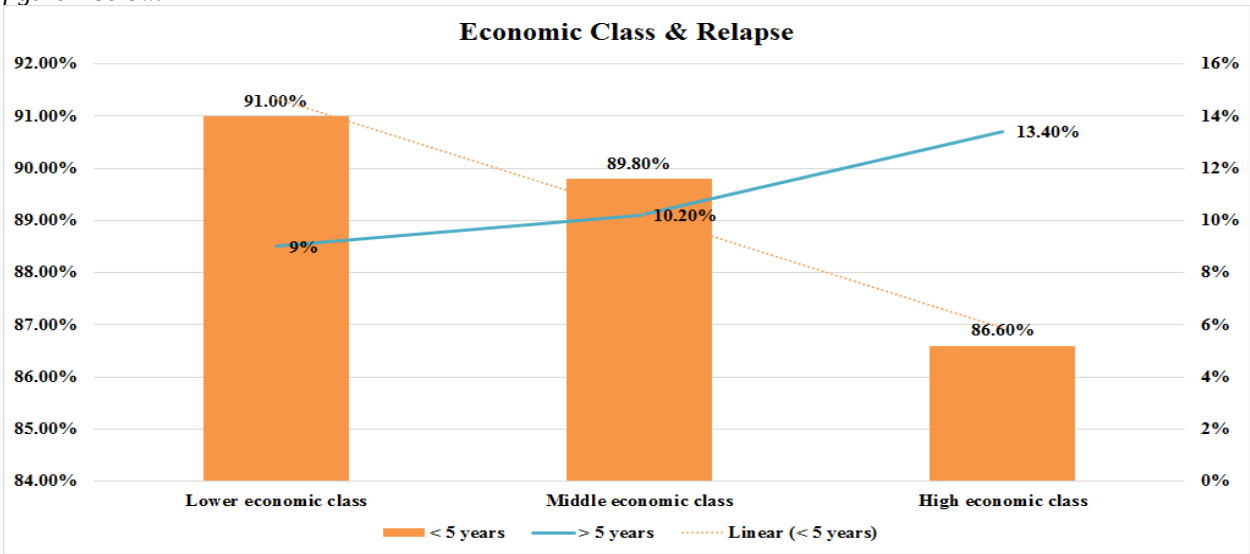

Fig 2: Patients belonging to all socioeconomic classes encountered relapse, recurrence and/or re-infection within five years. Chance existed to develop the disease after 5 years as well but the probability was considerably less but to variable extent. Low socioeconomic class had greatest chance o encounter relapse within five years of successful treatment and least chance of developing it after five years. The phenomenon is reverse for patients belonging to the high socioeconomic class. The middle economic class remained at a moderate probability level as compared to the other socioeconomic classes.

Among cases of relapse within 5 years, 95.6% took medicine without supervision, 86.6% were supervised by the family and 84% by the health professional. Although we maintain that all patients were successfully treated, and adhered to medication regimen, but the strictness of the adherence is expected to vary.

