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Screening among Close Contacts of Tuberculosis Patients in ALMANAGIL Locality, Gezira State, Sudan (2017-2020)

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Abstract

The back ground of the study was the Contact screening, as a strategy to identify recently infected individuals, is part of the tuberculosis (TB) elimination strategy. It follows risk stratification concerning the infectiousness of the index patient and the susceptibility of the contact for early detection .

The Objectives is to study the effect of Screening among close contacts of tuberculosis patients at Almanagil Teaching Hospital.

The methodology of the study is intervention analyzing data of the effect of screening among close contacts of TB patients, carried out in the period from 2017 to 2020 at Almanagil Teaching Hospital TB unit , included household contacts of tuberculosis patients. The data was collected by questionnaire and analyzed by computer using SPSS.

The result of the study a total of 400 close contacts patients with tuberculosis were recruited, females were predominant 211 (52.80%), most 159 (39.8.0%) in age group 35 -49 years, 388 (97 %) were from rural area, near half of participants had primary school level 259 (64.8%), 136 (34.0%) had a preschool education, 4 (1.0%) had higher secondary school, while 1 (03%) was postgraduate , 308 (77%) patients had 3-4 persons per room .

145 (36.3%) were first degree relatives. All studied close contacts with tuberculosis were accepted to perform screening of TB, investigations and examination. CXR was significant in 267 (66.8%) studied close contacts, Acid Fast Bacilli (AFB) was positive in 224 (56.0%) studied close contacts. 324 (81.0%) studied close contacts confirmed the diagnosis of TB, while 76 (19.0%) not confirmed TB.

Keywords

Tuberculosis,
Almanagil Teaching Hospital,
CXR,
AFB

Regarding the conclusion, the screening among close contacts of tuberculosis patients is an essential intervention to identify and reduce the number of infected patients that will progress to active disease and screening are the keys for effective tuberculosis control. The screening of close contact of tuberculosis patients showed that 81.0% were confirmed had tuberculosis. More than half of close contact had significant CXR and positive (AFB).

Introduction

Tuberculosis (TB) is an infectious disease caused by a bacterial organism named *Mycobacterium tuberculosis* (MTB) was identified and described on 24 March 1882 by Robert Koch and received the Nobel prize for that discovery, which transmitted from person to person by inhalation of the bacilli in droplets coughed or sneezed out by someone with infectious tuberculosis. Tuberculosis infects one third of the world's population and hence at risk of developing active disease[1]. It still remains to be a major public health problem among the under developed world, because of poverty, HIV pandemic, movement of displaced people and emergency of multidrug-resistant strains[1,2].

Tuberculosis is a bacterial disease caused by *Mycobacterium tuberculosis* complex which includes most of the time *M. tuberculosis* and occasionally by *Mycobacterium bovis*, *M, africanum* and *M. canett*. These organisms are also known as tubercle bacilli or Acid-fast-bacilli. When examining sputum containing tubercle bacilli processed by Ziehl-Neelsen stain under the microscope, the bacilli stained red. This is because they retain the primary dye even after washing with acid alcohol due to the waxy component of their cell wall[3].

Tuberculosis is a major global health challenge; mostly patients are identified in high-burden countries when they visit health care facilities ('passive case finding'). Contacts of tuberculosis patients are a high-risk group for developing the disease. Actively screening contacts of people with confirmed tuberculosis may improve case detection rates and control of the disease[4].

The WHO recommends active case finding for close contacts of a person with TB disease as one of the strategies for early diagnosis for TB and curbing transmission[5]. Typically, symptom screening is used to identify presumptive TB, which requires further investigation, and then using laboratory-based mycobacterial identification or chest X-rays to confirm or rule out the diagnosis is standard in many countries[6].

Tuberculosis (TB) remains one of the leading causes of mortality and morbidity worldwide. The World Health Organization (WHO) estimates that approximately one-third of the world population is infected with Mycobacterium *tuberculosis* (MTB).

Current TB control strategies have limited success in identifying all infectious TB source cases and their contacts in the community, especially in developing countries. Contact investigation among TB patients is a systematic evaluation to identify active disease or latent MTB infection (LTBI) among contacts of known TB patients. While it is a priority in high-income countries, human and financial resource constraints in many high-burden countries make contact investigation a low priority in the national TB control strategy. WHO has recommended two especially high-priority groups, children aged under 5 years and people infected with human immunodeficiency virus (HIV), who are at highest risk of progression to TB disease following contact with a TB patient in a household setting. Household contact investigations are considered as an important approach among other active-case finding strategies to increase TB case-detection rates and to interrupt the transmission of disease[7].

The period of tuberculosis treatment is divided into two phases; *an intensive initial phase* for a period not less than two months where 3-4 drugs, including rifampicin, are used and a *continuation phase* for a period not less than four months where at least two drugs are used. The duration of treatment should be not less than six months, WHO provides technical support to the Federal Ministry of Health in the managements of multidrug –resistant TB cases and contact management.

WHO also advocates, and provides support to address, the problem of TB in conflict – affected and post-conflict area. Technical support is given to the national TB program through capacity-building to accelerate the implementation[7]. Health education for the patients and their relatives about tuberculosis resembles an important element for cure.

1.1.1. Problem of the study:

Sudan is a large country with a diverse population and various environments. Poverty levels are high with a gross national income per capita of less than two thousand dollars. The country has a high burden of tuberculosis (TB) with an estimated 50.000 incident cases during 2009, when the estimated prevalence was 209 cases per 100.000 of the population. Few studies have been undertaken on TB in Sudan[1].

Tuberculosis an old disease and a major public health problem in the world so far. In 1993 WHO declared tuberculosis to be an urgent global problem .And it's one of the 10 causes of death in the world.

Close contacts have a higher risk of developing tuberculosis than the general population.

No screening of the contact s of TB patient to detect new cases.

1.2. LITERATURE REVIEW

1.2.1. Definitions of tuberculosis (TB):

Tuberculosis (**TB**) is an infectious disease usually caused by *Mycobacterium tuberculosis* (MTB) bacteria.[8] Tuberculosis generally affects the lungs, but can also affect other parts of the body.[1] Most infections do not have symptoms, in which case it is known as latent tuberculosis.[8] About 10% of latent infections progress to active disease which, if left untreated, kills about half of those affected.[8]

1.2.2. Epidemiology:

Presently, one-quarter of the world's population is thought to be infected with TB.[9] New infections occur in about 1% of the population each year.[10] In 2017, there were more than 10 million cases of active TB which resulted in 1.6 million deaths.[11] This makes it the number one cause of death from an infectious disease.[11] More than 95% of deaths occurred in developing countries, and more than 50% in India, China, Indonesia, Pakistan, and the Philippines.[11] The number of new cases each year has decreased since 2000.[8] About 80% of people in many Asian and African countries test positive while 5–10% of people in the United States population test positive by the tuberculin test.[12] Tuberculosis has been present in humans since ancient times.[13]

Tuberculosis is the second-most common cause of death from infectious disease (after those due to HIV/AIDS).[14] The total number of tuberculosis cases has been decreasing since 2005, while new cases have decreased since 2002.[15] China has achieved particularly dramatic progress, with about an 80% reduction in its TB mortality rate between 1990 and 2010.[16] The number of new cases has declined by 17% between 2004 and 2014.[17] Tuberculosis is more common in developing countries; about 80% of the population in many Asian and African countries test positive in tuberculin tests, while only 5–10% of the US population test positive.[13] Hopes of totally controlling the disease have been dramatically dampened because of a number of

factors, including the difficulty of developing an effective vaccine, the expensive and time-consuming diagnostic process, the necessity of many months of treatment, the increase in HIV-associated tuberculosis, and the emergence of drug-resistant cases in the 1980s.[13]

In developed countries, tuberculosis is less common and is found mainly in urban areas. Rates per 100,000 people in different areas of the world were: globally 178, Africa 332, the Americas 36, Eastern Mediterranean 173, Europe 63, Southeast Asia 278, and Western Pacific 139 in 2010.[16] In Canada and Australia, tuberculosis is many times more common among the aboriginal peoples, especially in remote areas.[17,18] In the United States Native Americans have a fivefold greater mortality from TB, and racial and ethnic minorities accounted for 84% of all reported TB cases.[19,20]

The rate of TB varies with age. In Africa, it primarily affects adolescents and young adults.[21] However, in countries where incidence rates have declined dramatically (such as the United States), TB is mainly a disease of older people and the immunocompromised (risk factors are listed above).[12,22] Worldwide, 22 "high-burden" states or countries together experience 80% of cases as well as 83% of deaths.[23]

1.2.3. Signs and symptoms:

General signs and symptoms include fever, chills, night sweats, loss of appetite, weight loss, and fatigue.[14] Significant nail clubbing may also occur.[24]

The classic symptoms of active TB are a chronic cough with blood-containing sputum, fever, night sweats, and weight loss. It was historically called "**consumption**" due to the weight loss.[8,25] Infection of other organs can cause a wide range of symptoms.[14]

1.2.4. Classification of tuberculosis:

1.2.4.1. Pulmonary:

If a tuberculosis infection does become active, it most commonly involves the lungs (in about 90% of cases).[13,26] Symptoms may include chest pain and a prolonged cough producing sputum. About 25% of people may not have any symptoms (i.e. they remain "asymptomatic").[13] Occasionally, people may cough up blood in small amounts, and in very rare cases, the infection may erode into the pulmonary artery or a Rasmussen's aneurysm, resulting in massive bleeding.[14,27] Tuberculosis may become a chronic illness and cause extensive scarring in the upper lobes of the lungs. The upper lung lobes are more frequently affected by tuberculosis than the lower ones.[14] The reason for this difference is not clear.[13] It may be due to either better air flow,[12] or poor lymph drainage within the upper lungs.[14]

1.2.4.2. Extrapulmonary:

In 15–20% of active cases, the infection spreads outside the lungs, causing other kinds of TB.[28]These are collectively denoted as "extrapulmonary tuberculosis".[29] Extrapulmonary TB occurs more commonly in people with a weakened immune system and young children. In those with HIV, this occurs in more than 50% of cases.[29] Notable extrapulmonary infection sites include the pleura (in tuberculous pleurisy), the central nervous system (in tuberculous meningitis), the lymphatic system (in scrofula of the neck), the genitourinary system (in urogenital tuberculosis), and the bones and joints (in Pott disease of the spine), among others. A potentially more serious, widespread form of TB is called "disseminated tuberculosis", also known as miliary tuberculosis.[14] Miliary TB currently makes up about 10% of extrapulmonary cases.[30]

1.2.5. Causes:

1.2.5.1. *Mycobacteria:*

The main cause of TB is *Mycobacterium tuberculosis* (MTB), a small, aerobic, nonmotile bacillus.[14] The high lipid content of this pathogen accounts for many of its unique clinical characteristics.[31] It divides every 16 to 20 hours, which is an extremely slow rate compared with other bacteria, which usually divide in less than

an hour.[32] *Mycobacteria* have an outer membrane lipid bilayer.[33] If a Gram stain is performed, MTB either stains very weakly "Gram-positive" or does not retain dye as a result of the high lipid and mycolic acid content of its cell wall.[34] MTB can withstand weak disinfectants and survive in a dry state for weeks. In nature, the bacterium can grow only within the cells of a host organism, but *M. tuberculosis* can be cultured in the laboratory.[35]

Using histological stains on expectorated samples from phlegm (also called "sputum"), scientists can identify MTB under a microscope. Since MTB retains certain stains even after being treated with acidic solution, it is classified as an acid-fast bacillus.[12,34] The most common acid-fast staining techniques are the Ziehl–Neelsen stain[36] and the Kinyoun stain, which dye acid-fast bacilli a bright red that stands out against a blue background.[28] Auramine-rhodamine staining[37] and fluorescence microscopy[30] are also used.

