

‘AN EMERGING RESEARCH ON TUBERCULOSIS’

Project report submitted in partial fulfillment for the award of the degree of

BACHELOR OF PHARMACY

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Enrollment no. 1712102046/ Admission no.17SMAS102052]

IN BRANCH OF PHARMACY

SCHOOL OF MEDICAL ALLIED SCIENCE

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MAY-2021



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CERTIFICATE

This is to certify that the project entitled “AN EMERGING REASEACH ON TUBERCULOSIS’ by “MOHD ASAD ADDMISON NO :17SMAS102052” for the award of bachelor of Pharmacy “ degree , comprises of the bonafide research work done by him at Department of Pharmacy , school of medical & allied sciences, Galgotias University, Greater Noida under my guidance and supervision and to my full satisfaction.

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DECLARATION

The project report entitled AN EMERGING REASEACH ON TUBERCULOSIS' is the compilation of work of "MOHD ASAD ADDMISON NO :17SMAS102052" under supervision of Dr. Md. Aftab Alam Assistant Professor Department of Pharmacy, GALGOTIAS UNIVERSITY Greater Noida U.P India. All pictures, Figures and information used in project are taken various sources are true and best of my knowledge.

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ACKNOWLEDGEMENT

Praise to be Almighty God who made me able to carry out the present study successful. I feel highly privileged while starting my dissertation work with acknowledge of the genuine help and support received from others who made this research project possible for me.

I deem it a great pleasure record my heartfelt gratitude to my supervisor for his valuable guidance.

I express my gratitude to my friends and my co workers for their moral support, advice, affection Co-operation, and functional freedom that mad me to set goal and achieved this task. The episode of my acknowledgement would not be complete without mentioning thanks to Dr. P. K Sharma , Dean of our school and Dr. Vijay Singh, H.O.D , Department of pharmacy for sculpting another milestone in my academic journey.

Last but not the least I wish to express my gratitude to my lovely parents for their patience and constant support. They provided me with every opportunity to succeed.

MOHD.ASAD

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Abstract

Tuberculosis (TB) is a common and preventable illness caused by Mycobacterium tuberculosis (MTB) that typically affects the lungs, leading to symptoms such as coughing, fever, and chest pain. In spite of the fact that current research in the past few years has provided important insights into TB transmission, treatment, and prevention, many challenges remain. It is hoped that these findings will help to reduce the frequency of and eventually eliminate TB. The illness significantly impacts overall health, often co-occurring with HIV/AIDS, which increases mortality rates. This review explores the historical context of TB, as well as current research on drug development, pathogenesis, and the immune response. It also discusses the challenges of TB treatment and the need for continued research to improve outcomes and reduce the global burden of this disease.

Introduction

The historical backdrop of TB since 1800s to the current "Simply rest and have nutritive food varieties" was the proposal taken by patients inside the 1800s contaminated with (TB) or recent alluded to as utilization, Partner in Nursing versatile ailment that occasionally influences the lungs bringing about extreme hacking, high fever, and chest torments . This secretive disorder, the Latin-began name portrays the pole type of the Bacillus which enhance higher seen once the German researcher Koch make public known that Mycobacterium tuberculosis caused TB in 1882. This progressive discovery, adjacent to the next revelations of fluid which is in 1890 and thusly the Bacillus-Calmette Guerin (BCG) vaccinium in 1908 moreover antituberculosis drug begin in 1943, offered trust to the decimation of an infection fatal than the plaque. Death rates extensively decreases from the first to middle-twentieth century; be that as it may, financing for investigation dwindled and somewhere in the range of 1970 and 1990, medication and vaccinium advancements eased back . With the beginning of the Guides widespread and safe shear TB rates increased once more, and immediately, premium in TB examination and obstruction. The by this point the symptomatic and therapy devices important to battle the affliction were generally old and methods to manage and hinder the ailment were grown, along with the Straightforwardly found therapy Short-Course (Spots) scheme in 1993, with the expansion of the Dabs in addition to program to manage multidrug safe (MDR) TB in 1998 [1,3]. despite the fact that current investigation inside the previous four years has given significant knowledge into TB transmission, conclusion, and

treatment, a great deal of stays to be found to viably diminish the occurrence of and ultimately annihilate Tuberculosis. The ailment actually puts a pressure on general wellbeing, being exclusively next to HIV/Helps in exacting high deaths. it's been reportable that in 2011 only, there have been concerning eight.7 million new cases and one.4 million passings because of TB, with concerning 2 billion people inactively contaminated [3].

