TREATMENT STRATEGIES OF MULTI-DRUG RESISTANT MYCOBACTERIUM TUBERCULOSIS

Abid Rashid[1*], Muhammad Akram[2], Muhammad Daniyal[3,4], Asmatullah Khan[5,6], Muhammad Younas[7], Naheed Akhtar[8], Imtiaz Mahmood Tahir[8]

ABSTRACT: Tuberculosis is one of the greatest killing diseases of modern times. WHO and UNICEF are assisting BCG vaccination campaign in more than 60 countries. Treatment of Mycobacterium tuberculosis infection is done via current standard regime of all allopathic medicine by is limited by side effect and low rates of treatment completion. We reviewed data from PubMed, Google scholar, Cochrane Library, EMBASE and recent published papers on treatment strategies, etiology, diagnosis and phytotherapy of tuberculosis in peer-reviewed International Journals. Various studies represented by publication made up of in vitro , in vivo anti-mycobacterial activities, systematic reviews and recent research articles on tuberculosis. The manuscript is prepared as a review with the objective of discussingconventional and herbal treatments of tuberculosis and documenting the medicinal plants used for treatment of tuberculosis. Further clinical trials should be conducted for their use in tuberculosis. Directorate of Medical Sciences, Government College University Faisalabad

1. Department of Eastern Medicine and Surgery, Directorate of Medical Sciences, Government College University Faisalabad, Pakistan.
2. TCM and Ethnomedicine innovation and Development Laboratory, school of Pharmacy Hunan University of Chinese Medicine, Changsha, 410208, China.
3. College of Biology, Hunan Province Key Laboratory of Plant Functional Genomics and Developmental Regulation, Hunan University, Changsha, 410082, China.
4. Laboratory of Neuroanatomy & Neuro psychobiology, Department of Pharmacology, Ribeirão preto Medical school of the university of Sao Paulo, AV. Bandeirantes, 3900, Ribeirão Preto, 14049-900, SãoPaulo, Brazil.
5. Department of Eastern Medicine and Surgery, School of Medical and Health Sciences of the University of Poonch Rawalakot, Hajira Road, Shams Abad, Rawalakot 12350, Azad Jammu and Kashmir, Pakistan.
6. Faculty of Pharmacy and Alternative Medicine, The Islamia University Bahawalpur, Pakistan.
7. College of Allied Health Professional, Directorate of Medical Sciences, GC University Faisalabad, Pakistan.

Corresponding author:
drabidrashid37@gmail.com

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INTRODUCTION

Tuberculosis is a communicable, chronic, granulomatous disease, caused by mycobacterium tuberculosis. It usually involves the lungs but may affect any organ or tissue of the body. The appearance of resistance to drugs prescribed to manage tuberculosis (TB), and mainly multi drug-resistant TB (MDR-TB), has become an important public health issue in numerous countries and barrier to successfulworldwide TB control. In several other countries, the level of drug resistance is unidentified and the treatment of cases with MDR-TB is insufficient. In countries wherever resistance of drugs has been recognized, particular actions required to be taken within tuberculosis control programs to deal with the difficulties through suitable management of cases and implementation of approaches to stop the spread and propagation of drug-resistant tuberculosis such as MDR-TB. Tuberculosis is an infectious disease, which involves lungs and other organs of the body causative organism of the disease is mycobacterium tuberculosis. Mycobacterium tuberculosis is a slow growing organism and many of them