The *M. tuberculosis* complex (MTBC) includes four other TB-causing mycobacteria: *M. bovis*, *M. africanum*, *M. canetti*, and *M. microti*.[38] *M. africanum* is not widespread, but it is a significant cause of tuberculosis in parts of Africa.[39,40] *M. bovis* was once a common cause of tuberculosis, but the introduction of pasteurized milk has almost completely eliminated this as a public health problem in developed countries.[12,41] *M. canetti* is rare and seems to be limited to the Horn of Africa, although a few cases have been seen in African emigrants.[42,43] *M. microti* is also rare and is seen almost only in immunodeficient people, although its prevalence may be significantly underestimated.[44]

Other known pathogenic mycobacteria include *M. leprae*, *M. avium*, and *M. kansasii*. The latter two species are classified as "nontuberculous mycobacteria" (NTM). NTM cause neither TB nor leprosy, but they do cause lung diseases that resemble TB.[45]

1.2.6. Risk factors:

A number of factors make people more susceptible to TB infections. The most important risk factor globally is HIV; 13% of all people with TB are infected by the virus.[15] This is a particular problem in sub-Saharan Africa, where rates of HIV are high.[46,47] Of people without HIV who are infected with tuberculosis, about 5–10% develop active disease during their lifetimes; in contrast, 30% of those coinfected with HIV develop the active disease.[24]

Tuberculosis is closely linked to both overcrowding and malnutrition, making it one of the principal diseases of poverty.[13]Those at high risk thus include: people who inject illicit drugs, inhabitants and employees of locales where vulnerable people gather (e.g. prisons and homeless shelters), medically underprivileged and resource-poor communities, high-risk ethnic minorities, children in close contact with high-risk category patients, and health-care providers serving these patients.[48]

Chronic lung disease is another significant risk factor. Silicosis increases the risk about 30-fold.[49] Those who smoke cigarettes have nearly twice the risk of TB compared to nonsmokers.[50] Other disease states can also increase the risk of developing tuberculosis. These include alcoholism[13] and diabetes mellitus (three-fold increase).[51]

Certain medications, such as corticosteroids and infliximab (an anti-αTNF monoclonal antibody), are becoming increasingly important risk factors, especially in the developed world.[13]

Genetic susceptibility also exists,[46] for which the overall importance remains undefined.[13]

1.2.7. Transmission:

Tuberculosis may infect any part of the body, but most commonly occurs in the lungs (known as pulmonary tuberculosis).[14] Extrapulmonary TB occurs when tuberculosis develops outside of the lungs, although extrapulmonary TB may coexist with pulmonary TB.[14]

Tuberculosis is spread through the air when people who have active TB in their lungs cough, spit, speak, or sneeze.[8,52]

People with latent TB do not spread the disease.[8] Active infection occurs more often in people with HIV/AIDS and in those who smoke.[8] Diagnosis of active TB is based on chest X-rays, as well as microscopic examination and culture of body fluids.[53] Diagnosis of latent TB relies on the tuberculin skin test (TST) or blood tests.[53] When people with active pulmonary TB cough, sneeze, speak, sing, or spit, they expel infectious aerosol droplets 0.5 to 5.0 µm in diameter. A single sneeze can release up to 40,000 droplets.[54] Each one of these droplets may transmit the disease, since the infectious dose of tuberculosis is very small (the inhalation of fewer than 10 bacteria may cause an infection).[55] People with prolonged, frequent, or close contact with people with TB are at particularly high risk of becoming infected, with an estimated 22% infection rate.[56] A person with active but untreated tuberculosis may infect 10–15 (or more) other people per year.[57] Transmission should occur from only people with active TB – those with latent infection are not thought to be contagious.[13] The probability of transmission from one person to another depends upon several factors, including the number of infectious droplets expelled by the carrier, the effectiveness of ventilation, the duration of exposure, the virulence of the *M. tuberculosis* strain, the level of immunity in the uninfected person, and others.[58] The cascade of person-to-person spread can be circumvented by segregating those with active ("overt") TB and putting them on anti-TB drug regimens. After about two weeks of effective treatment, subjects with nonresistant active infections generally do not remain contagious to others.[56] If someone does become infected, it typically takes three to four weeks before the newly infected person becomes infectious enough to transmit the disease to others.[59]

1.2.8. Pathogenesis:

About 90% of those infected with *M. tuberculosis h*ave asymptomatic, latent TB infections (sometimes called LTBI),[60] with only a 10% lifetime chance that the latent infection will progress to overt, active tuberculous disease.[61] In those with HIV, the risk of developing active TB increases to nearly 10% a year.[54] If effective treatment is not given, the death rate for active TB cases is up to 66%.[57]

TB infection begins when the mycobacteria reach the alveolar air sacs of the lungs, where they invade and replicate within endosomes of alveolar macrophages.[12,62,63] Macrophages identify the bacterium as foreign and attempt to eliminate it by phagocytosis. During this process, the bacterium is enveloped by the macrophage and stored temporarily in a membrane-bound vesicle called a phagosome. The phagosome then combines with a lysosome to create a phagolysosome. In the phagolysosome, the cell attempts to use reactive oxygen species and acid to kill the bacterium. However, *M. tuberculosis* has a thick, waxy mycolic acid capsule that protects it from these toxic substances. *M. tuberculosis* is able to reproduce inside the macrophage and will eventually kill the immune cell.

The primary site of infection in the lungs, known as the "Ghon focus", is generally located in either the upper part of the lower lobe, or the lower part of the upper lobe.[12] Tuberculosis of the lungs may also occur via infection from the blood stream. This is known as a Simon focus and is typically found in the top of the lung.[64] This hematogenous transmission can also spread infection to more distant sites, such as peripheral lymph nodes, the kidneys, the brain, and the bones.[12,65] All parts of the body can be affected by the disease, though for unknown reasons it rarely affects the heart, skeletal muscles, pancreas, or thyroid.[66]

Tuberculosis is classified as one of the granulomatous inflammatory diseases. Macrophages, T lymphocytes, B lymphocytes, and fibroblasts aggregate to form granulomas, with lymphocytes surrounding the infected macrophages. When other macrophages attack the infected macrophage, they fuse together to form a

giant multinucleated cell in the alveolar lumen. The granuloma may prevent dissemination of the mycobacteria and provide a local environment for interaction of cells of the immune system.[67] However, more recent evidence suggests that the bacteria use the granulomas to avoid destruction by the host's immune system. Macrophages and dendritic cells in the granulomas are unable to present antigen to lymphocytes; thus the immune response is suppressed.[68] Bacteria inside the granuloma can become dormant, resulting in latent infection. Another feature of the granulomas is the development of abnormal cell death (necrosis) in the center of tubercles. To the naked eye, this has the texture of soft, white cheese and is termed caseous necrosis.[67]

If TB bacteria gain entry to the blood stream from an area of damaged tissue, they can spread throughout the body and set up many foci of infection, all appearing as tiny, white tubercles in the tissues.[68] This severe form of TB disease, most common in young children and those with HIV, is called miliary tuberculosis.[69] People with this disseminated TB have a high fatality rate even with treatment (about 30%).[30,70]

In many people, the infection waxes and wanes. Tissue destruction and necrosis are often balanced by healing and fibrosis.[67] Affected tissue is replaced by scarring and cavities filled with caseous necrotic material. During active disease, some of these cavities are joined to the air passages (bronchi) and this material can be coughed up. It contains living bacteria, and thus can spread the infection. Treatment with appropriate antibiotics kills bacteria and allows healing to take place. Upon cure, affected areas are eventually replaced by scar tissue.[67]

1.2.9. Diagnosis:

1.2.9.1. Active tuberculosis:

Diagnosing active tuberculosis based only on signs and symptoms is difficult,[71] as is diagnosing the disease in those who have a weakened immune system.[72] A diagnosis of TB should, however, be considered in those with signs of lung disease or constitutional symptoms lasting longer than two weeks.[72] A chest X-ray and multiple sputum cultures for acid-fast bacilli are typically part of the initial evaluation.[72] Interferon-γ release assays and tuberculin skin tests are of little use in the developing world.[73,74] Interferon gamma release assays (IGRA) have similar limitations in those with HIV.[74,75]

A definitive diagnosis of TB is made by identifying *M. tuberculosis* in a clinical sample (e.g., sputum, pus, or a tissue biopsy). However, the difficult culture process for this slow-growing organism can take two to six weeks for blood or sputum culture. Thus, treatment is often begun before cultures are confirmed.[78,77]

Nucleic acid amplification tests and adenosine deaminase testing may allow rapid diagnosis of TB.[71] These tests, however, are not routinely recommended, as they rarely alter how a person is treated.[77] Blood tests to detect antibodies are not specific or sensitive, so they are not recommended.[78]

1.2.9.2. Latent tuberculosis:

The Mantoux tuberculin skin test is often used to screen people at high risk for TB.[72] Those who have been previously immunized with the Bacille Calmette-Guerin vaccine may have a false-positive test result.[79] The test may be falsely negative in those with sarcoidosis, Hodgkin's lymphoma, malnutrition, and most notably, active tuberculosis.[12] Interferon gamma release assays, on a blood sample, are recommended in those who are positive to the Mantoux test.[77] These are not affected by immunization or most environmental mycobacteria, so they generate fewer false-positive results.[80] However, they are affected by *M. szulgai*, *M. marinum*, and *M. kansasii*.[81] IGRAs may increase sensitivity when used in addition to the skin test, but may be less sensitive than the skin test when used alone.[82]

The US Preventive Services Task Force (USPSTF) has recommended screening people who are at high risk for latent tuberculosis with

either tuberculin skin tests or interferon-gamma release assays.[83] While some have recommend testing health care workers, evidence of benefit for this is poor as of 2019.[84] The CDC stopped recommending yearly testing of health care workers without known exposure in 2019.[85]

1.2.10. Management:

Treatment of TB uses antibiotics to kill the bacteria. Effective TB treatment is difficult, due to the unusual structure and chemical composition of the mycobacterial cell wall, which hinders the entry of drugs and makes many antibiotics ineffective.[86]

Treatment requires the use of multiple antibiotics over a long period of time.[8] Antibiotic resistance is a growing problem with increasing rates of multiple drug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB).[8]

Latent TB is treated with either isoniazid alone, or a combination of isoniazid with either rifampicin or rifapentine.[87,88] The treatment takes at least three months.[58,87,89] People with latent infections are treated to prevent them from progressing to active TB disease later in life.[90]

Active TB disease is best treated with combinations of several antibiotics to reduce the risk of the bacteria developing antibiotic resistance.[13]

1.2.10.1. New onset:

The recommended treatment of new-onset pulmonary tuberculosis, as of 2010, is six months of a combination of antibiotics containing rifampicin, isoniazid, pyrazinamide, and ethambutol for the first two months, and only rifampicin and isoniazid for the last four months.[13] Where resistance to isoniazid is high, ethambutol may be added for the last four months as an alternative.[13]

1.2.10.2. Recurrent disease:

If tuberculosis recurs, testing to determine which antibiotics it is sensitive to is important before determining treatment.[13] If multiple drug-resistant TB (MDR-TB) is detected, treatment with at least four effective antibiotics for 18 to 24 months is recommended.[13]

1.2.10.3. Medication administration:

Directly observed therapy, i.e., having a health care provider watch the person take their medications, is recommended by the WHO in an effort to reduce the number of people not appropriately taking antibiotics.[91] The evidence to support this practice over people simply taking their medications independently is of poor quality.[92] There is no strong evidence indicating that directly observed therapy improves the number of people who were cured or the number of people who complete their medicine.[92] Moderate quality evidence suggests that there is also no difference if people are observed at home versus at a clinic, or by a family member versus a health care worker.[92] Methods to remind people of the importance of treatment and appointments may result in a small but important improvement.[93]

