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# Drug Resistance Among Pulmonary Tuberculosis Patients Attending A Tertiary Care Hospital: A Cross Sectional Study From Etawah,Uttar Pradesh.

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***Abstract***
***Background:*** *Tuberculosis is the most widespread infectious disease which poses a serious threat to the health and development of the country. Drug resistant tuberculosis is a major constraint to successfully controlling tuberculosis.*
***Objectives:*** *To find out drug resistance and its socio-demographic co-relates among pulmonary tuberculosis patients.*
***Methods:*** *The present cross-sectional study involved cases of sputum-positive pulmonary tuberculosis diagnosed between February 2012 to January 2013 attending UP RIMS & R, Hospital, Saifai, Etawah. Sputum-positive TB cases were subjected to mycobacterial culture and first-line drug-susceptibility testing (DST) excluding pyrazinamide at JALMA, Agra, Uttar Pradesh. Information regarding socio-demographic co-relates was elicited using a pre-tested semi-structured questionnaire.*
***Results:*** *Out of the fourty culture positive patients 8 (20.0%) were found to be resistant.*
***Conclusion:*** *While this providing the aproximate information about prevalence of drug resistance in the region and this may help in further planning long term surveillance studies to know the trend of drug resistance in this area.*
***Key Words:*** *Drug Susceptibility Test, Drug Resistance, pulmonary tuberculosis*

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## I. Introduction

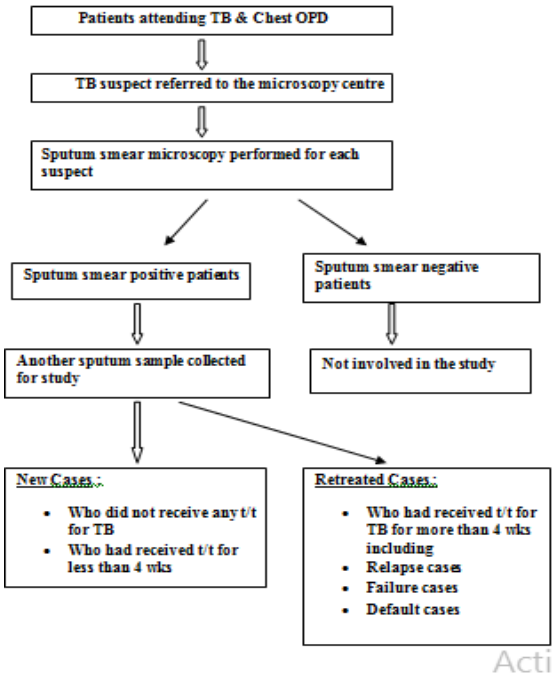
Drug resistant TB is rapidly emerging condition affecting health care system to a significant proportion. Despite the availability of effective chemotherapy tuberculosis (TB) still remains a major public health problem in most of the countries of the world. Average number of cases declined in the 70's leading to a sense of relief. But, in the last two decades, the world has witnessed an alarming rise of tuberculosis. Unfortunately, TB has not only struck back, it has returned with vengeance in a deadly form called 'Drug-resistant tuberculosis'. Globally, 3.7% (2.1–5.2%) of new cases and 20% (13–26%) of previously treated cases were estimated to have multidrug resistance tuberculosis. There were an estimated 310 000 (range, 220 000–400 000) multidrug resistance tuberculosis cases among notified TB patients with pulmonary TB in 2011. Almost 60% of these cases were in India, China and the Russian Federation[(1)]. Drug resistant tuberculosis is a man made problem. While tuberculosis is hundred percent curable, Drug resistant tuberculosis is difficult to treat. Inadequate and incomplete treatment and poor treatment adherence has led to a newer form of drug resistance. A combination of contributing factors has led to the current public health crisis: a failing National Tuberculosis Programme, denial and lack of compliance on the part of patients, lack of regulation of doctors in private practice, governmental policy failure and corruption, social and economic problems, and a growing HIV epidemic. This situation must be combated on several fronts, including promoting social change; increasing government funding; seeking global aid; implementing DOTS, and NGO programs; integrating TB and HIV programs; funding research; enacting regulatory legislation; and establishing continuing medical education programs among private practitioners[(2)]. Unfortunately, the situation in low income countries that carry 95% of the global TB burden is not favourable. TB diagnosis still relies upon sputum smear microscopy. The management of Drug resistant tuberculosis remains problematic though guidelines for DOTS-plus programs have been developed, and cheaper second-line drugs are becoming available. The diagnosis of Drug resistant tuberculosis requires that tuberculosis patients must be tested for susceptibility to drugs. The Global Plan to Stop tuberculosis 2011–2015 includes targets that is, by 2015 all new cases of tuberculosis considered at high risk of multidrug resistance tuberculosis (estimated at about 20% of all new bacteriologically-positive cases

globally) and all previously treated cases should undergo drug susceptibility testing. Likewise, all patients with multidrug resistance tuberculosis need to be tested for extensive drug resistant tuberculosis. Increasing the coverage of diagnostic drug susceptibility testing is urgently needed to improve the diagnosis of multidrug resistance tuberculosis and extensive drug resistant tuberculosis. This study is designed to find out drug resistance and its socio-demographic co-relates so that people can be made aware about the reasons that leads to emergence of drug resistance and timely effective measures can be applied to control the situation.

