Effect of antituberculosis treatment on human liver

Preeti Dharmik, Ashok Gomashe*, Radha Dolas and Trisha Dhargave
Shri Shivaji Science College, Congress Nagar, Nagpur-440012, (M.S.), India

*: Corresponding Author
Dr. Ashok V. Gomashe
Department of Microbiology
Shri Shivaji Science College,
Congress Nagar, Nagpur-440012,
(M.S.), India
Email: drgomashe@rediffmail.com, preetidharmik5@gmail.com

ABSTRACT:

Antituberculosis treatment is the common cause of drug induced liver injuries or hepatotoxicity in the patients. It has been proved in many studies that the effect occure due the elevated level of the liver enzymes like ALT, AST, ALP.The study was carried on the patients of DOTs centre at Shree Ramjivan Choudhary Medical Hospital and Research Centers and all the estimation were done in Sarasvati Pathology laboratory, Mahal, Nagpur. During three months observation the elevated level of the liver enzymes like ALP and SGPT has been detected in most o the patients. Out of 20 patients, who include 14 males and 6 females, the elevated level of SGPT was found in two males. One male showed the levels of both the enzymes and reported to have drug induced hepatitis. In females no such effects was found on the liver as the level of the enzymes were found raised but the levels were within the normal range. Thus, it can be concluded that the antituberculosis treatment impose hazardous on the patients liver leading to hepatotoxicity or drug induced liver injuries, most commonly drug induced hepatitis. Results obtained vary for person to person depending upon the immune response mounted by the individual.

INTRODUCTION:-

Tuberculosis is a disease caused by *Mycobacterium tuberculosis* mostly in lungs. *M. tuberculosis* is pathogenic bacteria; it was first isolated by Robert Koch in 1882. The organisms shows mycolic acid on its cell surface, hence does not stain with normal bacteriological stain but is able to stain with acid fast stain and therefore classified as acid fast Gram positive bacteria [1].

In lungs it is taken up by Alveolar macrophages but these macrophages fails to digest the bacteria as the cell wall prevents the phagosomes to fuse with lysosomes. This is known as Pulmonary Tuberculosis [2].

Apart from lungs the bacteria may enter the blood stream and cause the infection in other organ such as kidney, brain, spine and other vital organ, this is known as extrapulmonary tuberculosis. It includes TB meningitis, TB of bones, TB of lymph glands and TB of abdomen, etc [3].

The infection is spread through air, droplets due to forceful activities like coughing, sneezing, etc. the person at high risk of exposure are HIV infected patients, coworker in industries especially working in mines, construction works, crushing and hospital staffs of DOT centers, etc [2].

For treatment of tuberculosis U. S. Food and Drug Administration [FDA] approved 10 drugs [4]. Out of these four drugs are most commonly used . They are –

- Isoniazid (INH).
- Rifampicin. (Rifampin)
- Ethambutol (EMB)
- Pyrazinamide(PZA)

Starting with the treatment of tuberculosis initially four drugs are prescribed which are called as the extensive period or initial phase which continues for two months following the continuation period in which drugs are reduced to two which continues for 4-8 months depending upon condition of patients. [4]

These antituberculosis treatments though very effective have many side effects on patient's liver. As compared to another treatments such antimicrobial and anticonvulsants etc antituberculosis treatment is found to be main cause of drug induced hepatitis or hepatotoxicity. [5]

The drugs and its side effects are:

1. Isoniazide [INH]:-

This drug is effective bactericidal against some strain of Mycobacterium species like *M. bovis , M. tuberculosis, M. kanaess.* Isoniazid first undergoes acetylation and get converted into acetyl isoniazide which further hydrolysed into two products acetyl hydrazine and isoniotinic acid. Some part is converted into hydrazine. This causes the hepatotoxicity of liver [6] and Asparate transaminase level get elevated at first few months.