1.2.10.4. Medication resistance:

Primary resistance occurs when a person becomes infected with a resistant strain of TB. A person with fully susceptible MTB may develop secondary (acquired) resistance during therapy because of inadequate treatment, not taking the prescribed regimen appropriately (lack of compliance), or using low-quality medication.[96] Drug-resistant TB is a serious public health issue in many developing countries, as its treatment is longer and requires more expensive drugs. MDR-TB is defined as resistance to the two most effective first-line TB drugs: rifampicin and isoniazid. Extensively drug-resistant TB is also resistant to three or more of the six classes of second-line drugs.[94] Totally drug-resistant TB is resistant to all currently used drugs.[95] It was first observed in 2003 in Italy,[96] but not widely

reported until 2012,[97] and has also been found in Iran and India.[16,98] Bedaquiline is tentatively supported for use in multiple drug-resistant TB.[99] XDR-TB is a term sometimes used to define *extensively resistant* TB, and constitutes one in ten cases of MDR-TB. Cases of XDR TB have been identified in more than 90% of countries.[23]

1.2.11. Prognosis:

Progression from TB infection to overt TB disease occurs when the bacilli overcome the immune system defenses and begin to multiply. In primary TB disease (some 1–5% of cases), this occurs soon after the initial infection. However, in the majority of cases, a latent infection occurs with no obvious symptoms.[12] These dormant bacilli produce active tuberculosis in 5–10% of these latent cases, often many years after infection.[24]

The risk of reactivation increases with immunosuppression, such as that caused by infection with HIV. In people coinfected with *M. tuberculosis* and HIV, the risk of reactivation increases to 10% per year.[12] Studies using DNA fingerprinting of *M. tuberculosis* strains have shown reinfection contributes more substantially to recurrent TB than previously thought,[100] with estimates that it might account for more than 50% of reactivated cases in areas where TB is common.[101] The chance of death from a case of tuberculosis is about 4% as of 2008, down from 8% in 1995.[13]

1.2.12. Prevention:

Tuberculosis prevention and control efforts rely primarily on the vaccination of infants and the detection and appropriate treatment of active cases.[13] The World Health Organization has achieved some success with improved treatment regimens, and a small decrease in case numbers.[13]

Prevention of TB involves screening those at high risk, early detection and treatment of cases, and vaccination with the bacillus Calmette-Guérin (BCG) vaccine.[102,103,104] Those at high risk include household, workplace, and social contacts of people with active TB.[104]

1.2.12.1. Vaccines:

The only available vaccine as of 2011 is Bacillus Calmette-Guérin (BCG).[105] In children it decreases the risk of getting the infection by 20% and the risk of infection turning into active disease by nearly 60%.[106] It is the most widely used vaccine worldwide, with more than 90% of all children being vaccinated.[13] The immunity it induces decreases after about ten years.[13] As tuberculosis is uncommon in most of Canada, the United Kingdom, and the United States, BCG is administered to only those people at high risk.[107,108,109] Part of the reasoning against the use of the vaccine is that it makes the tuberculin skin test falsely positive, reducing the test's usefulness as a screening tool.[109] A number of new vaccines are currently in development.[13]

1.2.12.2. Public health:

The World Health Organization declared TB a "global health emergency" in 1993,[13] and in 2006, the Stop TB Partnership developed a Global Plan to Stop Tuberculosis that aimed to save 14 million lives between its launch and 2015.[110] A number of targets they set were not achieved by 2015, mostly due to the increase in HIV-associated tuberculosis and the emergence of multiple drug-resistant tuberculosis.[14] A tuberculosis classification system developed by the American Thoracic Society is used primarily in public health programs.[111]

1.2.12.3. Stigma:

Slow progress in preventing the disease may in part be due to stigma associated with TB.[23] Stigma may be due to the fear of transmission from affected individuals. This stigma may additionally arise due to links between TB and poverty, and in Africa, AIDS.[23] Such stigmatization may be both real and perceived; for example, in Ghana individuals with TB are banned from attending public gatherings.[112]

Stigma towards TB may result in delays in seeking treatment,[23] lower treatment compliance, and family members keeping cause of death secret[113] – allowing the disease to spread further.[23] In contrast, in Russia stigma was associated with increased treatment compliance. TB stigma also affects socially marginalized individuals to a greater degree and varies between regions.[112]

One way to decrease stigma may be through the promotion of "TB clubs", where those infected may share experiences and offer support, or through counseling. Some studies have shown TB education programs to be effective in decreasing stigma, and may thus be effective in increasing treatment adherence.[112] Despite this, studies on the relationship between reduced stigma and mortality are lacking as of 2010, and similar efforts to decrease stigma surrounding AIDS have been minimally effective.[112] Some have claimed the stigma to be worse than the disease, and healthcare providers may unintentionally reinforce stigma, as those with TB are often perceived as difficult or otherwise undesirable.[23] A greater understanding of the social and cultural dimensions of tuberculosis may also help with stigma reduction.[113]

1.2.13. Tuberculosis in Sudan:

TB is a concern in Sudan, as it is a high TB burden country in the Eastern Mediterranean Region/World Health Organization (EMR/WHO)[114,115]. In 2017, 21054 cases of TB were notified in Sudan[116].

Internal displacement enhances this high incidence of TB in Sudan[117]. Tuberculosis care and treatment is provided by the National Tuberculosis Control Program under the auspices of the Ministry of Health and by a number of non-governmental organizations (NGOs) who provide care to displaced persons, including those living in refugee camps[114]. Treatment is also provided by the private sector [117]. At the time of this study the Sudan National TB Program treatment policy was for an intensive phase of rifampicin, isoniazid, pyrazinamide and streptomycin daily under direct supervision for two to three months until the patient became smear negative followed by eight months of isoniazid and ethambutol[117]. Thioacetazone was previously used in the place of ethambutol[118,119]. Patients unable to attend on a daily basis were put on a 12-month regimen excluding rifampicin. Smear-negative pulmonary patients and non severe extra-pulmonary cases were given isoniazid and ethambutol daily for twelve months, supplemented by daily streptomycin injections during the initial phase[114]. While some NGOs refer patients to the national program others provide treatment using their own regimens. TB treatment in the private sector is not regulated[117].

The emergence and spread of strains of tuberculosis that are resistant to the drugs used in standard first line treatment poses a serious threat to attempts to control the disease[120]. Drug resistance in *M. tuberculosis* arises through the selection of spontaneous mutations by inadequate therapy. Resistance to multiple drugs arises through sequential selection of mutations. Resistance to both the key drugs rifampicin and isoniazid is termed multi drug-resistant tuberculosis (MDR-TB). Patients with MDR-TB frequently fail to be cured by standard drug treatment and may remain infectious and a potential source of onward transmission. Treatment for MDR-TB requires alternative chemotherapy for at least 18 months using more expensive drugs[121] of heightened toxicity[122,123]. In Sudan treatment is provided at the Abu-Anga Teaching Hospital[124], where the drugs available are ciprofloxacin, ofloxacin, cycloserine, ethionamide and amikacin[117]. From 2005 to 2008 small numbers of patients were treated for MDR-TB[124] but in 2009 ninety four patients commenced second line treatment, thirty five were new patients and fifty nine were retreatment cases[115]. The prevalence of drug resistant TB in Sudan is not known. A previous study undertaken in central Sudan during 1965 reported high levels of resistance to the anti-tuberculosis drugs available at that time[125]. Cure rates have improved considerably since the establishment of the National Tuberculosis Control Program and introduction of short course chemotherapy, but no

surveys of drug susceptibility have been reported[114,126].

1.2.14. Screening for tuberculosis:

1- Tuberculin skin testing:

The tuberculin skin test (TST) in its first iteration, the Mantoux Test, was developed in 1908. Conceptually, it's quite simple: tuberculin (also called purified protein derivative or PPD) is a standardised dead extract of cultured TB, injected into the skin to measure the person's immune response to the bacteria. So, if a person has been exposed to the bacteria previously, they should express an immune reaction to the injection, usually a mild swelling or redness around the site. There have been two primary methods of TST: the Mantoux test, and the Heaf test. The Heaf test was discontinued in 2005 because the manufacturer deemed its production to be financially unsustainable, though it was previously preferred in the UK because it was felt to require less training to administer and involved less inter-observer variation in its interpretation than the Mantoux test. The Mantoux test was the preferred test in the US, and is now the most widely used TST globally[127].

2- Mantoux test:

The Mantoux test is now standardised by the WHO. 0.1 ml of tuberculin (100 units/ml), which delivers a dose of 5 units is given by intradermal injection into the surface of the lower forearm (subcutaneous injection results in false negatives). A waterproof ink mark is drawn around the injection site so as to avoid difficulty finding it later if the level of reaction is small. The test is read 48 to 72 hours later.[16] The area of induration (NOT of erythema) is measured transversely across the forearm (left to right, not up and down) and recorded to the nearest millimeter[128].

3- Heaf test:

The Heaf test was first described in 1951.[129] The test uses a Heaf gun with disposable single-use heads; each head has six needles arranged in a circle. There are standard heads and pediatric heads: the standard head is used on all patients aged 2 years and older; the pediatric head is for infants under the age of 2. For the standard head, the needles protrude 2 mm when the gun is actuated; for the pediatric heads, the needles protrude 1 mm. Skin is cleaned with alcohol, then tuberculin (100,000 units/ml) is evenly smeared on the skin (about 0.1 ml); the gun is then applied to the skin and fired. The excess solution is then wiped off and a waterproof ink mark is drawn around the injection site. The test is read 2 to 7 days later.[129]

- Grade 0: no reaction, or induration of 3 or less puncture points;
- Grade 1: induration of four or more puncture points;
- Grade 2: induration of the six puncture points coalesce to form a circle;
- Grade 3: induration of 5 mm; or more
- Grade 4: induration of 10 mm or more, or ulceration

The results of both tests are roughly equivalent as follows:

- Heaf grade 0 & 1 ~ Mantoux less than 5 mm;
- Heaf grade 2 ~ Mantoux 5–14 mm;
- Heaf grade 3 & 4 ~ Mantoux 15 or greater

4- Tuberculin conversion:

Tuberculin conversion is said to occur if a patient who has previously had a negative tuberculin skin test develops a positive tuberculin skin test at a later test. It indicates a change from negative to positive, and usually signifies a new infection.[129]

5- Boosting:

The phenomenon of *boosting* is one way of obtaining a false positive test result. Theoretically, a person's ability to develop a reaction to the TST may decrease over time – for example, a person is infected with latent TB as a child, and is administered a TST as an adult. Because there has been such a long time since the immune responses to TB has been necessary, that

person might give a negative test result. If so, there is a fairly reasonable chance that the TST triggers a hypersensitivity in the person's immune system – in other words, the TST reminds the person's immune system about TB, and the body overreacts to what it perceives as a reinfection. In this case, when that subject is given the test again (as is standard procedure, they may have a significantly greater reaction to the test, giving a very strong positive; this can be commonly misdiagnosed as Tuberculin Conversion. This can also be triggered by receiving the BCG vaccine, as opposed to a proper infection. Although boosting can occur in any age group, the likelihood of the reaction increases with age.[130]

Boosting is only likely to be relevant if an individual is beginning to undergo periodic TSTs (health care workers, for example). In this case the standard procedure is called two-step testing. The individual is given their first test and in the event of a negative, given a second test in 1 to 3 weeks. This is done to combat boosting in situations where, had that person waited up to a year to get their next TST, they might still have a boosted reaction, and be misdiagnosed as a new infection.[131] Here there is a difference in US and UK guidelines; in the US testers are told to ignore the possibility of false positive due to the BCG vaccine, as the BCG is seen as having waning efficacy over time. Therefore, the CDC urges that individuals be treated based on risk stratification regardless of BCG vaccination history, and if an individual receives a negative and then a positive TST they will be assessed for full TB treatment beginning with X-ray to confirm TB is not active and proceeding from there.[132] Conversely, the UK guidelines acknowledge the potential effect of the BCG vaccination, as it is mandatory and therefore a prevalent concern – though the UK shares the procedure of administering two tests, one week apart, and accepting the second one as the accurate result, they also assume that a second positive is indicative of an old infection (and therefore certainly LTBI) or the BCG itself. In the case of BCG vaccinations confusing the results, Interferon-γ (IFN-γ) tests may be used as they will not be affected by the BCG.

