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TO STUDY THE PRESCRIPTION ANALYSIS OF TUBERCULOSIS DRUGS AND MAINTAINING THE SAFETY AND EFFICACY OF TUBERCULOSIS DRUG

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➢ ABSTRACT

This analysis examines the prescription patterns and treatment regimens for tuberculosis (TB), emphasizing the standard first-line therapy comprising isoniazid, rifampicin, pyrazinamide, and ethambutol. The effectiveness of these medications, their potential side effects, and the importance of adherence are discussed. Regular monitoring for hepatotoxicity and other adverse reactions is essential to ensure patient safety. Strategies to improve adherence, such as Directly Observed Therapy (DOT) and patient education, are critical in achieving successful treatment outcomes. Additionally, the analysis highlights the necessity of susceptibility testing to identify drug-resistant TB and the potential use of second-line therapies. Ultimately, a comprehensive approach to TB management is vital for effective treatment and reducing transmission.

➢ **KEYWORD:** Tuberculosis, TB, TB treatment, TB prescription, Isoniazid.

➢ INTRODUCTION

Tuberculosis (TB) is a disease caused by germs that are spread from person to person through the air. TB usually affect the lungs, but it can also affect other part of the body such as lungs, kidney, or spine. Tuberculosis is a chronic granulomatous disease cause by mycobacterium tuberculosis. It affects 1/3rd of world population. In 1999 WHO reports showed 3.5 million of HIV patients in India are infected with tuberculosis and mycobacterium Avium complex (MAC). Now 21st century ICMR 2001 reports showed about 4 million compared total

worldwide rang of 11 million patients.

- **AIM AND OBJECTIVE**

To study the prescription analysis of tuberculosis drugs and maintaining the safety and efficacy of tuberculosis drugs.

- **Objective**

1. To determine the trend of drugs used in the patient with having tuberculosis.
2. To identify the adverse drug reaction or drug-drug interaction in prescribed drug.
3. To determine and analysis which molecules are regularly used for tuberculosis patients in the particular region.
4. Diagnose and treat all TB patients promptly to reduce morbidity and mortality.
5. Prevent transmission of TB to others through proper infection control measures.

Tuberculosis (TB) is an infectious disease that primarily affects the lungs parenchyma. It may also be transmitted to other part of the body, including the meninges, kidney, bones, and lymph node. The primary infectious agent mycobacterium tuberculosis is an acid-fast aerobic rod that grows slowly and is sensitive to the heart and ultraviolet light.

Tuberculosis (TB) leading caused by death world. It is the world second most common cause of death from infectious disease after HIV/AIDS.

India has the highest burden of tuberculosis in world, accounting for 20% of global incidence of TB. This is due to the neglect of TB as a public health problem and mismanagement of TB patient in both public and private sector. Thus the success of any global effort to control tuberculosis is critically dependent on the success of such an effort in India.

In a study on the role of private practitioners in national tuberculosis control programme, it was found that 90% of them prescribe drug that are used in short course chemotherapy and 67% depend upon the advice of representative of pharmaceutical firms about current treatment of tuberculosis. Apart from causing prolonged morbidity and increased mortality from the disease, poor prescribing practices also fuel the emergence and spread of drug resistant organism, and are most certainly n of the reason why india accounts for over a 5^{th} of the global MDR-TB (multi drug resistant tuberculosis) burden, with indicators showing a rising trend.

The national TB control programme was started in 1962 with the aim to detect cases earliest and treat them. In the district, the programme is implemented through the district tuberculosis center and the primary health institutions.

- **Discovery of agent**

Different antitubercular agents have been discovered from time to time some such important agents are streptomycin (1944). Isoniazid (1950). Rifampin (1970). Fluroquinolone (2nd generation 1990). Other new agents which are added in 2nd generation are macrolides and rifampicin congers. According to applicability of tuberculocidal agent. Drugs are classified as a first line and second line.

Classification

First line drug	Second line drug
Isoniazid	Para-amino salicylic acid (PAS)
Rifampicin	Ethionamide
Pyrazinamide	Cycloserine
Streptomycin	Macrolides antibiotics

First line agents having more advantages compare to second line agent. They exhibit high efficacy along with low toxicity levels. While second generation agents are characterized by low efficacy and high toxicity, due to this reason this agents area used in special circumstances.

- **First line agent**

1) Isoniazid:- (INH)

Isoniazid was develop in 1952, and become the most active drug for the cure of tuberculosis. Isoniazid is an vital component treatment regimen. It is a tuberculocidal and inhibits fast multiplying bacilli. Isoniazid is active in both acidic as well as alkaline medium. Structurally, it resembles t pyridoxine.

Mechanism of action:- isoniazid is a product and it catalyzed by mycobacterial enzyme peroxidase (encoded by katG gene) activated into biological active from of isoniazid which inhibit the mycolic acid synthesis which is important constituents of mycobacterial cell wall. Mycolic acid is a waxy lipid and make up the maximum component of cell wall. Thus, isoniazid inhibit the lipid content of cell wall of mycobacterial cell.

- **Antimicrobial activity**

1) High activity against both intracellular and extracellular and extracellular tubercle bacilli.
2) Atypical micro bacterial are not inhibited except M. kansasii.

- **Mechanism of resistance**

Resistance may developed due to the following reason-

1) Due to use of isoniazid alone, resistance develops after 2-3 months of isoniazid.
2) Mutation are targeted site (inhA) of isoniazid
3) Mutation in katG gene responsible for inactivation of isoniazid
4) Loss of concentrating process of isoniazid.