2. Pyrazinamide:-

The pyrazinamide is converted into pyrazinoic acid with the help of enzyme pyrazinamidase , which gets accumulate in bacteria cell and it get binds to ribosomal subunits thus inhibiting trans- translation activity[8]. The main causes of drug induce hepatitis along with its side effects like nausea, vomiting, sideroblastic anemia, fever, etc. Similarly, Rifampicin and Ethambutal have potent activity against M. tuberculosis but along with that it induce hazardous side effects on patients liver like hepatitis, jaundice, liver failure in severe case .

It is found that during antituberculosis therapy the level of liver enzymes such as Alkaline phosphatase [ALP] , Serum Glutamic Pyruvate Transaminase [SGPT] , Serum Oxaloacetic Transaminase [SGOT] or Aspartate Transaminase [AST] get elevelated from its normal range hence cause toxicity or malfunction of human liver [9] .

Hence the current study investigate the two liver enzymes ALP and SGPT in patients by

1) Collection of blood sample form patients.
2) Separation of serum.
3) Serological diagnosis of the serum sample:
    - Test for estimating the level of ALP.
    - Test for estimating the level of SGPT.

MATERIAL AND METHOD:-

The study was conducted on the patients of DOTs centre Shri Ramjivan Choudhari Memorial Hospital and Research centre, Mahal, Nagpur. All the estimations were performed in Saraswati Pathology Laboratory, Mahal, Nagpur.

Total 20 patients were kept in observation for subsequently three months. The study type is observative.

1) For collection of blood sample:

- Gloves were worn before taking the sample.
- Blood was drawn from the median cubital vein which runs on the inner part of the forearm.
- Tourniquet was then placed on the upper part forearm, tight enough to make the vein bulge.
- The vein was gently patted to look at its size.
- Best angle was found from which to draw blood.
- Sterile needle was inserted into the vein with smooth , fast motion
- The syringe was pulled back to start filling the tube with blood.
- Needle was disposed in proper place and gauze was applied on patient's wound, holding it to apply pressure.

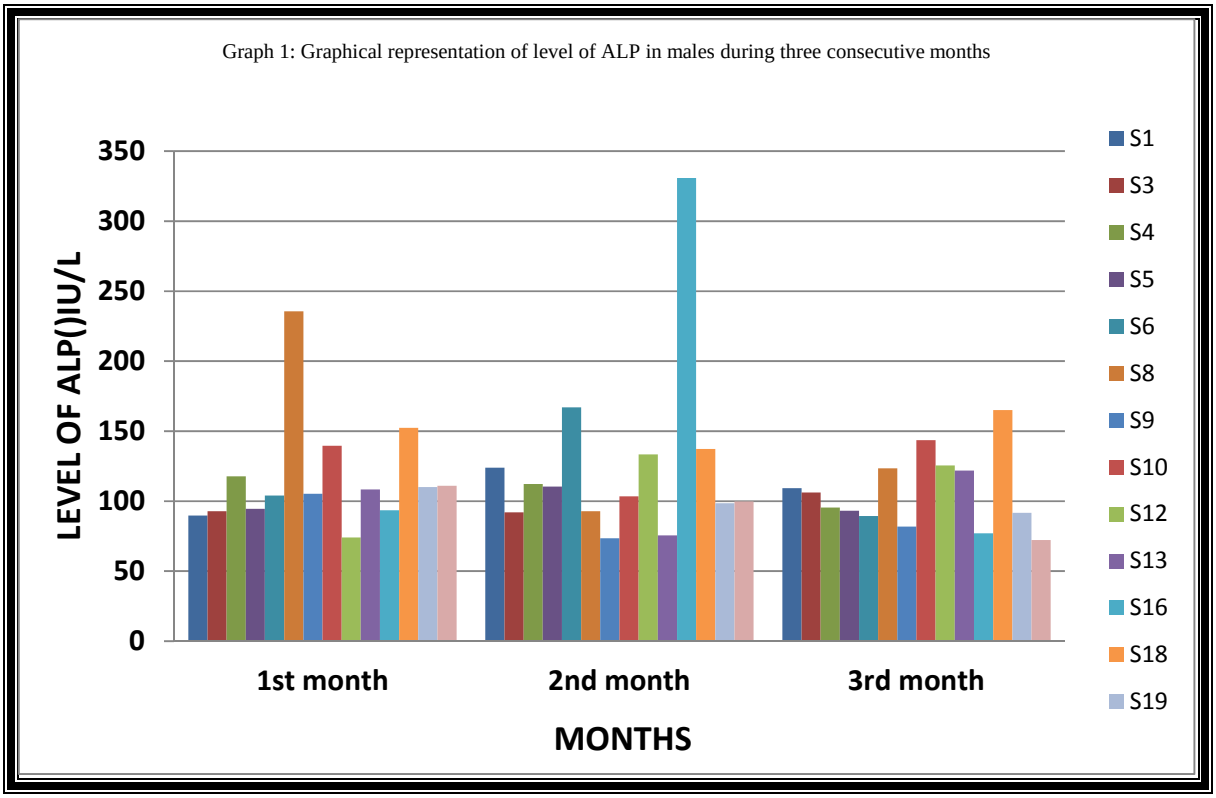
2) **For estimation of ALP:**
   - **1**ml of working solution (ACCUREX biomedial pvt. Ltd.) Was taken in the tube.
   - To it 0.02 ml (20µl) of serum sample was added.
   - Sample mixture was mixed thoroughly
   - Sample was then aspirated in an autoanalyser
   - The normal range of ALP is **72-250 IU/L.**
3) **For estimation of SGPT:**
   - 1ml of working solution was taken in another specimen tube.
   - To it 0.1ml (100µl) of serum was added
   - Sample mixture was mixed thoroughly
   - Sample was then aspirated in an autoanalyser
   - Reading as noted down
   - The normal range for SGPT is **5-49IU/L**