6- Interpretation:

According to the U.S. guidelines, there are multiple size thresholds for declaring a positive result of latent tuberculosis from the Mantoux test: For testees from high-risk groups, such as those who are HIV positive, the cutoff is 5 mm of induration; for medium risk groups, 10 mm; for low-risk groups, 15 mm. The U.S. guidelines recommend that a history of previous BCG vaccination should be ignored. For details of tuberculin skin test interpretation, please refer to the CDC guidelines (reference given below).

The UK guidelines are formulated according to the Heaf test: In patients who have had BCG previously, latent TB is diagnosed if the Heaf test is grade 3 or 4 and have no signs or symptoms of active TB; if the Heaf test is grade 0 or 1, then the test is repeated. In patients who have not had BCG previously, latent TB is diagnosed if the Heaf test is grade 2, 3 or 4, and have no signs or symptoms of active TB. Repeat Heaf testing is not done in patients who have had BCG (because of the phenomenon of boosting). For details of tuberculin skin test interpretation, please refer to the BTS guidelines (references given below).

Given that the US recommendation is that prior BCG vaccination be ignored in the interpretation of tuberculin skin tests, false positives with the Mantoux test are possible as a result of: (1) having previously had a BCG (even many years ago), and/or (2) periodical testing with tuberculin skin tests. Having regular TSTs boosts the immunological response in those people who have previously had BCG, so these people will falsely appear to be tuberculin conversions. This may lead to treating more people than necessary, with the possible risk of those patients suffering adverse drug reactions. However, as Bacille Calmette-Guérin vaccine is not 100% effective, and is less protective in adults than pediatric patients, not treating these patients could lead to a possible infection. The current US policy seems to reflect a desire to err on the side of safety.

The U.S. guidelines also allow for tuberculin skin testing in immunosuppressed patients (those with HIV, or who are on immunosuppressive drugs), whereas the UK guidelines recommend that tuberculin skin tests should not be used for such patients because it is unreliable.

7- Interferon-γ testing:

The role of IFN-γ tests is undergoing constant review and various guidelines have been published with the option for revision as new data becomes available. CDC: MMWR Health Protection Agency:UK. There are currently two commercially available interferon-γ release assays (IGRAs): QuantiFERON-TB Gold and T-SPOT.TB.[133] These tests are not affected by prior BCG vaccination, and look for the body's response to specific TB antigens not present in other forms of mycobacteria and BCG (ESAT-6). Whilst these tests are new they are now becoming available globally.

CDC recommends that QFT-G may be used in all circumstances in which the TST is currently used, including contact investigations, evaluation of recent immigrants, and sequential-testing surveillance programs for infection control (e.g., those for health-care workers)[133].

8- HPA Interim Guidance:

The HPA recommends the use of IGRA testing in health care workers, if available, in view of the importance of detecting latently infected staff who may go on to develop active disease and come into contact with immunocompromised patients and the logistical simplicity of IGRA testing[133].

9. Drug-resistant strains:

It is usually assumed by most medical practitioners in the early stages of a diagnosis that a case of latent tuberculosis is the normal or regular strain of tuberculosis. It will therefore be most commonly treated with Isoniazid (the most used treatment for latent tuberculosis.) Only if the tuberculosis bacteria does not respond to the treatment will the medical practitioner begin to consider more virulent strains, requiring significantly longer and more thorough treatment regimens. There are 4 types of tuberculosis recognized in the world today:

- Tuberculosis (TB)
- Multi-drug-resistant tuberculosis (MDR TB)[134]
- Extensively drug-resistant tuberculosis (XDR TB)[135]
- Totally drug-resistant tuberculosis (TDR TB)[136]

1.2.15. Household contact/ tuberculoses contact:

Tuberculosis (TB) contacts are people who have close contact with patients with infectious TB. As they are at high risk for infection (and in line with the End TB strategy). Close contacts of patients with infectious tuberculosis are at increased risk of developing *Mycobacterium tuberculosis* infection and disease[137,138]. The risk of tuberculosis in individuals with latent *M. tuberculosis* infection (LTBI) is estimated to be 5%–10% over the course of a lifetime, with approximately half of cases occurring within the first 2 years after exposure[139,140].

TB contacts should be investigated systematically and actively for TB infection and disease. Such interventions are called ‘tuberculosis contact investigations’. They contribute to early identification of active TB, thus decreasing its severity and reducing transmission of *Mycobacterium tuberculosis* to others, and identification of latent TB infection (LTBI), to allow preventive measures.[138]

Contacts are commonly investigated in high-income countries with low TB burdens and in settings in which a TB elimination policy is implemented, in order to identify persons with early active TB or who have recently been infected. People identified as infected are then treated for LTBI with isoniazid for at least 6 months (usually 9 months) or with shorter combination regimens including isoniazid and rifampicin[137]

TB contact investigations are rarely and inconsistently carried out in resource-limited settings. In most low- and middle-income countries, it is included in the national policy to control and prevent TB; however, in the vast majority of countries, it is either not undertaken or is implemented on the basis of no or poor standards, because of the absence of clear definitions of index cases, contacts and procedures. Furthermore, the health personnel who should be involved are usually not clearly identified[137]

Information on the contribution of routine contact investigations to early TB case detection is scarce in these countries or is non-standardized, thus precluding an assessment of its impact on reducing transmission.[137]

Many studies in countries with a high TB incidence have shown that the prevalence may reach 5% or more among contacts, particularly among household members. Other data suggest that contact investigations could be particularly useful for identifying childhood TB. Furthermore, contact investigation can help identify people who require careful follow-up, such as those who were exposed to an index case of multi-drug-resistant or extensively drug-resistant TB or people infected with HIV, whose risk for rapid progression to active TB is very high. [138,140]

Effective investigation of TB contacts within national TB programmes and other services can result in the detection of a significant number of cases. WHO estimates show that, worldwide, highly infectious, smear-positive pulmonary TB develops in over 4 million people annually.[137]

Early identification means a better chance of cure and, especially, a reduction in further transmission. Furthermore, contact investigation allows identification of people who are latently infected and at high risk for active TB, who can be treated preventively.

The WHO policy document recommendations for investigating contacts of persons with infectious tuberculosis was prepared to guide national TB programme staff and all agencies and organizations involved in TB prevention, care and control to establish strategies for sound TB contact investigation practices. The document was elaborated after an extensive literature review and with contributions from experts around the world. It states the fundamental principles and procedures for an appropriate approach to TB contact investigation, and annexes 1 and 2 provide further details to understand these principles. The hope is that these evidence based guidelines will be translated into country policy and practice, so that an additional neglected intervention can be put in place and, ultimately, contribute to elimination of TB. [138]

The World Health Organization (WHO) estimated that two-fifths of new TB cases are undiagnosed and more country-specific actions are needed to identify these missing cases to achieve the global goal of ending the TB epidemic by 2035[141]. Contact tracing among household family members is one of the active case-finding strategies that has been proposed to increase the case detection rate[142]. In 95 studies from low- and middle-income settings included in a systematic review, the prevalence of TB from household contact tracing varied from 2.1 to 10.1%[143,144]. Efforts for early diagnosis of TB through effective case finding programs are needed to reduce the rate of TB transmission and to reduce the case detection gap.

Due to the limitations of current passive case-finding strategies and the global urgency to improve TB case-detection rates, WHO has called for more evidence on innovative ways of TB screening, especially from low-income countries. An integrated approach among individuals who are presumed to have TB but do not present to a health service (as commonly seen in the passive case finding approach), has gained interest to enhance the detection rate for early diagnosis and treatment of TB in high prevalence countries.[145].

1.2.16. Health education of TB:

Health education is important to empower patients and encourage their contribution towards

tuberculosis (TB) control. Health education activities are integrated into services provided at the primary health care (PHC) level. Despite recent World Health Organization (WHO) reports about a declining global trend, the burden of tuberculosis (TB) in Sudan remains unacceptably high[146]. The high incidence of active TB infection, high proportion of latent infection and comorbidity significantly undermine effective TB control.[147]. For instance, drug-resistant forms of TB have spiralled largely as a result of late detection, poor treatment and management, and failure to retain TB patients on treatment[148,149,150].

Besides the high disease burden and systemic limitations, patients themselves may undermine TB control efforts through poor or high-risk infection control practices or non-adherence to treatment[151,152]. Poor/unhelpful patient conduct, negligence and resistance to participation in appropriate TB control efforts are motivated by individual, socio-economic and structural factors[151,152]. Negative behaviours and attitudes can be the direct result of patients' own choices or the indirect result of a lack of knowledge[153]. Thus, empowering patients with appropriate and correct information and engendering positive attitudes towards TB and its curability is critical for the effective control of the disease. There is increasing recognition among researchers, health workers, and policy makers that encouraging patients to play a more active role in their health care improves the quality and efficiency of health care, and ultimately population-level health outcomes.[154].

Health education is an important tool to foster patient empowerment and encourage their contribution towards TB control. In a study conducted in KwaZulu-Natal, TB-HIV co-infected patients found it easier to adhere to anti-retroviral treatment than anti-TB treatment, citing limitations such as poor communication, low patient involvement, and poor provider supervision of treatment by the TB programme. Contrarily, the success of the HIV programme has been associated with commitment to provide adequate health education, treatment literacy and support to patients.[154]

In Sudan, health education activities are integrated into services provided at the PHC level. Health care workers are responsible for health education, information dissemination, and supporting patients through face-to-face consultation, health education campaigns, social mobilisation for different health programmes, and distribution of health education materials and media.

At most PHC facilities, due to lack of space, health education is conducted in large group lecture sessions in the waiting area facilitated by dedicated health educators or nurses. Although these strategies may broaden health education reach, their actual impact on patient knowledge retention and attitudes and practices is generally not well established in the current setting. Previous research on patients' TB-related knowledge, attitudes and practices revealed significant deficits in their levels of awareness regarding symptoms, transmission, prevention, and treatment of TB among various communities. The lack of TB awareness was shown to impact negatively on individual health-seeking behaviour, attitudes towards TB and infection control practices.[154].

1.2.17. Previous related studies:

A cross-sectional study by Mulusew, et al [155] was conducted between October and December 2016 among shopkeepers in Bahir Dar City, Northwest Ethiopia. Sputum samples were collected stained with Ziehl Neelscn staining technique and examined microscopically. Data were analysed by using SPSS [or Windows and descriptive statistics was used to present figures. A total of 103 subjects were included in the study, of these 70 (68%) were males. The mean age of the participants was 36.1 with standard deviation of 13.1 years. The majority 36 (35%) were in the age group 31-50. Similarly, most of the study subjects 61(59.2%), 67(55.3%), 53 (51.5%) carne from rural areas, were farmers and illiterates, respectively.

A descriptive epidemiological study was carried out in Nairobi by Perpetual[156] about the risk factors in the transmission of tuberculosis. Study was conducted on 258 patients presenting with pulmonary tuberculosis. Patients' sputum were collected for laboratory analysis and patients were required to respond to a structured questionnaire 011 risk factors for transmission. Data among stratified groups were compared using bivariate analysis. Statistical significance was considered at $p < 0.05$. Results showed that there were significantly more males than females associated with pulmonary tuberculosis infection ($\chi 2 = 0.963$; df = 1; $p < 0.05$). Monthly income was significant in disease transmission with 222 (86.0%) of the patients earning less than 100$ and 90 (34.9%) earning less than 50$ per month ($p < 0.05$, 95% CI). One hundred and seventy three patients (67.1%) were unemployed or running small businesses. Only 85 (32.9%) were in formal employment. Results showed 166 (64.3%) patients were living in single rooms with 110 (42.6%) living with more than two people with a maximum of 10 people in a single room. Only 73 (28.3%) were living alone in a single room and only 7 families (2.7%) were living in houses with five or more rooms. Alcohol consumers and smokers were 102 (39.5%) and 93 (36%) respectively. Half of the patients 137 (53.3%) had not completed secondary education with only 16 (6.2%) having completed tertiary education. Recurrent cases were 54 (21%) while those exposed to the disease either at home or working place were 75 (29.2%). Out of 171 patients who agreed to test for HIV, 46 (26.9%) were positive. Marital status had no effect on incidence of disease. Conclusion: Emphasis should be given to creating awareness of the risk factors associated with transmission of tuberculosis in order to reduce the rate of infection.

