IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

Treatment Of Active Pulmonary And Extra-Pulmonary Tuberculosis with Co-morbidities in Adult Patients Admitted to The Government Tertiary Care Hospital in Mandya: A Cross-Sectional Study

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Abstract:
Tuberculosis (TB) has been a health problem that, despite all global efforts, they claimed 1.3 million deaths globally in 2020, with an increase to 1.4 million people in 2021. Due to difficulty in diagnosis and treatment of TB cases during Coronavirus pandemic in 2019, it reversed years of progress in the field. Tuberculosis is communicable disease caused by the bacteria *Mycobacterium tuberculosis* which commonly affects the lungs. The treatment of tuberculosis is complicated by many factors, and it is very crucial to evaluate the effectiveness of drug therapy to improve the quality of life for the tuberculosis patients. Adults who are suffering with multiple disease states are known to suffer more from tuberculosis infection hence, an appropriate treatment must be provided for such patients. The main objective of the study is to enhance the knowledge regarding tuberculosis's association with co-morbidities. And also, to describe the treatment pattern involved in it. In a tertiary care hospital, a cross sectional study was conducted for a duration of 6 months which involved 90 tuberculosis affected patients with various co-morbidities. The study assesses the presence of different co-morbidities and their treatment pattern in the individual patient by collecting the data from the patient's medical record. Statistical analysis i.e., descriptive analysis was done. The primary outcomes were to assess the prescribed drugs for the treatment of active pulmonary (PTB) and extra-pulmonary tuberculosis (EPTB) and secondary outcomes were focused on the association of tuberculosis with co-morbidities and their treatment pattern. The present study showed that among 90 patients, 30% of patients had extra-pulmonary tuberculosis and 70% of patients had pulmonary tuberculosis. The majority of the co-morbidities with tuberculosis were under respiratory system-related diseases (48.8%). Most of the patients were with anaemia (35.5%). In conclusion, co-morbidities are present in many tuberculosis patients and are associated with poor quality of life and increased morbidity. Identification and correction of co-morbidities is based on treating the underlying cause which may improve their clinical outcome.

Keywords: Tuberculosis, Extra pulmonary tuberculosis, Comorbidities, National Tuberculosis Elimination Programme (NTEP), World Health Organization (WHO).

Introduction:

Tuberculosis (TB) is a non-communicable disease caused by the bacteria *Mycobacterium tuberculosis* which often affects the lungs.[1] As per the WHO 2022 Incidence Report, about 10.6 million people became ill with TB in 2021, with immune-compromised patients accounting for about 7% of the total. Epidemiological survey data for the year 2021 showed a higher infection rate among males compared to females.[2] Countries having burden of TB also face the burden of concomitant co-morbidities. These include respiratory diseases, cardiovascular diseases, liver diseases, skin disorders, etc. These co-morbidities interact with TB infection at many levels. They may aggravate the infection from latent to active or disseminated TB causing difficulty in diagnosis which may lead to ineffective treatment or it might cause restriction in using the anti-tubercular therapy (ATT). Moreover, TB infection aggravates the co-morbidities leading to hindrance in diagnosing and managing these co-morbidities.
Several studies have been conducted showing the association of TB with Anemia, Diabetes mellitus (DM), Human Immune Virus (HIV), Chronic Obstructive Pulmonary Disease (COPD), undernutrition etc. However, in the current scenario treatment of TB associated with co-morbidities has not assumed much importance. These studies have shown that co-morbidities can lead to increased susceptibility, aggravation and mortality due to TB infection. Therefore, this study is conducted to study the treatment of active pulmonary and extra-pulmonary TB associated with co-morbidities in a tertiary care hospital in Mandya. This will reflect the need for integrated Tb treatment with the management of co-morbidities which will result in the decline in mortality caused due to co-morbidities of TB.

Materials and Methods:

An observational study was conducted which was cross-sectional in nature. Before the commencement of the study, approval from Institutional Ethical Committee for the research was obtained. All the patients attending the pulmonology outpatient and inpatient department of a teaching hospital Mandya institute of medical science (MIMS) during the study period of 6 months, who were diagnosed at that time with TB and associated comorbidities or were already diagnosed were chosen as subjects for the study. Sample size of 90 patients were enrolled in the study.

