

ATT (ANTI TUBERCULOSIS TREATMENT) DRUG COMPLIANCE WITH PULMONARY TUBERCULOSIS AND ITS PREVALENCE IN SOUTHERN PUNJAB

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ABSTRACT:

One third of all human population is dealing with asymptomatic TB. We conducted research to estimate positive pulmonary TB cases and ATT compliance in rural area of Rohilanwali, Southern Punjab. Rural health center (RHC) Rohilanwali's laboratory was the center for diagnosis and provision of free ATT drugs via National TB control Program (NTP) under DOTS guidelines. Eight villages population was included in study that was almost 3lac, sampling was simply random including male and female of each age group, only PTB positive cases were included in research. In first three quarters of 2018 there were 417 pulmonary TB cases (229 bacteriologically confirmed & 188 clinically confirmed), while it was 524 positive cases in 2019 (198 bacteriologically confirmed & 326 clinically confirmed). The number of cases who had clinically confirmed increased to the patients who were bacteriologically confirmed. In 2018 first three quarters out of 417 PTB cases 117 have been cured, 285 completed the treatment, 04 of patients lost follow up and 11 positive cases expired. In 2019 out of 2314 suspects with chronic bronchitis there were 524 PTB cases, 39 patients had cured, 214 patients have completed the treatment, 270 patients were under treatment, 18 relapses were reported and only one patient had expired. ATT compliance is quite worthy as it is confirmed by cured cases and lesser number of relapses. The above given data reveals increasing incident rate of PTB but with low mortality rate as compared to the 2018 reports. The main reason for dissemination of

infection was poor hygiene, lack of health education and quack's practice that is leading causes of increasing incident rate.

KEY WORDS:

ATT (Anti tuberculosis treatment), PTB (Pulmonary Tuberculosis), Relapse, prevalence

INTRODUCTION:

There are almost 7.7 billion people living on earth. Plethora of deadliest diseases has taken over growing human population. An ancient disease named TB that has killed 2 billion people in past 200 years is caused by rod like acid fast bacilli named *Mycobacterium tuberculosis*(1). With the passage of time and treatment bacteria and viruses develop resistance against drugs that is termed as ant-microbial resistance (AMR). Due to the frequent and inappropriate use of drugs to treat Tuberculosis resulted in drug resistant (2). It is categorized under two main types of TB. The first one is cured with first line treatment or drug sensitive TB (DS-TB), while the other one is multidrug resistant TB (MDR-TB)(3), it is the only major air born drug resistant epidemic (1). Drug resistant TB is more costly than DS-TB, only one in three is diagnosed with Drug resistant TB (DRTB), one in four is treated and half of them are successfully cured. It is estimated that if the problem is not addressed properly the global economy have to pay US 17trillion dollars. DR-TB is not invincible up till now. Compendious approaches are required to be taken that may lessen the DR-TB effects on humanity and the end results would be of great benefits in future. DR-Tb is a major threat to global health security. It is estimated that one third of all deaths due to AMR are due to TB, killing 230,000 human in 2017. If it is not administer it could raise more than ten folds to 10 million annually by 2050. DR-TB affects more than half a million people globally mostly cases are reported in developing and third world countries (1).

Mycobacterium tuberculosis was first discovered by a German physician Robert Koch on 24th march, 1882 in Berlin; for his discovery he was awarded with Nobel Prize in physiology and medicine in 1905; since 1982 24th march is celebrated as world TB day (4). Currently one third

of human population is infected by tuberculosis globally; there two major types of infection asymptomatic infection is termed as “Latent TB Infection” on the other hand patient with symptomatic TB has “Active TB Infection”. Tuberculosis is a global health threat though it is preventable and curable yet, each of active TB may lead 10 to 15 further infections annually if left untreated (5, 6). It’s highly contagious though it takes time to be a symptomatic infection; it can spread through water droplets while sneezing, coughing, singing, talk, highly condensed and suffocated living areas (6, 7 & 8). After 1993 world health organization (WHO) declared TB global emergency and Direct Observed Treatment, short course (DOTS) strategy was adopted (6). After implementation more than 20 million of patients were treated and more than 16 million were cured of TB by 2004. Nevertheless, progress was slow in sub-Saharan Africa and Eastern Europe (9). Two third of TB cases reported in Asia, it even faces new challenges like TB/HIV co-infection, multidrug resistant TB (MDR-TB) and childhood TB which are hindering the TB control efforts (9).

