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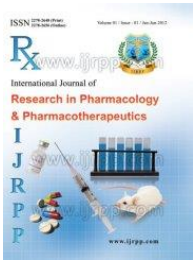

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Research article ***Open Access***

To find the prevalence of HIV infection in pulmonary tuberculosis patients admitted in a secondary and tertiary care hospital of a rural area in Tamil Nadu – A retrospective study

R.Nivetha[1], Dr. M. Saravana Kumar M.D[2]*

[1]Final year M.B.B.S student, DSMCH, Perambalur,
[2]Head of Department (Pharmacology), Dhanalakshmi Srinivasan Medical College & Hospital, Perambalur, TN (India)

***Corresponding author: Dr.M.Saravanakumar M.D**
Email: sharavankumar1923@yahoo.co.in

ABSTRACT

Background

Tuberculosis and HIV infections are the major health problems, especially in rural areas like Perambalur. Tuberculosis kills 1.8 million people per year worldwide. Unsuccessful treatment programmes for disease control and continued transmission are contributing to the emergence and spread of multidrug-resistant (MDR) tuberculosis (i.e., bacillary resistance to at least rifampicin and isoniazid). The spread of HIV infection has produced new challenges in the diagnosis and treatment of tuberculosis.

Methods

A retrospective study was conducted among 836 patients with the help of a proforma that consists of relevant details of patient taken from the treatment card. The data was collected among people who were pulmonary tuberculosis positive within the period of two years from January 2015 to December 2016.

Results

Among these pulmonary TB positive patients, 94 were found to be co-infected with HIV infection as per the data collected from District Head Quarters Hospital, Perambalur. The prevalence of TB with HIV co-infection was about 11.2%. These patients were presented with various atypical clinical presentations. 97% of pulmonary TB co-infected with HIV with these atypical presentations belongs to younger age group (10 to 27). The age group were majority of co-infection was between 30 to 40 years. The prevalence of co-infection has been reduced as compared to previous years, due to effective and supportive measures.

Keywords: Tuberculosis; TB – HIV co-infection; Rural areas, Tuberculosis, Prevalence, HIV status

INTRODUCTION

It is estimated that 7 per cent of all deaths and about quarter of all preventable deaths in the world are directly attributable to tuberculosis infection [1]. The percentage of the annual risk of reactivation at 8 per cent among HIV infected persons compared to 0 per cent in HIV uninfected. Although the prevalence and incidence of tuberculosis infection were similar for both HIV-Seropositive and HIV-Seronegative patients, the risk of active tuberculosis was elevated only for seropositive subjects [2]. In developing countries too, Bermejo et al have predicted that the incidence of tuberculosis will double as the prevalence of HIV infection reaches 13 per hundred adults [3]. The spread of HIV infection has produced new challenges in the diagnosis and treatment of tuberculosis. Diagnosis of tuberculosis is more difficult to establish in HIV infected persons as they may present atypical radiographic patterns [4] especially when CD4 cell counts are less than 200 cells/mm^3. Patients co-infected with HIV and tubercle bacilli also show more extra-pulmonary involvement [5].

Tuberculosis kills 1.8 million people per year worldwide. Unsuccessful treatment programmes for disease control [6, 7] and continued transmission are contributing to the emergence and spread of multidrug-resistant (MDR) tuberculosis (i.e., bacillary resistance to at least rifampicin and isoniazid).

Immune reconstitution inflammatory syndrome, IRIS which can include exacerbation of symptoms, new or worsening clinical signs and deteriorating radiological appearances have been associated with the improvement of immune function seen in HIV infected patients starting HAART in the face of M. tuberculosis infection. However delaying antiretroviral therapy increases the risks of further opportunistic events. Allowing at least two weeks of anti- tuberculous therapy before commencing HAART allows some reduction in the burden of mycobacterium. If the CD4 count is less than 100 then antiretroviral should be started at about 2 weeks of anti-TB medication, if the CD4 count is above 200 then initiation of HAART may wait for at least 6 weeks after the start of anti- tuberculous therapy. [8]

The human immunodeficiency virus (HIV) pandemic presents a significant challenge to global tuberculosis (TB) control. TB is a leading preventable cause of death among people living with HIV. To mitigate the dual burden of TB/HIV in populations at risk of or affected by both diseases, the Stop TB Department and the Department of HIV/ AIDS of the World Health Organization (WHO) published an Interim policy on collaborative TB/HIV activities in 2004 [9].