STUDY CRITERIA:

a) Inclusion criteria:

1. Patients with pulmonary, extra-pulmonary and drug-sensitive TB (DS-TB) with co-morbidities
2. Age group ≥18 years admitted with complaints of TB and associated co-morbidities.
3. Patient giving informed consent

b) Exclusion Criteria:

1. Patients with Drug-resistant TB (DR-TB).
2. Pregnant and lactating patients.
3. Having a psychiatric disease that induces incorporation of questionnaire investigation.

METHOD OF DATA COLLECTION (STUDY TOOLS):

All the data relevant to the patients were collected from patient's medical record and through the counselling. The Patient's medical records included: socio-demographics details, diagnosis of TB and comorbidities, habits of the patients (smoker or alcoholic), vital signs (blood pressure, pulse rate), laboratory data and details of drugs prescribed including anti-tubercular drugs (frequency dose and duration) along with the drugs prescribed for co-morbidities.

ANALYSIS:

Descriptive statistics has been applied in the present study. To generate graphs and tables, data is entered in Microsoft Excel and Word. Simple percentage calculation will be done to arrive at conclusion for our study.

Results

A total of 90 patient's data was collected from MIMS hospital during six months. Among those 90 patients, 70 (78%) were males and 20 (22%) were females. Most common age group in males were 65-74 (27.1%) years and in females were 55-64 (30%) years. Pulmonary tuberculosis was seen in 63 (70%) patients of which 50 were male patients and 13 were female patients and 27 (30%) patients had extra-pulmonary tuberculosis of which 20 were male patients and 7 were female patients. A total of 7 types of Extra-pulmonary tuberculosis were diagnosed among 90 patients, they are Pleural effusion (55.1%), Peritoneal TB (6.8%), Abdominal TB (13.8%), Spinal TB (6.8%), Tubercular lymphadenopathy (10.3%), TB meningitis (6.8%) and Syn-pneumonic effusion (6.8%) (shown in figure 1). Pleural Effusion was more commonly diagnosed EPTB among the population in which males were higher in number as compared to females.

Figure 1: Distribution of patients based on extra-pulmonary tuberculosis.

