PREVALENCE OF SECONDRY INFECTIONS WITH OPPORTUNISTIC BACTERIA IN DRUG ADDICTS SUFFERING FROM TUBERCULOSIS

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ABSTRACT

Secondary infections are the most common complications in patients of tuberculosis. In the present study the prevalence of opportunistic organisms was assessed among tuberculosis patients with respect to drug addiction, an important predisposing factor to acquire secondary and opportunistic infections. Moreover, the antibiotic sensitivity testing of these isolates was also performed. Clinical specimens were collected from hospitalized tuberculosis patients and were characterized to species level by using standard diagnostic criteria. Out of 510 tuberculosis patients, 199 (39%) were addicted to tobacco, cannabinoids, opioids or alcohol. The most frequently isolated bacteria from these patients were *Pseudomonas aeruginosa, Klebsiella pneumonia, Acinetobacter calcoaceticus, Moroxella catarrhalis, Streptococcus viridans* and coagulase positive and negative Staphylococci. Emergence of multi drug resistance among Gram positive and Gram negative organisms was noted against most of the broad spectrum antibiotics such as penicillin derivatives and cephalosporin of first and second generation. The results of present study highlight that drug abuse not only enhances incidence of tuberculosis but also results in causing complications in such patients by prevalence of secondary infections by multi-drug resistant microorganisms. Prompt management of such patients is of prime importance to minimize complications.

Key words: Tuberculosis, secondary infection, opportunistic bacteria, drug addiction, cannabinoid, opioid.

INTRODUCTION

Addiction to drugs like tobacco, cannabinoids, opoids or alcohol suppresses immune system which in turn increases the susceptibility of individual to develop any disease. Such addict persons are also at high risk to develop and consequently spread Tuberculosis. For instance, the chance for developing active tuberculosis is twice in heavy alcohol drinkers as compared to non habitual alcohol drinkers (Perlman *et al*., 1995; Friedman *et al*., 2003; Deiss *et al.,* 2009). There is also a positive association between tobacco smoking and pulmonary tuberculosis, although the exact mechanism is not known. It is possible that the nicotine in tobacco smoke might interfere with the immune response of the host to *Mycobacterium tuberculosis*. Besides, addiction has also been associated with development of disease compliances problem, relapse and drug resistance among tuberculosis patients (Kolappan and Gopi, 2002, Goetsch *et al*., 2012).

The active course of tuberculosis not only causes severe damage to immune system but also results in hormonal changes which cause further lowering of immune system (Sain *et al.,* 1991; Naz and Tarfiq, 2004). The suppression of human defence mechanism during the course of active tuberculosis brightens the chances for attack by opportunistic organisms. These organisms may invade any part of the body and may cause secondary infections. These organisms not only invade lungs and other organs and cause secondary infections but also in some cases these organisms enhance the severity of the primary disease. The most important obstacle in control of the secondary infections is the emergence of multiple drug resistance. When ever, the infections are caused by such resistant organisms, the treatment become a great problem (Sain *et al.,* 1991; Naz and Tariq, 2005; Nessa *et al.,* 2008).

In view of the above the present study was conducted to evaluate the incidence of opportunistic organisms in addict tuberculosis patients and the antibiotic resistance pattern of organism isolated from these patients.

MATERIALS AND METHODS

Subject

The study comprises to 510 tuberculosis patients, admitted to Ojha Institute of Chest Diseases, Karachi. A questionnaire was completed for each patient, consisted of demographic details, clinical findings and addiction habit noted either from patients case file or obtained from their physician.

Collection of Specimens

Clinical specimen: sputa, pleural effusion and bronchial aspirations were collected from the patients by following standard protocols (Forbes *et al*., 2002).

Direct Smear Examination

All the clinical specimens were Gram stained and observed under the microscope

Culture for Isolation

All the specimens were processed for the isolation and characterization of microorganisms. Blood agar medium and MacConkey`s agar medium were used for primary isolation of organisms. Other media were also used depending on suspected organisms.

Characterization of Organisms

All the pure cultures were characterized to species level by using standard diagnostic criteria (Forbes *et al*., 2002). The criteria included study of morphological, cultural, biochemical and physiological characteristics.