ORIGIN OF TUBERCULOSIS

The highly successful human pathogen *Mycobacterium tuberculosis* has an extremely low level of genetic variation, which suggests that the entire population resulted from clonal expansion following an evolutionary bottleneck around 35,000 years ago [10]. Here, we show that this population constitutes just the visible tip of a much broader progenitor species, whose extant representatives are human isolates of tubercle bacilli from East Africa. In these isolates, we detected incongruence among gene phylogenies as well as mosaic gene sequences, whose individual elements are retrieved in classical *M. tuberculosis*. Therefore, despite its apparent homogeneity, the *M. tuberculosis* genome appears to be a composite assembly resulting from horizontal gene transfer events predating clonal expansion. The amount of synonymous nucleotide variation in housekeeping genes suggests that tubercle bacilli were contemporaneous with early hominids in East Africa, and have thus been coevolving with their human host much longer than previously thought. These results open novel perspectives for unravelling the molecular bases of *M. tuberculosis* evolutionary success.

Mycobacterium tuberculosis, the agent of tuberculosis, is a highly successful human pathogen and kills nearly 3 million persons each year. This pathogen and its close relatives sum up in a single and compact clonal group dating back only a few tens of thousands of years. Using genetic data, the researchers have discovered that human tubercle bacilli from East Africa represent extant bacteria of a much broader progenitor species from which the *M. tuberculosis* clonal group evolved. They estimate that this progenitor species is as old as 3 million years. This suggests that our remote hominid ancestors may well have already suffered from tuberculosis. In addition, the researchers show that tubercle bacilli are able to exchange parts of their genome with other strains, a process that is known to play a crucial role

in adaptation of pathogens to their hosts. Thus, the *M. tuberculosis* genome appears to be a composite assembly, resulting from ancient horizontal DNA exchanges before its clonal expansion. These findings open novel perspectives for unravelling the origin and the molecular bases of *M. tuberculosis* evolutionary success, and lead to reconsideration of the impact of tuberculosis on human natural selection.

PATHOGENESIS

Tubercle bacilli are transmitted between people by aerosols generated when an infectious person coughs. Based on whether it is the first time a patient is infected, TB is divided into a primary and secondary type.

In primary pulmonary TB the organism is inhaled and usually in the periphery of the lung, is phagocytised and innate immunity initiated. The phagosed organism stimulates the proliferation and activation of T cells. This results in formation of granuloma. The primary granulomatous reaction characteristically occurs in the peripheral part of the lung close to the pleura in virtually any part of the lung. This lesion is called Ghon focus. Airway obstruction, segmental pulmonary TB, bacteraemia and military TB and pulmonary haemorrhage may complicate primary TB.

In secondary tuberculosis, some patients become re infected with M. tuberculosis or experience reactivation of dormant disease in the Ghon focus or complex. Latent M. tuberculosis infection is present in one-third of the world's population. Less than 10% of infected individuals, however, develop active disease. [11]

MORPHOLOGY

The disease is usually bilateral, with one side often less affected than the other. Especially the upper lobes show large cavities and smaller cavities often contain caseous material, but many also be empty. The cavity itself is surrounded by a rim of caseous material flanked by organizing granulomatous inflammation and variable fibrosis and scarring towards the periphery of the wall. [12]

MULTIDRUG RESISTANCE TUBERCULOSIS (MDR-TB)

Tuberculosis kills 1.8 million people per year worldwide. Unsuccessful treatment programmes for disease control and continued transmission are contributing to the emergence and spread of multidrug-resistant (MDR) tuberculosis (i.e., bacillary resistance to at least rifampicin and isoniazid. Data from Kwazulu Natal, South Africa, suggest that almost all patients with extensively drug-resistant (XDR) tuberculosis are HIV-positive, with a fatal outcome. **Emergence of multidrug resistant tubercle bacilli (MDRTB) has been reported in the United States with most of the outbreaks of MDRTB having occurred in HIV infected persons [13].** Hence there is a need to monitor the impact of the HIV epidemic on tuberculosis in India.

HUMAN IMMUNODEFICIENCY VIRUS (HIV)

The human immunodeficiency virus (HIV) attacks the body's immune system. A healthy immune system provides a natural defence against disease and infection. If the immune system is damaged by HIV, it increases the risk of developing a serious infection or disease, such as cancer.