reside inside thesuch as cells macrophages. Hence, prolonged therapy is required to for the treatment of tuberculosis.A single drug should not be used for the treatment of tuberculosis, because of thedevelopment of resistant organisms (1). Hence, a combination of at least two ormore drugs is required for the successful treatment of tuberculosis (2). It is spread by air borne infection. The major route of infections is via the respiratory tract (more rarely via the oral route). Once organisms have been inhaled, they establish themselves in the periphery of the lungs, and elicit a host inflammatory response (largely via macrophages). Spread to regional lymph nodes may also cause hilar adenopathy (3). Tuberculosis is found worldwide especially in industrial establishments, in overcrowded living and low socioeconomic groups. However, with tuberculosis control program the prevalence of disease is showing downward trends all over the world. Primary complex or initial infection of tuberculosis of ten goes unnoticed. In others, it causes reactionary phase as mild continuous fever. Early primary lesions heal with calcification of pulmonary, tracheobronchial, or other regional lymph glands where the infection get entertain 90-95% persons but there is always danger of activation in life under adverse environmental conditions or lowering of internal resistance. The initial infection may disseminate via lymphatics to manifest as pulmonary tuberculosis or extra-pulmonary tubercular infection.(4) Prevalence of tuberculosis is increasing and there is need to prevent this transmission. Tuberculosis is seen in patient with diabetes mellitus type 1.(5) Tuberculosis is mostly seen in HIV patients because HIV infection impairs the immune system of patient and patient become susceptible to tuberculosis. It usuallyinvolves the lungs but may affect any organ or tissue in the body. Egyptian and Greco-Roman civilization has recorded tuberculosis disease of spinal cord. Tuberculosis may occur as fresh infection or reactivate from its dormant stage. It has been seen that new infection occurs in young population and older people suffer from tuberculosis due to reactivation of Tuberculosis (6). Now, tuberculosis is considered one of the manifestations of HIV. Tuberculosis is being treated by WHOs directly observed treatment (DOTS) strategy, which is considered reliable and effective method of therapy (7). Tuberculosis was the major cause of death in poor countries before emergence of modern medicine. Tuberculosis affects one-third population of world population most of the cases are in subcontinent. This disease is still prevalent in developing countries. First line therapy is of 6 months thatincludes: pyrazinamide, ethambutol, isoniazid and rifampicin. Second line therapy is given after failure of first line therapy due to drug resistance. Second line therapy includes drugs such as ethionamide, capreomycin, fluor quinone, kanamycin, para-amino salicylate and cyclol serine (4).These drugs are effective earlier in tuberculosis but resistance has been developed against these drugs (8). Andhave few side effects (Table 1). This disease was more common in immune-competent people. Tuberculosis primarily affects the lungs and can spread in other parts of the body with passage of time.After making diagnosis of tuberculosis, First line treatment is initiated. If first line treatment-fails then physician can consider it a matter of multi drug resistant tuberculosis. Tuberculosis is a global public health problem. Tuberculosis is increasing rapidly in underdevelopedcountries. This disease has been neglected in past. In developing countries, most of the

TB patients are mishandled because of low medical facilities. In this way, patients remain un diagnosed for a long time and when they come to hospital, the complications of tuberculosis are developing. Tuberculosis was considered disease of poor people and its occurrence was mostly in overcrowded family, prisoners, and places with less oxygen (9). Allopathic medicines are used to treat tuberculosis but they exert side effects Herbal medicines are becoming popular among people of developing countries.

Plants activity against tuberculosis has been identified from different sources such as literature review of books of phytomedicine, microbiology and published papers on phyto-therapy of tuberculosis. Traditional healers prescribe herbal medicine as remedies against fever and other symptoms of tuberculosis (10). Active compounds have been isolated and studied for their activity. Several medicinal plants are used to treat this infection. Resistance is of two types; one is called multi drug resistant TB(MDR-TB) and second is called extensively drug resistant (XDR-TB). MDR- TB is resistance to first line therapy andXDR-TB is resistance to second line therapy. Medicinal plants are in use to treat tuberculosis in all over the world. Medicinal plants are used by all cultures of world since ancient times (11-13). Tuberculosis is treated by directly observed treatment (DOT) (14). This disease is more common in uneducated persons as compared to educated communities. More commonly, the disease is found in person working in factories especially cotton mills in India and Pakistan People working in factories should be screened for AFB in sputum (15).In the future, we should be attentive withreference to the spread of the extensively drug resistant(XDR)strains of tuberculosis worldwide. MDR tuberculosis strains are resistant to any fluoroquinolone drug and a 2nd line injectable drug. MDR and XDR tuberculosis can be managed merelythrough appropriate planning andimplementation of tuberculosis control programmers in worldwide. A “broad-tiered” association between the community and private sectors can be helpful in the prevention and control of MDR and XDRtuberculosis (16).