The reason for this audit is to highlight the present writing on clinical claim to fame, pathologic cycle, therapy, and the executives of TB, so as {to higher to raised to higher} see the disorder in order to give better treatment through novel investigation and general wellbeing endeavors.

The study of disease transmission, transmission, symptomatic apparatuses: predominance, transmission component, TST/IGRAs .There are bound danger category that are part of inclined to getting it contaminated including: youthful grown-ups (all the more unexceptionally guys), those in agricultural nations, medical care staff UN office are round the affliction oft, and individuals whose insusceptible frameworks are feeble, as those that have HIV or bad habit to smoke . Indeed, TB is that the main clarification for death in those infect with HIV and HIV-TB concurrent has been wide examined. for sure, nonnative singles and individuals UN office dwell in devastated zones or any place insufficiency illness is winning are a great deal of without a doubt to incite contaminated [2]. The host's have inadequacy in lymphokine (IL)- 12 advancing the T assistant (Th) one

reaction is likewise another consider the expanded powerlessness to contamination [7]. There are various conditions that will cause a dangerous for weakness to MTB contamination like polygenic infection, maturing, semipermanent utilization of corticosteroids, TNF-a blockers, diversification in ergocalciferol receptors, diversification in IL-12 and IFN-g qualities. Be that as it may, these various conditions will not be referenced altogether here.

MTB contamination is noninheritable by inward breath of irresistible vaporized particles liberated from shut contacts [6,8]. A greater part of individuals UN office breathe in MTB mount a decent reaction inside the lungs bringing about undefeated restraint inside the development of MTB, prompting the microorganism transforming into lethargic; this condition is generally seen as idle {tuberculosis |TB |T.B. |infectious sickness} or LTBI immunocompetent inactive individuals are tainted with MTB anyway don't blessing indications and don't send the infection to others [2,6]. it's notable that 1/3rd of the total populace is idly tainted with MTB [6]. From inert disease, the contamination will get to a lively state [5]. concerning 5e10% of LTBI cases are in peril to advancing from disease to dynamic (essential) TB . Those with HIV and distinctive problem individuals, similar to those with disease or by and by taking immunosuppressing prescription have the following danger of creating dynamic TB.

The World Wellbeing Association (WHO) reportable that "33% of the total populace has contaminated with TB. Holding reliable Robert Koch's explanation

that the ailment is fatal than the plague or plague cholera [1,6], concerning 9,000,000 people was tainted with Tuberculosis and concerning one.5 million surrendered to the disorder in 2013 [2]. In 2004, TB was at fault for a couple of.5perc of all passing inside the world. The social unit is generally the area of openness in more-and low-trouble nations, the' contamination rates are higher in zones like clinics or penitentiaries [4]. Predominance of the disorder in such settings relies upon harmfulness, regular insusceptibility, and weakness.

While TB might be blessing in any general public in any of the country, a larger part of these passings reportable, about 95%, happened in low-and center pay nations any place assets are a ton of confined, with a lion's share of cases becoming visible in Asian country and China. Those with infected HIV are most in danger of acquiring tainted with TB, and concerning 80th of HIV contaminated people with TB snooze Dark Africa [4,8]. In differentiation, in low-trouble nations very much like the u. s., exclusively 100% of public with TB are contaminated with HIV in 2008 just 12, 904 TB cases was reportable with the rate being four.2 per 100,000. while symptomatic progressions are made inside the previous four years, 80th of TB cases overall are engaged in 22 nations [1] 27 nations along with Asian nation, China, and Russia, are at fault for concerning eighty fifth of MDR TB cases . Regrettably , more current data isn't there on account of the maximum of world police examination and inclusion frameworks [8]. for sure, there still remaining parts a deficient seeing anyway one individual

will secure the ailment while another doesn't, the' they're presented to a comparable danger factors, or an approach to higher affirm dormant to dynamic TB movement . Since a larger part of public with TB have idle disease [6], the occasion of late demonstrative and hide devices and principles has gotten essential to manage the ailment. Interferon-gamma unharness examines (IGRAs) are acclimated analyze LTBI, however the fluid investigate symptomatic test indicative assay} (TST) actually stays the principal savvy test.