- **Pharmacokinetics**

Isoniazid is absorbed orally and radially diffuse into all body tissue and fluids.

It get metabolized in liver by N-acatylation. Genetic variation has been observed in its metabolism of isoniazid while in lo acetylators it is around 3 hours because of less metabolism. Thus the status of acetylation may influence the isoniazid toxicity in which slow acetylators are more susceptible to develop peripheral neuritis and hepatotoxicity isoniazid is more susceptible to develop peripheral neuritis in slow acetylators because of increased in the pyridoxine excretion in urine and decreased in peripheral utilization of pyridoxine because of inhibition of enzyme pyridoxine kinase which is required to convert the pyridoxine to active pyridoxyl phosphate. The metabolites excreted in urine.

- **Clinical use**

1) Isoniazid is a first choice of drug for all types of tuberculosis.

- Adverse reaction:-

1) CNS toxicity: memory loss, psychosis and seizures are outcome of CNS toxicity
2) Hepatoxicity: - the most frequent result hepatotoxicity is increased in aminotransferase and hepatitis.

- **Drug intraction**

1) Isoniazid inhibit the metabolism of phenytoin, carbamazepine, diazepam, warfarin thus result in toxicity of interacting drug.
2) Para amino salicylic acids inhibit the metabolism of isoniazid thus resulting into increase half-life of isoniazid.

- **Second line drug**
- **Para-Aminosalicy acid (PAS)**

Para aminocylic acid is bacteriostatics and highly specific to mycobactereiun tuberculi while it is usefully others. Most common non-tuberculous mycobacteria are not inhibited by the drug. Mechanism of action appears to be very similar to that of the sulfonamide inhibits the folate synthesis in mycobacterium tuberculi while is against sulfonamide susceptible bacteria.

- **Pharmacokinetics**

Para-aminosalicylic is radially absorbed on oral administration. It is distributed throughout the body while CSF levels are low. The drug has a half- life of about 1 hour and concentrations in plasma are negligible within 4-5 hour after a single dose. It is compenting with isoniazid for its metabolism because both are metabolized by same pathway example acetylation. There is an increasing half-life of isoniazid addministetered along with para-aminosalicylic acid over 80% of the drug is excreated in the urine excreation of amino-salicylic acid is greatly retarded by renal dysfunction probenecid decresed the renal excreation of this agent. Para-aminosalicylic acid is gastric irritant thus the drug is best addministered after meals.

- **Adverse effect**

1) Gastrointestinal problems including anorexia, nausea epigastria pain, abdominal distress and diarrhea.
2) Hypersensitivity reactions, fever, malaise, joint pains, and sore throat may be present
3) Skin eruption, hematological abnormalities including leukopenia, agranulocytosis, eosinophilia, lymphocytosis and thrombocytopenia are seen.

- **Mechanism**

Similar to isoniazid, ethionamide is an inactive prudrug which is converted into active from in presence of FAD-containing monoxygenase, into a sulfoxide which is converted which is non-toxic to mycobacteria. Ethionamide inhibits mycobacterial growth by inhibiting the activity of the enzyme that is inhibited by isoniazid resulting into inhibition of mycolic acid biosynthesis and consequent impairment of cell-wall synthesis.

- **Treatment of tuberculoasis**

>The first rules of TB treatment are:-

1) Enough drugs at least 3-4 drugs should be used.

2) The right drugs should be chosen according to its antimicrobial sensitives.
3) Enough milligrams of each drug should be used according to body weight of patients.
4) Enough doses should be given to patient.
5) Attention to monitoring of laboratory studies and clinical course of therapy.

- **Regimen/ therapy for tuberculosis treatment**

In conventional therapy, the treatment was given for period of 12-18 months. It includes isoniazid and thiacetazone/ethambutol with or without streptomycin. There was high failure rate with this regimen and poor compatible from patients. In 1995, WHO worked on new regimen and development standards short course regimen for periods of 6-9 months. In the conventional regimen get reduced from 12 months to 9 months because pyrazinamide is more effective during first 2-3 moths of administration of drug and during this period there is more inflammatory changes in tubercular patient which is more favorable condition to pyrazinamide. Thus, combination of isoniazid and rifampicin and pyrazinamide reduced the conventional therapy from 12-18 moths to 6-9 moths. This combination is more effective and less toxic. The new regimen is possible because of greater understanding of biology of tuberculi and property of anti-TB drugs.

- **Modified regimen in tuberculosis**

Resistance drug (s)	Treatment modifications
H	REZ continue for 12 months.
R	Extent the treatment with HEZ for 12-18 months.
H,R	Extent the treatment with HRE for 9 months.
Z	Extent the treatment with HRE for 9 months.
HRZ	E+ second line agent for 24 months.
HRE	Second line agent for >24 months.
HREZ	Z+ second line agent for >24 months.

- **Treatment of tuberculosis in AIDS patients**

HIV infected patients are most pone for the infection of TB watched closely. Infant of infection because of their weak immune system. Adverse reaction to anti-TB are common in such type of patient.

Such types of patients are treated by short course therapy immediately after diagnosis of TB. It is as follow.

- Initial phases are given by HRZE for 2 months and therapy immediately after diagnosis with HR for next 7 months so there compulsory to give the therapy for 9 or 6 months respectively.

- Mycobacterium avium complex infection is most common in AIDS patient and such type of patient is treated by using azithromycin/ clarithromycin and ethambutol with second line agent rifambutin. Fluoroquinolone may be added in therapy
- Lifelong therapy is needed in such type of patient and for prophylyxis of MAC in HIV clarithromycin or azithrhromycin is given.
- All the anti-TB agent are compatible but baby should be watched closely. Infant should receive BCG vaccination and isoniazid should be given for prophylaxis.