Tuberculosis is a highly contagious disease caused by *Mycobacterium tuberculosis*; it lasts throughout life course and determines the formation of tubercles in different parts of the body (8). TB bacilli has an ancient origin, it has survived for 70,000 years and currently infects 2 billion people worldwide (12) with around 10.4 million cases every year and one third of human population at risk of developing active TB (13). When the infection affects the lung parenchyma, it is called „pulmonary tuberculosis“. When the infection affects other parts of the body, it is called „extra-pulmonary tuberculosis“. Examples of extra pulmonary TB includes pleural effusion (pleural TB), lymphadenopathy (glandular tuberculosis), miliary TB, genito-urinary TB, pericardial disease (pericardial TB), and tuberculosis meningitis. Patients usually complain of constitutional symptoms (fever, night sweat, weight loss) and local features related to the site of disease. A patient with both pulmonary and extra-pulmonary TB should be classified as a case of pulmonary TB (11).

According to an estimate Pakistan is 5th country out of 25 with highest burden of TB infection (10). Bacilli Calmette Guérin (BCG) is the current vaccine for TB first used in 1921 (14). It was widely used after world war 2 and introduced in Pakistan in 1947 (15). Advancement in TB control was

started with discovery of Streptomycin in 1944 that targets the 30s bacterial ribosome and derived from a soil Actinomycetes (16), P-amino salicylic acid (PAS) in 1946 and Isoniazid in 1951 helped in better cure for tuberculosis (17). TB is more prevalent in males as compare to female while this reverses in childhood population (18). Some people resist TB more effectively as compare to others and his susceptibility is associated with HLA-DR2 in Asian population (19). Most of cases are reported in Asia (55%) followed by Africa (30%), Eastern Mediterranean region (7%), European region (4%) and the region of Americas (3%). Top 5 infected countries were India, China, Afghanistan, Indonesia and Pakistan. India and China collectively accounted for 35% of these new cases. More or less some 1300,000 people died of TB in 2009 and sixty thousands of them belonged to Pakistan (11). Prevalence of TB in Pakistan is 350 infected individuals out of 100,000 (11)

It's the courtesy of joint venture by National TB control Program NTP and Ministry of National Health Services, Regulations and Coordination; Government of Pakistan.

MATERIALS AND METHODS:

DIAGNOSIS:

Following strategies were associated in research for diagnosis of TB infected patients. Though TB is curable and preventable but it's still lethal and contagious that make it difficult to handle. A patient with TB is not that easy to be detected, as one third of human population is carrier of TB. Asymptomatic infection (latent TB Infection) is curable but difficult to be detected while active TB is easy to be detected by AFB-staining. TB is an insidious infection; it takes time to develop signs and symptoms. When a patient has developed typical symptoms like night sweating, weight loss, fever and TB like cough since 2-3 weeks, he has already infected many people nearby (11, 20). Physician team from our group diagnosed patient with cough and put them on first line empirical antibiotic treatment according to the SOPs. As a result the patients with 2-3 week cough, sudden weight loss, fever and night sweating were referred to clinical lab tests.

LABORATORY DIAGNOSIS:

Detection of AFB from concentrated sputum and pulmonary exudates have great importance in clinical diagnosis and epidemiological investigation of infection. Yet it is the mostly used detection method in developing countries (11, 20). About 60% to 70% of all TB cases are diagnosed by sputum Smear examination with the help of two traditional microscopy methods namely fluorescence microscopy (FM) and the Ziehl-Neelsen (ZN) though ZN method is widely used in developing countries because of simplicity and cost effective method. (11, 20)

As mycobacterium tuberculosis is a chronic infection that leads to elevated ESR and monocytes. Therefore further confirmation is done via Erythrocyte Sedimentation Rate (ESR) test that is recommended by concerned physician; as a result of one research study 99% of patients with TB have elevated ESR. It's an accessory test for TB positive patients. While its normal range is 0-10 despite its value will be >30 (11, 22). While C-reactive protein test is used as an accessory test in confirming TB infection. Another confirmatory test is chest X-ray, there are white shadowed patches on chest X-ray that reveals the damaged lungs and severity of infection; while patients with negative sputum reports can be further diagnosed by CT-Scan and Magnetic resonance imaging (MRI) (23, 24, 25).

There is another mechanical approach to diagnose mycobacterium tuberculosis by GENE Xpert MTB assay. Its working is based on polymerase chain reaction; it detects the genetic sequence of Mycobacterium tuberculosis and amplifies it (26). We don't have the facility but Gene Xpert diagnosed patients from Nishter medical University Multan are here for follow up.

