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Review Article

Towards controlling the HIV and tuberculosis co-epidemic

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ABSTRACT

The coinfection of Tuberculosis and HIV are discussed and the Impact of HIV Infection on the Pathogenesis of Tuberculosis, on the Clinical Course of Tuberculosis, on Tuberculosis Control Programme Treatment of HIV-Related Tuberculosis is reviewed. Tuberculosis remains one of the serious diseases that affect the health as well as the economy of the country. HIV infection has contributed to a significant increase in the worldwide incidence of tuberculosis.

HIV positive patients with tuberculosis respond well to antituberculosis therapy, as long as the regimen contains isoniazid and rifampicin. The treatment of HIV-related tuberculosis requires proper monitoring because of possible drug-drug interactions, frequent drug toxicities, and paradoxical reactions. For HIV-infected persons with CD4 counts less than 100 cells/mm3, daily therapy is prescribed during the initial phase (first 2 months), followed by either daily therapy or thrice a week doses during the continuation phase. Drug-induced hepatotoxicity is common in HIV-infected patients.

The TB epidemic has been a challenge to control due to its coexistence with the HIV epidemic. It creates enormous problems that need to be overcome with great precision. In order to mount a more meaningful response to the co-epidemic, close collaboration needs to develop between the TB and HIV control programmes. The Three I's [ICF (Intensified case finding for TB), IPT (Isoniazid preventive therapy) and IC(Infection control)] must be viewed as an integral component of prevention, care and treatment services and an essential part of universal access, as indispensable as patient monitoring, antiretroviral is or co-trimoxazole.

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INTRODUCTION

HIV/AIDS and tuberculosis (TB) are commonly called the "deadly duo" and are closely linked since the emergence of AIDS and constitute the main burden of infectious disease in resource limited countries (HIV TB Coinfection et al., 2007). HIV coinfection is the most powerful known risk factor for progression of M. tuberculosis infection to active disease, increasing the risk of latent TB reactivation 20 fold (Getahun et al., 2010).

Mycobacterium tuberculosis–HIV coinfections pose particular diagnostic and therapeutic challenges and exert immense pressure on health care systems in African and Asian countries with large populations of co infected individuals. HIV infection has contributed to a significant increase in the worldwide incidence of Tuberculosis (AIDSCAP 1996; Raviglione et al., 1992). By producing a progressive decline in cell-mediated immunity, HIV alters the pathogenesis of tuberculosis, greatly increasing the risk of developing the disease in co-infected individuals and leading to more frequent extra-pulmonary involvement and a typical radiographic manifestation. Although HIV-related tuberculosis is both treatable and preventable, incidence rates continue to ascend in developing nations. In the individual host the two pathogens, M.

tuberculosis, and HIV potentiate one another, accelerating the deterioration of immunological functions and resulting in premature death if untreated.

HIV promotes both the progression of latent TB infection to active disease and relapse of disease in previously treated patients. The two diseases represent a lethal combination since they are more destructive together than either disease alone because of the following reasons: 1) Tuberculosis is harder to diagnose in people who are HIV positive. 2) Tuberculosis progresses faster in people who are HIV positive. 3) Tuberculosis in HIV positive is fatal if undiagnosed or left untreated. 4) Tuberculosis occurs early in HIV positive. The hallmark of HIV infection is a progressive depletion and dysfunction of CD4+ T lymphocytes, coupled with defects in macrophage and monocyte function. Because CD4+ T lymphocytes and macrophages have a central role in anti-mycobacterial defenses, dysfunction of these cells places patients with HIV infection at high risk for primary or reactivation TB disease. Various lines of evidence indicate that inborn errors of immunity, as well as genetic polymorphisms, have an impact on susceptibility to TB and HIV (Moller et al., 2010). Estimates by the World Health Organisation (WHO) indicate that there are more than 9 million new active cases of TB and nearly 2 million deaths per year (World Health Organization, 2010), and that 2.6 million new cases of HIV infection and 1.8 million AIDS related deaths occur per year (UNAIDS, 2010). Some 14 million individuals worldwide are estimated to be dually infected (Getahun et al., 2010). TB is the largest single cause of death in the setting of AIDS (Small PM. Tuberculosis research, 1996) accounting for about 26% of AIDS related deaths (Raviglione et al., 1995), 99% of which occur in developing countries (Dye et al., 1999).