Determination of Antimicrobial Susceptibility

Disc diffusion susceptibility test was employed for antimicrobial susceptibility test (Bauer *et al.,* 1966; Forbes *et al.,* 2002).

RESULTS

Of 510 tuberculosis patients 39% (199/510) were addicted to hazardous substances such as tobacco (82.9%), cannabinoid (8.0%), opioid (4.5%) and alcohol (4.5%). Among the addict tuberculosis patients, 54.3% (108/119) showed some complications like non subsiding fever, marked cough, haemoptysis, raised ESR and leukocytosis in spite of taking anti-tuberculosis drugs (Fig.1).

A total number of 306 isolates were obtained from addict tuberculosis patients comprising 27.1% Gram negative bacilli 56.5% Gram positive cocci and 16.3% Gram negative cocci. The most frequently isolated bacteria were *Pseudomonas aeruginosa* (9.5%), *Klebsiella pneumonia* (9.0%), *Acinetobacter calcoaceticus* (3.5%), *Moroxella catarrhalis* (14.5%), *Streptococcus viridians* (44.2%) and coagulase positive and negative Staphylococci (20.6%) (Table.1).

Table 1. Incidence of organisms isolated from addict tuberculosis patients.

Bacilli			**Cocci**		
Gram Negative Bacilli	**NO.**	**%**	**Gram Negative Cocci**	NO.	%
Acinetobacter baumanni	1	0.5	*Moraxella catarrhalis*	29	14.5
Acinetobacter calcoaceticus	7	3.5	*Neisseria flavescens*	2	1.0
Acinetobacter lwoffi	8	4.0	*Neisseria lacatmica*	7	3.5
Citrobacter freundii	1	0.5	*Neisseria mucosa*	10	5.0
Enterobacter aerogens	1	0.5	*Neisseria sicca*	2	1.0
Escherichia coli	4	2.0	Total Gram Negative Cocci	50	16.3
Flavobacterium odoratum	1	0.5			
Kingella kingae	3	1.5	**Gram Positive Cocci**		
Klebsiella pneumonia	18	9.0	*Micrococcus cryophilus*	18	9.0
Moraxella liquifaciens	3	1.5	*Micrococcus luteus*	1	0.5
Moraxella osloensis	1	0.5	*Micrococcus roseus*	3	1.5
Morganella morganii	1	0.5	*Micrococcus varians*	13	6.5
Proteus mirabilis	3	1.5	*Staphylococcus aureus*	9	4.5
Pseudomonas acidovorans	2	1.0	*Staphylococcus epidermidis*	30	15.0
Pseudomonas aeruginosa	19	9.5	*Staphylococcus saprophyticus*	11	5.5
Pseudomonas alcaligenes	5	2.5	*Streptococcus viridans*	88	44.2
Pseudomonas diminuta	1	0.5	Total Gram Positive Cocci	173	56.5
Ps. pseudoalcaligenes	2	1.0			
Serratia liquifaciens	2	1.0			
Total	83	27.1	Total	223	72.9
Total number of isolates =306					