## II. Material & Methods

The present cross-sectional study was conducted to find out drug resistance and its socio-demographic co-relates at UP RIMS & R, Hospital, Saifai, Etawah. Patients attending TB & Chest OPD and who were found to be suspected of TB were referred to the microscopy centre of the institute where they were diagnosed for TB with the help of sputum smear microscopy (using florescent method of staining). The patients who were found to be smear positive were contacted again by the investigator to get another sample at the earliest possible time for study purpose. Two days (Wednesday and Friday) in a week were fixed to collect sputum sample. At the same time when sample was collected, information regarding socio-demographic profile was also obtained regarding age, sex, marital status, previous treatment status, socio-economic condition etc. Sputum was collected in a sterilized disposable vial and packaged to withstand leakage of contents, shock, pressure changes and other conditions. Sputum sample vials at their neck were packed with a plastic seal which prevented leakage and than all the vials that to be transported together were packed into secondary containers made of strong cardboard with enough absorbent material so that if they are damaged or leak the fluids will be absorbed. Biohazard sign was applied over every box and transported to National JALMA Institute for Leprosy & other Mycobacterial Diseases (NJIL & OMD), Agra. A preservative viz., an equal volume of a mixture of 1% CPC and 2% sodium chloride (NaCI) solution was added to sputum in equal proportion so that sample remained useful if there was any delay in transportation. In the National JALMA institute the specimens were further processed and the same was subjected to culture & sensitivity for M. tuberculosis. Culture was performed on LJ Media, which is solid growth medium specially used for culture of Mycobacterium, notably Mycobacterium tuberculosis. It is selective as well enriched media that inhibits the growth of other bacteria, while accelerating the growth of M. tuberculosis. Typical colonies of M. tuberculosis were rough, crumbly, waxy, non-pigmented (cream coloured) and appeared after a period of 6 to 8 weeks. For DST there are phenotypic as well as genotypic methods available in which phenotypic mostly used. There are three indirect type of phenotypic methods namely, resistance ratio method, absolute concentration method and proportion method. In the present study DST was carried out on solid media by applying proportion method (gold standard test). Drug sensitivity carried out for all first line drugs except pyrazinamide against Tuberculosis. Verbal informed consent was obtained from all patients and they were told about the purpose of study and assured about the confidentiality of data. The Ethical approval was obtained from Institutional Ethical Committee of UP RIMS & R, Saifai.

**3.1 Flow chart for recruitment of subjects:**



The present study includeded 127 patients. Culture was done on 91 of these patients by LJ method. Drugs sensitivity test applied, for the four first line drugs on 40 patients, who were culture positive and 8 were found to be resistant among them. Those who were found to be resistant were telephonically informed about their resistance status and reffered to the lucknow for DOTS+ treatment.

## III. Results

Results showing the distribution of 40 cases who were found to be culture positive. Table 1 showing distribution of 40 cases regarding their socio-demographic characteristic. Maximum no. of the subjects were hindu male belonging to OBC caste. Married were 72% and mainly had rural background. Literate were 63% and included mainly primary school age group. Agriculture and labour was found to be the main occupation among them. Most of them were smoker as well as alcoholic and living in kutcha house with overcrowding and inadequate ventilation. Subjects mainly belonged to joint family with socio-economic status of class 3 and 4. Many of them were using wood as main fuel for cooking.