A study on improving detection of tuberculosis among household contacts of index tuberculosis patients by an integrated approach in Myanmar: a cross-sectional study by Kyaw, et al. (2018)[157] Household contacts of index TB cases who had been receiving treatment for at least 3 months were prospectively investigated by an integrated approach which included modification of screening methods and active facilitation of screening investigations as follows. Initial chest x-ray (CXR) was performed for all contacts at the responsible facilities followed by sputum specimen collection for those aged ≥15 years and gene Xpert MTB/RIF examination. Transportation of all household contacts to health facilities and transportation of sputum samples for smear and gene Xpert MTB/RIF examination at centers were arranged by the research team to ensure that all household contacts received all investigations. Risk factors for TB among household contacts were identified by multiple logistic regression models. The results showed that out of 174 household contacts, 115 were ≥ 15 years and 59 were < 15 years. The percentage of TB cases detected among the household contacts was 13.8%. There were 14 (12.2%) positive TB cases among the 115 contacts aged ≥15 years while 10 (16.9%) of those aged < 15 years had clinical signs and symptoms of TB with an abnormal CXR. Risk factors among household contacts for TB were being a caretaker of an index case, active and passive smoking, and drinking alcohol.

A previous study by Mandal, et al.[158] aimed to determine the effectiveness of contact tracing for both pulmonary and non-pulmonary tuberculosis (TB). The authors studied contact tracing in South East of Scotland, Edinburgh TB Clinic, UK, for 3 years. New index cases of both pulmonary and non-pulmonary TB were identified from reviewing TB nurses records. Pulmonary involvement was excluded from all non-pulmonary cases. Active TB was diagnosed as per the national TB guidelines. Latent TB was diagnosed based on history, tuberculin skin test and interferon γ release assay. TB contacts were identified from reviewing TB nurses notes on index TB patients. A positive screening episode was defined as identification of either active or latent TB in a contact following relevant investigations. Results showed that a total number of positive screening episodes for pulmonary TB was 43.1% and non-pulmonary TB was 26.1%. Of these, 78.8% were household contacts and 21.2% were casual contacts.

A study conducted by Mary, et al., (2019)[159] on risk and timing of tuberculosis among close contacts of persons with infectious tuberculosis. They prospectively enrolled patients ≥15 years of age with culture-confirmed pulmonary tuberculosis and their close contacts at 9 health departments in the United States and Canada. Close contacts were screened and cross-matched with tuberculosis registries to identify those who developed tuberculosis. The results showed that tuberculosis was diagnosed in 158 of 4490 contacts (4%) of 718 index patients with tuberculosis. Of tuberculosis cases among contacts, cumulative totals of 81 (51%), 119 (75%), 128 (81%), and 145 (92%) were diagnosed by 1, 3, 6, and 12 months, respectively, after the index patients' diagnosis. Tuberculosis rates among contacts were 2644, 115, 46, 69, and 25 cases per 100 000 persons, respectively, in the 5 consecutive years after the index patients' diagnosis. Of the tuberculosis cases among contacts, 121 (77%) were identified by contact investigation and 37 (23%) by tuberculosis registry cross-match. In conclusion, Close contacts to infectious patients with tuberculosis had high rates of tuberculosis, with most disease diagnosed before or within 3 months after the index patient' diagnosis.

A cross-sectional study was conducted by Gebremedhin, et al.,[160] on household Contact Screening Adherence among Tuberculosis Patients in Northern Ethiopia, from April 10 - June 30, 2013 in five urban districts of Amhara region, where 418 patients receiving treatment at tuberculosis clinic were interviewed. All patients were interviewed using structured and pre-tested questionnaire. Bringing at least one household contact to TB clinic was regarded as adherent to household contacts screening. Bivariate and multiple logistic regressions were used to investigate association. The results showed that the overall adherence to household contact screening in Amhara region was 33.7%. Adherence was higher among Muslims than Christians. Adherence was high if patient took health education from Health Care Worker [AOR: 3.22, 95% CI: 1.88 to 5.51] and 2.17 times higher if patient had sufficient knowledge on tuberculosis [AOR: 2.17, 95% CI: 1.29 to 3.67] during interview. Relationship with contact was a significant [AOR: 0.4, 95% CI: 0.2 to 0.9] social related factor. In conclusion, one third of tuberculosis patients adhered to household contact screening in health facilities during their treatment course. Promoting knowledge of tuberculosis in the community and continuous health education to tuberculosis patients are recommended.

A study conducted by Huddart, et al.,[161] aimed to examine how TB knowledge and infection prevention behaviors change over the course of treatment. A total of 6,031 of publicly treated TB patients with NGO-provided treatment support health workers was compiled in nine Indian cities from March 2013 to September 2014. At the beginning and end of TB treatment, patients were asked about their knowledge of TB symptoms, transmission, and treatment and infection prevention behaviors. The results showed that Patients beginning TB treatment (n = 3,424) demonstrated moderate knowledge of TB; 52.5% (50.8%, 54.2%) knew that cough was a symptom of TB and 67.2% (65.6%, 68.7%) knew that TB was communicable. Overall patient knowledge was significantly associated with literacy, education, and income, and was higher at the end of treatment than at the beginning (3.7%, CI: 3.02%, 4.47%). Infection prevention behaviors like covering a cough (63.4%, CI: 61.2%, 65.0%) and sleeping separately (19.3%, CI: 18.0%, 20.7%) were less prevalent. The age difference between patient and health worker as well as a shared language significantly predicted patient knowledge and adherence to infection prevention behaviors.

1.3. JUSTIFICATION

- The importance of this study stems from study of tuberculosis among individuals who are in close contact with the patient in order to detect positive cases.
- To know the reality of tuberculosis in the study area.

- Need to know the prevalence of disease among close contact.
- Providing medical advice and guidance to close contacts of confirmed tuberculosis patients.
- Addition to Sudanese studies and reached in this field.

1.4. OBJECTIVES

1.4.1. General objective:

To study the effect of screening among close contacts of tuberculus patients at Almanagil Teaching Hospital.

1.4.2. Specific objectives:

1. To screen close contact of passively diagnosed tuberculus patients.
2. To identify suspected cases among close contact and confirm them by more investigations (CXR and sputum analysis).
3. To build the capacity of health workers in tuberculosis control program who participated in the study.
4. To raise the awareness and minimize the stigma among close contacts through health educations during home visits.

2. PATIENTS AND METHODS

2.1. Study design:

The study is intervention analyzing data of the effect of screening and health education among close contacts of TB patients , conducted during the period October 2017 – October 2020. All tuberculosis cases who were diagnosed during this period and their close contacts who agreed to participate in the study were recruited , thus home visits were conducted by pre agreed upon dates. The home visits were conducted by public health specialist , medical assistant and lab technician who were working in the unit of TB at Almanagil Teaching Hospital, all were supervised by consultant of internal medicine. The household contacts were screened for TB and referred to the unit of TB at Almanagil Teaching Hospital and investigated for tuberculosis by chest X ray and sputum examinations .

Those who were found to be positive by sputum examination or chest X-ray were treated according to the national treatment protocol. Those who were found to be from the high risk groups (under five children and elderly) and negative by chest X-ray and sputum examination were given prophylactic treatment with INH.

2.2. Study duration:

The study was carried out in the period from 2017 to 2020.

2.3. Study area:

Sudan is one of African developing countries with a total population of 38 million and area of 2.5 million km2 Sudan is shouldering about 8-10% of the disease burden in the Eastern Mediterranean Region (EMRO) with an estimated incidence of 79/100000 new cases annually that is a total of 30, 028 / year. The case detection rate is only 30%.

Gezira state is one of the central state of Sudan with an area of 35,000 square kilometer and a total population of 4 million.

It is the second populous state after Khartoum state the capital of the country; approximately more than 1/10th of country population reside in this state. The state is divided into seven localities. One of them is selected as the study locality (Almanagil locality , Almanagil Teaching Hospital TB Unit).

Almanagil locality has 3 units of TB:

1. Almanagil Teaching Hospital TB Unit.
2. Alhuda Hospital TB Unit.
3. Algamosy Hospital TB Unit.

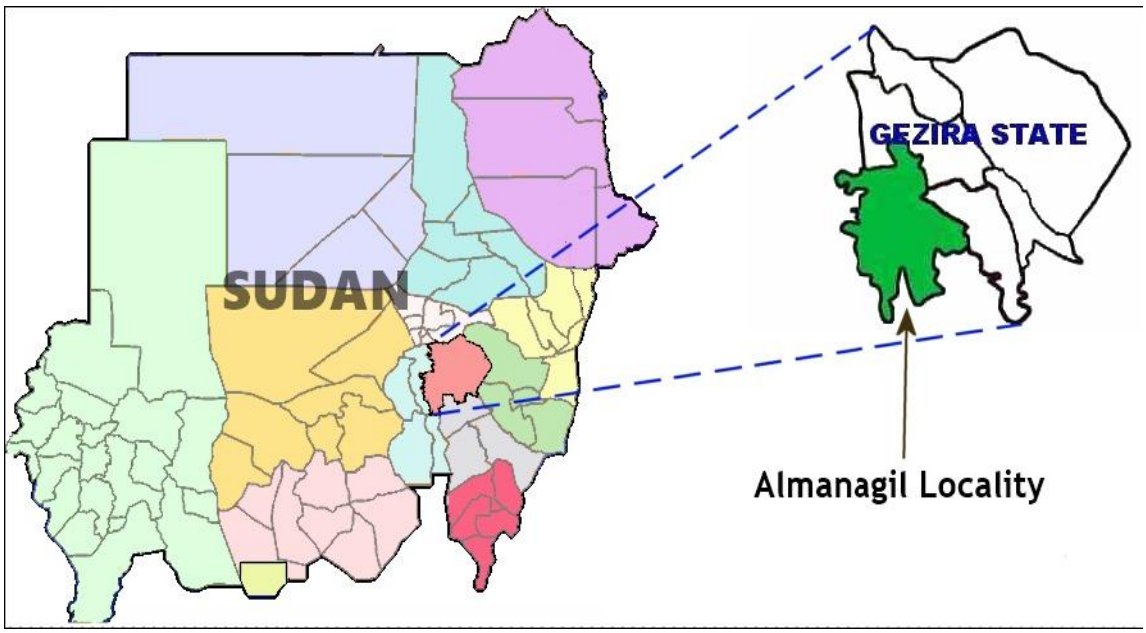
Almanagil Teaching Hospital TB Unit considered as referral center of TB in the locality because of full staffs whose supervised by consultant of internal medicine in addition to full equipment's of investigation of TB ,beside the location of the unit inside the central and referral hospital in the locality (Almanagil Teaching Hospital) .

Almanagil Teaching Hospital includes many departments (Medicine, Surgery, obstetrics & Gynaecology, Paediatrics, ENT, Ophthalmology, Dermatology, Orthopedics and Renal center.

Almanagil Teaching Hospital TB Unit is responsible for diagnosis, investigations, treatment, follow up and registration of TB pt and the close contacts of TB pt. In addition to that , it is providing prophylaxis treatment for those contacts with TB patients (HIV and children under 5 years).

The staff members of TB Unit includes medical assistance, 2 lab. technicians, lab assistance, statistician and health workers, this staff under supervision of Ministry of Health in the state, by chest consultant. All related to national TB program .

Fig. 1: The location of Almanagil Locality in Gezira state in Sudan in 2018



2.4. Study population :

All household contacts of tuberculosis patients (pulmonary or extra pulmonary) cases diagnosed in Almanagil Teaching Hospital TB Unit , during the study period who agreed to participate in the study by verbal or written consent, were recruited, for children consent was obtained from their gardens.

Phases of the Study :-

Phase one.

Field study was aimed to determine the method which achieved the study objectives, this was achieved through preparing of the questionnaire and screening of the close contacts of tuberculus pt with follow up for data collection.

Total duration of the study was three years, from October 2017 – October 2020, the research was undertaken place in Gezira state (Almanagil Teaching Hospital TB Unit).