There are some other tests but rural health center **Rohilanwali** is out of such test facilities despite serving the patients with AFB staining, C-reactive protein (CRP) test, X-ray, ESR test and referring serious and complex patients for Gene X-pert to nearby District headquarter (DHQ) or Tehsil headquarter (THQ) hospital. Other than Gene X-pert mycobacterium can be diagnosed by culturing MTB on Lowenstein Jensen Medium (LJ Medium) but it is time taking. Another test is TUBERCULIN test. A purified protein derivative (PPD) is injected intra-dermally 4 fingers below elbow and reaction is measured after 72 hours a positive patient would have 5mm or more wheal size on arm surrounded by zone of erythema; only induration has to be measured (11). The specificity of **Monteux** test for pulmonary as well

as extra-pulmonary TB increases as the size of induration increases reaching 86% at induration of more than 15 mm (11, 27). Patients with complicated cases relapses and patients who have completed the cure are referred to THQ, DHQ and Private Laboratories for Gene X-pert Test.

MEDICATION STRATEGY:

After screening test and final diagnosis next step towards cure is medication for the management of TB infection. There are three different stages of prevention and control of TB. Primary prevention includes health education regarding severity of infection; secondary prevention includes proper diagnosis and treatment of suspect via above given techniques to ensure that a real suspect is under cure and tertiary prevention includes rehabilitation of infected patients (11). Medication includes Myrin-P {Rifampicin (150mg), Isoniacida (75 mg)} and Myrin-P forte {Rifampicin (150mg), Isoniacida (75mg), Pirazinamide (400mg) and Etambutol clorhidrato USP (275mg)}. These ATT (Anti Tuberculosis Treatment) drugs are provided to the patients without any cost according to the National TB control program (NTP). It's a well-managed system where hospital's employees (lady health visitors) are regulated to visit the infected family on regular basis to ensure the compliance of treatment by assigning this duty to an educated or responsible individual in family. Hospital's staff regularly updates the patients regarding their medication and assigned laboratory test in time for better cure. These all standard operating procedures are the part of Direct Observatory treatment short course (DOTS) system according to NTP guide lines.

All the patients were in direct contact to respective medical officers who were participated in research. Our team worked keenly in clinical diagnosis and laboratory diagnosis; despite we conducted regular visits to infected families to evaluate their life standards and conditions they were living in. Complicated and MDR cases were referred for culture test. Though Gene X-pert was enough in diagnosing DRTB (Drug Resistant TB) but culture tests were referred for confirmation. ALL collected data was filled in already built forms and MS excel sheets were created for statistical evaluation.

RESULTS & DISCUSSION:

Rural health center (RHC) Rohilanwali was elected as center with higher incident rate of TB. There are almost 300,000 of population that is being facilitated with medical services via this medical center. Our team has been working since last 9 months; collaborating with patients from eight different union councils (Rohilanwali, Manka bhutta, Marha, Manik pur, Aloday wali, Ibraheem wali, Ganga & Umarpur Janubi). Our core focus for research was prevalence of Pulmonary TB and its compliance with provided treatment following (DOTS) SOPs under the guidelines of National TB control Program (NTP). There were 2,314 patients that were suspected of having TB in last 09 month's OPD of 215215 patients and referred for laboratory diagnosis and confirmatory tests by respective medical officers. Patients with night sweat, fever, TB like cough and weight loss were referred for AFB smear staining and chest X-ray. All routine and confirmatory tests were done in BSL-2 initial level laboratory ensuring the safety of all colleagues and workers there in laboratory. SOPs and Biosafety rules were followed strictly. As a result out of 2314 plausible patients there were 524 TB cases reported with pulmonary Tuberculosis.

As per final results, we found that there were 542 numbers of patients who were suffering from pulmonary TB. 207 cases were reported in first three months, 202 in second quarter and 115 from July to September with 7, 8 & 3 relapse cases respectively. After final confirmation these patients were dealt following D.O.T.S guidelines, a specific TB card was issued to the patients with a brief knowledge about severity of infection and drug dose was adjusted according to the patient's weight. Patient's personal data was collected for visits and regular follow up of ATT drug compliance.