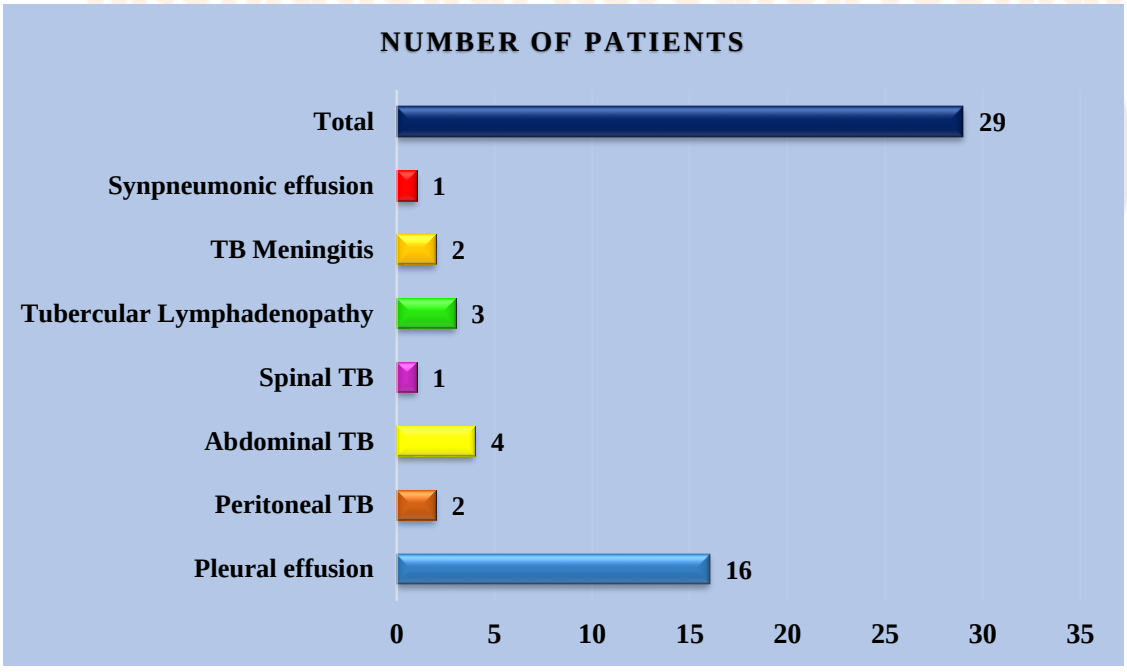

Figure 1 shows the patient distribution of different types of extra-pulmonary tuberculosis. Pleural effusion (16) was most common followed by abdominal TB (4), tubercular lymphadenopathy (3), peritoneal TB (2), TB meningitis (2), syn-pneumonic effusion (1) and spinal TB (1)

Figure 2: Patient distribution based on most common co-morbidities.

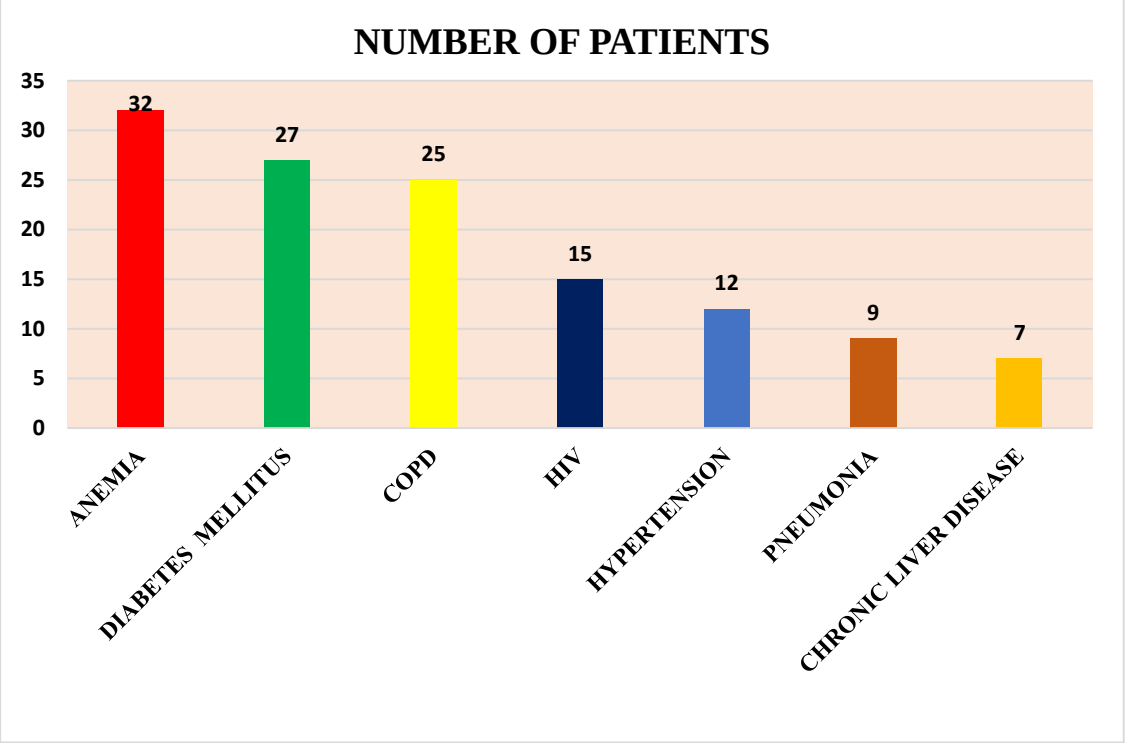

Figure 2 shows that anemia is the most common co-morbidity followed by diabetes mellitus, COPD, HIV, hypertension, pneumonia and chronic liver disease

Table 1: Distribution of patients based on co-morbidities

SYSTEMS	CO-MORBIDITIES	PERCENTAGE
RESPIRATORY	Chronic obstructive pulmonary disease	27.7%
	Pneumonia	10.0%
	Pneumothorax	3.33%
	Bronchitis	6.66%
	Emphysema	1.11%
CARDIOVASCULAR	Hypertension	13.3%
	Congestive cardiac Failure	1.11%
	Ischemic heart disease	3.33%
	Myocardial Infarction	1.11%
LIVER	Chronic Liver Disease	7.77%
	Hepatitis	7.77%
ENDOCRINE	Diabetes Mellitus	30.0%
	Hypothyroidism	2.22%
GENITOURINARY	Stricture Urethra	1.11%
	Pyelonephritis	1.11%
NEUROLOGIC	Cerebrovascular accident	6.66%
	Seizure	4.44%
	Nicotine dependent syndrome	1.11%
LYMPHATIC	Cervical Lymphadenopathy	1.11%