India a country with over 1.21 billion people has the highest burden of tuberculosis TB in the world, accounting for 20% of the global incidence of TB, and an even higher share of global incidence of multi drug resistance (MDR) TB, thus the success of any global effort to control TB and MDR-TB critically dependent on the success of such an efforts in india. The india national TB programme (NTP) was launched in 1962, but suffered from inadequate program funding, managerial weaknesses, irregular drug supply and multiplicity of treatment regimens (2) with low rate of cases detection and treatment completion (30%), high rates of default (40-60%). And counting high mortality (50 per 100,000) the NTP failed (2). Acknowledgement this reality, a revised national tuberculosis control programme (RNTCP) was launched by the government of india in 1997, based on the global DOTS programme (directly observed treatment, short curse) strategy which aim to have an epidemiologic impact by achieving 70% case detection and 85% cure rates. By 2006 100% of the indian population was covered by the DOTS programme, making this scale-up one of india's most significant public health accomplishment. The RNTCP has resulted in impressive improvements in cure rates (currently >80% in new infectious cases), sub-stantial decline in death rates with low rates of default (<10%) (3.4)

Despite this success, india continues to have an estimated annual incidence of more than 2 million TB cases. While the problem of TB in india is characterized by high incidence, high prevalence, and high rate of transmission of TB infection (5), available estimates of the TB burden have been inconsistent. The most recent world health organization (WHO) estimate of TB morbidity and mortality for india are show in 1 contrast, the tuberculosis research center (TRC) in india estimated the burden to be substantially higher, with 8.5 million cases of TB of all forms in the year 2000, including 3.8 million smear-position cases and 0.8 million cases of extra-pulmonary TB. This was based on surveys conducted in india, where the prevalence of culture-positive and smear-positive pulmonary TB were found to be 605 per 100,000 and

323 per 100,000 respectively, considerably higher than the WHO estimates.

The problems of drug resistance TB, HIV co-infection, and the social costs of TB in india are staggering. With an estimate annual incidence of 99,000 cases of TB in India. Currently, less than 1% of MDR-TB patients have access to effective treatment, and there is an urgent need for scale-up f access to MDR treatment. India has an estimated 2.27 million people who are HIV infected and at the higher risk of developing TB. Although case fatality rates have declined, the number of persons drying from TB is unacceptably high. TB has a devastating impact on patients and families. The mean cost (direct or indirect) can be high as 40% of the annual income, pushing poor families into further debt and destitution. The costs of TB to the nation have been computed to be 3 billion per year.

Why is TB such a big problem in India, despite the success of the DOTS program? TB is a disease of poverty, with several known social determination (e.g. malnutrition and tobacco smoking)

Treatment in the private sector is often started based on serology is often started based on serology results, with potentially disastrous consequences for patients as diagnostic practices lead to wrong and or delayed diagnosis inflates costs of care, could explain the delay of 1-2 months before a TB patient get diagnosed, and the reason why even those patients who do reach a DOTS center do so after initially visiting 6-9 healthcare providers. Thus, undiagnosed TB, delayed diagnosis and mismanaged TB continues o fuel the TB epidermis.

- **Management of adverse reaction to anti-TB agent**

1) Minor reaction to anti-TB agent is managed symptomatically without altering the regimen in TB patients.
2) If there is serve from of reaction to anti-TB agent then one need to stop the therapy and reintroduce after reaction has subsides.
3) If serve reaction like heamolysis, thrombocytopenia, renal failure occurs then should not reintroduced rifampin in TB patient.
4) Hepatotoxicity is common reaction with anti-TB agent and it is common with isoniazid. Rifampicin and pyrazinamide. When the combination therapy used in treatment then hepatotoxicity occurs frequently.
5) If hepatitis develops stop the regimen and continue with streptomycin and ethambutol; fluroquinolone may be added to this therapy.

6) When the reaction clears, HRZ added to above regimen but one by one and identify the culprit drug which potentiates to causes hepatitis.

➢ MATERIAL AND METHODS

All the patients attending a department of pulmonary medicine outdoor patient department at government at government medical collage and hospital, Nagpur, who gave history of previous treatment with anti-tuberculosis drugs by previous treatment with anti- tuberculosis drugs by private practitioners. Were requested to deposit a Xerox of their prescriptions, were requested for this study. 105 prescription under RNTCP (as per RNTCP treatment card) were includes in the study. The 1st recent prescription of anti TB drugs of each patient was enrolled in the study. Any modification in the regime on account of adverse drug reaction or co mortifies excluded the diagnosed drug resistance tuberculosis was excluded from the study.

The data from these prescriptions along with the demographic data of the patient taking treatment in both groups was then entered into a Microsoft excel programme especially designed for Microsoft excel programme especially designed for the study and then subsequently analyses. Proportion method was used for data analysis and comparison of parameters among the two groups. The two proportion Z test was utilized for comparing parameters" (Viz. RNTCP prescriptions and private practitioner prescriptions). Significance was measured at level of < 0.05 and < 0.01 was considered highly significant. The prescriptions were then evaluated by software programme as per the recent WHO guidelines and a prescription was labeled to be correct if it fulfill all of the following criteria:

1) At least 4 first line anti TB drugs were prescribed
2) All the drugs were in doses as per weight as per WHO recommendations.
3) All the drugs were prescribed to be taken at once at the same time.
4) The prescription did not contain any second line anti TB drug since all diagnosed drug resistance TB patients were excluded from the study.

