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## ORIGINAL ARTICLE

## Candidaemia In Disseminated TB

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## ABSTRACT

**Context:** Disseminated TB patients are invariably immunocompromised and are susceptible to opportunistic infections. Candidaemia is an under-recognised infection in India. Therefore, we planned to evaluate the prevalence, survival and risk factors for the development of this infection in disseminated TB patients in a tertiary care hospital in southern India.

**Aims:** To assess the prevalence of invasive candidiasis / candidaemia in disseminated TB patients in India and to determine the survival of these patients and risk factors for the development of candidaemia in disseminated TB patients

**Settings and Design:** A prospective study conducted after obtaining the institutional ethical committee's approval.

**Methods and Material:** Disseminated TB patients who came between February 2005 and February 2006 were included in the study after obtaining informed consent from the patients with assured confidentiality. The sources of the fungal culture were blood and ascitic fluid.

**Statistical analysis:** Fisher's test, the level of significance was set at  $< 0.05$

**Results:** 103 disseminated TB patients were enrolled into this study, but the prevalence of candidaemia was just 5 %. Intravenous broad spectrum antibiotics ( $P < 0.001$ ), oral broad spectrum antibiotics ( $P < 0.01$ ) and indwelling catheters ( $P < 0.01$ ) were the three important risk factors. Non candida albicans species were predominantly present.

**Conclusions:** Candidaemia has a low prevalence in Indian climatic conditions. If the risk factors associated with this infection are avoided, survival can be improved.

**Key-words:** Candidaemia, disseminated TB

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### Introduction

There were an estimated 9.2 million new cases of TB in 2006 (139 per 100 000 population),

including 4.1 million new smear-positive cases (44% of the total) and 0.7 million HIV-positive cases (8% of the total). This is an increase from the 9.1 million cases in 2005, due to population growth. India, China, Indonesia, South Africa and Nigeria rank first to fifth respectively, in terms of the absolute numbers of cases. The African Region has the highest incidence rate per capita (363 per 100 000 population). There were an estimated 14.4 million prevalent cases of TB in 2006. There

were an estimated 0.5 million cases of multidrug-resistant TB (MDR-TB) in 2006. In 2006, there were an estimated 1.5 million deaths from TB in HIV-negative people and 0.2 million among people who were infected with HIV. In 2007, a total of 202 (out of 212) countries and territories reported TB notification data to WHO for 2006. A total of 5.1 million new cases (out of the estimated 9.2 million new cases) were notified for 2006 among these 202 countries and territories, of which 2.5 million (50%) were new smear-positive cases. The African, South-East Asian and Western Pacific regions accounted for 83% of the total case notifications[1].

Candidaemia is an under recognised infection in India [2]. Therefore, we planned to evaluate the prevalence, survival and risk factors for the development of this infection in disseminated TB patients in a tertiary care hospital in southern India.

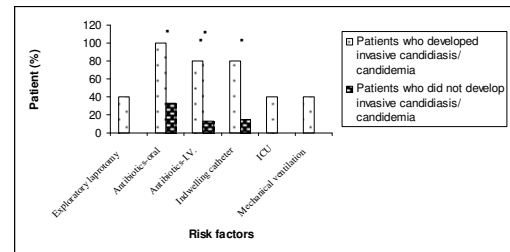
**Subjects and Methods**

Disseminated tuberculosis was defined in patients after the isolation of *Mycobacterium tuberculosis* from blood or bone marrow, from a liver biopsy specimen, or from specimens from 2 noncontiguous organs in a single patient [3]. Because the radiological appearance of miliary shadowing has relatively low sensitivity and specificity for the detection of disseminated tuberculosis, patients with a single positive culture for *M. tuberculosis* of a specimen from any site (except blood, bone marrow, or liver biopsy specimens) and a chest radiograph report by a radiologist of miliary shadowing, were not included in this study [3]. Disseminated TB patients who reported between February 2005 and February 2006 were included in the study after obtaining informed consent from the patients with assured confidentiality. The sources of fungal culture were blood and ascitic fluid. The identification of the *Candida* species was done at SRL Ranbaxy, Mumbai. Of the patients who did not develop candidaemia, 15 were randomly chosen for the comparison in statistical analysis.

**Results**

103 disseminated TB patients were enrolled into this study in the specified time interval.

All of them were on the standard anti tubercular drugs which come under the DOTS regimen- INH, Rifampicin, Pyrazinamide and Ethambutol. 5 disseminated TB patients had invasive candidiasis / candidaemia and therefore, a prevalence of 5 % in the present study during February 2005 to February 2006. 1 of them had Non Hodgkin’s lymphoma and was on Vincristine 2mg, Adriamycin 60mg and Endoxan 800mg for the past 1 month, 3 were HIV positive and were on Zidovudine, Lamivudine and Nevirapine. 1 had Insulin Dependent Diabetes Mellitus and was on 39-46 units of insulin/subcutaneously/day. Patients with invasive candidiasis/ candidaemia received either oral Fluconazole or liposomal Amphotericin B. The long term survival was 20%.



▪ P <0.01 ▪▪ P<0.001

[Table/Fig 1]: Risk factors for candidemia in disseminated TB

Fishers Exact test: level of significance set at P<0.05

Broad spectrum antibiotics, both intravenous (P<0.001) and oral (P<0.01) and indwelling catheters (P<0.01) were the statistically significant risk factors in the disseminated TB patients who developed invasive candidiasis / candidaemia. The other comorbid conditions which were observed were HIV and diabetes, but these were not statistically significant.

**Discussion**

In the present single centre study, only 5 cases were identified and the prevalence was very low, since the climate in India protects against systemic candidial infections.

*C. parapsilosis* was isolated from 3 specimens (60%), *C. tropicalis* from 1 specimen (20%) and *C. albicans* from 1 specimen (20%).

Candida species	n =5	Outcome	Cause of death

<i>C. parapsilosis</i>	1	Survived	
<i>C. Parapsilosis</i>	1	Death on 15 day	Adult Respiratory Distress Syndrome
<i>C. Parapsilosis</i>	1	Death day 7	Fungal Septicemia
<i>C. tropicalis</i>	1	Death day 14	Upper GI bleed
<i>C. albicans</i>	1	Death day 9	Fungal Septicemia

[Table/Fig 2]: Candida infection and outcome

Hence, we could not apply the multiple log regression (cox) which would have been the appropriate statistical method if the numbers were higher. Studies done in western countries have associated the development of systemic candidiasis with risk factors such as exploratory laprotomy, oral broad spectrum antibiotics, immunocompromised states, ICU admissions, indwelling catheters and mechanical ventilation [2],[4]. But in our set up and in disseminated TB patients, the risk factors were the use of broad spectrum antibiotics, both intravenous (  $P<0.001$ ) and oral (  $P<0.01$ ) and indwelling catheters (  $P<0.01$ ) [Table/Fig 1]. If the known risk factors were avoided, the survival could have been improved. Further studies with higher number of patients are needed to validate the observed results; however, in patients who did not respond to antitubercular therapy, it is worth investigating them for candidaemia.

## Conclusion

In our set up and in disseminated TB patients, the risk factors were the use of broad spectrum antibiotics, both intravenous (  $P<0.001$ ) and oral (  $P<0.01$ ) and indwelling catheters. If the known risk factors were avoided, the survival could have been improved. Candidaemia, when undiagnosed, can definitely lead to 100% mortality. Early diagnosis and treatment can improve the prognosis.

The present study results suggest the emergence of non *Candida albicans* species in Indian climatic conditions. [Table/Fig 2]

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