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STUDY TO KNOW INCIDENCE OF DRUG INDUCED HEPATITIS IN PATIENTS USING ANTI- TUBERCULOSIS DRUGS AND ITS RISK FACTORS

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Abstract:

Objective: *To identify risk factors for anti-tuberculous drugs influence hepatitis (ATDH) among tuberculosis patients.*

Study Design: *A retrospective study.*

Place and Duration: *In the Jinnah Hospital, Lahore in Gastroenterology and Pulmonology department for three years period from February 2013 to February 2016 after the approval from the ethical committee of Jinnah Hospital, Lahore*

Methodology: *The medical records of tuberculosis 3056 cases were reported for three years was collected and data analyzed for ATDH done. TB inclusion criteria identified based on the National Tuberculosis Program (NTP) has been documented. ATDH and Non-ATDH data were analyzed in the SPSS version 17 and full fisheries and chi-square tests.*

Results: *198 cases were diagnosed as ATDH which include 66 (33.01%) women and 134 (66.99%) males, 43.2 years was the mean age, SD 9.5 treatment and ATDH as follow up period were selected for the study. ATDH in patients was found to be significant statistically (p = 0.0001, OR: 13.92) (OR: 7.6, p = 0.0002) and (OR: 11.3, p = 0.0001) was the difference between intravenous injection ATDH and HIV infection.*

Conclusion: *ATDH had the highest prevalence among patients suffering from HCV infection, HIV and IVDU infection.*

Key words: *Tuberculosis, drug-induced hepatitis, national tuberculosis program.*

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INTRODUCTION:

A major public health issue worldwide is Tuberculosis (TB). Mycobacterium tuberculosis infect 1/3rd of the world's population, and it is estimated that every year 800,000 new cases of tuberculosis occur. In Pakistan, it is an important cause of mortality and morbidity. National Tuberculosis Program (NPT) TB management is divided into two phases, isoniazid, rifampicin, pyrazinamide and ethambutol are standard 6 months. The intensive phase continued with isoniazid and rifampicin in the second phase and then two more with four drugs. The most serious and common side effects of isoniazid, pyrazinamide and rifampicin is Hepatotoxicity and may cause these reactions in the treatment of tuberculosis. Previous studies have shown that patients treated with a standard combination therapy against tuberculosis containing approximately 10%, isoniazid and rifampicin, aspartate aminotransferase (AST) and alanine aminotransferase (ALT), such as suddenly rise in serum hepatocellular enzymes 1-2% most hepatic reactions are attributed to fámaco.8 risk factors (ATDH) due to hypersensitivity to antituberculosis drugs, but some hepatitis caused by hepatitis. These are phenotype, age acetylated, poor nutrition, alcoholism, HIV infection and chronic hepatitis B infections and ADDH may increase risk. C. Other factors are promoted include the co-administration of tuberculosis, Asian ethnic, female, eg inducing enzymes (anesthetic agents and barbiturates) and improper drugs use. Pancreatic liver dysfunction usually occurs during the first weeks of intensive phase of t tuberculosis treatment. Patient education, especially with risk factors for hepatitis symptoms and laboratory follow-up (AST and ALT), is necessary to enhance the outcome of hepatitis patients who are afflicted during TB treatment. This study was conducted to determine the risk factors for ATDH in TB patients, considering the lack of studies on epidemiology to assess ATDH risk factors resulting from Ahvaz NPT regimen.

MATERIALS AND METHODS:

This retrospective study was held in Jinnah Hospital, Lahore in Gastroenterology and Pulmonology department for three years period from February 2013 to February 2016 after the approval from the ethical committee of Jinnah Hospital, Lahore. The medical records of tuberculosis 3056 cases were reported for three years was collected and data analyzed for ATDH done. TB inclusion criteria identified based on the National Tuberculosis Program (NTP) has been documented. Criteria for diagnosis for Positive pulmonary tuberculosis (PTB +) spread with two positive cases for acid-acid bacilli at least (SSP-ARB), chest radiography suggesting Bacillus or tuberculosis plus M. tuberculosis and SSP-defined AFB-positive SSP-AFB or marrow culture. Clinical findings are defined as TB plus negative pulmonary tuberculosis (PTB) antibiotic treatment with more C-X (implanted TB) and three negative sputum smear (SSK-ARB) two weeks later. Other diagnostic criteria were tuberculosis, meningitis, and computerized tomography and microbial studies. Miliary or extrapulmonary tuberculous cerebrospinal fluid was analyzed. The diagnosis of ATDH is based on clinical findings of high ALT and laboratory results. he / she had one of the following, especially the ATDH diagnosed that there was no obvious reason for liver function tests:
Serum is 5 times above the normal limit of ALT (40 U / L) and the absence of hepatitis symptoms and symptoms. Clinical hepatotoxicity was diagnosed if ALT ATDH symptoms were elevated, including vomiting, nausea, jaundice and weakness. Patients with ALT at high baseline were not included in the study. For each drug induced anti-tuberculous hepatitis case, without ATDH three patients were selected randomly as controls. Medical history, demographic characteristics, HIV, incarceration, HCV drug dependence, HBV serologic, underlying diseases, TB treatment in both cases (ATDH patients) and side effects of medication and other health problems during control. The data were analyzed in the SPSS 17 version and with full fishery tests and chi-square. In this study, TB patients are followed for 12 months (months, 3, 6, and 12) after treatment (6 months minimum) and after treatment completion. ATDH and follow-up were recorded throughout the treatment period.