MDR-TB

It is TB resistant to rifampicin and isoniazid. These medications are recommended to all patients with tuberculosis (17). Method of transmission Ingestion of polluted nourishment and drain are hazard factors. The time frame from disease to beginning of tuberculosis i.e. disease period might be weeks or months or years relying upon have parasites relationship and dosage of contamination. The dangers of contamination and ailment are firmly identified with the closeness of contact, degree of the sickness ,sputum inspiration of the source case and the host parasite relationship.

Morphology

Shape of mycobacterium tuberculosis is club shaped. It is non-capsulated, non motile and non spore forming (18).

Forms of mycobacterium tuberculosis

Human type Bovine type

Sources of infection

In human type, sputum or excreta of tuberculosis patient is major source of infection. In bovine type, infected milk from cows suffering from tuberculosis is source of infection (19).

Predisposing factors

Tuberculosis can occur in any stage of life. Individuals suffering from malnutrition are more susceptible to tuberculosis. There is no inherited immunity against tuberculosis (20). Environmental factors: which lower thebody resistance such as: malnutrition, poverty, overcrowding unhygienic conditions, alcoholism and heavy

smoking. Pathological factors: which lower the body resistance e.g. diabetes mellitus, lymphoma and cytotoxic drugs.

Symptoms

Symptoms vary and may be nonspecific. The outset of tuberculosis is insidious and early symptoms vary from one individual to other. Most of the patients are asymptomatic and are only diagnosed ontuberculin test and x-ray chest. Ery the mano do summary be seen on the shin and thigh. There is usually steady and progressive loss of weight and this isassociated with general malaise and fatigue

.Persistent pyrexia is present characteristically raised in the evening and lowered in the morning. Heavy night sweats accompany the pyrexia. In some cases, cough is associated with blood stained sputum (21).

CASEFINDINGTECHNIQUES

- **Tuberculin test**

Tuberculins are preparations obtained in a number of ways from the human and bovine strains of the tubercle bacillus. Inboth human and veterinary practice, tuberculin may be applied as a diagnostic agent to determine whether the person or animals is or has been infected with mycobacterium. The tuberculin may be applied by intra cutaneous injection. Thistest is performed to know that patient is suffering from tuberculosis or was affected in his life. In this test, an antigen is injected under skin. Patient suffering from tuberculosis will have a wheel flare phenomenon on the injected site (22-23).

- **X-Ray examination**

X-rays how's white spot that is due to reaction of immune system against mycobacterium tuberculosis. Enlargementof the hilar or paratracheal lymphnodes, parenchymal pulmonary lesions , tuberculous pneumonia, collapse of segment or lobe, pleural effusion may be seen(24)

- **Sputum examination**

Sputum is checked for presence of mycobacterium tuberculosis. In pulmonary tuberculosis, sputum smear is taken to check infection but in case of extra- pulmonary involvement, specimen from affected site should be investigated for histological, culture and microscopy. Early morning sample is usually checked for tuberculosis. If sputum report indicates presence of acid-fast bacilli then further evaluation should be done (25)

- **Histology of biopsy specimen**

Biopsy specimens are taken from superficial lymph nodes, liver, bone marrow, and trachea (26)

- **Biochemical markers**

Biochemical markers for tuberculosis include adenosine deaminase test and bromide partition test, which have a sensitivity and specificity ranging from 90-95%.

- **Gas chromatography technique**

Gas chromatography technique detects mycobacterial fatty acids in sputum and CSF(27)

- **DNA probes**

These have been developed to identify mycobacterial DNA. Sensitivity of this test is 90%(28).