Impact of HIV infection on the pathogenesis of tuberculosis

Tuberculosis can develop through the progression of the newly acquired disease, reactivation of dormant infection, or exogenous re-infection. According to a report of a genotypic study, about 30-40% of new cases were due to recent infection with rapid progression to disease. HIV infection or AIDS was an independent risk factor for recent possession of infection and rapid progression to disease. Infection with M tuberculosis can occur when an individual exposed to an infectious environment (Edwards et al., 1996). These tubercle bacilli reach the pulmonary alveoli; they may be ingested by alveolar macrophages. Survived tubercle bacilli multiply within the macrophage and ultimately spread to other areas of the body. Although macrophage function is defective in HIV-infected patients, it is not evident that HIV-positive persons are more likely prone to tubercular infection than the HIV-negative person (Meltzer et al., 1990). Once a person gets the infection, the risk of rapid development is much greater between HIV infected persons, due to impaired host ability to contain the new tubercular infection in HIV infected individuals.

Immune defected individuals having M tuberculosis infection showed approximately a 10% lifetime risk of development of tuberculosis. Several studies demonstrated active tuberculosis among HIV-infected individuals showed positive tuberculin skin test. Though, the rate of active tuberculosis varied significantly depending on the population and region. Infection with M tuberculosis in an immune compromised individual is thought to present significant protective immunity against exogenous re-infection (Hopewell et al., 2000). However, re-infection has been reported in both HIV-negative (Nardell et al., 1986; Shafer et al., 1995) and positive individuals (Small et al., 1993; Horn et al., 1994; Hawkens et al., 1993; Osset et al., 1995). Tuberculosis can occur early in the course of HIV infection due to increased virulence in immunocompetent individuals with M tuberculosis as compared to infections with other opportunistic pathogens (eg, Pneumocystis jiroveci). Several studies reported the median CD4 T-cell count was >300 cells/mm3 in a HIV-infected person possessing pulmonary tuberculosis (De Cock et al., 1992). On the other hand, patients with primarily extra-pulmonary infection or disseminated disease, the CD4 T-cell count may be much lower. Although tuberculosis can be a relatively early manifestation of HIV infection, it is important to note that the risk of developing tuberculosis, and of disseminated infection, increases as the CD4 T-cell count decreases. Immunocompetent individuals infected with M. Tuberculosis have approximately a 10% lifetime risk of developing TB. Infection with M. Tuberculosis in an immunocompetent person is thought to confer significant protective immunity against exogenous reinfection (Hopewell et al., 2000).

Impact of HIV on the clinical course of tuberculosis

The clinical presentation of pulmonary tuberculosis may differ extensively in both immunocompetent and immunocompromised hosts. Generally, the clinical presentation is similar in both type of patients (HIV-infected patient and HIV-uninfected patients), but the signs and symptoms (such as fevers, weight loss, and malaise) may be due to HIV itself and causes the possibility of tuberculosis ignored. Symptoms are usually present for weeks to months, and the acute onset of fever and cough is more suggestive of a non-

mycobacterial pulmonary process. If there is no response to antimicrobial therapy, however, the possibility of tuberculosis should be considered. In HIV-infected patients, clinical manifestations of pulmonary tuberculosis reflect different levels of immunosuppression. Earlier in the course of HIV disease, tuberculosis is more likely to present as the classical reactivation-type disease, whereas patients with advanced immunosuppression are more likely to present with findings consistent with primary tuberculosis.

