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AN ASSESSMENT OF ANTI-TUBERCULAR INDUCED HEPATITIS AMONG PULMONARY TUBERCULOSIS PATIENTS: A CROSS-SECTIONAL DESCRIPTIVE RESEARCH

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Abstract:

Objective: *We aimed to assess and evaluate the anti-tubercular agents (ATT) induced hepatitis among the patients of pulmonary tuberculosis (PTB).*

Material and Methods: *We conducted this cross-sectional research to assess ATT induced pulmonary TB among 95 patients at Jinnah Hospital, Lahore in the timeframe of February to November 2017. The patients were selected in the age bracket of (16 – 65) years. We completed baseline measurements of Liver Function Tests (LFTs) which included Bilirubin, AST and ALT for every patient at the time of sample selection after meeting the research criteria. The same procedure was also repeated at an interval of one month to know the possible variations. Ethical approval and consent of the patients were also secured before the commencement of research. We told the pros and cons of this particular research to every patient who participated in the research study. Research made statistical analysis with the help of SPSS software.*

Results: *In the age bracket of (16 – 65) years, the mean age of enrolled patients was (37.95 ± 14.46) years. In terms of gender distribution, we enrolled 51 male patients (53.7%) and 44 female patients (46.3%). Male was predominant over females in terms of the population proportion. An onset of ATT induced hepatitis was reported among 35 patients in the total of 95 patients having a proportion of (36.8%).*

Conclusion: *We conclude that ATT induced hepatitis is among repeated complications which are commonly reported in the patients of PTB (Pulmonary Tuberculosis). Therefore, the one-month follow-up is mandatory for all patients. Doctors, as well as patients, need to educate themselves about the adverse outcomes of ATT induced hepatitis. Moreover, an in-time diagnosis and management of the disease are also important.*

Keywords: *Pulmonary Tuberculosis (PTB), Antitubercular Agents (ATT), Liver Injury, Drugs, Hepatotoxicity, Rifampin (RIF), Isoniazid (INH), Ethambutol and Pyrazinamide (PZA) and Liver Function Test (LFT).*

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INTRODUCTION:

Tuberculosis (TB) is undoubtedly an infectious disease which is significant all over the world [3]. In the estimates of 2012, the reported TB cases and associated deaths are respectively 8.6 million and 1.3 million all over the world. Newly diagnosed TB patients receive standard treatment of four drugs which include rifampin (RIF), isoniazid (INH), ethambutol and pyrazinamide (PZA). However, these drugs also offer associated adverse outcomes such as hepatotoxicity (toxic effects) [4 – 6]. Recently an author reported the ATT induced hepatitis frequency among (19.67%) patients [7]. A number of hepatotoxic reactions have a direct relation with hypersensitivity of the drugs and also related to the intake of dose [8 – 9]. Rifampicin and Isoniazid induced damage includes lipid peroxidation, oxidative stress, choline deficiency which leads to a reduction of phospholipids protein synthesis with variation in the configuration of the wall, decreased level of glutathione and CYP2E1 activation [10].

ATT induced hepatitis severity ranges from asymptomatic liver enzymes alteration to acute symptomatic hepatitis; this acute hepatitis is a complication caused by acute renal function failure [11]. Reported clinical factors include malnutrition, older age, female gender involvement, HIV infection, alcoholism, & HCV infections [9]. The patients having toxic effects are at an increased risk which requires a proper, safe, timely and risk-free modification and identification. This particular research will be very much helpful for the upcoming studies on the same topic as it identifies ATT induced hepatotoxicity among patients. It also helps in the early identification and detection of the disease to counter possible side-effects. The monitoring of associated symptoms and LFT will also be easier than ever before because of increased disease awareness for the physicians and patients. Therefore, we aimed to assess and evaluate the anti-tubercular agents (ATT) induced hepatitis among the patients of pulmonary tuberculosis (PTB).

MATERIAL AND METHODS:

We conducted this cross-sectional research to assess ATT induced pulmonary TB among 95 patients at Jinnah Hospital, Lahore in the timeframe of February to November 2017. The patients were selected in the age bracket of (16 – 65) years. We did not include those patients who presented jaundice history, abnormal baseline LFTs, ATT drugs high dose intake, hepatotoxic drug intake and consuming alcohol. We completed baseline measurements of Liver Function Tests (LFTs) which included Bilirubin, AST and ALT for every patient at the time of sample selection after meeting the research criteria. The same procedure was also repeated at an interval of one month to know the possible variations. Ethical approval and consent of the patients were also secured before the commencement of research. We told the pros and cons of this particular research to every patient who participated in the research study. Research made statistical analysis with the help of SPSS software.

