A STUDY ON LFT MONITORING IN ATT AND THE SPECTRUM OF ANTI-TUBERCULOUS DRUG INDUCED LIVER INJURY

INTRODUCTION

Drug reactions are often under reported and majority of drug reactions are minor. Some cases of adverse drug reactions may be major events like hepatotoxicity or nephrotoxicity. DILI is one of the leading causes of acute liver failure in the US, accounting for 13% of cases of acute liver failure; these events pose a major challenge for drug development and safety. Antimicrobials and agents for the central nervous system are the most common causes of DILI and health foods or dietary supplements account for 7% of cases of DILI in the US. In India and other developing countries, ATT is the most important drug implicated in DILI. Anti Tuberculous drug induced liver injury is mostly due to inadequate evaluation of risk factors and “inappropriate dosing”. Worldwide, incidence of Anti Tuberculous DILI, between 5 to 33%. This wide variation may be due to the predilection of TB towards developing countries than West. Even developed nations have a recent surge after the global HIV pandemic of HIV during 80s. In India, a nation contributing significant proportion of TB cases, the incidence of ATT DILI ranges between 33 to 35%.
AIM OF THE STUDY

**Primary Aim:**

1. To identify DILI even before onset of symptoms, which may prevent serious drug induced Acute Liver failure.
2. To identify the risk factors for DILI due to Anti Tubercular Treatment.
3. To formulate the way of monitoring for DILI in patients who are started ATT

**Secondary:**

1. To study the Prevalence of ATT DILI in patients with deranged baseline LFT values.
2. To study the Incidence of Hepatic adaptation and its significance in monitoring patients on ATT

**MATERIALS AND METHODS**

This is a prospective study from our Institute, Department of Digestive Health and Diseases. Government peripheral Hospital Anna Nagar., a tertiary care Centre, fed by a chest clinic and many DOTS (Directly Observed Short Term Chemotherapy) centers.

The study period is from January 2014 to January 2015.
THE STUDY GROUP:

The Study population is patients who are registered under dots and started on ATT, at chest clinic, Govt. Kilpauk medical college. They were patients diagnosed with TB, pulmonary or extra pulmonary. Also, they were not on previous anti-TB chemotherapy higher than two weeks.

All patients were followed till the end of their ATT COURSE and LFT was monitored.

EXCLUSION CRITERIA:

1. HIV POSITIVE AND ON HAART,
2. PREGNANT FEMALEs,
3. POSTPARTUM 3 MONTHS,
4. PATIENTS ON CANCER CHEMOTHERAPY,
5. AGE LESS THAN 18 YEARS
6. MORIBOUND STATE

LFT and clinical monitoring in patients who are selected under the inclusion criteria in the study were followed up till the end of their therapy by serial LFTs. Patients were divided into two groups according to their baseline LFT as follows,
1. **GROUP 1** – PATIENTS WITH NORMAL BASELINE LFT VALUES

2. **GROUP 2** – PATIENTS WITH BASELINE ALTERED LFT VALUES

LFT was done baseline and every week for the first month, then fortnightly for the next 2 months and then monthly until the end of therapy. Patients with clinical and lab evidence of DILI were evaluated for risk factors.

All results were analysed for both groups. Patients with referred with ATT DILI to this tertiary care were analyzed for Risk factors and the Demographic profile of DILI.

Finally the incidence of DILI in both groups was analysed.

The incidence of hepatic adaptation was analysed.

Also, the mortality rate in patients taking ATT and significance of risk factors in, mortality of DILI was analysed.
An ATT DILI criterion is taken according to American Thoracic Society Guidelines-2006, when any one of these three criteria was met ATT was stopped.

1. S.Transaminases >3 ULN with Symptoms
2. S.Transaminases >5ULN without Symptoms
3. Any increase in Bilirubin

DILI Grading is according to WHO criteria. Grading (WHO)Grade

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<thead>
<tr>
<th>Grade</th>
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<tbody>
<tr>
<td>1</td>
<td>( \leq 2.5x \text{ ULN} )</td>
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<td>2</td>
<td>2.6 –5x \text{ ULN}</td>
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RESULTS:

The incidence of Drug induced liver injury in Group 1 & 2 Both is 11.7%

Incidence of DILI in Group 1 is 9.48%

Incidence of DILI in Group 2 is 20.7%

Patients with normal baseline LFT had stastically significant incidence of DILI of 9.4%\((p<0.001)\)
Mortality Rate:

a. Mortality due to ATT, among the total study population is 4.1%. (n=145)

Mortality due to ATT among Group 1 is 2.5%.

Mortality due to ATT in Group 2 is 10.3%

The cause specific mortality rate for Group 1 patients with DILI - 27.2%

The cause specific mortality rate for Group 2 patients with DILI - 50%

Mortality among Group 2 (n=25)

The mortality rate in Patients on ATT in Group 2 is 10.3%

There is statistical significance between patients recovered and not recovered in Group 2. (p<0.001)

Mortality in females - Group 1

Females have higher Odds for DILI deaths compared to males.

Since there were no females died of DILI in Group 2, p value and odds ratio was not applicable.

Diabetics have higher Odds in DILI related mortality than Non Diabetics in Group 1.

Since there were no diabetics, who died in Group 2, p value and Odds ratio was not applicable.
CONCLUSION

1. There is increased incidence of DILI in patients with
   Altered Baseline LFT values.

2. Females with Normal baseline LFT have higher Odds for DILI deaths
   than
   Males.

3. Diabetics with Normal baseline LFT, have higher Odds for DILI deaths
   than Non Diabetics

4. The patients with altered baseline LFT values have higher mortality with
   ATT

5. Periodic monitoring of LFT prevents mortality in DILI.