RESULT AND DISCUSSION:

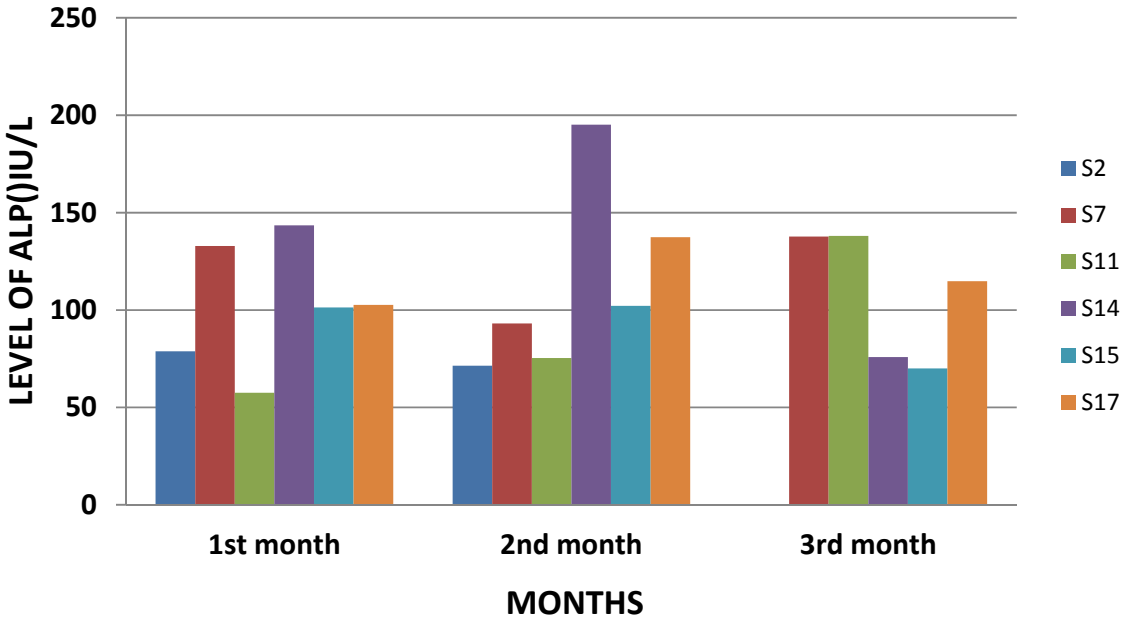
Drug induced liver injuries, hepatotoxicity are common cause of antituberculosis treatment. Regimen for treatment was found to impose many side effects on the liver of patients suffering from tuberculosis. The side effects occurring due to the antituberculosis treatment was observed in most of cases of different age groups. The effects can be studied by testing the level of liver enzymes in the patients within the interval of weeks to months.