Phase two: Data collection for TB pt :

Diagnosis for the primary data for Tuberculosis patient were determined from registration of Almanagil Teaching Hospital TB Unit before & during the study . A total of 160 tubercolous patients were included in our study while the remaining (144) were excluded for various reasons and from those registry books of the TB pt were extracted the close contacts of diagnosed tuberculus pt .

Phase Three: Screening of close contacts of tuberculus pt

The staff of Almanagil Teaching Hospital TB Unit who mainly participated in the study included medical assistance, lab.Technician , statistician and health worker were well trained to explain the aim of the study ,giving health education for close contacts of tubercolous patients & data collection. Data were collected from close contacts through design questionnaire included the personal data (sex ,age ,residence ,.level of education ,house condition & investigations , in addition to pre & post test for health education of TB .

The total number of close contacts of tuberculosis patient was 1050 person, (38%) of them participated in the study of No. 400, and (62%) of No. 650 did not participate in the study or absent during the household visit .Then the researcher had screened 400 close contacts with necessary information of TB then filled the questionnaires , beside investigations and examinations of TB.

Before visiting, a call was made to close contacts to inform him of the visiting, then arranged the day and suitable time, and discussed the possibility of meeting all close contacts. Call was made using the telephone number extracted from TB unit registers. Then the time was set for whom accepted the visit & were willing to participate in the study .

The factors assessed were demographic data, number of the close contacts of tubercolous patients , level of education, age, sex,, occupation, knowledge of TB disease, TB symptoms, number of family members and housing condition.

Then screening with history (symptoms and signs of TB) during the household visits, then to the TB unit for investigations (CXR & sputum analysis) and examinations in order to diagnosis and giving treatment according to TB protocol who had confirmed TB, then follow up to all close contacts .

2.4.1. Inclusion criteria:

- All age group in contact with tuberculosis patients were included (pulmonary or extra pulmonary).
- Close contacts of diagnosed tuberculosis patient before & during the study .

2.4.2. Exclusion criteria:

- Diagnosed tuberculosis patients.
- Close contacts of tuberculosis patients not available at time of study.
- Close contacts of tuberculosis patients who refused to be part of study.

2.5. Sample technique:

The sample size was selected as total coverage, where as all contact of TB patients were screened for TB during the study period.

2.5. Sample size:

The sample size was determent according to the formula:

$$N = \frac{Z^2 \times PQ}{d^2}$$

Where:

N= desired sample size (when the population 10.000)
Z= Standard normal deviate ; usually set at 1.96(or a~2), which correspond to 95% confidence level.
P= proportion in the target population estimate to have a particular characteristic. If there is no reasonable estimate, use 50% (i.e 0.5)
Q= 1-p (proportion in the target population not having the particular characteristics).
d= degree of accuracy require, usually set at 0.05 level.
Accordingly, the sample size is 384 of close contacts.
The sample of the study is approximately (400) sample.

2.6. Data collection tools:

The data was collected by pre-designed questionnaire (Appendix) through direct interview of close contacts of all diagnosed tuberculus patients before & during study period (2017 - 2020) , after explained the purpose of the study and took their verbal consent, then health education to the contacts about TB, after that investigations were performed to close contacts, included CXR and sputum analysis, in order to confirm diagnosis of TB.

Methods of Data collection:

The closed contacts will be determined from diagnosed tuberculus patients before & during study period (2017 -2020) at Almanagil Teaching Hospital TB Unit records , to do the following methods.

1. Closed contacts questionnaire
2. Screening & Diagnosis of closed contacts by (history ,symptoms and signs ,investigations(CXR & sputum analysis).

The following definitions were used:

- **Household contact:** an individual that shared the same house with the index case for a period of at least 3 months leading up to the time of diagnosis of the index case.

- **Screened household contacts:** Close contacts of tuberculus patients who had TB screening in the interval (days) between the day treatment was started of the index case and the interview date of the household.

- **Secondary case:** a household contact who was diagnosed to have TB in the interval (days) between the day start of treatment of the index case and the day of interview of the household.

- **Prolonged cough:** unexplained cough of more than two weeks duration occurring between the start of treatment of the index case and the interview of the household.

2.7. Study variables:

- **Dependent variables:** Tuberculosis, close contact, screening, investigations, health education, tuberculosis patient.

- **Independent variables:** sociodemographic characteristic (age, gender, residence ..etc).

2.8. Data analysis:

To obtain more accurate and precise evaluation. The collected data was organized into a master sheet, and then entered the computer which analyzed by using Statistical Package for Social Sciences (SPSS) version 25. The results obtained were presented in tables and figures. Chi-squire test was performed to correlate between variables. The level of significant was considered if P. value < 0.05.

2.9. Ethical consideration:

- Ethical approval was obtained from Gezira University, Ethical committee of Faculty of Medicine and Department of Family and Community Medicine.
- A letter was issued to the Ministry of Health Research Department, then to Preventive Department and to TB program of Gezira State.
- Permission was taken from Almanagil Teaching Hospital Administration in order to collect information.
- Consent was taken from all participants after explain the purpose of the study.
- The questionnaire was coded for confidentiality.
- No intervention with hospital protocol.

4. RESULTS

This chapters deals with data analysis. Which presented in tables & figures.

Result of close contacts of tuberculosis patient

The total number of close contacts of tuberculosis patient was 1050 person, only 400 of

them participated in the study which represent (38%) , and 650 which represent (62%) did not participate in the study or absent during the household visit , so the total number of 400 sample of close contacts that were covered & accepted to perform screening of TB, investigations and examination, also were recruited to evaluate effects of health education among them.

Figure 1 :- The socio-demographic data of the close contacts of tuberculosis patients in the study showed that females were predominant 211 (52.80%), and male 189 (47.30%) .

Figure 2 The most of close contacts of tuberculosis patients 159 (39.8.0%) in age group 35 -49 years, and 75 (18.8%) were from 5-18 years, 127 (31.8%) were from 19-34 years and 39 (9.8 %) were from 50 & above years.

Figure 3 The most of close contacts of tuberculosis patients regarding the residency 388 (97 %) were from rural area and 12 (3%) were from urban area .

Figure 4 the consanguinity of close contacts with tuberculosis patients, 145 (36.3%) were first degree relatives, 128 (32.0%) were second degree relatives and 123 (30.8%) were third degree relatives, while others 4 (1.0%).

Figure 5 the level of education of close contacts of tuberculosis patients, about half of participants had primary school level 259 (64.8%) and 136 (34.%) were pre school and 4 (1.0%) were secondary school and 1 (0.3%) were postgraduate.

Figure 6 shows house condition among close contacts of tuberculosis patient included in the study, 81 (20.0%) patients had 1-2 persons per room, 308(77%) patients had 3-4 persons per room, and 11 (2.8%) patients had >5 persons per room.

Figure 7 The socio-demographic data of the close contacts of tuberculosis patients in the study showed that the majority of the family income of the participants with low income (<2000) 303(76%) and with middle income (2000-5000) 83 (21%) while with high income >5000 ,14 (0.3%).

Figure 8 shows the results of investigations of close contacts , that CXR was significant in 267 (66.8%) of studied close contacts and not significant in 133 (33.2%)

Figure 9 shows the results of investigations of close contacts according to AFB was positive in 224 (56.0%) of studied close contacts and negative in 176 (44%).

Figure 10 shows the diagnosis of studied close contacts, 324 (81.0%) of studied close contacts confirmed the diagnosis of TB, while 76 (19.0%) not confirmed TB .

Figure 1: Distribution of studied the close contacts of TB patients according to gender

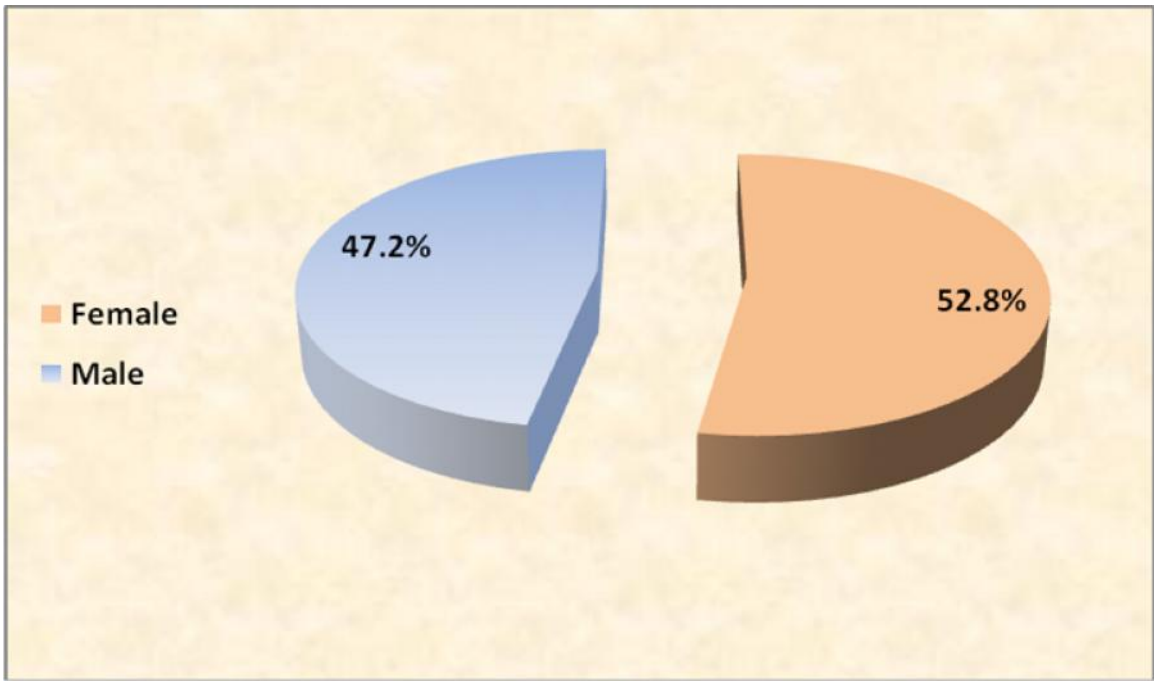


Figure 2: Distribution of studied the close contacts of TB patients according to age

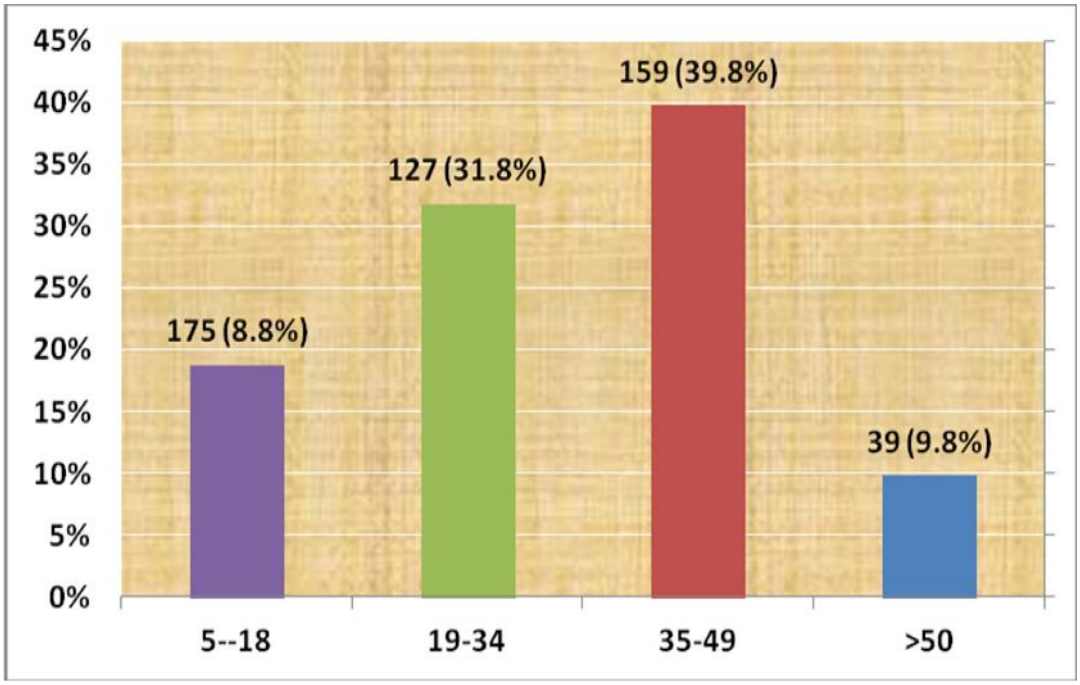


Figure 3: Distribution of studied the close contacts of TB patients according to residence