RESULTS:

By the NPT regime, 792 cases were treated. Male were 489 (61.8%) and female were 304 (37.92%). During the treatment and follow-up period, a total of 90 patients (5%), including females 66 (33.08%) and (66.92%)133 were male, 43.2 years was the mean age and 9.5 SD were recorded as ATDH. In two hundred (60.98%) patients, in the first two months ATDH occurred after treatment. With ATDH associated four deaths occurs only.

Table-I: Demographic characteristics and risk factors for drug hepatotoxicity among tuberculosis patients under treatment in Khuzestan Health Center.

Variables		*ATDH (Cases, n=198) N (%)*	*Non ATDH (Control, n=594) N (%)*	*P value*	*Odds ratio OR, 95% CI*
Sex	Male	133 (67.2)	356 (59.9)	0.07	1.4, 0.9-1.9
	Female	65 (32.8)	238 (40.1)		
Age (Year)	>35	145 (73.2)	316 (53.2)	0.0001	2.4, 1.7-3.4
	<35	53 (26.8)	278 (46.8)		
Smoking		79 (39.9)	169 (28.4)	0.003	1.7, 1.2-2.3
IVDU		109 (55)	58 (9.7)	0.0001	11.3, 7.7-16.7
Imprisonment		58 (29.3)	71 (11.9)	0.0001	3.1, 2.1-4.5
Alcohol consumption		8 (4.0)	7 (1.2)	0.01	3.5, 1.3-9.9
Viral co infection	HBV	16 (8.1)	25 (4.2)	0.04	2.0, 1.1-3.8
	HCV	61 (30.8)	18 (3.0)	0.0001	14.2, 8.2-24.9
	HIV	14 (7.1)	6 (1.0)	0.0001	7.5, 2.8-19.7
Cavitary TB		57 (28.8)	112 (18.8)	0.004	1.7, 1.2-2.5

ATDH: Anti TB drug induced hepatitis, IVDU: Intravenous drug users, HBV: Hepatitis B virus, HCV: Hepatitis C virus, HIV: Human immunodeficiency virus, OR: Odds ratio, CI: Confidence interval

Previous viral infections (B and C) were found in 78 cases (39.09%), with incarnation and intravenous drug injection in the majority (78%). Other results of non-ATDH (control) and ATDH (case) are given in Table-I.

DISCUSSION:

In this age of work, they were considered to inject risk factors for smoking, drug dependence for ADHD, imprisonment, alcohol consumption, viral hepatitis and HIV coinfection. The rate of HCV infection was statistically significant (p = 0.0001, OR: 14.2) in patients without ATDH ATDH, in fact, HCV patients were higher than those who were negative for HCV risk. Similar findings were found in other studies. As in other studies, we found a relationship between HBsAg positivity and hepatotoxicity development. In fact, the effect of HBV infection is much less than the effect of HCV. This can be attributed to routine inoculation against HBV since it is not possible to achieve a full effect of each risk factor. As a result, it was difficult to establish a close relationship with different parameters, such as associating hepatotoxicity with these parameters. Moreover, since most of the participants in our study were weak, it was difficult to see the relationship between malnutrition and hepatotoxicity. Because the study takes place only in a health center located on the eastern shore, the economic status of the whole country and the representation of the ethnic group may be a problem.

CONCLUSION:

As in previous studies, smoking has been considered as risk factors for ADHD, including injecting drug dependence, incarceration, viral hepatitis, alcohol consumption and HIV coinfection, HCV infection, infection. By IVDU and HIV, We recommend that patients who are infected with HIV, HCV, and who are dependent on IVD should undergo an initial liver function screening test and be followed closely with the follow-up tests during treatment. We also recommend further study to investigate why these risk factors contribute to the hepatotoxicity development and to elaborate in detail the risk factors not addressed in this study.

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