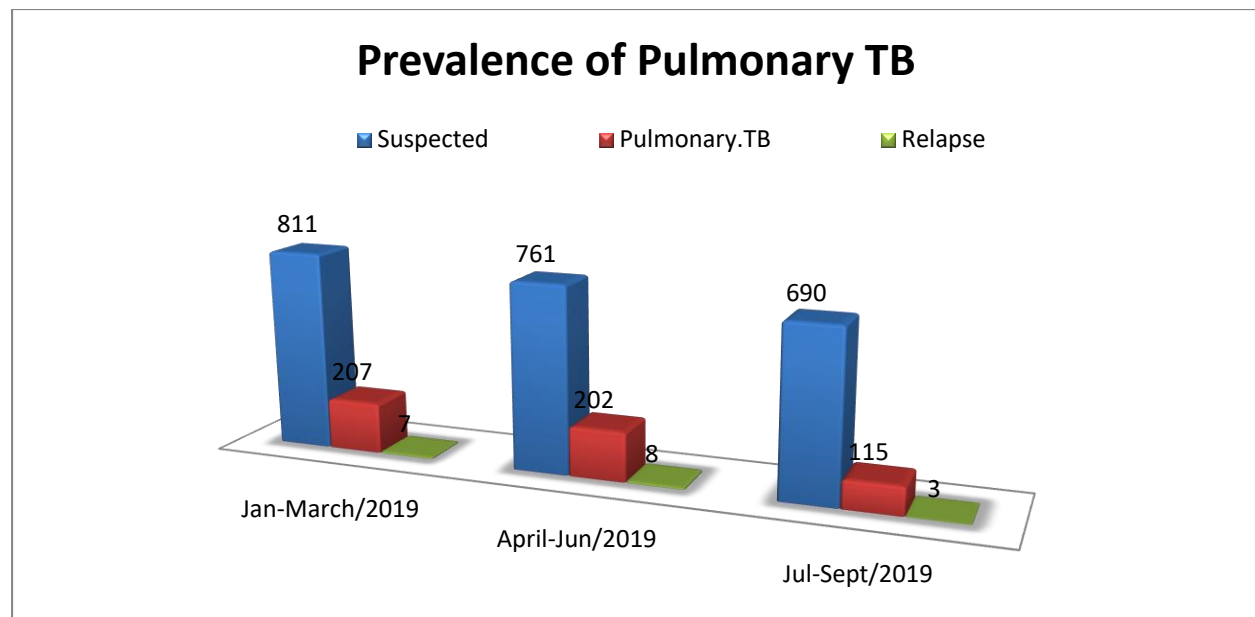


Chart 1; Reveals the prevalence of pulmonary TB among 2314 suspects that was 524 in last 09 months. In an OPD of 215215 patients there were 524 actual TB patients from January, 2019 to September, 2019. 542 P-TB patients including relapse cases in last 09 months.

In comparison of last year's 09 months a considerable variation is observed. There were 417 of total reported pulmonary TB cases in last year (145, 129, 143 patients in Quarter 1, 2 & 3 respectively). Out of 417 patients 117 get cured (35, 37 & 45 cured in Quarter 1, 2 & 3 respectively); on the other hand 285 patients completed the treatment (104, 85, 96 patients completed the cure in Quarter 1, 2 & 3 respectively). While 11 patients get expired with severity of infection (03, 06 & 02 died in Quarter 1, 2 & 3 respectively) and team lost the follow-up by 04 of infected individual (03 & 01 lost in Quarter 1 & 2). The patients with severe bronchitis and pneumonia were greater in number in 2019 as compare to the patients reported in 2018. Same was the pattern with increasing pulmonary TB cases. The no. of pulmonary TB patients was in 2018 first three quarters was 417 collectively while it was 542 in 2109.