RESULTS:

In the age bracket of (16 – 65) years, the mean age of enrolled patients was (37.95 ± 14.46) years. In terms of gender distribution, we enrolled 51 male patients (53.7%) and 44 female patients (46.3%). Male was predominant over females in terms of the population proportion. An onset of ATT induced hepatitis was reported among 35 patients in the total of 95 patients having a proportion of (36.8%).

Detailed outcomes analysis is as under (Table – I and II):

Table – I: Gender Distribution

Gender	Number	Percentage
Male	51	53.7
Female	44	46.3

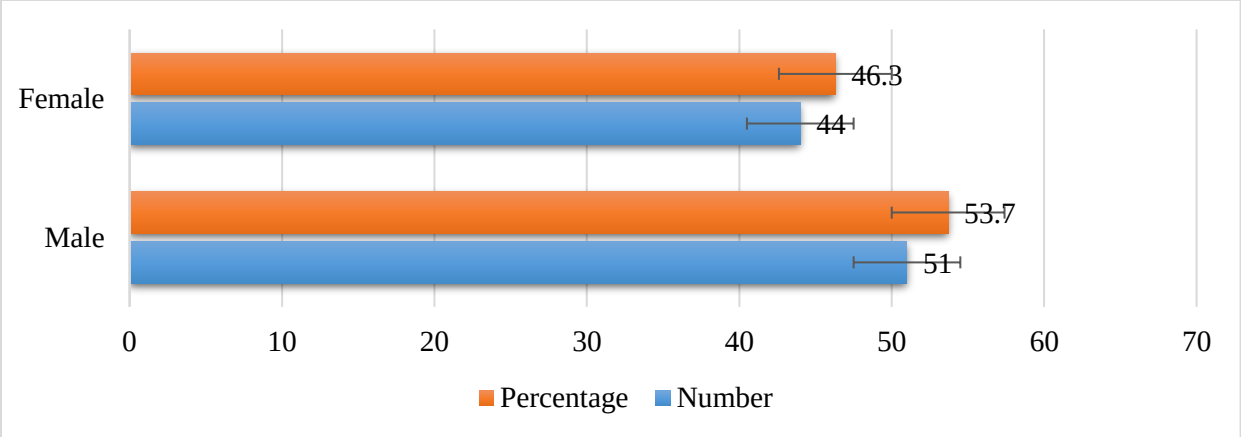
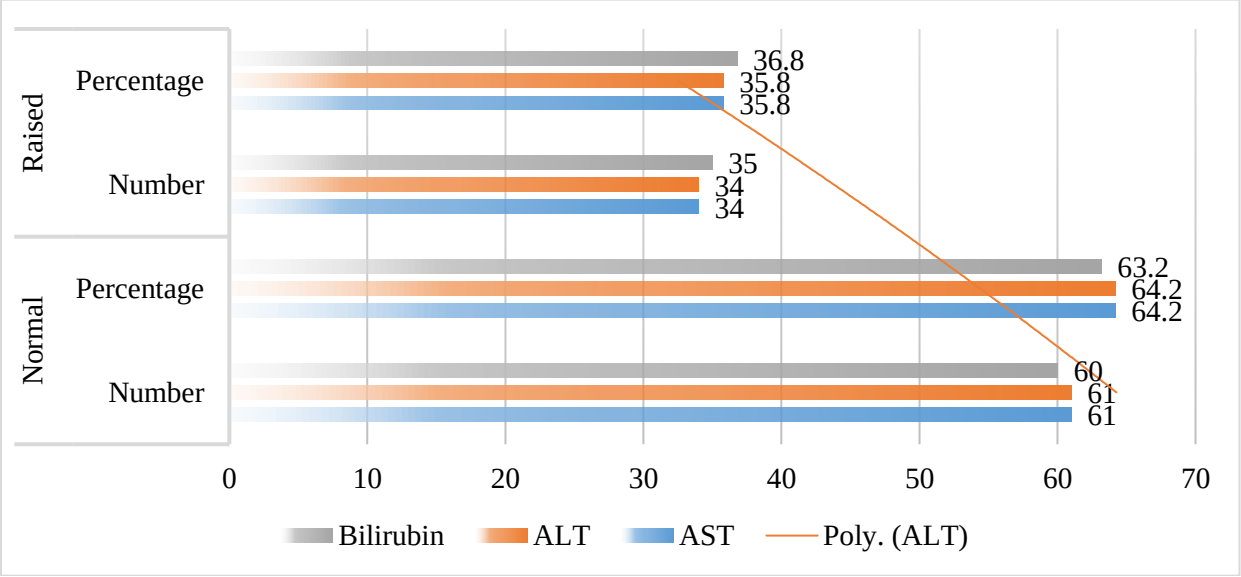