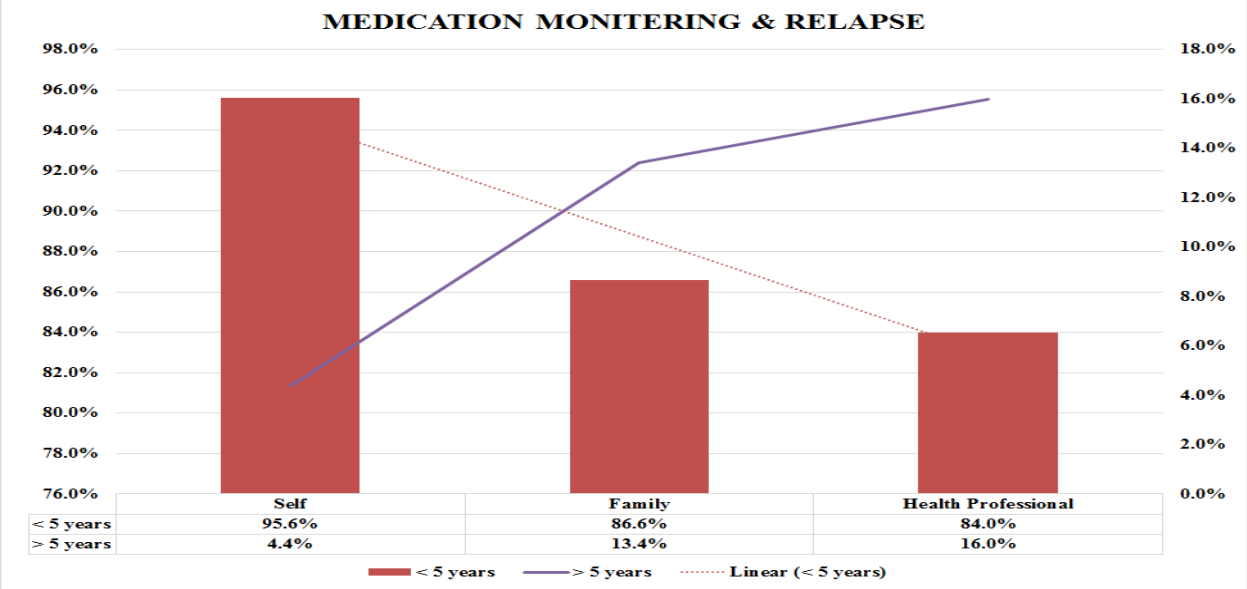

Fig 3: The patients that took medication under supervision of health professionals had lesser incidence of relapse, recurrence or reinfection within five years of treatment whereas patients who whose treatment was unsupervised showed greater incidence of relapse within five years of completion of initial treatment. The scenario reversed as it did in the earlier two figures. Family supervision reduced the chances of relapse within the initial five years following treatment but to a lesser extent than professional supervision.

Urban areas are less affected with TB relapse within 5 years than the rural areas. Non-smokers are more affected within 5 years while smokers are comparably less affected with TB. Incomplete treatment too lead to a faster relapse among patients. Details are depicted in the figure 4 below.

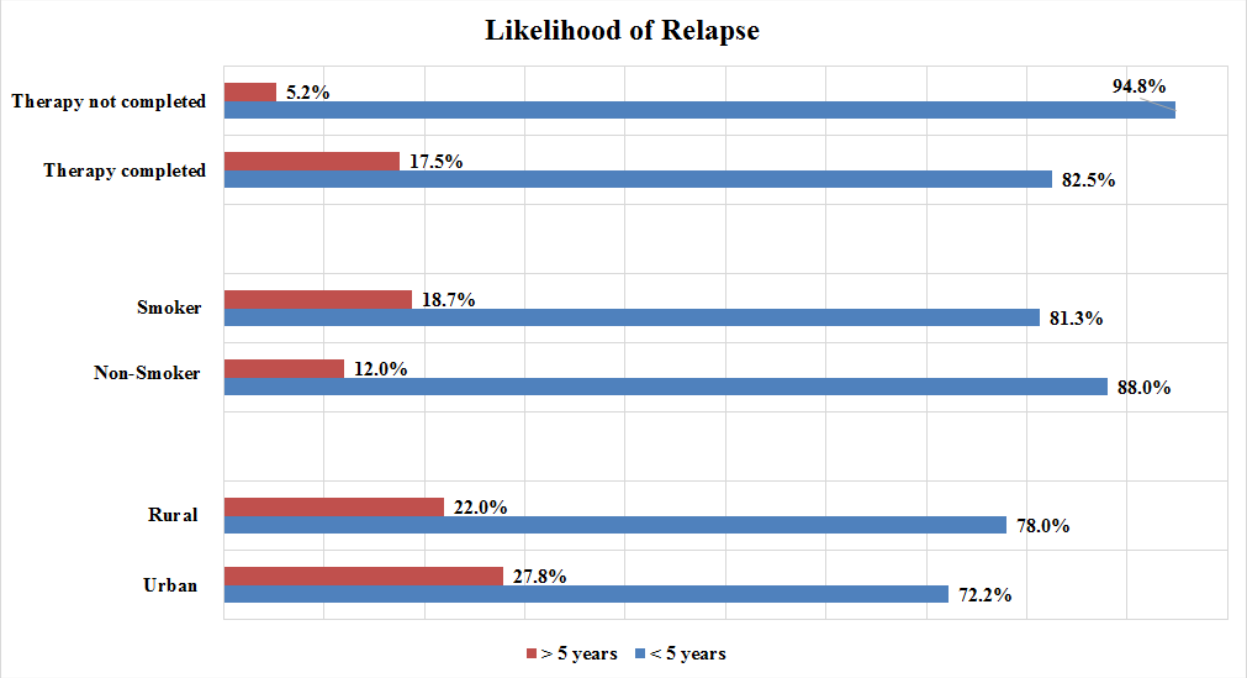

Fig 4: The likelihood of early relapse (within five years of treatment) is greater in rural than in urban population. Similarly the likelihood is greater in patients who did not complete the course of the treatment. Smoking however, exhibits an unusual relationship. One in which smokers are less likely to encounter a relapse than non-smokers within five years of treatment.