The occurrence of extra-pulmonary tuberculosis is increased in HIV-infected individuals. Low CD4 T-cell counts are associated with an increased rate of occurrence of extra-pulmonary tuberculosis, positive mycobacterial blood cultures, and atypical chest radiographic findings, reflecting a failure of the impaired immune response to control infection. The sign and symptoms in patients with extrapulmonary tuberculosis may be specific to the involved site, such as lymphadenopathy, headache, meningismus, pyuria, abscess formation, back pain, or (Jones et al., 1993) abdominal pain. These findings in HIV-infected patients can present a diagnostic challenge. Whenever possible, diagnostic specimens should be examined for acid-fast bacilli (AFB) and cultured for mycobacteria.

Impact of HIV on tuberculosis control programme (Hargreaves et al., 2003; Joshi et al., 2004)

When occurrence of HIV/TB is common in the large population, health providing services may face various problems to cope the large and rising numbers of patients having tuberculosis with following possible consequences-(i) under-diagnosis of sputum smear-positive pulmonary tuberculosis (ii) over-diagnosis of sputum smear-negative pulmonary tuberculosis (iii) high mortality rate during treatment (iv) inadequate supervision during tuberculosis treatment (v) high rate of tuberculosis recurrence. In order to control the lethal combination of HIV -Tuberculosis, it is therefore essential that the HIV and TB control program should work closely together.

Diagnostic tools for TB

The chest radiography is the basis of diagnosis for pulmonary tuberculosis. The typical findings in reactivation tuberculosis may include upper lobe infiltrations and cavities, whereas intrathoracic lymphadenopathy and lower lobe disease are seen in primary tuberculosis. In HIV-infected persons with higher CD4 T-cell counts (e.g., >200 cells/mm3) the radiographic pattern tends to be one of reactivation disease with upper lobe infiltrates with or without cavities (Post et al., 1995). In HIV-infected persons who have a greater degree of immunosuppression (e.g, CD4 T-cell count <200 cells/mm3), a pattern of primary disease with intra-thoracic lymphadenopathy and lower lobe infiltration may be seen. A high index of suspicion must be maintained in evaluating an HIV-infected patient with symptoms suggestive of tuberculosis, even after chest radiographs may appear normal (Greenberg et al., 1994; Long et al., 1991). The finding of low-density lymph nodes with peripheral enhancement on a contrast-enhanced chest computed tomography scan is highly predictive of tuberculosis. For instance, immunocompromised patients are likely to have cavitary lung disease than HIV-uninfected TB patients, and up to a fifth of HIV patients coinfected with pulmonary TB with culture positive disease have normal chest radiographic findings (Perlman et al., 1997; Pepper et al., 2008).

Patients having the suspicion of pulmonary tuberculosis should have 3 sputum specimens obtained on 3 consecutive days, and these specimens should be examined for Acid Fast Bacilli and cultured for Mycobacterium. Positive smear for Acid Fast Bacilli does not confirm the diagnosis of tuberculosis because the acid-fast stain detects mycobacteria other than *M tuberculosis*, which may include *M. avium* intracellular complex or *M kansasii*. If the sputum smear is positive for Acid Fast Bacilli, empiric therapy for tuberculosis should be initiated until identification is established. The rate of Acid Fast Bacilli smear positivity has varied from 31% to 89% in HIV-positive patients (Gary et al., 1996). Generally, the rate of smear positivity correlates with the extent of radiographic disease. For example, patients with cavitary lesions due to active tuberculosis will almost always have positive smears, whereas minimal disease on chest radiograph showed a negative smear. However, positive smears may be seen with relatively little radiographic involvement in HIV-infected patients. When sputum specimens are Acid Fast Bacilli smear-negative, further evaluation (e.g. bronchoscopy with broncho alveolar lavage and transbronchial biopsy) may be required. In this evaluation, a rapid diagnosis of tuberculosis is done by histology and Acid Fast Bacilli smear test on specimens obtained by bronchoscopy (Kennedy et al 1992).