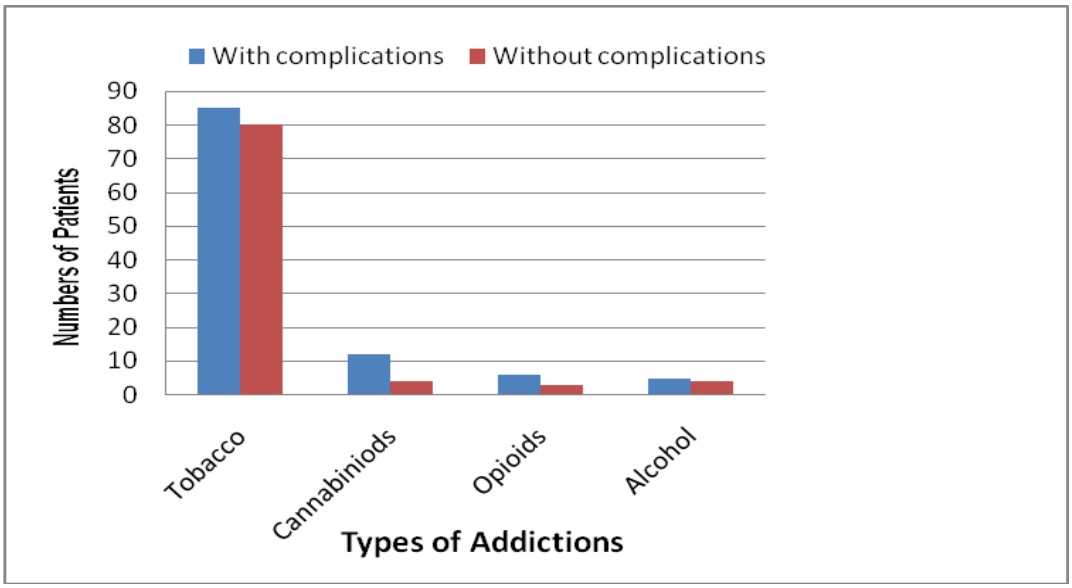

Fig. 1. Distribution of tuberculosis patients with respect to addiction habit and complications.

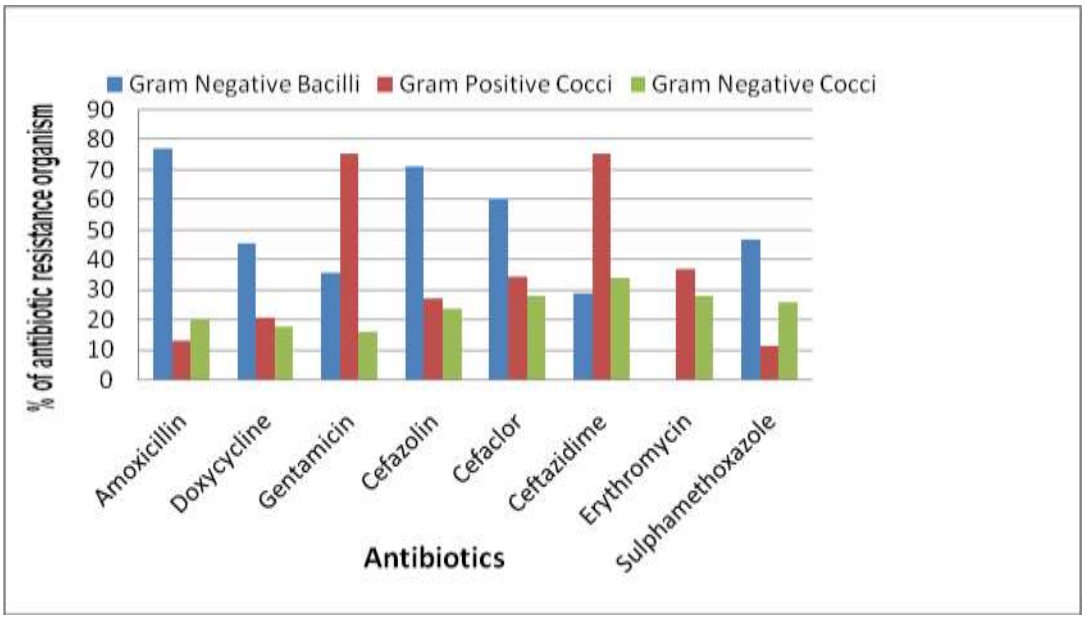

Fig. 2. Emergence of antibiotic resistance among organisms isolated from addict tuberculosis patients.

The antibiogram pattern of organism revealed resistance against most of commonly used antibiotics. The Gram negative bacilli exhibited higher resistance against Amoxicillin (77.1%), Cefazolin (71.7%) and Cefaclor (60.44%). However, most of Gram positive cocci were found resistant to Gentamicin (75.7%) and Ceftazidime (75.7%). While, the Gram negative cocci revealed resistance against Ceftazidime (34%) and Erythromycin (28%) (Fig.2). The emergence of resistance of these organisms against remaining antibiotics used in the study was also noted.