HIV infects particular cells, called CD4 cells that are found in the blood. CD4 cells are responsible for fighting infection. After they become infected, the CD4 cells are destroyed by HIV. Although the body will attempt to produce more CD4 cells, their numbers will eventually decline and the immune system will stop working.

HIV is spread through the exchange of bodily fluids. This most commonly happens during unprotected sexual contact, such as vaginal, oral and anal sex. People who inject illegal drugs and share needles are also at risk of catching HIV. The condition can also be spread from a mother to her unborn child.

There is no cure for HIV and no vaccine to stop you becoming infected. However, since the 1990s, treatments have been developed that enable most people with HIV to stay well and live relatively normal lives.

PATHOGENESIS

The lentivirus human immunodeficiency virus (HIV) causes AIDS by interacting with a large number of different cells in the body and escaping the host immune response against it. HIV is transmitted primarily through blood and genital fluids and to newborn infants from infected mothers. The steps occurring in infection involve an interaction of HIV not only with the CD4 molecule on cells but also with other cellular receptors recently identified. Virus-cell fusion and HIV entry subsequently take place. Following virus infection, a variety of intracellular mechanisms determine the relative expression of viral regulatory and accessory genes leading to productive or latent infection. With CD4+ lymphocytes, HIV replication can cause syncytium formation and cell death; with other cells, such as macrophages, persistent infection can occur, creating reservoirs for the virus in many cells and tissues. HIV strains are highly heterogeneous, and certain biologic and serologic properties determined by specific genetic sequences can be linked to pathogenic pathways and resistance to the immune response. The host reaction against HIV, through neutralizing antibodies and particularly through strong cellular immune responses, can keep the virus suppressed for many years. Long-term survival appears to involve infection with a relatively low-virulence strain that remains sensitive to the immune response, particularly to control by CD8+ cell antiviral activity. Several therapeutic approaches have been attempted, and others are under investigation. Vaccine development has provided some encouraging results, but the observations indicate the major challenge of preventing infection by HIV. Ongoing research is necessary to find a solution to this devastating worldwide epidemic [14].

SYMPTOMS

Rapid weight loss

- Recurring fever or profuse night sweats
- Extreme and unexplained tiredness
- Prolonged swelling of the lymph glands in the armpits, groin, or neck
- Diarrhoea that lasts for more than a week
- Sores of the mouth, anus, or genitals
- Pneumonia
- Red, brown, pink, or purplish blotches on or under the skin or inside the mouth, nose, or eyelids
- Memory loss, depression, and other neurologic disorders

IMPACT OF CO-INFECTION

Tuberculosis and human immunodeficiency virus (HIV) are intimately associated and thus require an integrated approach from health services. All the interventions for HIV-infected people need to be integrated into a combined TB/HIV programme delivered at facilities convenient to patients, preferably by the same or closely connected staff. Increased nosocomial and community exposure to M. tuberculosis may play a role in the increased risk of contracting TB in HIV-infected patients, but HIV-associated impairment of one or more immunological mechanisms play an important role. HIV infects macrophages and CD4+ T cells essential in granuloma formation in TB. Co infection will therefore impair cell-mediated immune responses to M. tuberculosis infection. Tuberculosis and HIV co infection is also likely to be associated with extensive virus-induced and activation-induced cell loss and with the suppression of lymphocyte regeneration and maturation. HIV co infection weakens the granulomatous host response to M. tuberculosis, resulting in increased reactivation of latent mycobacterium.

GEOGRAPHICAL DISTRIBUTION

The prevalence of HIV infection in tuberculosis patients reported here shows an increase from 3.19 per cent in 1991 to 20.1 per cent in 1995. The prevalence of HIV infection in TB patients reported by a retrospective study in DebreMarkos referral hospital – Ethiopia from 2008 to 2013 is decreased from 49.2% to 44.6%. [15] The prevalence of HIV infection among tuberculosis patients was reported to be 59% in Zambia, 57% in Uganda, 16% in Kenya and 0.7% in Thailand [16]. In USA the HIV seroprevalence in tuberculosis patients increased from 10.6% in 1985 to 39% in 1990 [17]. HIV seroprevalence of 4.7 per cent among tuberculosis patients was reported in an earlier study from western India [18]. A study from south India has reported an increase in HIV seroprevalence among tuberculosis patients from 0.77 per cent in 1991 to 3.4 per cent in 1993 [19]. The HIV seroprevalence among STD

patients showed increase from 1 in 1989 to 10 per cent in 1993 in Tamil Nadu [20]. A recent study in 2015 has estimated that 55% of TB cases have been reported among people living with HIV. It is an 18 fold increase as compared to data since 2004 globally. According to this study, 4 million people who had HIV & TB co-infection have died globally. 1.4 million Died with TB infection alone and 8 million with HIV alone [21]. In general there is an overall 18 times rise of HIV prevalence in PT patients.