**Table-1**: Distribution of Participants according to their Socio-demographic characteristic:

| S. No | Specification | No. | % |
|---|---|---|---|
| 1. | Gender | | |
| | Male | 34 | 85 |
| | Female | 6 | 15 |
| 2. | Religion | | |
| | Hindu | 37 | 92.5 |
| | Muslims | 3 | 7.5 |
| 3. | Caste | | |
| | General | 10 | 25 |
| | OBC | 21 | 52.5 |
| | SC | 9 | 22.5 |
| 4. | Marital status | | |
| | Married | 29 | 72.5 |
| | Unmarried | 7 | 17.5 |
| | Widower | 4 | 10 |
| 5. | Family background | | |
| | Rural | 39 | 97.5 |
| | Urban | 1 | 2.5 |
| 6. | Literacy Status | | |
| | Illiterate | 15 | 37.5 |
| | Literate | 25 | 62.5 |
| 7. | Occupation | | |
| | Agriculture | 11 | 27.5 |
| | Labour | 12 | 30 |
| | Unemployed | 8 | 20 |
| | Service | 9 | 22.5 |
| 8. | Smoker | | |
| | Yes | 25 | 62.5 |
| | No | 15 | 37.5 |
| 9. | Alcoholic | | |
| | Yes | 24 | 60 |
| | No | 16 | 40 |
| 10. | Type of house | | |
| | Kutcha | 23 | 57.5 |
| | Pucca | 10 | 25 |
| | Semi-pucca | 7 | 17.5 |
| 11. | Overcrowding | | |
| | Present | 36 | 90 |
| | Absent | 4 | 10 |
| 12. | Family type | | |
| | Joint | 27 | 67.5 |
| | Nuclear | 13 | 32.5 |
| 13. | Ventilation | | |
| | Adequate | 6 | 15 |
| | Inadequate | 34 | 85 |
| 14. | Fuel used for cooking | | |
| | Dung | 2 | 5 |
| | Gas | 4 | 10 |
| | Wood | 34 | 85 |
| 15. | Socio-economic Classification | | |
| | Class 3 | 16 | 40 |
| | Class4 | 18 | 45 |
| | Class 5 | 6 | 15 |

Table 2 reveals drug resistant status of those 40 cases, 8(20%) were found resistant among them.

**Table-2**: Distribution of Participants according to Drug Resistance Status

| S. No | Status of Drug Resistance | No. | % |
|---|---|---|---|
| 1. | Susceptible | 32 | 80 |
| 2. | Resistant | 8 | 20 |

Table 3 depicts association between drug resistance and socio-demographic characteristics. Looking at the association between gender and drug resistance 24% male were found resistant and all the females were susceptible but the association was not statistically significant. Cases who belonged to other caste were 30% resistant while only 16% of OBC were resistant but this association between caste and resistance was not significant. Similarly association of drug resistance with marital status and literacy were not statistically significant. Occupation distribution presented that 36% of subjects were resistant in agriculture group and 24% smokers and 31% alcoholic were resistant but the association was not found to be statistically significant. Subjects who were living in semi-pucca house were more resistant and those in joint family with inadequate ventilation were found to be more resistant and the association was not significant. Among the study participants who were using gas as cooking fuel were more resistant but the association was not significant. Participants who were treated for tuberculosis in past 32% of them were resistant while among new cases only 6% were resistant and the association between drug resistance and prior treatment were found statistically significant.

**Table-3**: Association between drug resistance status and socio-demographic characteristic

| S.No | Specification | Drug resistance status | | Test of Significance |
|---|---|---|---|---|
| | | Susceptible | Resistant | |
| 1. | Gender | | | |
| | Male | 26(76.5%) | 8(23.5%) | p=0.318 |
| | Female | 6(100%) | 0(0%) | |
| 2. | Caste | | | =0.833 |
| | Others | 7(70%) | 3(30%) | P=0.36 |
| | OBC | 25(83.3%) | 5(16.7%) | df=1 |
| 3. | Marital Status | | | |
| | Married | 21(72.4%) | 8(27.6%) | p=0.08 |
| | Unmarried | 11(100%) | 0(0%) | |
| 4. | Literacy Status | | | =0.667 |
| | Illiterate | 13(86.7%) | 2(13.3%) | p=0.414 |
| | Literate | 19(76%) | 6(24%) | df=1 |
| 5. | Occupation* | | | |
| | Agriculture | 7(63.6%) | 4(36.4%) | |
| | Labour | 11(91.7%) | 1(8.3%) | p=0.65 |
| | Unemployed | 6(75%) | 2(25%) | |
| | Working | 8(88.9%) | 1(11.1%) | |
| 6. | Smoker | | | =0.667 |
| | Yes | 19(76%) | 6(24%) | p=0.414 |
| | No | 13(86.7%) | 2(13.3%) | df=1 |
| 7. | Alcohol | | | =2.1 |
| | Yes | 11(68.8%) | 5(31.2%) | p=0.14 |
| | No | 21(87.5%) | 3(12.5%) | df=1 |
| 8. | Type of House* | | | |
| | Kutcha | 19(82.6%) | 4(17.4%) | p=1.000 |
| | Pucca | 8(80%) | 2(20%) | |
| | Semi-pucca | 5(71.4%) | 2(28.6%) | |
| 9. | Overcrowding | | | |
| | Present | 28(78.8%) | 8(22.2%) | p=0.56 |
| | Absent | 4(100%) | 0(0%) | |
| 10. | Family Type | | | |
| | Joint | 20(74.1%) | 7(25.9%) | p=0.236 |
| | Nuclear | 12(92.3%) | 1(7.7%) | |
| 11. | Ventilation | | | |
| | Adequate | 6(100%) | 0(0%) | p=0.236 |
| | Inadequate | 26(76.5%) | 8(23.5%) | |
| 12. | Fuel Used* | | | |
| | Dung | 2(100%) | 0(0%) | p=1.000 |
| | Gas | 3(75%) | 1(25%) | |
| | Wood | 27(79.41%) | 7(20.59%) | |
| 13. | Prior Treatment | | | =4.26 |
| | Yes | 15(68.2%) | 7(31.8%) | p=0.039 |
| | No | 17(94.4%) | 1(5.6%) | df=1 |