Positive cultures for M tuberculosis confirm the diagnosis of tuberculosis. According to a report, around 85% of tuberculosis cases are culture positive. Culture study requires rapid diagnostic techniques because culture results may not be available for 2-6 weeks. These rapid diagnostic techniques may include nucleic acid amplification tests which detect unique nucleic acid sequences in the M tuberculosis complex. The U.S. Food and Drug Administration have approved nucleic

acid amplification tests, the Amplified *Mycobacterium tuberculosis* Direct Test and the Amplicor *Mycobacterium tuberculosis* Test for the diagnosis purpose to a newly untreated patient. The Amplified *Mycobacterium tuberculosis* Direct Test is used to diagnose both type of samples (smear-positive or smear-negative samples), while Amplicor *Mycobacterium tuberculosis* Test is used for smear-positive samples. A negative result from nucleic acid amplification tests does not discard the presence of active tuberculosis and required antitubercular therapy. The analytical value of nucleic acid amplification testing will vary depending on the sensitivity and specificity of the test in the laboratory, as well as on the dominance of M. tuberculosis and other mycobacteria.

Treatment of HIV-related tuberculosis

HIV-positive patients with tuberculosis respond well to antituberculosis therapy. Direct observation of treatment is very important for HIV-infected TB patients. The treatment of HIV-related tuberculosis requires close monitoring because of frequent drug toxicities, possible drug-drug interactions, and paradoxical reactions. Hence, the DOTS strategy that promotes adherence to therapy should be used for all patients with HIV-tuberculosis. The majority of the patients with HIV infection respond well to DOTS. For the treatment of EPTB patients having HIV infection, category I is to be used under the DOTS strategy. All HIV co-infected TB patients should receive a Rifampicin containing regimen.

The relapse rate of tuberculosis is low in HIV-infected tuberculosis patients who complete a full course of the non-Rifampicin-containing short-course treatment regimen. The use of none- Rifampicin containing regimens and treatment interruptions due to drug reactions and intercurrent opportunistic infections, are associated with an increased risk of relapse of tuberculosis. The relapse rates tend to be higher if they are treated with conventional regimens or a short-term treatment regimen which uses Isoniazid and Ethambutol during the continuation phase, or if the treatment has not been directly observed. DOTS strategy can prevent the emergence of multidrug-resistant tuberculosis and also will reverse the trend of MDR-TB. The 2010 meta-analysis examined the efficacy of daily versus thrice weekly dosing of TB medications and found that in a pooled analysis daily dosing during the continuation phase of TB treatment was associated with improved TB outcomes (Khan et al., 2010). The WHO currently recommends daily administration of TB treatment at least for the intensive phase of therapy in persons with HIV coinfection (WHO Rapid Advice 2010).

Antiretroviral therapy (ART) (National AIDS control organization et al., 2004)

Three first line drugs are being used (Stavudine, Lamivudine, Nevirapine). Treatment of tuberculosis patients coinfected with HIV cannot be envisaged without Rifampicin. In HIV-TB co-infection, treatment should be first administered for tuberculosis under the DOTS strategy and ART should be started after the completion of the tuberculosis treatment. In patients with very low CD4 counts requiring concomitant administration of ART and antituberculosis treatment, the ART regimen should be modified by replacing Nevirapine with Efavirenz. On completion of tuberculosis, such patients can be switched back to nevirapine.

Nevirapine shows interaction with Rifampicin. To avoid the problem of drug interaction between Rifampicin and Nevirapine, Rifampicin can be started after DOTS is completed. In the later stage of immunosuppression, co-administration of ARV drugs and antitubercular drugs may be required with some modification in the ARV regimen.