The high prevalence of HIV among tuberculosis patients seen here clearly shows that HIV has already made an impact on the tuberculosis situation in India. This information would be useful while accurately estimating the magnitude of the impact of HIV infection on the tuberculosis situation in the population. No data are available about the incidence of tuberculosis in HIV infected persons in our district especially in rural areas. Currently there is no information on HIV infected tuberculosis patients in our area**.** Studies on the diagnosis and management of tuberculosis patients with HIV infection are also lacking. Voluntary testing of tuberculosis patients may be encouraged in order to detect tuberculosis patients with HIV infection.

OBJECTIVES

Primary objective

To evaluate HIV status in pulmonary tuberculosis patient in a secondary & tertiary health centre.

Secondary objective

To study the clinical scenario including presenting features, radiological features in pulmonary tuberculosis patients through the case sheets available in my study centre.

MATERIAL AND METHODS:

- Sputum positive / x-ray positive / both
- Treatment cards of patients confirmed with pulmonary tuberculosis.
- Relevant data for my study are taken from the treatment cards.

METHOD

In a retrospective cohort study, we analysed the case records of patients (all age group) those who are diagnosed as pulmonary tuberculosis between January 2015 to December 2016 with the help of a proforma that consists of relevant details of patient taken from the treatment card.

STUDY DESIGN

- Retrospective study.
- Patient's complete details that are available in chest medicine ward, those who are diagnosed as pulmonary tuberculosis earlier.
- **Age group**: all age group
- All cases of pulmonary tuberculosis which are screened for HIV and other investigations like CXR will be taken.
- Proforma with details of the patient with tuberculosis is taken from the treatment card.

Study Area

- Government headquarters hospital, Perambalur.

Study Population

As per complete data available.

Study Period

1 year [2017 to 2018]

Inclusion Criteria

- Patients diagnosed as pulmonary tuberculosis.
- Patients in follow up with ATT.

EXCLUSION CRITERIA

Incomplete case details will be excluded.