- **Antibody detection**

The sensitivity of these tests varies between50-90%, while these tests are around 92-95% specific.

- **Supportive investigations**

CBCESR

CSF examination Ultrasound abdomen CT scan

MRI

Fundoscopy

TREATMENT

Mycobacterial infections are difficult to cure because they are slow growing organisms, dividing only once in 1-2 days, even in the most favorable conditions (29).They can be dormant especially in less favorable

Circumstances such as closed caseous lesion and may persist for many years although they are less sensitive. The caseation and fibrosis also tends to block the blood vessels supplying the necrotic area. The general health of tuberculosis patient is usually poor. Patients may be anemic and undernourished. These patients should be provided with maximum physical and mental rest. Their nourishmentshould be improved. If facilities areavailable, severely ill patient should be admitted to a sanatorium .Studies of the effectiveness of vaccines to produce immunity to tuberculosis are constantly in progress. The vaccine known as BCG (prepared from bacillus calmette guerin) is a freeze-dried preparation of the culture of an attenuated strain of bovine tuberculosis originally isolated by two bacteriologists, Calmette and Guerin. The main point of difference concerned the relative safety of the vaccine ,but refinements in the processing and improvement in the testing have now assured a safe, nontoxic product for human use. European physicians have accepted BCG vaccine for a number of years, and endorsement by American investigators was forth coming during the 1950s. Immunologic protection against tuberculosis is only relative and is not permanent or predictable .The vaccine is recommended primarily for use for people whose exposure to tuberculosis is unusually high or when other means of control are inadequate. It should be used only with in dividual who give a negative tuberculin skin test. All cases should receive at least three drugs, followed by a maintenance phase of two drugs (30). First line drugs are isoniazid, pyrazinamide ,rifampicin, and ethambutol. Second line drugs are aminoglycosides (streptomycin, amikacin, and kanamycin), fluoroquinolones (ciprofloxacin, levofloxacin), cell wall inhibitors (cycloserine), other protein synthesis inhibitors (capreomycin), and antifolate (aminosalicylic acid), related to rifampin (ribabutin, rifapentine), and relatedto isoniazid(ethionamide) and oxazolidinone(linezolid). Instead of supplying the drugs to the patient for self-administration at home, the patient is called to the clinic and administered the drugs under supervision. This ensures that the drugs are actually consumed. Because of the difficulties in organizing such supervised treatment every day, intermittent ,twice-weekly regimes were tested and found effective. These are called directly observed therapies. DOTS are mandatory when drugs are prescribed less often than daily; when drugs are prescribed to be taken daily, or the regimen is on self-administration basis (31). Isoniazid, rifampicin, and streptomycin are given for 2 months and for next 4 months isoniazid and rifampicin. Isoniazid, rifamipicin, ethambutol or pyrazinamide are prescribed for 2 months and isoniazid and rifampicin for next4 months. Isoniazid, rifampicin, ethambutol are given for 2 months and for next 7 months isoniazid and rifampicin. Isoniazid isa drug that is prescribed in tuberculosis. Its taken orally. It is taken in combinationwith other drugs . Vitamin B6 deficiency has been observed as side effect of isoniazid. Isoniazid is effective in checking progress of primary complex or initial infection to fully-fledged pulmonary disease in most of the cases (32). Primary complex formation may reveal mild continuous temperature with constitutional symptoms in a group of children and others. It is necessary to exclude clinical disease before starting isoniazid alone as prophylactic drug; otherwise, isoniazid resistant bacilli may emerge. Persons receiving isoniazid to be told the possibility of hepatitis ,drug fever ,and rash as adverse effects and that drug