The TST and IGRA work by mensuration the reaction of Immune system microorganisms to TB antigens

4.1 TST

In the antiquated TST, fluid refined macromolecule side project (PPD) combination of proteins from TB are intradermally infused into somebody, exacting a sort IV postponed touchiness skin response, if the singles either prior presented to mycobacterial proteins blessing inside the vaccinium or lastly presented to the mycobacteria disease. to check whether the individual is contaminated with Tuberculosis the elements to the skin response is estimated; normal spot the equivalent old} is between 48 and 72 h and a cut-off from zero.74 at five millimeter to zero.40 at fifteen millimeter. Notwithstanding, the TST is thought to manual for bogus positive reactions in those that are BCG vaccinated and the bogus contrary reactions in immunological confusion singles.

4.2 IGRAs

The IGRAs are part of touchy and the explicit (81e88% contrasted with 70th affectability for the TST) however, they're high-ticket and specialized. They notice the free of protein IFN-g from White blood cells that respond to antigens that are not found inside the BCG vaccinium . A blood test is taked from a private and along these lines the unharness of IFN-g is estimated. pointers ceaselessly swap for IGRA use. In North American country and in some parts of European nations, it's even been encouraged that IGRAs and hence the TST be utilized along to analyze LTBI, anyway these tests aren't complete.

[Generally speaking, having an improved comprehension of anyway the ailment creates in singles from a dormant to dynamic TB by trademark hazard factors identified with more-and low-trouble nations can work with bring about the occasion of higher symptomatic apparatuses and can improve our comprehension of the reaction in TB. Pathologic cycle and invulnerable reaction: the communications among MTB and consequently the host cell . depict the underlying battle of tuberculosis once it attacks the host exploitation the statement: "Everything is set the essential day, that gets the very longest day". When the microbes M. Tuberculosis is indrawn by means of beads unfurl through individual to-individual contact, macrophages will phagocytose and murder the bacilli. Nonetheless, if the bacilli aren't slaughtered, all through that underlying association, they will multiply inside nerve fiber cells and the alveolar macrophages at a quick rate, sign the gathering of IL-1-a, IL-1b, and distinctive

host unfortunate cytokines. This reaction is intercede by design acknowledgment receptors (PRRs) [7,11] communicated by macrophages and nerve fiber cells that acknowledge microorganism related atomic examples (PAMPS) communicated on MTB [11]. Cost like receptors work with take-up MTB, that incites Associate in Nursing intracellular sign course to give the cytokines. Notwithstanding, medicament cytokines work with the disease by restricting host cell unfortunate reactions. all through the underlying intrinsic reaction, MTB multiplies inside the host cell, causing demise by means of the harmfulness issue ESX1 sort VII emission framework, on its own terms and whenever it's pre-arranged, postponing the accommodating reaction [7,12]. In doing subsequently, TB might be an unmistakable affliction in this a perceptible cell reaction happens once a far longer time-about 2e12 weeks once disease [4,6]. nerve fiber cells carry mycobacteria to the mediastinal lymphatic tissue (MLN), any place antigen-introducing cells (APCs) actuate T cells [13]. Bacilli are stacked onto significant natural marvel convoluted (MHC) class II, preparing Th one IFN-g-emitting antigen explicit T cells that transition to the respiratory organ. With the actuation of the accommodating reaction, every effector CD4p and CD8p T-cells are iatrogenic MTB will gather transformations all through this point [7] and cytokines are much of the time made, as IFN-g Mycobacteria will adjustment the outflow of their qualities and consequently their antigens to avoid T-cell acknowledgment [7]. when the ceaseless creation of cytokines T cells limit the nature macrophages and actuate them for expanded perform [13]. a sort one