	Central Lymphadenitis	1.11%
GIT	Gastritis	3.33%
	Anemia	35.5%
	Hemoptysis	2.22%
SKIN	Stevens-Johnson Syndrome	1.11%
	Erythroderma	3.33%
INFECTION	Human immunodeficiency virus	16.66%
	Oral Candidiasis	2.22%
OTHERS	Fibrothorax	1.11%
	Hypoalbuminemia	7.77%
	Hyperuricemia	1.11%

A total of 29 types of co-morbidities (Table 1) were diagnosed and these co-morbidities are categorized into various systems. The systems included cardiovascular system-related disease (18.8%), respiratory system-related disease (48.8%), liver disease (15.5%), genitourinary system-related disease (2.22%), central nervous system-related disease (12.2%), endocrine system-related disease (32.2%), skin disease (4.44%), gastrointestinal tract related disease (37.8%), infection (18.8%) and other diseases (9.99%). The most common comorbidity was Anemia (35.5%) followed by diabetes mellitus (30.0%), chronic obstructive pulmonary disease (27.7%) and human immunodeficiency virus (16.66%). In our study, among 90 patients, 23 (26.0%) patients were smokers, 3 (3.0%) patients were alcoholic, 13 (14.0%) patients were both alcoholic and smoker and 51 (57.0%) were non-alcoholic and non-smoker. Maximum patients in the population had no habits of smoking and consumption of alcohol.

Treatment for Pulmonary tuberculosis for all 63 patients included first-line anti-tubercular therapy given as fixed-dose combinations as per National Tuberculosis Elimination Programme (NTEP). The fixed-dose combination HRZE (isoniazid, rifampicin, pyrazinamide, ethambutol) for 2 months in the intensive phase and HRE for 4 months in the continuation phase. These drugs are given in oral route to the patients. (As shown in table 2)

Table 2: Drugs for treatment of pulmonary tuberculosis

REGIMEN FOR PTB	ROUTE	DRUG	DOSE
INTENSIVE PHASE	ORAL	T. ISONIAZID (H)	5 mg/kg daily
		T. RIFAMPICIN(R)	10 mg/kg daily
		T. PYRAZINAMIDE(Z)	25 mg/kg daily
		T. ETHAMBUTOL(E)	15 mg/kg daily
CONTINUATION PHASE	ORAL	T. ISONIAZID(H)	5 mg/kg daily
		T. RIFAMPICIN(R)	10 mg/kg daily
		T. ETHAMBUTOL(E)	15 mg/kg daily

Treatment for extra-pulmonary tuberculosis such as pleural effusion and syn-pneumonic effusion included Inj. Furosemide + ATT, for peritoneal TB T. Levofloxacin + T. Ethambutol and for the treatment of TB Meningitis, Abdominal TB and Spinal TB anti-tubercular therapy was given.

Figure 3: Distribution of patients based on treatment pattern of extra-pulmonary tuberculosis.