should be discontinued. Patients under treatment at home should be under direct observation to ensure regular intake of prescribed drugs (33).Rifampicin is used in tuberculosis (34). It is taken orally. Its trade name is Rifadin and Rimactane. Sensitivity reaction and digestive upset are usually seen by use of this drug. It inhibits the synthesis of RNA in the bacteria by inhibition of the enzyme known as DNA dependent RNA polymerase .It is bactericidal. Resistance to rifampicin mayoccur due to mutation in the gene of RNA polymerase of the mycobacteria. This will prevent the binding of rifampicin with the RNA polymerase of bacteria(35).Pyrazinamide kill and retard the growth of bacteria. This medication is prescribed in combination with other drugs. This drug is taken orally. This drug is available in tablet form in market. It is usually taken once a day. Chemically it is related to nicotinamide. It is bactericidal. Itis a cheap drug, which is given in combination therapy for tuberculosis. After oral administration ,it is well absorbed from the intestine, widely distributed into the tissues and the CSF when the meninges are inflamed. Resistance to the drug occurs by mutation in the gene responsible for the conversion of pyrazinamide to pyrizinoic acid. It can be used for the prophylaxis of tuberculosis along with ofloxacinor ciprofloxacin(36).Ethambutol is effective against mycobacterium tuberculosis and other mycobacteria. It inhibits the synthesis of arabinoglycan by inhibiting the enzyme arabinosyl transferase in the cell wall of bacteria. Arabinoglycan is an essential part of mycobacterial cell wall. Prevention of arabinoglycan formation will cause weakness of the bacterial cell wall, causing easy passage of certain lipid soluble anti-mycobacterial drugs into the bacteria. Ethambutol is prescribed in combination with other drugs. It is given orally. Visual disturbance is side effect of this drug. Other side effects include digestive upsets and allergic rashes. Resistance to ethambutol occurs by increased formation of ara binosyl transferase due to mutation of its gene. This causes increased expression of the gene responsible for the production ofara binosyl transferase (37). Ciprofloxacin is a broad-spectrum antibiotic that is used orally and is effective in tuberculosis. Nausea, vomiting, abdominal pain, andheadache are common side effects of this drug. It is available in market as ciloxan and ciproxin (38). Active immunization provides resistance in the body against specific disease by initiating antibodies formation in the body by antigenic stimulation(active immunization).BCG gives protection againstall types of tuberculosis for 15 years.

Mechanisms of drug resistance in M. tuberculosis

Understanding the method of drug resistance to anti-TB drugs not merely assists to put procedures into practice to restrict the extent of such resistance but also enables us to recognize genes linked with drug resistance (39). Most chromosomal mutations in the genome of M. tuberculosis that present resistance to anti-TB drugs happened unexpectedly (40). Johnson et al (2006) reported that speed of spontaneous mutation for RMP and INH is 3.1×10-8 and 3.4×10-6, respectively. The magnification of the above-discussed genetical terations causes drug- resistant Tb (41).

MEDICINAL PLANTS USED IN TUBERCULOSIS

Juniperusexcelsa

Juniperusexcelsa belongs to family Cupressaceae. Parts used are berries. It contains limonene, sandra copimaric acids, isocommunic, sesquiterpene 4-hydroxycedrol and pimiric acid (42). It is used in tuberculosis, diabetes. It is anti-oxidant, antimicrobial, antihypertensive

,antifungal and antileishmanial (43). Methanol and hexane extracts of *Juniperus excelsa* were found effective against mycobacterium tuberculosis (44).

***Lawsoniainermis* Linn**

Lawsoniainermis Linn belongs to family Lythraceae. Parts used are leaves, b a r k , flowers, seeds and oil. It contains lawsone, α-ionone gallicacid and hennotannic acid. It is used in abscess formation, tuberculosis and liver disorders (45).It is refrigerant , detergent, resolvent, blood purifier, astringent, sedative, alterative, and anti-inflammatory(46).Tuberculo static activity of *Lawsonia inermis* has been observed. Thisstudy was done *in vivo* and *in vitro*. There was significant inhibition of tubercle bacillifrom sputum at 6 microgram/ml of the extract. *In vivo* studies were conducted in mice and guinea pig. The herb showed significant effect at dose of 5mg/kg body weight. There was significant resolution of experimental tuberculosis following infection with *Mycobacterium tuberculosis* H37Rv(47).