Table – II: Liver Function Test Derangements

Liver Function Tests (Derangement)	Normal		Raised	
	Number	Percentage	Number	Percentage
AST	61	64.2	34	35.8
ALT	61	64.2	34	35.8
Bilirubin	60	63.2	35	36.8



DISCUSSION:

Our research shows a higher hepatotoxicity degree among patients because of induced Anti-tuberculous management. A higher striking rate of 35 patients in the total of 95 patients (36.8%) was positive for ATT induced hepatitis. Majority of preventable infections show a direct and significant association with Tuberculosis (TB) causing higher mortality rates all over the world [12, 13]. An in-time diagnosis followed by proper chemotherapy is mandatory and major treatment [14]. Extensive discussion is ongoing on the topic of hepatotoxic ATT induced adverse effects in various series in order to confirm the outcomes and frequency among the affected patients all over the globe [15, 16].

More research work is available in the Western literature which are developed countries; whereas, the scarcity of literature is common among underdeveloped nations of the world. Local research studied a total of five hundred TB patients and they

treated those patients with standard disease management therapy which is common for the first-line treatment of TB management [17]. Majority of the patients received Rifampicin, Isoniazid (INH), Ethambutol and Pyrazinamide (PZA) also known as four drug regimen therapy for TB patients. In order to predispose associated factors of hepatotoxicity, researcher documented and monitored examination and history of every patient.

We reported nine patients of raised transaminases (3.8%) and twenty-one patients of overt hepatitis (4.2%). Over hepatitis was reported in twenty-one patients out of which seven were male and fourteen patients were female. Among these patients, one death case (0.2%) was also reported who died due to Acute Fulminant Hepatitis. Research reported 35 patients of ATT induced hepatitis (36.8%) which is comparable to the outcomes of this research [18]. A higher rate of hepatotoxicity has been reported in the said study than our series which may have an association with hepatotoxicity categorization such as acute fulminant hepatic failure and overt hepatitis.

Change in the DIH (Drug-Induced Hepatitis) is because of Anti-TB chemotherapy which includes four regimen therapy. Researchers also studied the DIH frequency among patients who were treated with chemotherapy of four regimens in the timeframe of different years including (1980 – 1983), (1987 – 1988), (1991 – 1992) and (1998 – 2000) (P-value = 0.01) [18]. However, the reported rates are less as reported in our series. In another research conducted in India detected seventy percent patients of ATT-induced hepatitis who were taking Pyrazinamide along with Rifampicin and INH. This hepatotoxicity rate is much higher to our reported rate. Whereas, our research is cross-sectional descriptive in design which carries no control group for comparative analysis and the other research is actually case-control research [19].

Another research was also conducted in Iran (National TB Center) which compared drug-induced hepatitis in the timeframe of (2006 – 2008) and reported 99 out of 761 patients of DIH (13.0%). These patients developed DIH in the course of an anti-TB management programme. The reported rate is below our reported rate of DIH. However, no significant variation was reported in terms of nationality, gender, opium intake and smoking between both hepatitis and control groups with a significant P-Value of (> 0.05). The patients with an age factor above sixty-five years presented a significantly higher rate of DIH with a significant P-Value of (0.019) [20].

CONCLUSION:

We conclude that ATT induced hepatitis is among repeated complications which are commonly reported in the patients of PTB (Pulmonary Tuberculosis). Therefore, the one-month follow-up is mandatory for all patients. Doctors, as well as patients, need to educate themselves about the adverse outcomes of ATT induced hepatitis. Moreover, an in-time diagnosis and management of the disease are also important.

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