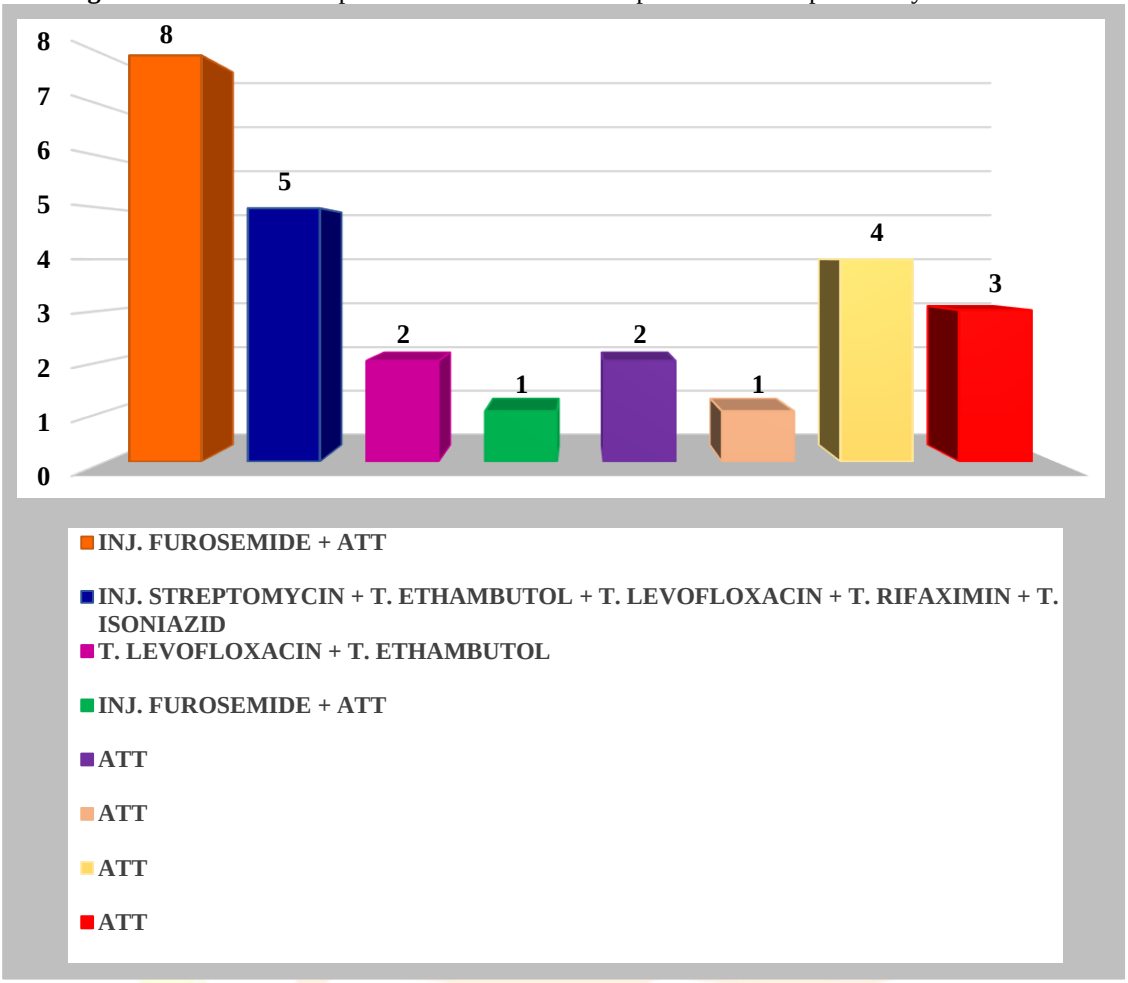

Figure 3 shows the treatment pattern of extra-pulmonary tuberculosis. It shows that 8 patients were given Inj. Furosemide + ATT followed by 5 patients Inj. streptomycin + T. ethambutol + T. levofloxacin + T. rifaximin + T. isoniazid, 2 patients T. levofloxacin + T. ethambutol, 1 patient Inj. furosemide + ATT and other patients were given ATT.

Treatment given for the most common co-morbidities in MIMS hospital is enlisted in Table 3.

Table 3: Treatment pattern for common co-morbidities.

CO-MORBIDITIES	MOST COMMONLY PRESCRIBED DRUGS	PERCENTAGE
ANAEMIA	T. FERROUS SULPHATE AND FOLIC ACID	35%
DIABETES MELLITUS	T. METFORMIN	30%
COPD	NEB. LEVOSALBUTAMOL + IPRATROPIUM + BUDESONIDE	68%
HIV	T. TENOFOVIR+LAMIVUDINE+EFAVIRENZ	46%
HYPERTENSION	T. ENALAPRIL+AMLODIPINE	42%
PNEUMONIA	NEB. LEVOSALBUTAMOL + IPRATROPIUM + BUDESONIDE	45%
CHRONIC LIVER DISEASE	T. URSODEOXYCHOLIC ACID	34%
HEPATITIS	INJ. NAC AND SYP. LACTULOSE + T. UDILIV	30%
HYPOALBUMINEMIA	T. BENADON + PROTEIN POWDER	71%
BRONCHITIS	INJ. PIPERACILLIN+TAZOBACTAM	33%
CEREBROVASCULAR ACCIDENT	INJ. MANNITOL AND T. ATORVASTATIN + T. CLOPIDOGREL	86%
SEIZURE	T. PHENYTOIN	51%