Isoniazid preventive therapy

Isoniazid preventive therapy for HIV/TB co-infection may play a crucial role in limiting a possible increase in the number of symptomatic tuberculosis (Selwyn et al., 1989; Halsey et al., 1998) this approach is supported by the knowledge that tuberculosis in the HIV infected is predominantly caused by endogenous reactivation of dormant foci, that it can happen with a higher frequency than in the general population, and that the disease can, therefore, be prevented by chemotherapy (Narain et al., 2002)

Prevention challenges

Successfully treating HIV/TB treatment is complicated. There are drug-to-drug interactions between the complex drugs regimens required to treat both diseases, and paradoxically, people with HIV/AIDS can develop something called Immune Reconstitution Inflammatory Syndrome (IRIS), an over-reaction of the immune system that inflames TB. Studies are underway to determine the best antiretroviral drugs to administer, how to manage IRIS and the optimal duration of TB treatment in HIV patients. These studies are critically important because successful TB treatment can prolong the lives of people with HIV by at least two years and probably longer if they get started on AIDS medicines. The emergence of drug resistant TB in countries with a high HIV prevalence poses an additional public health threat, not only to people with

HIV but also to the broader community. However, people with HIV are at a much greater risk of mortality from multidrug resistant (MDR)-TB and recent case series, reporting on extensively drug resistant (XDR)-TB in people living with HIV in Africa, suggest a greater than 95% mortality rate. Urgent action is thus required to prevent, diagnose and treat TB in people living in these countries.

Drug-resistant tuberculosis

Paralleling the increase in tuberculosis cases in the United States was an increase in the number of cases of drug-resistant tuberculosis. HIV infection was shown to be a risk factor for having drug-resistant tuberculosis, independent of geographic location, history of prior therapy, age, or race. Recent studies have found that HIV-seropositive patients are more likely to develop acquired drug resistance (ADR) than seronegative cases (Nolan et al., 1995; Bishai et al., 1996; Bradford et al., 1996; Luftey et al., 1996). In a case-control study involving 16 cases of ADR in San Francisco between 1990 and 1994, AIDS, nonadherence to the tuberculosis treatment regimen, and gastrointestinal symptoms were each independently associated with the acquisition of drug resistance. During the study period one of every 16 AIDS patients with tuberculosis, and either gastrointestinal symptoms or nonadherence developed ADR. Of note, most of the patients developed mono rifampin resistant tuberculosis, which is an unusual form of ADR. It is not clear why acquired mono rifampin- resistant tuberculosis would be more likely to arise in HIV-1 seropositive persons, although malabsorption of antituberculosis drugs has been postulated as a causative factor.

Drug-drug interactions

Successful therapy for tuberculosis requires that HIV infected individuals take anti-tuberculosis drugs for a minimum of 6 months, in addition to potentially large numbers of other medications. Certain antituberculosis drugs may interact adversely with medications commonly used by HIV-infected individuals. Understanding these drug-drug interactions can prevent drug toxicity and possible treatment failures. Combination ART is commonly used for the treatment of HIV infection. These agents are divided into nucleoside reverse transcriptase inhibitors (NRTIs), NNRTIs, and PIs. The rifamycin derivatives accelerate the metabolism of the PIs and NNRTIs resulting in subtherapeutic levels and the potential development of viral resistance to these important agents (CDCP update. 1996). Of the available rifamycins, rifampin is the most potent inducer of the P450 enzymes and thus produces significant reductions in the serum concentrations of the PIs and NNRTIs. Rifabutin, which is a less potent inducer of the P450 enzymes, can be substituted for rifampin in the treatment regimen. However, because the PIs and NNRTIs affect the metabolism of rifabutin, resulting in altered serum levels and the possibility of drug toxicity, adjustments in rifabutin dosage are often necessary.

Paradoxical reaction

On 2–4 April 2008 the WHO HTM/HIV/AIDS and HTM/TB Departments, in collaboration with other key partners, convened a meeting of international stakeholders to develop recommendations for WHO and guidance for national programs and their partners for implementation of the Three I′s for people living with HIV. The meeting was an important step on the path towards improved services for people living with HIV and there was the clear consensus on several key conclusions and concrete actions (WHO Three I′s Meeting, 2008).