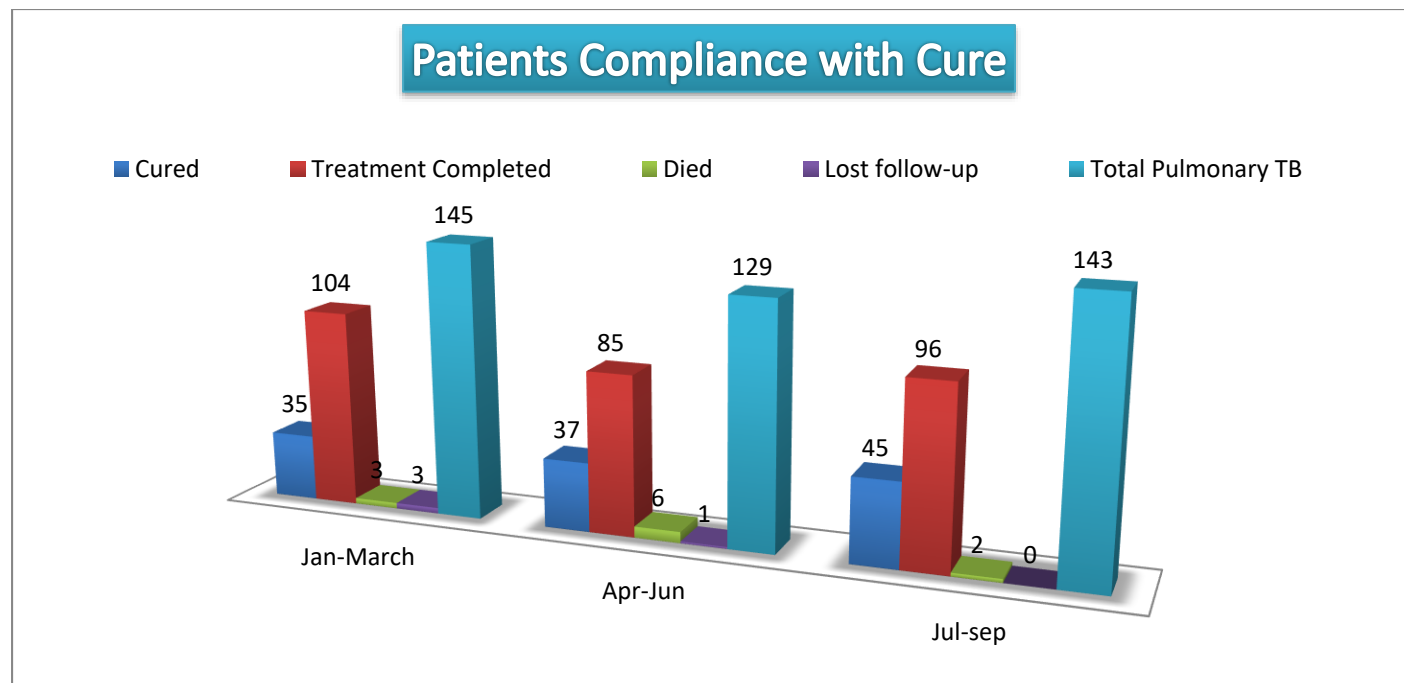


Chart 2; Shows the no. of patients who have completed the treatment, cured, died with infection, lost the follow up and total no. of cases from Jan, 2108 to September, 2018.

As for as the cure and patients compliance with given TB drugs is concerned; here it is noteworthy that treatment is effective and efficacious if patients strictly follow the treatment guide lines. Completely cured individual are tested via Gene X-pert with regulated intervals of time to ensure the complete eradication of infection. Patients who were taking ATT drugs completed the assigned treatment course of six months, nine months or twelve months either. They were diagnosed thrice with negative results after 3rd, 5th & 7th months of treatment. Negative results assured complete cure of TB infection; as he/she was confirmed bacteriologically for PTB (pulmonary Tuberculosis). But the patients who were confirmed clinically were under ATT course according to the guidelines of DOTS program. These patients completed the course and went through diagnosis timely as given above. 3 patients were died in first quarter, 6 patients were died in second quarter and 2 were dies in third quarter. These patients were having severe PTB and were diagnosed late. The core reason behind late diagnosis and increased severity of infection is quackery. Increased quake practice, increases the rate for severity in infections. This is not the only reason behind increased incident rate of PTB. The second major reason behind is

literacy rate. Mostly infected individuals were illiterate; their first choice for treatment is not a hospital but pilgrims and home remedies.

CONCLUSION:

ATT drug compliance is efficacious and effective for management of P.TB. It had saved many lives and blessed them with a healthy life. As for as prevalence concerned, it is increasing and there are two prospective we deducted from our research. Either DOTS program reporting has reached far off areas or active PTB patients are spreading the lethal infection due to the lack of knowledge of what they are dealing with. TB reporting is getting better, patients are following the treatment, here the national TB control program (NTP) and funding agencies should be appreciated. They are all eagerly struggling to support the NTP vision to make Pakistan TB free and better place to live. But still there is lot to be done. First and the foremost thing is public counseling and health education. This will increase the understanding for severity of infection and how to manage the problem. Secondly, Quake's practice should be banned with iron handed.

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