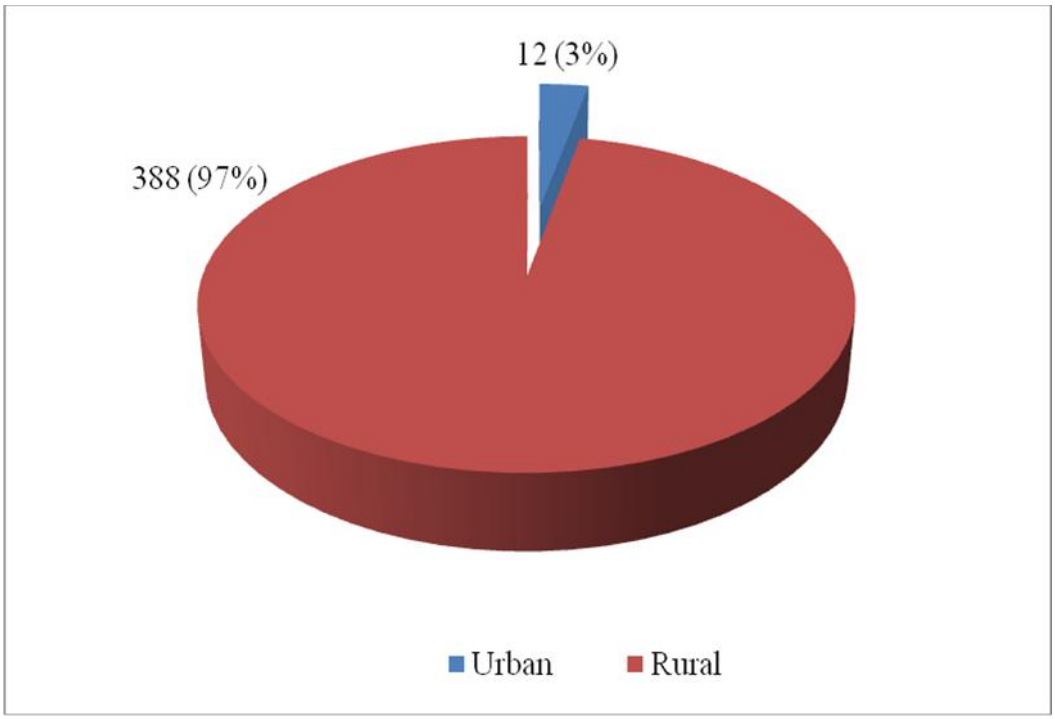


Figure 4: Distribution of studied the close contacts of TB patients according to consanguinity

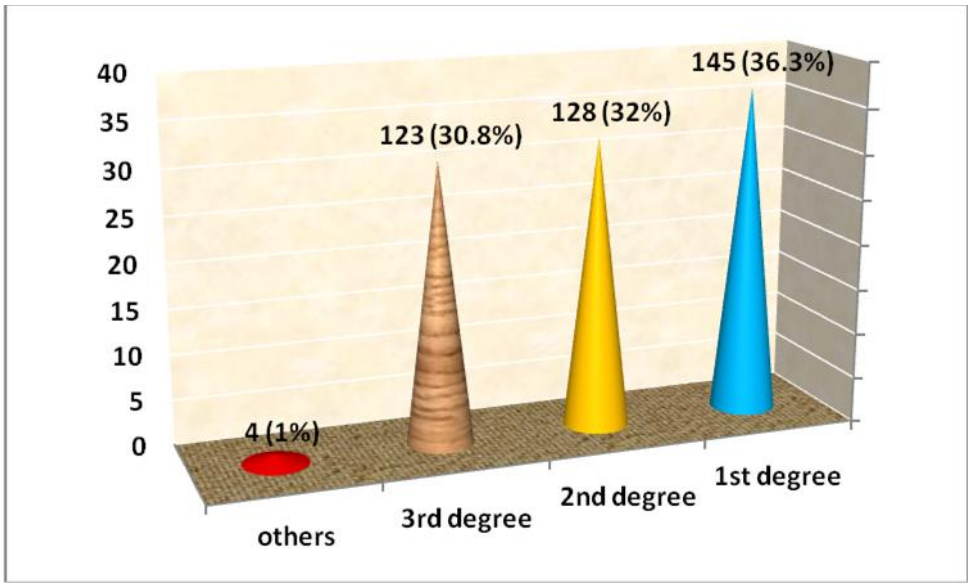


Figure 5: Distribution of studied the close contacts of TB patients according to educational level

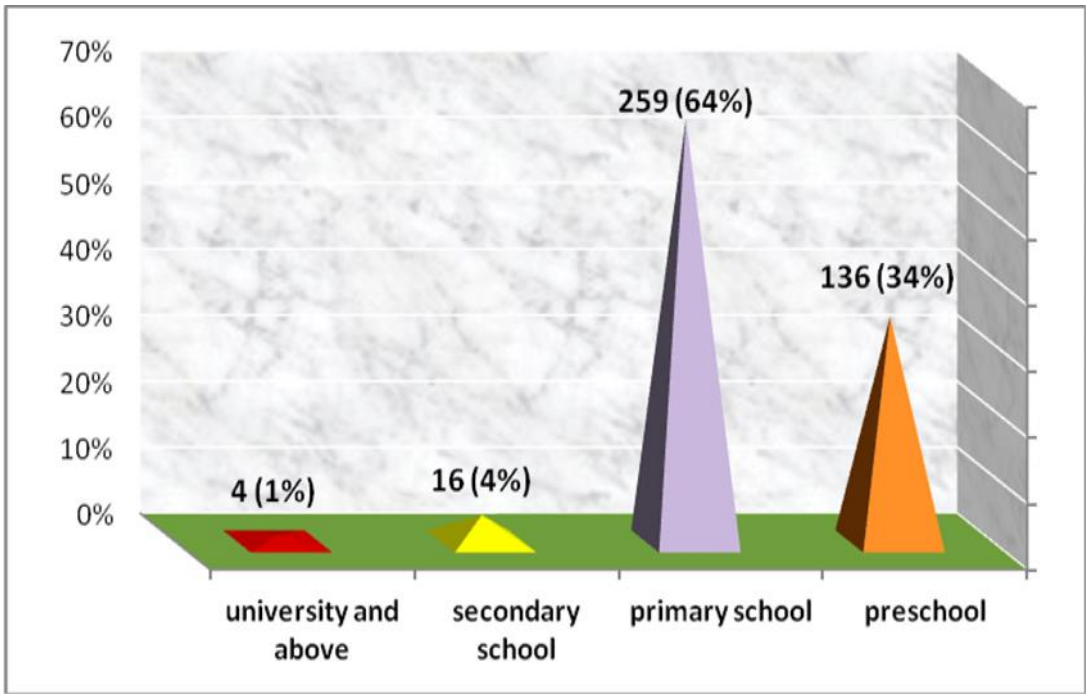


Figure 6: Distribution of studied the close contacts of TB patients according to house condition

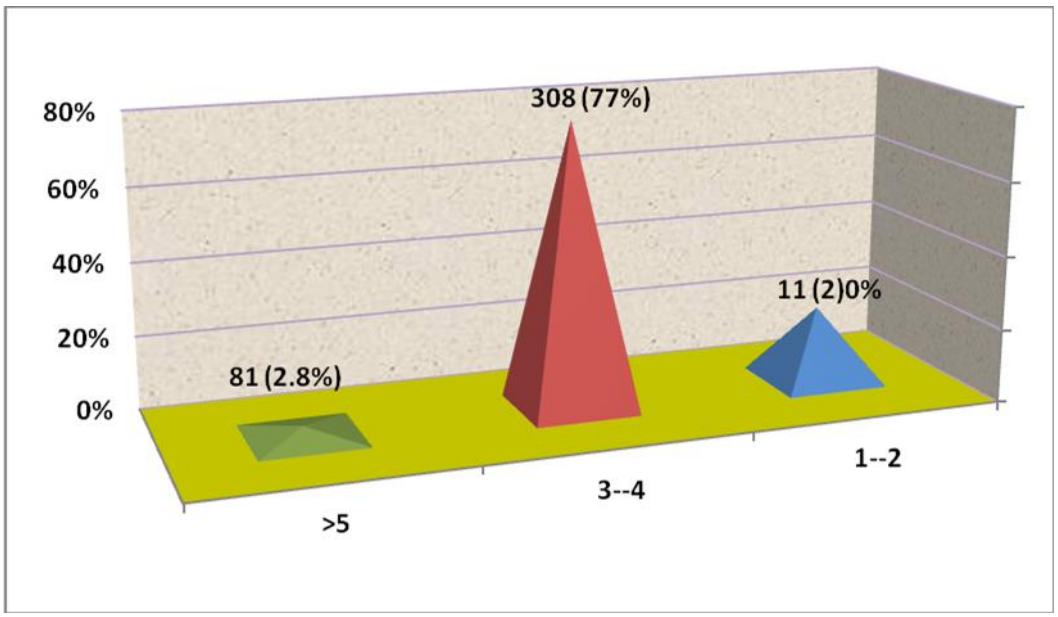


Figure 7: Distribution of studied the close contacts according to the Family income

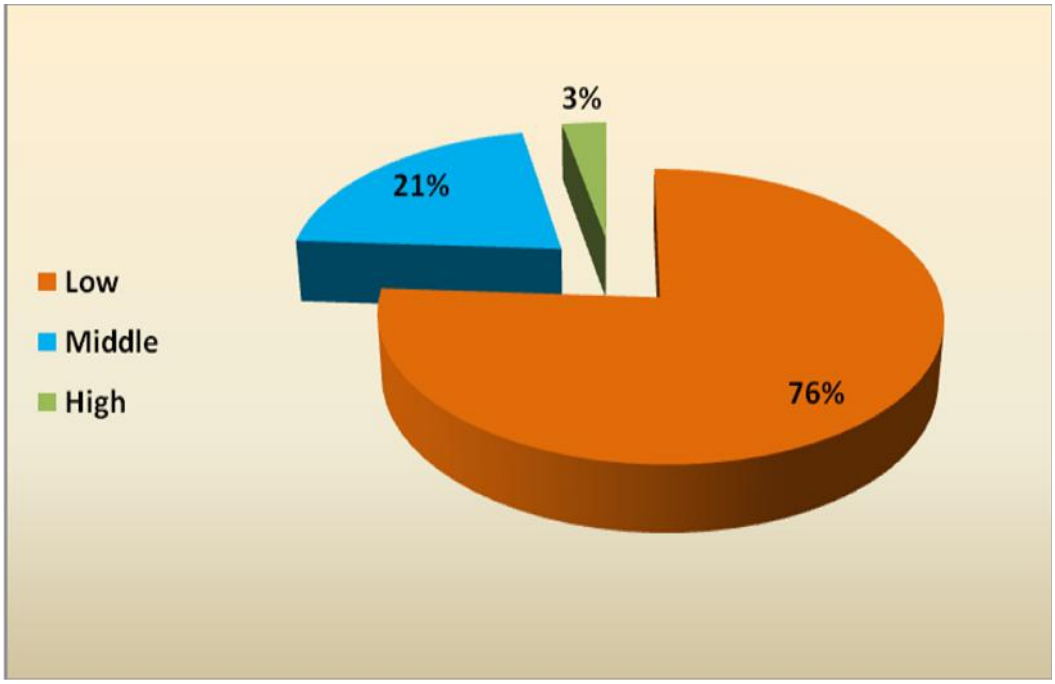


Figure 8 : Distribution of studied the close contacts of TB patients according to results of CXR