➢ Comparison of anti TB treatment parameters between private and public sector:

Sr. No.	Prescription dosing	Private practitioners	Public sector (RNTCP)	P value
1	Correct	10 (9.52%)	5 (4.76%)	0.1804
2	Faulty	95 (90.40%)	100 (95.24%)	0.1804
3	Suboptimal	56 (53.33%)	30 (28.57%)	0.0003

4	Overdose	56 (53.33%)	72 (68.57%)	0.0236
5	Factors for drug resistance	71 (67.62%)	30 (28.57%)	<0.0001

- *NS= not significant, **S= significant, ***highly significant.

- **Prescription by private practioners**

Out of the 105 prescriptions made by private practitioners, only 10 (9. 52%) were correct. The remaining 95% were faulty.

Suboptimal dosing was percent in 36 (34.29%) prescriptions, overdosing was present in 36.29% prescriptions and both suboptimal dosing as well as overdosing was percent in 20 (19.05%) prescriptions. Thus overall suboptimal dosing was comparison of parameters among the two groups.

1) Inclusion criteria

All the people attending respiratory medicine outpatient department/ inpatient department (OPD/IPD) and diagnosed with TB (pulmonary and extra pulmonary) aged more then 13 years, and registered at the study site tuberculosis unit during the study period were included.

2) Exclusion criteria

People diagnosed with drug resistance TB, critically ill/ moribund patients, PWTB not providing consent for the study, PWTB rifambutin base ATT regimen where ATT regimen had modified and PWTB deranged liver function tests/kidney function tests at baseline were excluded from the study.

Pretreatment investigation

1) Sputum smear for acid fast bacilli/ cartridge-bases nucleic acid amplification test
2) For all pulmonary TB patients: chest radiography,
3) HIV testing by enzyme-linked immunosorbent assay (ELISA) method and random blood sugar.

During the study period, any other investigation as clinically required was performed for ADR evaluation.

The standardized weight band-based daily FDC first line ATT regime under NTEP comprised of initial two months of intensive phase with isoniazid and other drugs related to the TB,

follow by the continuation phase of four months, at baseline and monthly intervals for six months after treatment commencement, patients were evaluated by doctors trained in NTEP standards for clinical evolution. The doctors trained in NTEP standards for clinical evaluation the occurrence of adverse events was the primary outcome variable. Before treatment initiation and throughout the all follow-up visits, all the patients and their family members were counseled about the possibly of adverse events and encouraged to report the. The doctor accessed the PWTB for possible adverse event at each follow-up appointment and recorded the same in case record forms. Thus, ant adverse events, found were noted and managed at each visit, depending on clinical and laboratory evidence. All ADRs are found in the study were reported to the pharmacovigilance program in india (PvPI). The servility of anti-TB related ADR was classified as in 1. Mild and 2. moderate

Inclusion criteria were pulmonary tuberculosis patients diagnosed as primary treatment failure (category 1st) or relapse case or resistance TB (category 2nd). Cases of either sex with age above 14 years and patients who were under DOTS. While patient's with history of hepatitis, renal or hepatic impairment; pregnant woman and age below 14 years were excluded from the study.

In total 34 patients were included in this study, of which 14 had received category, I, 4 anti-TB drugs that includes rifampicin, isoniazid, ethambutol, pyrazinamide. Another 20 patients received category II: 5 anti-TB drug that include rifampicin, isoniazid, ethambutol, pyrazinamide, and sparfloxacin. All the patients received the drug under direct observation therapy short- course (DOTS) – treatment program.

Primary variable were organ related adverse effect and biochemical parameters were estimated before (0 week) and 4 and 8 weeks after initiation of treatment.

Data was analyzed by x, one-way ANOVA with repeated measure design and post hoc test of significance was done by pair t test by using SPSS 11.

- **Example of collection of prescription**

Prescription	**Tablet**	**Contain**
Prescription 1st	1)AKT-3KIT 2)Tab-Blong 100 3)Powder nusowin	>Vit-b6 > Rifampicin+ ethambutol+isoniazid > Soya protein+ meltodextrin + skimmed milk powder

Prescription 2nd	1)Tab-Blong-100 2) AKT-3KIT	>Rifampicin+ ethambutol+isoniazid >Vit-B6
Prescription 3rd	1)Powder nusowin 2)tab-Blong-100	>Soya protein+ meltodextrin + skimmed milk powder >Rifampicin+ ethambutol+isoniazid
Prescription 4th	1) tab-Blong-100	>Rifampicin+ ethambutol+isoniazid
Prescription 5th	1)AKT-3KIT 2)Powder nusowin	>Rifampicin+ ethambutol+isoniazid >Soya protein+ meltodextrin + skimmed milk powder
Prescription 6th	1)tab-Blong-100 2)AKT-3KIT	>Rifampicin+ ethambutol+isoniazid >Vit-B6