The Three I′s to reduce the burden of TB disease among people living with HIV. There are three activities, known as the "Three I′s," that those providing care to people with HIV should do to protect them from TB infection, help prevent active disease from developing, and to identify active TB disease early and improve the chances of cure: some patients may experience a temporary exacerbation of symptoms, signs, or radiographic manifestations of tuberculosis after beginning antituberculosis treatment. This worsening has been referred to as a "paradoxical reaction" and has been noted to occur in HIV-infected patients with active tuberculosis. These reactions often develop after immune reconstitution has occurred in the setting of simultaneous administration of both antiretroviral and antituberculosis medications. Symptomatic therapy is sufficient for patients with a paradoxical reaction in whom the symptoms are not severe or life threatening.

Initiation of antiretroviral therapy in the coinfected patient

It is not unusual for the diagnosis of tuberculosis and HIV to be made simultaneously. In this setting, treatment of tuberculosis should be initiated immediately. When to initiate ART is a more difficult decision. Some experts argue that delaying treatment of HIV infection for 2 months, observing for any adverse effects from the tuberculosis medicines, and potentially decreasing the risk of a paradoxical reaction is a reasonable approach. On the other hand, effective ART can have a significant impact on HIV-related morbidity and mortality.

In patients already receiving ART, the regimen should be continued, and modifications to either the tuberculosis regimen or to the antiretroviral regimen can be made as indicated. Whether it is best to start ART as soon as possible or wait until antituberculosis treatment is well established is not clear at present, so the decision should be made on a case-by-case basis, taking into account factors related to both adherence (such as motivation and stability of living situation) and potential for complications (such as clinically active hepatitis C). Involvement of the patient in the decision of when to start ART is very crucial.

It is important to be aware of the potential problems that can occur when antituberculosis medications and antiretroviral agents are administered concurrently. Gastrointestinal complaints and rash are not uncommon with antituberculosis medications and these can be quite common with certain antiretroviral medications. A flu-like illness has been described with rifampin, which could be confused with an abacavir hypersensitivity reaction. Peripheral neuropathy is an adverse effect of INH as well as stavudine and didanosine. Elevated liver function tests can occur with INH, rifampin, pyrazinamide, and most of the NRTIs, NNRTIs, and PIs. In HIV infected persons with TB, ART should be initiated (or continued) during TB treatment regardless of the CD4 cell count. The SAPIT trial, conducted in patients with CD4 counts of ≤500 cells/μL, demonstrated a relative reduction in mortality of 56% for those who started ART during the 6 months of TB treatment compared with those who initiated ART after completion of TB therapy. The reduction in mortality was seen in patients with CD4 counts of ≤200 cells/μL as well as in those with CD4 counts of >200 cells/μL (Abdool Karim et al., 2010). The timing of ART initiation in relation to TB treatment start has been clarified further by the SAPIT (Starting ART at 3 Points in TB), CAMELIA (Cambodian Early versus Late Introduction of Antiretrovirals), and ACTG 5221 STRIDE studies (Blanc et al., 2011).

TB and HIV collaboration and integration: Opportunities and Challenges

• ICF: Intensified Case Finding for TB means regularly screening all people with or at high risk of HIV or in congregate settings (such as mines, prisons, military barracks) for the symptoms and signs of TB, followed promptly with diagnosis and treatment and then doing the same for household contacts. Simple questionnaires to screen for TB can be performed when people first seek HIV services (e.g., care, voluntary counseling, and testing, etc.) and/or by community-based organizations supporting people with HIV. ICF serves as the important gatekeeper for the two other I′s (infection control and isoniazid preventive therapy), facilitating rapid identification of TB suspects (allowing for triage and other steps to reduce TB transmission), and acting as the necessary first step for healthcare providers to confidently prescribe IPT to people living with HIV who do not have active TB.