PROFORMA

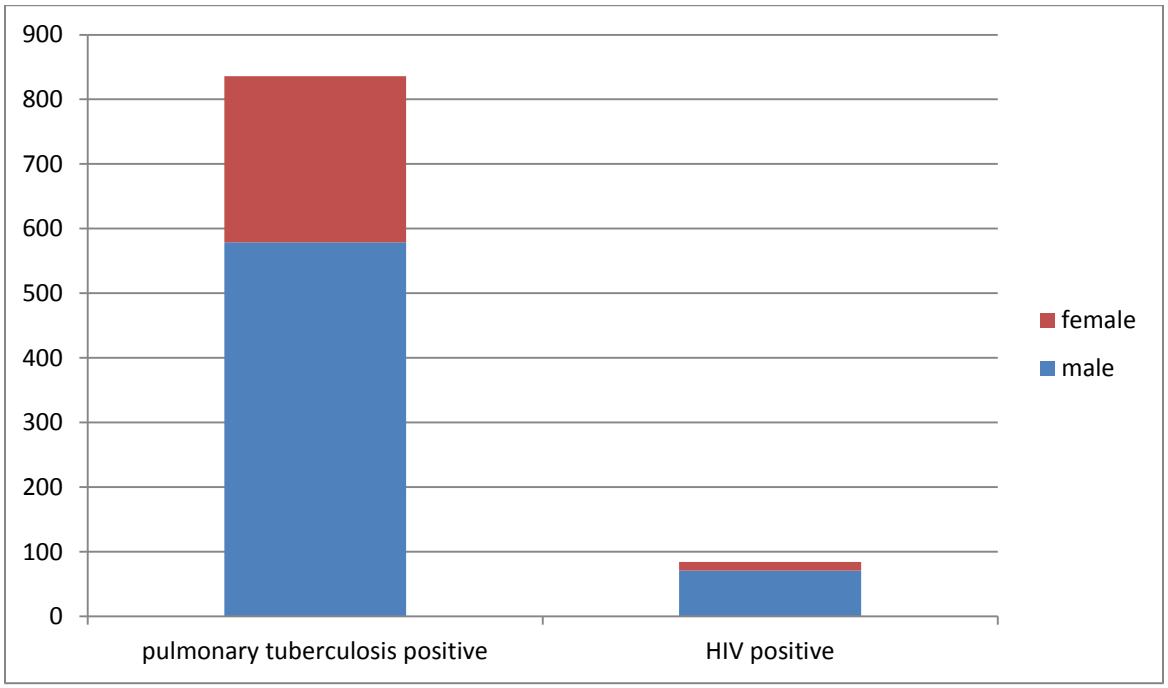
- Age/sex
- Body weight
- Occupation

- Smoking
- Alcoholism
- DM
- Hypertension
- Categorization

Category I	category II
a. New	a. Relapse
b. New sputum [+]	b. failure
c. New sputum [-]	c. others
d. New Extra Pulmonary	

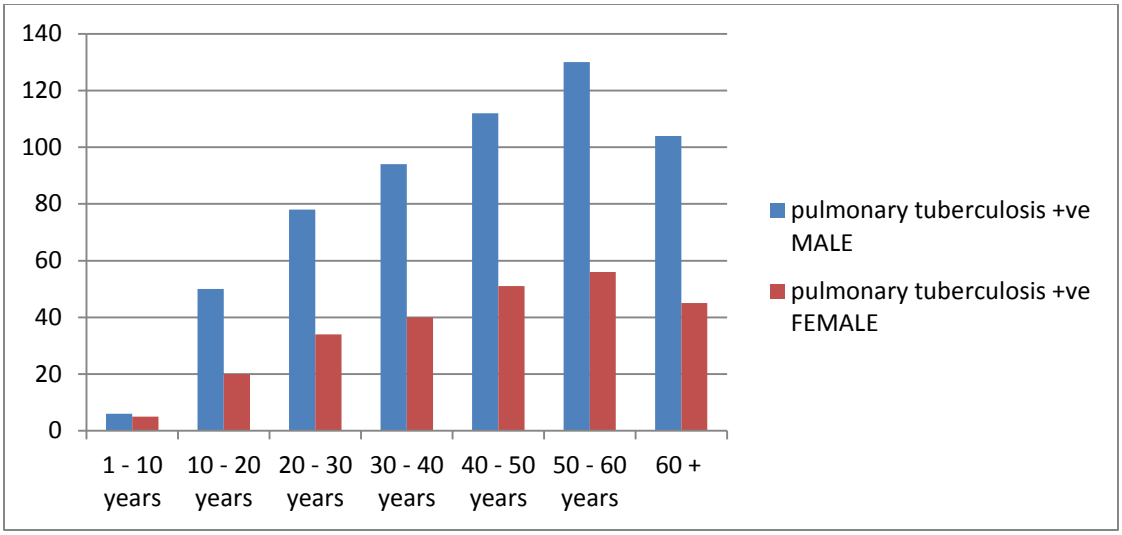
- Sputum test
- Chest x-ray
- Any previous H/o treatment
- HIV screening report