- Studies about the drug/ drug profile
- **First-line agent**

Drug	**Isoniazid**	**Rifampicin**
Mechanism of action	Isoniazid is a product and it is catalysed by the bacterial enzyme peroxidase encoded by katG-G gene, activities biological active form of isoniazid which inhibit the mycolic acid synthesis which is important constituent of mycobacterial cell walls, mycolic acid is a waxy lipid and make of the maximum component of cell wall thus, isoniazid inhibit the lipid content of cell wall mycobacterial cell,	Rifampicin strongly binds.to beta subunit of bacterial DNA-dependant RNA polymerase and inhibit RNA synthesis this polymerase enzyme is essential for the initiation and both of new RNA chain. There is conformational change in that enzyme rifampicin so the enzyme cannot initiate the new RNA chain formation. RNA chain of mammalian is not affected because the drug does not bind with mammalian RNA polymerase.
Antimicrobial activity	1) High activity against both intracellular and extra cellular tubercle bacilli. 2) A typical mycobacterium are not inhibited except M. kansasii.	-
Clinical use	Isoniazid is a first choice of drug for all types of tuberculosis.	Rifampicin is the major drug in management of tuberculosis and leprosy.
Pharmacokinetics	Isoniazid is absorbed orally and radially diffuses in to all body tissue and fluid. It gets metabolised in liver	Rifampicin is absorbed orally well and widely distrusted to isoniazid.

	by N- acetylation. Genetic variation has been observed in its acetylation, in fast acetylators plasma half life is found to be one house because of fast metabolism of isoniazide while in slow acetylators it is around 3 hours because of less metabolism.	Metabolism take place in liver and the metabolised are excreated mainly in bile and urine. Plasma half life is found to be 2-5 hours.

- **Second line agent**

Drug	**Para-Aminosalicylic acid**	**Ethionamide**
Mechanisma	Para-aminosalicylic is bacteriostatic and is highly specific to mycobacterium tuberculi while it is unaffected on others. Most non-tuberculosis mycobacterium are not inhibited but the drug. Mechanism of action appears to be very similar to that of the sulphonamides, it inhibited the folate synthesis in mycobacterium tuberculi while is inactive against sulphonamides-susceptible bacteria.	
Pharmacokinetic	Aminoglysides are a group of potent antibiotics primarily used to treat certain infection caused by aerobic gram negative bacteria they are used in treatment if sever infection of the abdominal urinary tract skin and soft tissue bones, cervix, blood, eye, ear, lungs and heart.	
Adverse effect	The main noted adverse effect of Aminoglysides are ototoxicity, nephroxicity neuromuscular blockage aminoglycosides induced toxicity has been reported occurred in 2-45% of adult Nephrotoxicity due to amino glycosides may appear in up to 10-25% of patients.	

- **Analysis**

In India, the overall prevalence of infection is 30%. More than 40% of the adult are infected with TB, and approximately 1.5 million cases are put on treatment every year. Every smear positive case can infect approximately, 10-15 cases, thereby increase in the pool of the infected person. The median survival from diagnosis to death was 23.5 days. With a minimum several time of two days and maximum of 1688 days the SD was 174.6 days and

the mean was 73 days. There are two kinds of test use to detect TB bacteria in the body test. A positive TB skin test or TB blood test only tells that a person has been infected with TB bacteria it does tell whether the person has latent TB infection (LTBI) or has progress to tuberculosis.

Most national TB studies in high burden countries have reported a higher burden of disease among men, with male-to-female. Tuberculosis blood test can be used to confirm the presence of latent TB or active TB. Immune system reaction to tuberculosis bacteria major used in high end technology through tuberculosis blood test. The most commonly prescribed tuberculosis blood test were QuantiFERON-TB gold in-tube test and T-spot tuberculosis test.

^There are some examples of prescription collection and there analysis:-

- **Prescription 1st**

1) AKT-3-KIT

Contain:- rifampicin + ethambutol + isoniazide

2) Tab-blog -100

Contain:- Vit-b6

3) Powder nusowin

Contain:- soya protein + maltose + skimmed milk powder

- **Prescription 2nd**

1) AKT-3-KIT

Contain:- rifampicin + ethambutol + isoniazide

2) Tab-blong -100

3) Contain:- Vit-b6

- **Prescription 3rd**

1) AKT-3-KIT

Content;- rifampicin + isoniazid + ethambutol

2) Tab-blong-100

Content:- vit-b6

3) Powder nusowin:-soya protein + maltose + skimmed milk

➢ **Prescription 4th**

1) AKT-3-KIT

Content;- rifampicin + isoniazid + ethambutol

2) Tab-blong-100

Content:- vit-b6

3) Powder nusowin:-

Contain:- soya protein + maltose + skimmed milk powder

4) tab-mega flexon

Content:- paracetamol + acetaminophen + tramadol

➢ **Prescription 5th**

1) AKT-3-KIT

Content;- rifampicin + isoniazid + ethambutol

2) Tab-blong-100

Content:- vit-b6

3) tab-mega flexon

Content:- paracetamol + acetaminophen + tramalol

➢ **Prescription 6th**

1) AKT-3-KIT

Content;- rifampicin + isoniazid + ethambutol

2) Tab-blong-100

Content:- vit-b6

3) Powder nusowin:-

4) Contain:- soya protein + maltose + skimmed milk powder

➢ **Prescription 7th**

1) AKT-3-KIT

Content;- rifampicin + isoniazid + ethambutol

2) Tab-blong-100 Content: - Vit- b6

Collect the prescription and analysed individual prescription.

⇩

We collect the prescription of the patients who suffered from tuberculosis,

⇩

Collect near about the 100-120 patients prescriptions who belong from the same region (Chatrapati Sambhajinagar)

⇩

Then we did studied about the drug and also find out the content which mainly contain in invidual drug.

⇩

After that we did studied about the prescribed drugs and find out the same kinds of drug which having the same contains.

⇩

In between the study we observed that the (AKT-3KIT is combination of isoniazid + rifampicin + ethambutol) drugs are regularly prescribed by the physician to the patients.