"invulnerable granuloma", made out of macrophages, neutrophils and monocytes, nerve fiber cells and T cells, is then molded inside the respiratory organ which may the board MTB development, as certain investigations have appeared, the it's right now felt that MTB will commandeer the tumor for its own benefit. MTB change the reaction of the tumor through IL-10, that attempts to smother the actuation of T cells and macrophages. inquisitively, knockout concentrates in IL10 show a little decrease in microorganism load, proposing that through advancement, MTB may use numerous pathways for its benefit. A "ongoing granuloma", that to boot comprises of frothy and macrophages and a fibrotic epitome, can result, bringing about morphological and valuable adjustments of these modifications are incredibly powerful and might shift among individuals and surprisingly inside a private, the it's muddled whether these changes ar intervene by host or by microorganism. there's a deferral between MTB contamination and T lymphocyte reaction . Up till this stage, TB is stifled to Associate in Nursing dormant, or inert sort, any place contaminated individuals don't blessing with manifestations and can't send the disorder [6,7]. inside the instance of LTBI, as referenced, mycobacterial development is controlled (however microorganism replication will happen) by accommodating insusceptibility before the affliction will create [4], by containing MTB inside granulomas [6,11,13] or by gas (NO) in mice or antimicrobial peptides in people [14]. Inactively tainted people show restored granulomas, "set apart by focal calcification related to fibrotic embodiment. Embodiment may stop

microorganism getaway or cutoff safe interruption, anyway this is regularly muddled [13]. Be that as it may, at some reason, even once a couple of long stretches of inertness, exogenous components [14], very much like the emitted macromolecule looking like revival advancing issue (Rpf), might be initiated, any place microorganism are returned from a stifled state to a lively state and may continue natural interaction [7,12].

Rpf cistron cancellations can be a component inside the movement from idleness to reactivation . for sure, poison antidote (TA) cistron sets, or incorporation upkeep factors encoded by MTB play an errand in choosing the change from idleness by assembling a toxic substance that gets killed by immune response that is then corrupted; the noxious substance will at that point murder the cell . Albeit, the guideline among inert and dynamic TB and subsequently the genuine condition of the microorganisms all through inertness stays to be more examined . it's at the adaptative invulnerable stage that Tuberculosis will clinically show in different manners by which, when it changes from a dormant to dynamic state; clinical sign relies upon any place mycobacteria multiply [4,6,14]. Expansion will happen inside the spine, hips, and subsequently the GI parcel, anyway by and large, multiplication occurs inside the lung; concerning eighty fifth of TB patients blessing with respiratory organ manifestations [6].

Treatment and antibodies

Antituberculosis prescription, BCG vaccinium, and medication obstruction The course of Tuberculosis treatment relies upon whether the singles is inside the inactive or dynamic stage on their possibility of hazard. In the event that an singles has as of late obtain contact with partner degree tainted individual and a TST is negative, LTBI treatment are regularly begun and proceeded if the TST result's positive once a 12-week window HIV patients ordinarily proceed with therapy the TST result can be negative N. Fogel/irresistible sickness 95 (2015) 527e531 529 [6]. Therapy of TB commonly includes a profoundly dynamic antiretroviral treatment, or a mix of numerous prescription, with partner degree concentrated starting 2-month segment by a more slow 4-to half year continuation area [4]. the most medicine used in the treatment of TB are: antibacterial medication (INH). looking on the remaining of the uncovered singles, the program changes and may be convoluted to follow. A medication program graph made by the Center for unwellness the board and obstruction (CDC) diagrams the spans and dosages for drug therapy all through explicit stages. if the MTB disengage is totally disposed, and PZA are frequently suspended once 2 months of treatment. antibacterial medication and RIF square measure proceeded for a very long time. Treatment will last from six to 9 months [6,8] or possibly as long as twenty months [6]. furthermore to the 5 fundamental antituberculosis prescription, the eubacteria bovis BCG vaccinium is that the current vaccinium acclimated emulate the regular insusceptible response to contamination [16]. despite the fact that the BCG vaccinium has been wide