Abrusprecatorius

Abrus precatorius belongs to family Fabaceae .Parts used are seeds, roots, pods, leaves and juice. It contains squalene, glycyrrizin, precabrin, hypaphorine, gallic acid, cholanic acid, abrusicacid, abrine. Abrin and abrinaline, trigonelline (48). It is used in insomnia, malaria, abdominal pain, urinary tract infections, jaundice, carcinoma ,venereal diseases, sore throat, arthritis, chestpain, diarrhea, gonorrhea, pleurisy, skin diseases ,itching ,tuberculosis ,asthma, inflammation ,wounds, stomatitis, headache, spermatorrhea ,generalpain ,hoarseness, aphthae of mouth and syphilis (48-49). It is aphrodisiac, expectorant ,diaphoretic and anthelmintic ,anti-inflammatory and demulcent. Limmat et al. (2004) reported the antitubercular constituents of *Abrusprecatorius.* Two compounds were isolated from this plant. Compounds are abruquinone Bandabruquinone G.Spectral analysis was done to elucidate the chemical structure of these compounds .Abruquinone Bhasanti tubercular activity(50).

Pandanustectorius

Pandanustectorius belongs to family Pandanaceae. Part used is fruit. It contains phytosterol sand triterpenes ,betasitosterol, stigmasterol, phenolics, flavonoids, neolignan ,lignans, coumarins, furanocoumarin and pandanusin A (51). It is used in leprosy, tuberculosis, small pox and leucoderma. Its antihypertensive and anti-tuberculosis. Tanetal.(2008) reported the anti-tubercular triterpenes and phytosterols from *Pandanustectorius*(52).

Alliumsativum

Allium sativum belongs to family Amaryllidaceae; Parts used are bulb, juice and seeds. It contains phytoncides, vitamins, allicin, flavonoids, essential oil, allyl prolyl disulfide, quercetin, cordine andfatty oil (53). It is used in asthma, pleuricy,bronchitis, TB, common cold, sore throat, pneumonia, cough, whooping cough, scabies, eczema, teeth problems, baldness, ticks, nipple looseness, headache, earache, diphtheria, hysteria, cholera, worms, fever, malaria, paralysis, bones, hypertension, impotency ,jaundice, cancer, peptic ulcer, tonsillitis, leucoderma and prostate cancer. It is appetizer, anti-fungal and anti-bacterial. Inhibition of mycobacteria by *Allium sativum* has been reported. In one study, various concentrations of *Allium sativum* were used to investigate its efficacy against *Mycobacterium tuberculosis.* Plant extract was able to inhibit 30 strains of mycobacteria. Concentration of drug was 1.34mg/ml to a high of3.35mg/ml of media.

Inulahelenium

Inulahelenium belongs to family Asteraceae, Parts used are leaves. It

contains iso-alantolactone, eudesmanolides and all oalantolactone.It is used in skin diseases and tuberculosis. It is antibacterial, antitumor, anti-tuberculosis and antistaphylococus .Antimycobacterial eudesmanolides from *Inula helenium* has been reported. A study was conducted to investigate anti mycobacterial compounds from *Inulahelenium*. Significant activity was observed against mycobacterium tuberculosis by use of chromatographic fractions of root extracts of thisplan.

Erythrina abyssinica

Erythrinaabyssinica belongs to the family Fabaceae. Part used is root bark. This plant contains alkaloids, flavones, triacontyl 4-hydroxycinnamate, octacosylferulate ,licoagrochalcone Aerycristagallin and tannins. It is anti-plasmodial, anti-HIV and anti-emetic. Root bark extract was investigated for its efficacy in rifampicin-resistant TB [54].

ADJUNCTIVE TREATMENT

Pyridoxine (VitaminB6)

The use of Pyridoxine is suggested for all adult patients initiated on TB therapy tostop peripheral neuropathy most usually caused by Isoniazid.