⇩

Some other drugs which also regularly prescribed by the physician are as follow:-

1) Tab-blong-100.

2) Tab mega-flexon.

Prevalence of PTB disease in population can vary due to demographic difference like sex and age. This study analysed the prevalence of PTB amongst the population in western Uganda and it has been revealed that prevalence PTB was highest in the age group 20-29 years old. This age bracket comprises of the youth whose behaviour and active participations in social activities predisposes them TB infection. The youth are fond of travelling frequently have most social contact and spend more time in settings that may be favourable to PTB transmission such as bars, cinema halls or night clubs. Conversely, no PTB case was recorded in age groups 10-19 years' old this age bracket is composed of teens whose movements are controlled by either their home family or study educational institutional the restricted moment trend was visible among the study participants where by teen accounted for the least recruitment for the advance.

The study found out and association between PTB disease and clinical symptoms all PTB positive cases presented with clinical manifestations of persistence fever cough, for two weeks night sweats and noticeable weight loss in the hierarchical order. During tb disease, the intraction between m. tuberculosis or endogenous pyrogens cytokines such as interleukin (IL_-1) IL- 6 tumour necrosis factor (TNF) Alfa with the organum vasculum of the lamina terminals OVTL lead to production of fever. The OVTL is highly vascular and lacks a blood

brain barrier, permitting it to be stimulated by m. tuberculosis, and other pyrogenic substances 20. Its stimulation leads to increase synthesis of prostaglandin. Which act on the hypothalamus result into an increasing body temperature 20. Although shorts term fever may be beneficial prolonged fever tend to extract a metabolic cost with depletion of muscles mass and essential nutrients leading to malnutrition that ultimately weak the immune system (21). We also observed those participants who tested positive for TB without fever had cough and any other symptoms (night sweats or noticeable weight loss). Meanwhile, more than half of the participant with fever also had night sweat when the human body is responding to cytokines induced by m. tuberculosis, hypothalamus reset body temperature to higher level for a later body temperature returns to normal and extra heat is loss by sweating. This shows that prediction of presumptive TB required more than one clinical symptom.

Cough was observed in almost 90% of participant who tested positive for TB we also found out that 10% of the non- coughing patient who tested negative for the disease lack other TB clinical symptoms. In people with TB disease, cough in reflex is stimulated by m. tuberculosis organisms that are pre dominantly transmitted via. Cough initiated by respiratory track nociceptible neurones. The cell wall of m. tuberculosis consist of a complex lipid called selfolipid-1 that stimulates nociceptive receptor to produced inflammatory neural peptides that induced cough in. there was a positive correlation between clinical symptoms and TB with cough and fever being good predicators of presumptive TB disease hence cough and fever are possible targets that can be explore for future better TB diagnostic innovation.

The physiological hypothesis point at biological differences between sexes that render once acceptable to disease biological explanation for the male bias in TB susceptibility include x-linked genetics and differences in immune response anatomy and nutrition status. The x-linked genetic factor play an important role as far as susceptibly TB disease is concern 9 gene are well understood to be associated with medallion susceptibility of m. tuberculosis disease of which to (IKBKB AND CYBB) are x-linked and thus, essentially only observed in male. The x-linked chromosome content approximately 11oo gene majority of each are immune modulatory compared to only 100 gene on the Y chromosome (11). The random inactivation of X-chromosome prevents gene dosing effect in female hence the result female always express the beneficial x-linked polymorphism inherited and are less vulnerable to deleterious mutations. On the contrary males are at the mercy of the x-linked chromosomes inherited from the mother. The objective of this study is to know the prevalence of pulmonary TB in

cases brought to tertiary care hospital with speciation of age and gender. Material and method- results and discussion- sputum acid-fast bacilli (AFB) smear microscopy was done by zieglneelsen (ZN) method. The study is carried out on 194 total valid samples. 5.15% of total samples are found positive for pulmonary TB. 3.22% of male and 8.57% of female are positive in age bracket of 41-60 years where as positive cases are present in all age bracket in female patients, the maximum cases are recorded in female patients. In female patients in age group 21-60 years. The pulmonary TB was higher (5.33%) in hospitalized IPD patient in comparisons to OPD patients 4.54% out of the IPD patient cases 4.16% male and 4. 54%. Female patients are found positive. The results of this study depict the maximum share of positive pulmonary TB cases are female patients. The positive cases from the OPD patients. The906ositivee cases from the OPD patients are 5.33%. Female patients in OPD recorded highest 13.33 positive cases. 5.15% samples conclusion – out of the tested samples are found positive. This percentage of the positive patients' cases of pulmonary TB out of tested sample in present study is higher than the national.

WHO recommended the use of rapid molecular diagnostic test as the initial dynamistic test in all person with signs and symptoms of TB. Rapid diagnostic test recommended by WHO include the expert MTB/RIF althea and truant assays. This test has high diagnostic accuracy and will lead to major improvement in the early detection of TB and drug resistance TB. A tuberculin skin test (TST) or interferon gamma release assay (IGRA) can be used to identified people with infection diagnosing multidrug-resistance and other resistance on of TB (c multi drug-resistance TB section below) a well as HIV-associated TB can be complex and expensive tuberculosis expensive is particularly difficult to diagnosed in children. Treatment tuberculosis disease is treated with antibiotics. Treatment is recommended for both TB infection and disease. The most common antibiotic use are;

Isoniazid, rifampin, pyrazinamide. Ethambutol and streptomycin.