## IV. Discussion

The present study was carried out to find out drug resistance and its socio-demographic co-relates. Maximum no. of the subjects were Male similar findings were given by ICMR survey(1955-58)[3] and Gupta S[4] et al. Tuberculosis seen among hindu and OBC category and this was similar to Agarwal A, Agarwal VK[5]. Subjects in our study mainly belonged to rural background and Agrawal A, Agrawal VK found 63% subjects with rural background. Literate were 63% and included mainly primary school age group, Raina et al[6] and Benner et al[7] found illiteracy as main contributing factor. Agriculture and labour was found main occupation among tuberculosis patients and similar findings were given by Agrawal A, Agrawal VK, Gupta RK et al[8] and Gupta S et al.

Most of the resistant cases were smoker as well as alcoholic. Prasad et al[9] and Linn et al[10] reported risk of TB higher among smoker and Gupta RK et al also found significant association between TB and smoking. Kolappan C et al[11] and Buskin et al[12] reported higher risk of TB among alcoholic. Significant no. of tuberculosis patients were living in kutcha house with overcrowding and inadequate ventilation. Gupta RK et al studied the relationship of TB with living standard and found that those living in "Kutcha" houses had a higher prevalence. Among the other social variables which were studied by Gupta RK et al overcrowding were found to be statistically significant in relation to the tuberculosis. Poorly ventilated living conditions and crowding are important factors for tuberculosis transmission according to Clark et al[13] and Sepkowitz[14]. Subjects mainly belonged to joint family with socio-economic status of class 3 and 4. Chowdhary et[15] al and Tiwari et al[16] reported that people belonging to the lower socio-economic group were the worst sufferers. Many of the tuberculosis patients were using wood as main fuel for cooking.

Present study find out overall drug resistance 20%. Mahadev B et al[17] in their study found that in hoogli district drug resistance was 1.9-13.7% and Paramsivan CN et al[18] found 20.25% drug resistance in their study.

The present study depicted that more resistant cases were found among hindu male and among those who belonged to OBC category and married but this association was not statisticaly significant. This may be due to high prevalence of hindu religion and other category in surrounding population. Resistant cases were more among literate group and most of the resistant cases were educated only upto primary school .This finding was similar to Bhatt G et al[19] who found resistance more prevalent among those who were educated upto primary school. The present study found that resistance more prevalent among agriculture and Nuruli Amin et al[20] also found in their study more resistance among the people involved in labour intensive occupation. Smokers and alcoholic were found more resistant and similar findings given by Marahatta SB et al[21]. Bhatt G et al and Gupta S et al in their study observed overcrowding to be a factor among TB resistant cases similar to our study. Bhatt G et al who also found that among 86% subjects ventilation was inadequate and we found similar findings in present study. Nuruli Amin et al in their study revealed that 60% of resistant subjects were living in kutcha house while in our study person living in semi-pucca house were found to be more resistant.The present study also revealed that overall resistance among previously treated cases was 31.8%. Ti T et al[22] found that 30.2% were resistant to any one of the drugs. In Karagoz T et al[23] study resistance among previously treated cases were 34.3%.

## V. Conclusion

India's RNTCP has taken cognisance of the high levels of MDR-TB and non-MDR drug resistance and has developed a response plan that aims to continue strengthening the programme's preventive activities against the development of 'new' DR-TB cases by provision of high quality DOTS services throughout the country, improving public-private partnerships for TB treatment, quality assured laboratory services. A strong tuberculosis programme that can reduce the incidence of drug resistance in the community and particularly directly observed therapy (DOTS) which is cost effective, will prove to be effective in treatment completion and in turn prove to be effective against generation of resistant strains. Newer drugs for tuberculosis are unlikely to come up in the near future and hence the key to success remains in adequate case finding, prompt and correct diagnosis and effective treatment of infective patients including careful introduction of second-line drugs to which the patient is susceptible. The major limitation of the present study is the small sample size and therefore, it is not representative of the population at large. In fact, this limitation was observed in most previous studies on MDR-TB. Nation-wide and State-wide representative data on the prevalence of MDR-TB are an urgent need of the hour to design effective empirical regimens, to monitor functioning and progress of the national TB control programme and for continued surveillance of DR-TB.

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