Most commonly prescribed drugs for other co-morbidities include: For the treatment for emphysema included neb. levosalbutamol + ipratropium bromide + budesonide given by inhalation route. The combination of olesoftmax lotion (liquid paraffin + white soft paraffin) + neosol F. cream (clobetasol + fusidic acid) + mucoprocin ointment + Inj. dexamethasone is prescribed patients having erythroderma with TB,

for hypothyroidism T. thyronorm taken once daily, for fibrothorax neb. levosalbutamol + ipratropium bromide + budesonide) 6th hourly. The treatment for Stricture urethra included oral drugs combination of T. cefixime + Syp. sucralfate + T. ACSP (aceclofenac 100mg + paracetamol 500mg + serratiopeptidase 15mg), for myocardial infarction combination of oral drugs T. atorvastatin 20mg + T. clopidogrel 75mg + T. Aspirin 150mg, for ischemic heart disease combination of 3 drugs T. atorvastatin + T. aspirin + T. clopidogrel. Inj. ranitidine + Inj. metronidazole is mostly given for patients with gastritis associated with TB. The treatment for pyelonephritis included T. ciprofloxacin taken orally twice a day. For oral candidiasis T. fluconazole and candidal mouth paint. The treatment for pneumothorax included oxygen supplementation and neb. levosalbutamol + ipratropium bromide + budesonide. The treatment for Stevens-Johnson Syndrome (SJS) included Inj. dexamethasone, momate f. cream (mometasone furoate + fusidic acid), tess oral gel (triamcinolone), moist dew lotion and betadine gargle (povidone- iodine). For cervical lymphadenopathy T. cyclosporine, saline compression, anabel oral gel (choline salicylate + lidocaine), central lymphadenitis includes T. Albendazole, for Hyperuricemia T. Allopurinol, for Congestive chest failure combination of T. Atorvastatin + T. Aspirin + T. Clopidogrel, for Hemoptysis included Inj. traxanemic acid+ Inj. vitamin K and Inj. hemsyl (ethamsylate) + Inj. pause (tranexamic acid) was given parenterally.

Discussion:

India is dealing with a huge burden of not only tuberculosis but also concurrent co-morbid conditions. The cross-sectional study was conducted to find the treatment of active pulmonary and extra-pulmonary tuberculosis associated with co-morbidities. The most common co-morbidity was Anemia followed by Diabetes Mellitus and Chronic obstructive pulmonary disease.

This study shows that males are more prone to tuberculosis associated with co-morbidities as compared to females. When compared with men, women were significantly associated with extra-pulmonary tuberculosis in their forties, fifties, and sixties. Female patients associated with pulmonary tuberculosis were lower when compared with men.[3] However, in our study, it is found that pulmonary and extra-pulmonary tuberculosis occur more in males than females.

Pleural effusion and abdominal TB were common in our study similar to a study conducted in North-East India in 2020.[4] There is no study conducted, where treatment for tuberculosis associated with all the co-morbidities has been studied. There are limited studies that involve treatment for certain co-morbid conditions present with TB such as TB-Hepatitis [5], TB-DM [6] etc. Our study found an association of 29 co-morbid conditions with tuberculosis infection. The treatment of each co-morbidity was studied in detail.

In another study conducted on tuberculosis and tuberculosis-diabetes co-morbidity in Revised National Tuberculosis Control Program (RNTCP) centres of Northern Madhya Pradesh, India [7], diabetes mellitus was found to be the most common co-morbidity. In our study Diabetes mellitus (30.0%) is also one of the common co-morbidities.

Thus, our study has shown that a large proportion of TB patients suffer from various co-morbid conditions, and therefore there is a need to integrate the TB treatment with the treatment of other co-morbidities. TB patients must be provided with wholesome treatment concerning their co-morbidities.

Acknowledgement:

The assistance from the Mandya Institute of Medical Sciences is gratefully acknowledged.

Conflict of interest:

Nil

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