RESULT



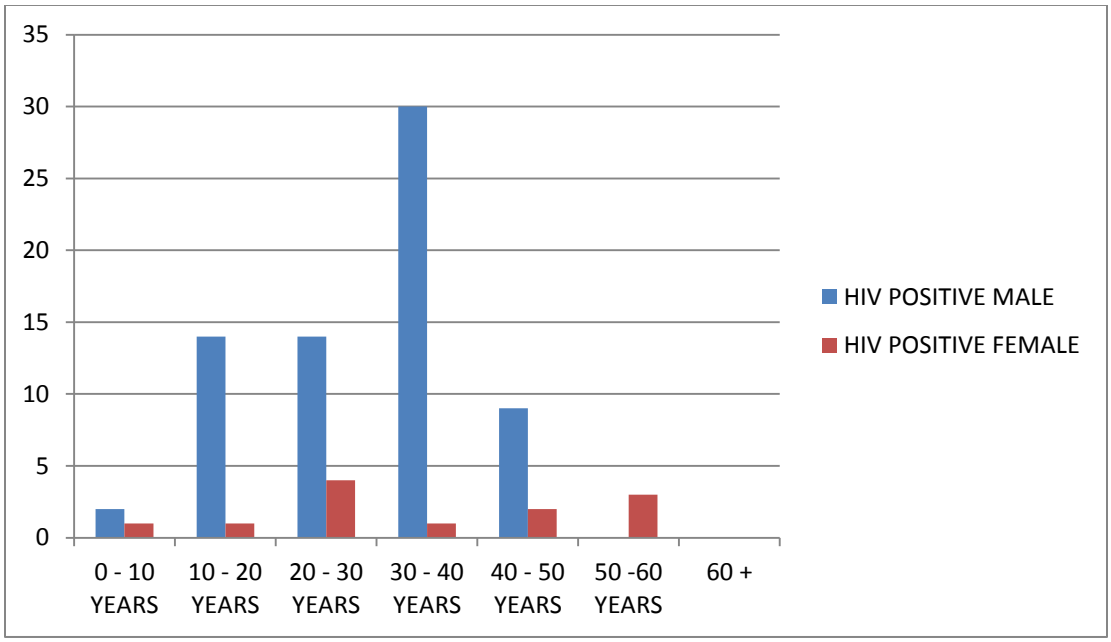
Total no. of PT positive cases with HIV positive in the year 2015 to 2016 (Chart: 1)

The total number of PT positive cases were 836 in which 579 were male and257 was female.



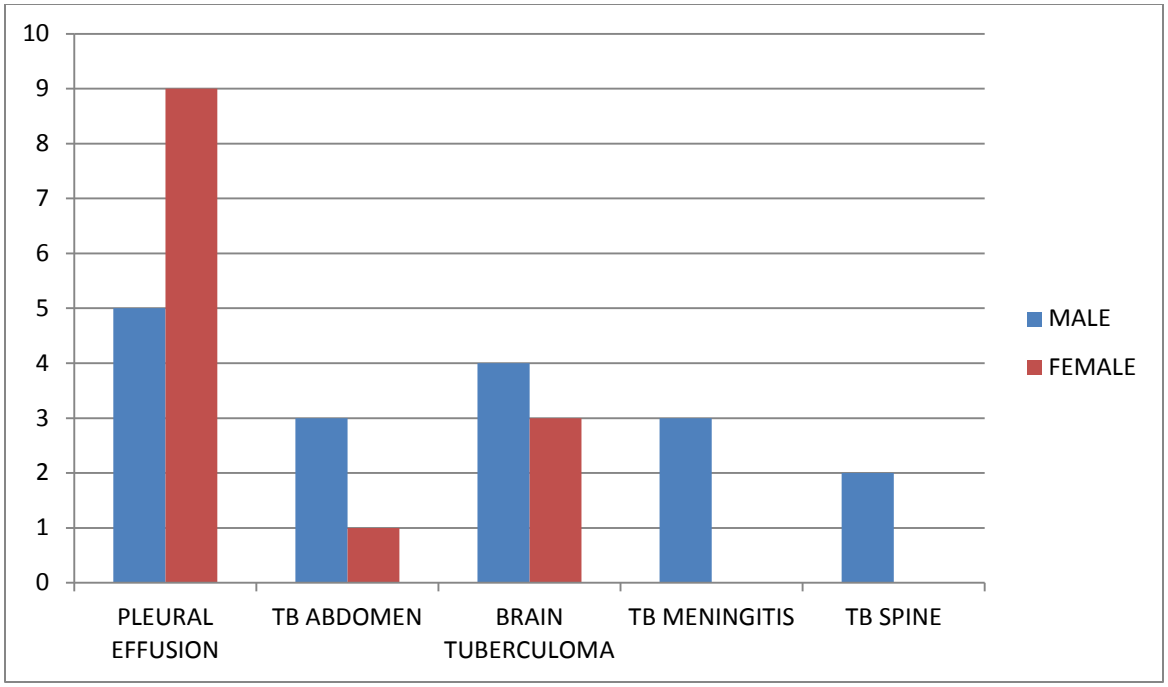
Total no. of PT positive cases according to their age group
(chart: 2)

The above chart indicates the details about PT positive patients among different age groups. The number of children affected among the age group 0 to 10 years are 11, between 10 to 20 years it is 70, between 20 to 30 years it is 112, between 30 to 40 years it is 134, between 40 to 50 years it is 163, between 50 to 60 years it is about 186, above 60 years it is 149. It is clear that, the age group which is affected in an increased number is between 50 to 60 years of age.