• IPT: Isoniazid Preventive Therapy for TB can safely be given to people living with HIV without TB disease, reducing the risk of developing TB by 33–67% for up to 48 months. It is currently recommended for all people living with HIV in areas with a prevalence of latent TB infection >30%, and for all people living with HIV with documented latent TB infection or exposure to an infectious TB case, regardless of where they live. More recently, evidence has shown that the combined use of isoniazid preventive therapy and antiretroviral therapy among people living with HIV significantly reduces the incidence of TB; and the use of IPT in patients who have successfully completed a course of TB therapy has been shown to markedly reduce the risk of subsequent TB cases.

• IC: TB Infection Control measures are essential to prevent the spread of M. tuberculosis to vulnerable patients, health care workers, the community and those living in congregate settings. Fundamentally, TB infection control is about the safety of people receiving or offering HIV care should not have to worry about being exposed to and infected with M. tuberculosis in the process. In light of the crisis of drug resistant TB in countries with a high burden of HIV, establishing facilities that are safe from TB has become an emergency situation for health services, prisons and other congregate settings, in general, but especially for HIV programs. Despite the considerable benefits, HIV programs have been slow to implement these TB-reducing services, resulting in missed opportunities to prevent many unnecessary cases of TB and related deaths. WHO recommends 12 collaborative HIV/TB activities; including 3I′s which should be seen as care prevention and treatment services for HIV infection. In addition to 3I′s for HIV/TB and other HIV prevention efforts, ART offers considerable hope for prevention of both HIV and TB, because the risk of developing TB approaches 10-20% per annum of immunocompromised persons.

CONCLUSION

Coinfections of *Mycobacterium tuberculosis*–HIV poses particular diagnostic and therapeutic challenges and emerges out as an immense pressure on health care systems in both African and Asian countries. It has been considered that tuberculosis can be a relatively early manifestation of HIV infection and is important to note

that the risk of developing tuberculosis, and of disseminated infection, increases as the CD4 T-cell count decreases. Both HIV and tuberculosis disease is more likely to present as classical reactivation-type disease. There are rapid diagnostic techniques which may include nucleic acid amplification tests which are used to detect unique nucleic acid sequences in the M tuberculosis complex. It has been found that co-administration of ARV drugs and antitubercular drugs may be required with some modification in the ARV regimen. At the later stage of immunosuppression. A crucial role may be played by Isoniazid preventive therapy for HIV/TB co-infection in limiting a possible increase in the number of symptomatic tuberculosis. Recent studies are underway and have found that HIV-seropositive patients are more likely to develop acquired drug resistance (ADR) than seronegative cases. Combination Anti Retroviral Therapy is commonly used for the treatment of HIV infection. A"paradoxical reaction" has been noted to occur in some patients experiencing a temporary exacerbation of symptoms, signs, or radiographic manifestations of tuberculosis after beginning antituberculosis treatment. Awareness of the potential problems that can occur when antituberculosis medications and antiretroviral agents are administered concurrently is very essential. It has been observed that the combined use of isoniazid preventive therapy and antiretroviral therapy. In the patient with HIV significantly reduces the incidence of TB.WHO has recommended 12 collaborative HIV/TB activities including 3I′s which can be seen as care, prevention, and treatment services for HIV infection.

The progress which has made towards controlling the dual HIV/TB epidemic is:

*Offering HIV testing and counseling to all TB patients,

*Providing Co-trimoxazole and Antiretroviral treatment (ART) to TB patients found to be infected with HIV.

*Screening people with HIV for TB disease and provision of TB preventive therapy once the active disease is ruled out. Appropriate TB treatment should be provided if the disease is diagnosed.

*Expediting the diagnosis and treatment of TB in people living with HIV by using revised diagnostic algorithm recommended by WHO in resource limited settings.

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