To be effective, this medication need to be taken daily for 4-6 moths. It is dangerous to stop the medication earlier without or medical advice. This can allow TB that is still a live to become resistant to the drugs. Tuberculosis that doesn't respond to standard drugs is called drug-resistance TB and required more toxic treatment with different medicine multi-drug resistance TB drug resistance emergence when TB medicine are used in appropriately through incorrect prescription by health care provider, poor quality drugs or patient stopping treatment pre-maturely, multi drug-resistance tuberculosis (MDR –TB) is a form of TB cause

by bacteria that do not response to isoniazid and rifampicin the two most effective first-line TB drugs. MDR-TB is treatable and curable using second line drug. However, second line treatment option required extensive medicines that are expensive and toxic, in some cases, more extensive drug resistance can be develop.

TB cause by bacteria the do not response to the most effective second line TB drug can live patient with very limited treatment option, TB remains a public crisis and a health security treat. Only above in five people with drug resistance TB access treatment in 2022. In accordance with WHO guideline, detection MDR cross line-TB requires bacterio-logical conformation of TB and testing for drug resistance using rapid molecular test or culture method. In 2022, new WHO guild line priorities a six month regimen-the capital BpaLM-line BpaLM – as a treatment of choice for eligible patients. The shorter duration. Lower pill burden and high efficacy of this novel regiment can help ease the burden on health system and save precious resource to further the diagnostic and treatment coverage for all individual needs. In the past, MDR-TB treatment used to last for at lead 9 months and up to 20 months WHO recommended expanded exist to all- oral regiments and HIV people living with HIV and 16 (uncertainty interval) 14-18 time more lightly to fall ill with TB disease than people without HIV. TB is the leading cause of death among elopes with HIV. And TB form a lethal comb nation, its spading the others progress. Without proper treatment, 60% of HIV – negative people with TB on average and nearly all HIV positive people with TB will die in 2022, above 167 000 people died of HIV associated TB. The percentage of notified TB patient who had a documented HIV test result 2022 was 80%, a form 76% in 2021, WHO reason has the highest burden of HIV associated TB, overall in 2022. Only 54% TB patient known to be living with HIV where on untried trivial thereby ART. WHO recommend of 12 component approach to collaborative TB HIV activities including action for prevention and treatment of infection and diastase to reduced death.

1) Proving global leadership to end TB through strategy development, political and multi-sector engagement, strengthening review accountability. Advocacy and partnership, including with CV society.
2) Shaping the TB research and innovation agenda and stimulating the generation, translation and dissentions on knowledge setting norms and standard on TB prevention and care promoting and fascinating there implementation.
3) Developing and promoting ethical and evidence- base policy option for TB prevention and care.

4) Ensuring the provision of specialised techniques support to member state and partner jointly with WHO reigns and country office catalysed in change and building sustainable and capacity stop and.
5) Monitoring and reporting on the status of the TB epidemic and progress in financing and implementation of the response of global, regional and country levels.

➢ CONCLUSION

A study has been done" and it concludes that the some common medicines are used for the TB in the particular (Chatrapati Sambhajinagar) region.

Are as follow

1) AKT-3KIT :- which is combination of- rifampicin, isoniazid, ethambutol,
2) Tab-blong-100 :- which is combination of vit-b6
3) Tab-mega-flexon :- which is combination of paracetamol,

In conclusion tuberculosis is distributed throughout the study hospital. At least in the clinical were positive to tuberculosis in all tested hospitals. The prevalence of tuberculosis was influenced was influenced by breed, age and body to cite this paper. India has the highest burden of tuberculosis in world, accounting for 20% of global incidence TB treatment is available both in private and public sector. Prescription of the immunotherapy of anti-TB drugs. Even this single drug was not prescribed in the correct dose of ethambutol for this adult patient weighing 39 kg would have been 585 mg to 780 mg per day per day single once a day dose as per the WHO guidelines, thus the inadequate number of anti-tuberculosis drugs and incorrect dosing make third regime faulty. Thus the indedequate dosing it need to be stressed here that he combination of drug prevent the appearance of resistance, because it avoid the selection of naturally resistance mutants, hence always adequate number of anti-tuberculosis in the patient. Single dose f administration of all anti tuberculosis drugs in the recommended doses is important so as to achieve the desire serum concentration of the drugs. Both these factor are extremely important to prevent emergence of drug resistance tuberculosis14.

On the other hand of overdosing, of anti-tubercular drugs was high in prescriptions, which is a risk factor for the drug toxicity can result in treatment failure and sometimes death if adequate care is not provided promptly. Also changes in treatment necessitated by toxicity can prolong duration of treatment especially in older patients.

A major causes of this drug toxicity is the absence of weight bands in patients weighing more than 30 kg. the current study revealed that all patients weighing more than 30 kg received the same 600mg of INH thrice weekly under the current WHO guidelines recommend an INH dose of 10 mg/kg according to these guidelines the 600 mg dose would be considered appropriate only for patients with weight>50kg there is a tendency to indian patient to receive high drug doses in terms of body weight indian patients to received high drug doses in terms of body weight later the recommended that adult drugs will be given in the recommended number of pills capsules irrespective of body weight later, recommended that adult patient weighing <30 kg of body weight and subsequently separate weight bands were instituted for the pulse program, (national TB program).

High doses increases toxicity without a commensurate increase in efficacy and low dosage may reduce efficacy and allow emergency of resistance. First line drugs should be taken as a single dose. Spitting first line drugs into several doses per day lower body weight.