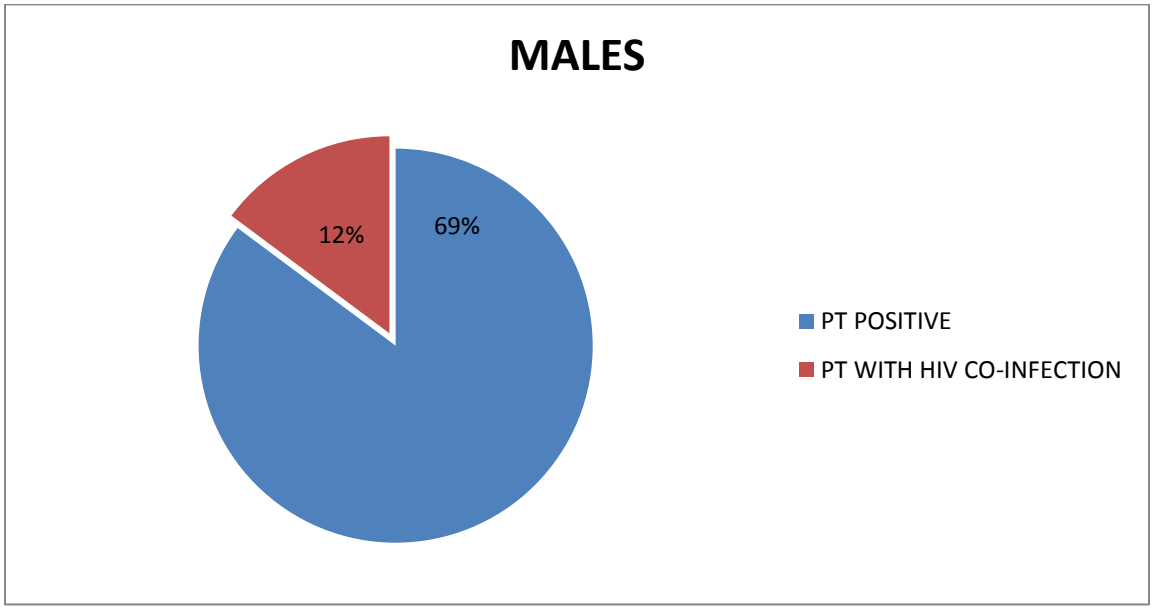
Total no. of HIV positive in PT patients according to their age group.
(chart: 3)

From the above chart (3), it is clear that the age group where HIV – Pulmonary TB co-infection is increased is between 30 to 40 years of age.



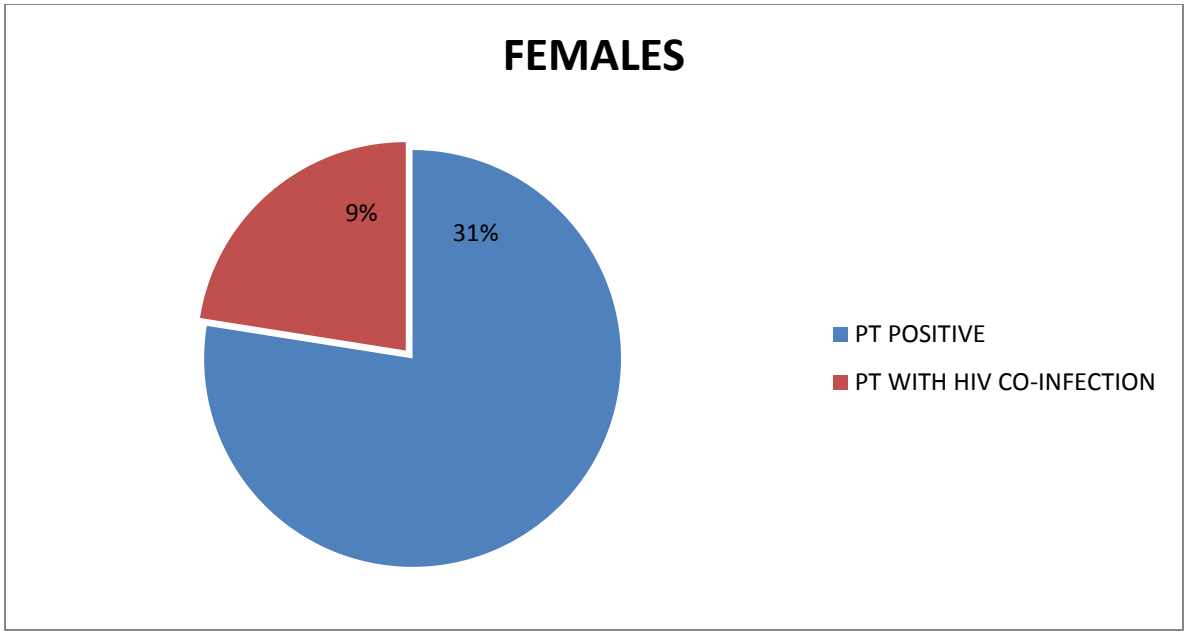
Atypical clinical presentations in HIV positive cases among PT patients (chart: 4)