DISCUSSION:

A systematic review of prospective cohort studies and randomised clinical trials performed in the 1990s by Panjabi et al. [24] estimated a median recurrence rate of 1,780 per 100,00 py (range 1000–4000) in low incidence countries at 12 months post treatment completion. Crofts et al. [21] recently investigated recurrences in England and Wales from 1998–2005 and found a recurrence incidence of 660 per 100,000 py among culture-confirmed pulmonary TB cases who completed treatment; TB incidence in the general population was 13 cases per 100,000 py in 2007. Likewise, Dobler et al. [22] reported an incidence of recurrence of 71 per 100,000 py among culture positive patients who had completed treatment in New South Wales, Australia between 1994–2006 (TB incidence in the general population was 6.5 per 100,000 py in 2005).

Few studies performed in medium incidence countries analyze such a large number of TB cases with a completed therapy in a population-based epidemiological study. However, our study has some weaknesses. First, the number of recurrent TB cases in the study is low due to a small sample population compared to the literary norms. Second, the project being retrospective in nature faced the trouble of faulty memory. However, given the relatively small time elapsed since initial onset of diesase, it should not have a significant influence on the risk factors found to be associated with recurrence in our study. Also, data regarding completion of treatment for a "history of TB treatment" could not be available for some patients. The lack of information about reinfection from the same strain could cause some cases of reinfection to be deemed relapses but that does not affect our outcomes since we are not investigating individual occurrences.

Our sample was plagued with high rates of disease recurrence after "successful" treatment. Despite the lack of data differentiating relapse from reinfection, high recurrence in such settings of drug resistance suggests that treatment programs will have limited impact in terms of reducing TB incidence.

Control of TB, and especially the disease caused by drug-resistant M. tuberculosis strains, seems unlikely in the face of these results. This conclusion is in contrast to a recent study from southern Mexico, in which a standard WHO treatment program was shown to reduce incidence of both drug-susceptible and drug-resistant TB [23]. However, this setting in southern Mexico did not have a high TB incidence prior to the implementation of WHO treatment program DOTS (42/100,000/year) and reports a 3% MDR TB level among new cases; these indices are considerably lower than most of the high TB-burden and high drug-resistance settings [24,25]. Additionally, it is likely that the patterns of M. tuberculosis drug resistance seen in Mexico are less complicated than those in Uzbekistan.

Although drug resistance is an important contributor to poor long-term outcomes in this context, other factors may be present; among new patients infected with pan-susceptible or mono-resistant M. tuberculosis strains. A central question arising from these data is whether these recurrences of disease were caused by true relapses or by reinfection with new strains of M. tuberculosis. If relapse is common, it suggests that patients who are declared to be "successfully treated" in the treatment program are not actually cured. Such treatment failure could result from inadequate treatment regimens, which in turn could arise through drug resistance, poor adherence to treatment, poor drug quality, or treatment regimens inadequate for this population, independent of drug resistance.

Alternatively, reinfection could be an important contributor to an apparently high treatment failure rate. High rates of reinfection might be caused by a high prevalence of infectious TB in the community, low levels of immunity among individuals completing TB treatment, HIV infection, or specific characteristics of circulating M. tuberculosis strains. Without DNA fingerprinting of strains at re-diagnosis, it is not possible to determine the relative contributions of relapse and reinfection in this study.

The data suggest, however, that the rate of TB recurrence is, at least, not decreasing throughout the observation period; since relapse is thought to predominate in the first 5 years after treatment completion [26], this suggests that both mechanisms may be involved.

In our setup, most patients are hospitalized for the intensive phase of treatment, maximizing adherence to treatment. Therefore, it seems that poor adherence may not wholly explain the high disease recurrence rates seen here. Rates of default from treatment are higher in the urban areas however, resulting in the finding that city residence contributes significantly to unsuccessful treatment. This is most likely the result of overcrowding in TB facilities and poorer motivation among health care workers. Such findings demonstrate that despite significant inputs, there remain problems in program quality that manifest in poor observation of treatment. Another possible explanation for high relapse may be poor drug quality.

Studies utilizing DNA fingerprinting of M. tuberculosis strains have shown that reinfection contributes more substantially to recurrent TB than previously thought [27], with between 12% and 77% of cases attributable to reinfection [28–32]. It is therefore plausible that in the high-prevalence, with

many infected persons harboring drug-resistant strains, reinfection may contribute substantially to TB recurrence.

CONCLUSION:

My study concluded that relapse, recurrence and re-infection of tuberculosis is affected by gender variation, social economic status, medical monitoring, TB regimen course, family history and smoking. Both before and after 5 years of initial treatment of disease. Further research on a wider sample space and more microbiologic technological resources can yield more elaborative outcomes.

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