We also observed those participants who tested positive for TB without fever had cough and any other symptoms (night sweats or noticeable weight loss). Meanwhile, more than half of the participant with fever also had night sweat when the human body is responding to cytokines induced by m. tuberculosis, hypothalamus reset body temperature to higher level for a later body temperature returns to normal and extra heat is loss by sweating. This shows that prediction of presumptive TB required more than one clinical symptom. If a patient develops drug resistance because if incorrect ingestion of medication, this is legal and ethical fault.

In an article on drug toxicity, published in 1986, the tuberculosis research canter concluded that: there is a tendency for indian patients to receive high drug doses in terms of body weight, as fixed doses which have been fixed for heavier western patients are transferred without adjustment to light weight indian patient" the view on this recommendation in 1997 had stated: for adult drug will be given in the recommended number of pills/ capsules irrespective of body weight, later the tuberculosis recommended that adult patient weighing <30 kg be given regimes according to body weight and subsequently seprate weight bands were instituted for this group. Also DOTS plus programme (national TB programmer for management of drug resistance tuberculosis) happen due to oversight, heavy rush of patients, lack of communication, etc. also lack of update or up gradation of exiting knowledge or not keeping pace with correct evidence based scientific principle of management as per current

guidelines are further contributing factors.

Programmatic constraint in field condition is condition is a factor that needs to be considered in programmatic management of TB in the public sector during assessment of correctness of TB prescriptions in the public sector. Possible solution to correct the high amount of faulty anti-TB prescription. There should be separate accreditation for prescription anti-TB drugs. Over the counter sale of anti TB drugs should not be allowed and responsibility of the treatment system for falling to organize treatment, including direct observation effectively.

In private sector, the specialty wise distribution of the anti-tuberculosis prescription revealed that correct proportion of anti-TB prescription was maximum in prescriptions prescribed by chest physicians. It is all cases for initiation of anti-TB drugs,

Treatment in the private sector is often started based on serology is often started based on serology results, with potentially disastrous consequences for patients as diagnostic practices lead to wrong and or delayed diagnosis inflates costs of care, could explain the delay of 1-2 months before a TB patient get diagnosed, The standardized weight band-based daily FDC first line ATT regime under NTEP comprised of initial two months of intensive phase with isoniazid and other drugs related to the TB, follow by the continuation phase of four months.

➢ DISCUSSION

In present study, anti-tuberculosis prescription were faulty in major prescription which is made by private practitioner and prescriptions. This data is in accordance with result found in similar other Indian studies.

Factors for emergence of drug resistance tuberculosis induced suboptimal dosing, spilt dosing, and inadequate number of drug tubercular drugs and prescription of second line anti TB drugs to non drug resistant tuberculosis patients.

In the current study, when comparing individual parameters, comparing individual parameters, the suboptimal dosing as well as overall factors for for drug resistance were high in prescription for private practitioner, when compared to prescription and this difference was statistically highly significant.

Thus factor for treatment failure and emergence of drug resistance were high in prescriptions by private practioners. Inadequate regimes which are most commonly prescribed in private

clinical practice increase the risk of treatment failure and relapse. This can be exemplified by one of the prescriptions in this prescriptions in this study anti- tuberculosis prescription by a private practitioner.

The prescription has only one anti- tuberculosis drug viz. a day. Thus in today's era also there are prescriptions of monotherapy of anti-TB drugs.

In several medical conditions like diabetes, malnutrition, HIV, tobacco-smoking and alcohol use are risk factors for TB and for poor TB treatment results. Therefore, it is important to identify these co-biddies in people diagnosed with TB in order to ensure early diagnosis and improve co-management.

Or the co-morbidity occurs when persons have more than one disease or conditions at the same time. Conditions described as comorbidies are often chronic or long-term condition. Latent tuberculosis infection and non- infectious com bridles: diabetes mellitus type 2, chronic kidney disease and rheumatoid arthritis.

This can result in the development of another chronic condition. When a parsing has two or more chronic conditions. Doctor may refers to this conditions as comorbid. A person with likely to develop comorbidities such as heart disease, sleep disorder, chance and the obesity. Most common comorbidities were hypertension, hypercholesterolemia/ hyperlipidaemia, depression gastrointestinal reflux disease, dyslipidaemia and osteoporosis.

➢ RESULT

A total of 108 prescriptions from private practitioner and 108 treatment cards were included in the study. The various parameters of anti-TB prescription in private and public sector are presented in this review.

Out of 108 prescriptions made by private practitioners, only 10 were correct. The remaining 95 were faulty. Overdosing was present in 36 prescriptions and both sub optional dosing as well as present in 20 prescriptions. Thus overall suboptimal dosing was present in 56 prescriptions and overdosing as present in 56 prescriptions. As per individual drug faulty prescription were found in 64 of out of 108 prescriptions in respect to rifampicin, in 58 out of 93 prescriptions in respect to pyrazinamide, in 48 out of 101 prescriptions. In respect of streptomycin. Anti-tuberculosis treatment was initiated with a minimum 4 drugs in 91 patients, with 3 drugs in 9 patients and monotherapy of one that is ethambutol.

- **Comparison of anti TB treatment parameters between private and public sector**

Sr.no	Prescription dosing	Private practitioners	Public sector (RNTCP)	P value
1.	Correct	10 (9.52%)	5 (4.76%)	0.1804
2.	Faulty	95 (90.40%)	100 (95.24%)	0.1804
3.	suboptimal	56 (53.33%)	30 (28.57%)	0.0003
4.	overdose	56 (53.33%)	72 (68.57%)	0.0236
5	Factors for drug resistance	71 (67.62%)	30 (28.57%)	<0.0001

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