The above chart(4) indicates that, patients with HIV – TB co-infection are more presented with other atypical presentations like pleural effusion which is more common among females and tuberculoma brain is more common among young adults (<20 years)



Percentage of Males Affected: (Chart: 5)

Among all PT patients, the majority of them affected are male subjects. They were 576 in number and are about 69%. The co-infection was found in about 71 subjects and it is 12%.



Percentage of Females Affected: (Chart: 6)

The females affected are comparatively less than males. They were about 257 in number and it is 31%. The co-infection is seen in 23 subjects and it is 9%.

DISCUSSION

Being it's difficult to diagnose and to treat PT patients especially co-infected with HIV infection makes a challenge in global tuberculosis control. In developing countries, the predicted prevalence of HIV in PT patients almost reaches 13/100 adults. In India, the available data regarding PT patients is not adequate. In Tamil Nadu, data regarding this scenario is not documented properly especially in backward rural areas like perambalur.

According to our study, about 836 patients confirmed PT positive were took into account retrospectively. Among these patients, there are 579 males and 257 females.

HIV status among these individuals was about 11.2%. Total number of HIV positive cases in all PT positive patients was 94. There were 71 males and 13 females found to be positive for HIV.

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In the demographic profile, the most common age group possessing PT positive falls in between 50 to 60 years of age (decreasing in order, proportion to decreasing age group). But HIV positive in PT patients falls in between 30 to 40 years of age group when compared to others (especially males).

In case of female subjects, HIV seropositive in PT patients was found to be between the age group of 20 to 30 years.

There are some atypical clinical features found in PT patients with HIV positive. They are, pleural effusion, which was found in 14 individuals, 4 patients revealed TB abdomen (females are more compared to male), 7 patients were presented with tuberculoma brain, TB spine were seen in 2 male patients, TB meningitis was found in 3 male patients. 97% of the HIV positive in PT patients who were having atypical clinical presentation belongs to younger age group (10 to 27 years of age).

9 among the HIV positive individuals are alcoholics and 8 individuals of HIV positive were drivers by profession

DATA

AGE GROUP	Pulmonary tuberculosis positive Male	Pulmonary tuberculosis positive Female	PT with HIV positive Male	PT with HIV positive Female
0 to 10	6	5	2	1
10 to 20	50	20	14	1
20 to 30	78	34	14	4
30 to 40	94	40	30	1
40 to 50	112	51	9	2
50 to 60	130	56	0	3
60 +	104	45	0	0

Special features of PT in HIV positive cases

Pleural effusion	5+9 (Male+Female)
TB abdomen	3+1 age (17 to 20)
Brain tuberculoma	4+3 m (age 15, 27, 27, 20) f (14, 10, 14)
TB meningitis	m 3
TB spine	m 2

CONCLUSION

Being it is a dangerous combination of two major killer diseases in developing countries like India. It is highly important to document the prevalence of HIV among TB patients. It is also important to know the prevalence of TB cases among HIV infected patiens. After 1993, there is no proper data available on related medical journals, but in some TB control programs or NADPH like programs the HIV status among TB patients is revealed.

So in our study, we evaluated the scenario in a rural area of Tamil Nadu between 2015 and 2016. Out of 836 pulmonary tuberculosis patients, HIV positive individuals were 94 which shows the seroprevalance in this perambalur district was about 11.2%. Among this HIV infected among TB patients, the male and female ratio is 12:9. More important is that the age group of 30 to 40 years is having the highest HIV status (32 patients).

The atypical presentations like tuberculoma, TB meningitis and TB spine were more common in males, especially less than 20 years of age.

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