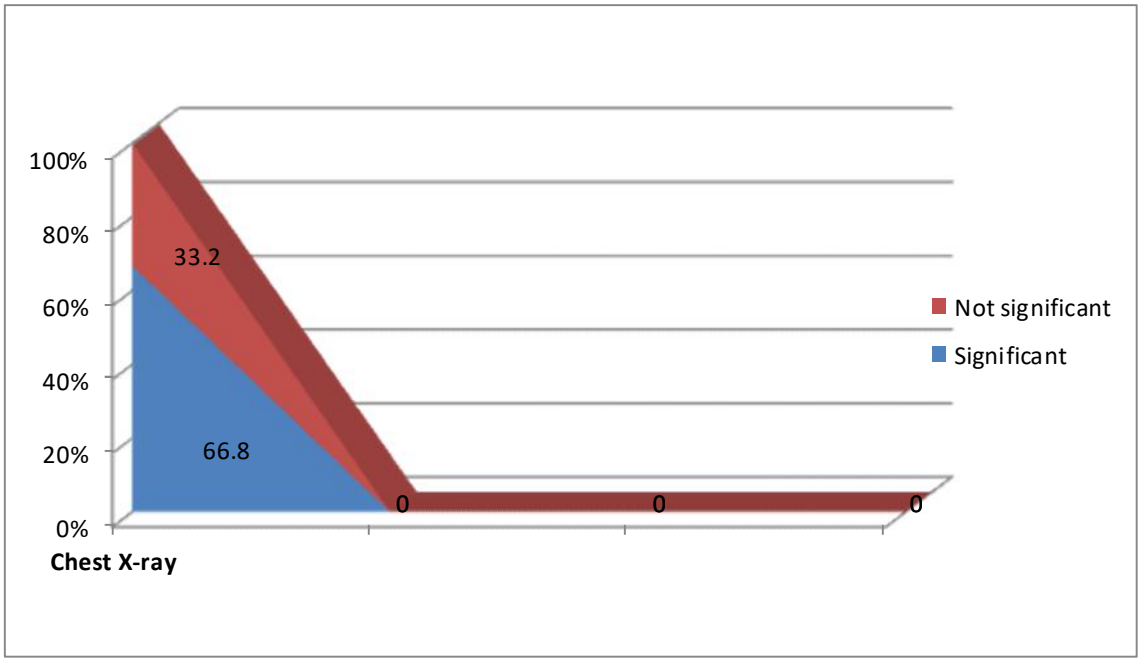


Figure 9 : Distribution of studied the close contacts of TB patients according to results of Acid Fast Bacilli (AFB)

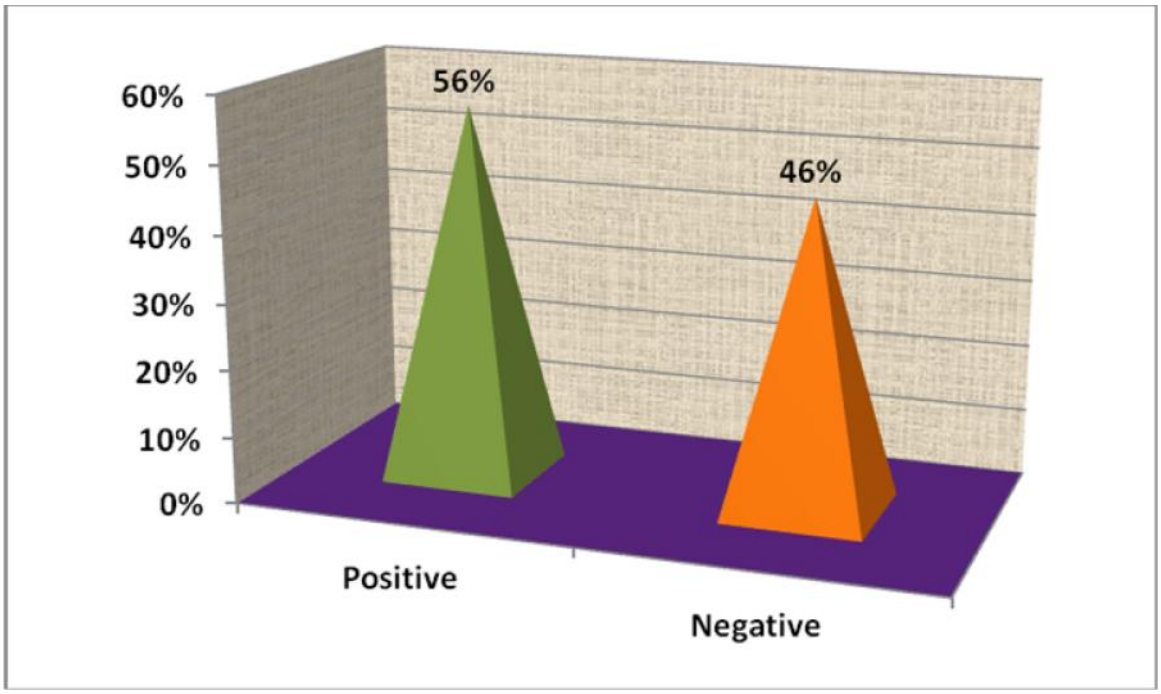
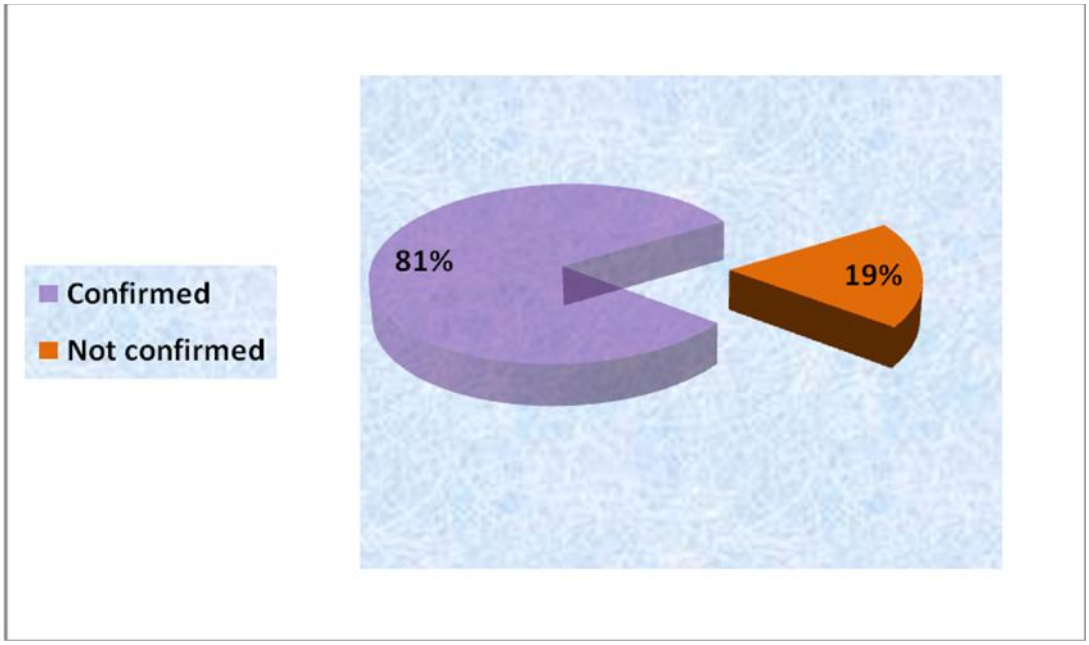


Figure 10: Prevalence of TB among studied the close contacts of TB patients according to confirmed diagnosis of TB



4.1. DISCUSSION

The Contacts of TB patients are at high risk of acquiring TB infection, depending on factors such as sources of infection, type of contact, and environmental characteristics[137]. Therefore, the search for infected subjects among relative of patients and household members with infectious tuberculosis is the best method of preventing later development of disease in populations.

Discussion of close contacts of tuberculosis patient

In this study the age of close contacts of the TB patients, the majority 159 (39.8%) in age group 35-49 years, 388 (97.0%) from rural area, 259 (64.8%) had primary school education. Our results somewhat similar to that found by Mulusew, et al.,[155] they found that the majority of close contact 36 (35%) were in the age group 31-50, most of the study subjects 61(59.2%), 67(55.3%), 53 (51.5%) carne from rural areas, were farmers and illiterates, respectively.

In our study, about half of participants of the close contacts of the TB patients had primary school level ,our finding in agree with that reported in study carried out in Nairobi by Perpetual, et al.[156] they stated that half of the patients 137 (53.3%) had not completed secondary education with only 16 (6.2%) having completed tertiary education.

In this study, the house condition among close contacts of tuberculosis patients showed that 308 (77.0%) had 3-4 persons per room , 81 (20.0%) patients had 1-2 persons per room and 11 (2.8%) patients had >5 persons per room. These compared with previous study Perpetual, et al.[156] findings; who mentioned that about 166 (64.3%) patients were living in single rooms with 110 (42.6%) living with more than two people with a maximum of 10 people in a single room. Only 73 (28.3%) were living alone in a single room and only 7 families (2.7%) were living in houses with five or more rooms.

In our study, the results of investigations showed that: CXR was significant in 267 (66.8%) studied close contacts, AFB was positive in 224 (56.0%) studied close contacts. Our results compared with a study by Kyaw, et al. (2018)[157] on detection of tuberculosis among household contacts of index tuberculosis patients.

The diagnosis among studied close contacts showed that 324 (81.0%) studied close contacts confirmed the diagnosis of TB, while 76 (19.0%) not confirmed TB. These findings compared with that found in the study conducted by Mandal, et al.[158] on which a total number of positive screening episodes for pulmonary TB was 43.1% and non-pulmonary TB was 26.1%. Of these, 78.8% were household contacts and 21.2% were casual contacts.

In conclusion, our study is intervention analyzing data of the effect of screening among close contacts of TB patients that provides important new information on the risk of tuberculosis over time in recent contacts of patients with infectious tuberculosis. Our findings support the important role of contact investigation as a means of identifying and treating new cases of active tuberculosis among contacts, and they underscore the importance of rapid screening and initiation of treatment for TB. These findings have important implications for tuberculosis prevention efforts worldwide, as well as for the design and interpretation of clinical trials of preventive therapeutic regimens.

4.2. CONCLUSION

- Screening among close contacts of tuberculus patients is an essential intervention to identify and reduce the number of infected patients that will progress to active disease and screening and health education are the keys for effective tuberculosis control.
- The screening of close contact of tuberculus patients showed that 81.0% were confirmed diagnosis of tuberculosis.
- More than half of close contact had significant CXR and positive Acid Fast Bacilli.

- Early detection of TB by screening through investigations is a well organized program & essential for effective TB prevention and control.
- Contact tracing in low-prevalence TB countries, for both pulmonary and Extra-pulmonary TB, is an essential intervention to identify and reduce the number of infected patients that will progress to active disease. This is the key for effective TB control.
- Empowering all (TB patients , close contact and communities)

by increasing their knowledge through proper education programmes could effectively contribute to the effort of controlling TB.

4.3. RECOMMENDATIONS

- Appropriate screening among close contacts of TB pt , should be undertaken to control infection program and prevent transmission of TB.
- Subjects in contacts with TB patients in high burden resource could benefit from periodical screening for early detection of TB infection and monitoring the progression to active TB.
- Close Contact screening need to be prompt to detect tuberculosis and maximize the opportunity to identify and treat TB infection, to prevent disease in new cases.
- Future research is needed to identify and test the effectiveness of feasible and affordable environmental control and respiratory protection measures in resource- constrained settings.
- The Stop TB Strategy is a key response for addressing the high global TB prevalence.
- Active case finding is to be streamlined within the national country tuberculosis control program activities.
- Regular home visit are to be conducted to all TB pt & their close contacts to deliver health education messages and to provide psychological and social support.
- Promoting knowledge of tuberculosis in the community and continuous health education to tuberculosis patients and their close contacts.

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