DISCUSSION

Addiction is always associated with psychological and physical problems. Among these, the socio-economic burden due to drugs results in mental stress, malnutrition, homelessness and unhygienic living conditions. Besides,

drug addiction also increases susceptibility of a person to many infectious diseases and there exist a long recognized relationship between addictive drugs and increasing rates of infections ((Friedman *et al*., 2003). With the advent of AIDS and its correlation with abused substances, it has been observed that these abused drugs have been serving as cofactors in progression of AIDS and in increasing the susceptibility to other infectious diseases (Mansell, 1984; Sofian *et al*., 2012). Among these drugs, tobacco and alcohol are recognized as legal in many countries and are consumed freely. However, marijuana, cocaine, heroin and other opiates are considered illegal but they are also in use through out the world by drug addicts. Addiction to these dugs whether legally or illegally has been always correlated with many major health problems such as infectious diseases (Nieman *et al.*,1993 ; Schepis *et al*., 2011; Honarvar *et al*., 2013).

The incidence of tuberculosis has been observed higher in addict persons and is continuously increasing with time. During the course of TB the addictive substances used by patients have many adverse effects which enhance the severity of primary disease and acquisition of secondary infections. In view of the above, the prevalence of addiction in TB patients was evaluated in the present study and it was observed that 39% of all the TB patients included in the study were found addict to different addictive substances. The substances abused by these patients were tobacco, opioids, alcohols and cannabinoids. The use of tobacco is so common and wide spread that it is rarely viewed as a form of drug abuse or as an addiction however it fits all of the accepted criteria which is needed for drug dependence. In Pakistan, tobacco is used in the form of cigarettes, pan with tobacco, beri etc. The most common addictive substance observed in this study among TB patients was tobacco as 82.9% of all dug addicts were tobacco addict. Interestingly, among these TB patients 51.5% also showed some complications in their primary disease as well which might be due to acquisition of secondary infections.

Cannabinoids are the psychoactive substances obtained from different parts of the *Cannabis* sativa plant. Charas, bhang, ghanja, hashish and marihuana are all the names of cannabis and its products (Parikh 1987). This form of addiction is also very common in our country but in the present findings only 8% addicts were in habit of abusing cannabinoids. But these patients exhibited more complications (75%) in their primary disease as compared to tobacco addicts (51.5%).

Among opioids, heroin is used most commonly in different parts of Pakistan as well as through out the world. The source of opium is *Papover somniferum.* Heroin is a refined form with powerful euphoric and hallucinogenic effect (Scott, 1969; Jaffe and Martin 1990), but it is also responsible for high degree of immunosuppression which might be one of the risk factor for the development of tuberculosis. Moreover, the TB developed in heroin addicts is of fulminating type with no hope of recovery (Novick *et al.,* 1986). Although in our study, the heroin addicts among TB patients were observed in less numbers i.e. 4.5% but the percentage of complications was much higher in these addicts. The prevalence rate of heroin addiction observed in present study was in contrast with previous reports where much higher prevalence rates of heroin addicts were observed (Rusen, *et al.,* 1999).

Similarly Alcohol abuse has been directly related to decreased liver functions and increased incidence of infectious diseases. The alcoholics have more chances to acquire pneumonia, tuberculosis, viral hepatitis and other lung diseases (Daaka *et al*., 1997; Lonnroth *et al*., 2008; Schmidt *et al*., 2013). This might be due to immunosuppression induced by alcohol. The alcohol consumption is very much low in our society as compared to figures documented in western literature (Poklis 1980). Religious restriction might be one of the factors behind this low consumption. This was also reflected in our study where only 4.5% of the total addicts were using alcohol but again these patients showed more cases of complications in their primary disease.

Secondary bacterial infections are the major complications observed in drug addict TB patient. *Moroxella catarrhalis, Pseudomonas aeruginosa, Klebsiella pneumoniae and Acinteobacter* species were found in significant number from these patients. The antibiotic resistance pattern of these isolates also showed marked resistance against most commonly used antibiotics. The secondary infections caused by such drug resistant organisms might be a cause of complication in these patients. Therefore there is a need for constant monitoring and prompt management of addict patients particularly those who are immuno-compromised or have some underlying disease such as tuberculosis.

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