controlled for more than eighty years and intensely incites Th one cells, its effectivity is incredibly factor, in accordance with a new survey by essayist [16]. it's exclusively confined insurance in grown-ups with respiratory . the necessity for a vastly improved vaccinium is clear; at the same time, limits in our information of that parts of BCG invulnerability square measure fundamental for long assurance against MTB stop in endeavors. In the course of recent years there been a competition to foster a vastly improved vaccinium. For what reason is there a particularly extravagant program including various prescription to treat Tuberculosis the arrangement exists in the fast unconstrained change pace of MTB . in spite of the fact that medication status tests square measure never-endingly performed to watch opposition, and inappropriate or lacking regimens will give drug obstruction . in accordance with the fourth world Drug police work Project directed from 2002 to 2007 in the UN office [2], concerning Revolutionary Organization 17 November of most recent obstruction cases had protection from at least one drug and concerning a couple of.9prcent had multi-drug opposition (MDR), or protection from at least antibacterial medication and RIF. antibacterial medication obstruction is that the most common kind [6]. An UN office report in 2009 measurable concerning three.3prcent of TB cases were MDR. Medication opposition keeps on making a huge wellbeing concern. In certain spaces, similar to Asian country, it totally was reportable in 2007 that fifty six.3% of most recent bodies of evidence were confirmation against any medication and twenty two.3% were MDR [8]. Yearly mortality was measurable

in 2009 to be 100 fifty,000 overall . As of late, broad medication obstruction (XDR), or MDR and protection from secondline medicine, has become an overall worry, with concerning unadulterated gold of XDR cases among MDR case in Russia in 2006 , and representing concerning 9/11 of MDR cases inside the world in 2013 [2].

Management of TB

Accomplishments, Spots, Stop Tuberculosis System accidentally, the UN organization reports says that a few nations have kept on possessing significant decreases in TB cases [2]; in Asian country at the TB predominance fell by concerning five hundredth. in light of demonstrative and treatment endeavors, concerning 37 million lives were saved somewhere in the range of 2000 and 2013. [2]. Nonetheless, the insufficiency of the BCG vaccinium, bogus positive screening tests, resistance to therapy , the intricacy of MTB and the consequently the slow down in creating novel clinical strength. In certain nations, similar to India, China, and Russia, TB rates square measure exclusively dropping gradually and still stay high [2]. to deal with this worry, a further therapy program is gone through by patients alluded to as straightforwardly found out clinical consideration short-run Dabs, Dabs in addition to was started as an extra thorough treatment procedure [1,4]. The UN office composed a Stop Tuberculosis Procedure [2], that diagrams six means to be share by all nations to downsize TB

on every local and public scales, determined to upgrade TB treatment, medical care encounters, and examination. it's the world's expectation that at least some of these points are accomplished inside the near future.

Summary and conclusion

Any place square measure we tend to and any place will we should go?

Understanding Tuberculosis has advanced from the suggestion inside the 1800s to "simply rest and eat feeding food varieties" . IGRAs will higher analyze LTBI than TST and subsequently the catarrhine model will give understanding into HIV co-contamination since it intently takes after human Tuberculosis.

Notwithstanding, an extra complete comprehension of idle improvement and of the securing and obsessive resistant reactions and cooperations in TB square measure enormously required in order to foster adequate prescription and imunizations [6,16]. probably action an individual's transcriptional mark may give an extra tweaked perception of the unwellness. this may work with downsize the amount of MDR cases and can be a greatly improved diverse to Specks clinical consideration . it's extraordinary that this unwellness has show a danger to general wellbeing since the 1800 regardless remedial headways are vain and moderate. during this competition to battle an unwellness that knows about no limits, it's important to claim a theoretical and clear comprehension of TB by and large. this may exclusively be executed if agreeable endeavors

among investigation, general wellbeing officials, clinical guide experts, and accordingly the overall population actually push the limits of our present information, relieving the world weight of TB.

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