In the current study, the concentration of ALP was found to be high in many patients serum during second and third month of observation. Study also showed high prevalence of ALP in males than in females. (Graph1, 2). Graph 1 showed that, level of ALP was found very high in patient S16 indication the occurrence of drug induced liver injuries while in others the level is within the normal range.

Graph 1: Graphical representation of level of ALP in males during three consecutive months



Graph 2: Graphical representation of level of ALP in females during three consecutive months



Graph 2 represents the level of ALP in female during three consecutive months. Our results are in accordance with the findings of Dinesh Koju et al[9] from Kathmandu, Nepal.

In addition to level of ALP, the level of SGPT was also determined during consecutive three month period. It has been found that out of 20 patients two male (i.e.,10%) was found to have very high level of SGPT during second month of treatment in the intensive phase, indicating that the patients were suffering from drug induced in the study of Habbib Ullah Khan et.al[10] from Pakistan.

Only one patient (i.e., 5%) was from found to have high level of ALP. The patient having high ALP and SGPT level showed the symptoms like nausea, vomiting, and high yellow colored urination indicating the occurrence of drug induced hepatitis.

As compared to results obtained in case of males, the levels of ALP and SGPT in females were found raised but were within the normal ranges so no hazardous effect were deducted in the lever during three months observation.

CONCLUSION:-

In conclusion, one can say that, in females no such effects was found on the liver as the level of the enzymes were found raised but the levels were within normal range. Thus it can be concluded that the antituberculosis treatment impose hazardous effect on the patients liver leading to hepatotoxicity or drug induced liver injuries, most commonly drug induced hepatitis. Results obtained vary from person to person depending upon the immune response mounted by the individual.

REFERENCE:-

[1] Ismael Kassim, Ray CG (2004). Sherris Medical Microbiology (4th ed.). McGraw Hill.
[2] Anantnarayan and Panikar, Textbook of microbiology, seventh edition,pp 351-364.
[3] Types of TB: library.thinkquest.org/C0126375/typs%20 of %20%20tb.html.

[4] "Core Curriculum on Tuberculosis: What the Clinician Should Know".Centers for Disease Control and Prevention(CDC), Division of Tuberculosis Elimination.2000,updated August 2003.
[5] Wbesite: http://www.mayoclinic.com/health/tuberculosis/DS00372/DSECTION= treatments-and-drugs.
[6] Marzuki O.A., Fauzi, et.al., "Prevalance and risk factor of Antituberculosis in
[7] Alma Tostmann, Martin J. Boere et.al., "Antitubeculosis Drug Indoced Hepatotoxicity : Concise up-to-date review", University of Nijmegen Medical Centre, Nijmegen The Netherland.
[8] Shi w Zhang, Jiang X, Yuan H, Lee JS, Barry CE, et.al.(2011), " Pyrazinamide inhibits trans- translation in *Mycobacterium tuberculosis*" , Sci.333(6049): 1630-1632.
[9] Dinesh Koju, B. S. Rao, et.al, "Occurance of side- effects from antituberculosis treatment in urban Nepalese population under DOTS treatment" , Kathmandu University Journal of Science, Engineering and technology, Vol. No. 1 September 2005.
[10] Habib- Ullah Khan, Muhammad Hussain Khan, et al., Pakistan, " Antituberculosis Therapy Induced Liver Injuries: frequency, management and outcome.", J. Med. Sci. (Peshawar print) July 2009, Vol. 17, No. 2: pp 99-102.