Multi-drug resistance (MDR-TB)

MDR-TB is TB resistant to at least rifampicin and isoniazid (and probably other medicines). Physician expert in treating tuberculosis should merely manage DR- TB. Pyrazinamide and/or ethambutol is firstline medicine while injectable medicines (amikacin, moxifloxacin,fluoroquinolone) are second line therapy. Aregimen should comprise of at least three (if possible five) medicines to which the bacteria is recognized to be vulnerable. Regardless of laboratory resistance, isoniazid may be placed in them an aging regimen and is suggested in the majority of patients where isoniazid resistance is reported to be at a small concentrationonl.

Primary resistance in tuberculosis

Primary resistance in tuberculosis refers to people infected with mycobacterium tuberculosis that is resistant to anti-TB medicines from the outset, before the anti-TB therapy. Transmission of drug resistant bacilli causes primary resistance that develops the drug-resistant tuberculosis between people who are primarily affected with drug-resistant strains.

Follow-up

During chemotherapy, the patient should be followed up regularly with the following investigations.

- ESR and hemoglobin percentage
- Diagnostic curettage after 6 months and then Yearly for five years
- Advice of a physician should be sought if there is an active pulmonary lesion or a next ra genital tract lesion.

Health education

Community health education is effective for the prevention and management of tuberculosis (Fig 1). Tuberculosis is not a dangerous ailment now, provided it is managed timely for the full-prescribed duration. This will likewise help in getting early case and to get co-operation of the general population.

Control of MDR-TB

Infection control is a major factor to stop propagation of MDR-TB. Key interventions are personal respiratory protection, environmental and administrative measures. The most important is the good administrative control in infection control of MDR-TB. Personal respiratory protection and environmental control measures will be taken in the presence of administrative control measures. These procedures must be adopted in all health services concerned in MDR-TB care. Successful management, control and prevention of appearance and propagation of drug-resistant TB at the

society level are needed to decrease the rising tendency in MDR-TB. Administrative control should not be replaced with environmental control measures; though, they are planned to decrease the quantity of infectious droplet nuclei in the air. These measures are controlling the airflow direction and maximizing natural ventilation. The use of fans to control the airflow direction and opening windows to enhance natural ventilation is fundamental to decrease infection in resource-limited locations. Common people and health care providers can be protected from being infected by personal respiratory protection. Now guidelines for drug resistant TB arewell understood and should be implemented. Obviously a directly observed treatment, short-course (DOTS) plan for affected persons is the most excellentweapon against MDR-TB and it includes political obligation with enhanced and constant financial plan, a uniform management regimen directly observed by a health care provider, a successful medicine supply and treatment system, case recognition through quality guaranted laboratories, and an evaluation and monitoring system with tuberculosis infection control impact measures. The policy also comprise saction stotackle TB infection control support and to hold operational research. The DOTS-plus, increased DOTS program has been introduced for treating MDR-TB in developing countries and this plan advocate further investment in services for culture and drug susceptibility testing for the recognition of drug-resistant TB and provision of suitable second-line drugs(55).

CONCLUSION

This review revealed that MDR-TB worldwide is a severe public health dilemma that wants to be addressed immediately. Numerous data showed that earlier contact of anti-TB therapy enhanced the hazard of MDR-TB worldwide. Therefore, strengthening timely case finding and appropriate management of drugsusceptible TB in light of WHO treatment guidelines to make sure proper management success rates is necessary. This will restrict the appearance of M/XDR- TB and stop the spread of the tuberculosis. As a result ,a quick build-up of MDR-TBidentification and management sites for the accomplishment of the DOTS-plus plan is vital to stop spread of this fatal infection in the country. Public should be given education through media about the spread of tuberculosis for early treatment and that disease is curable. Advice should be given to avoid factors like overcrowding, sneezing and coughing in open. Early finding of tuberculosis (TB) and starting better management would not merely allow a treatment of a patient but will also restrain the infection transmission and illness to others in the community. Early timely interventions can be cost effective in tuberculosis.

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Fig. 1: Prevention and control of tuberculosis