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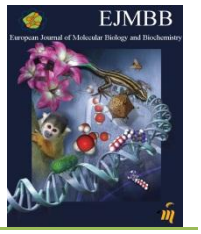

PATHOGENESIS AND EFFECT OF BCG VACCINATION AGAINST MYCO BACTERIUM TUBERCULOSIS IN ABDOMEN

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ABSTRACT

Tuberculosis (TB), one of the oldest known human diseases. It still is one of the major causes of mortality, since two million people die each year from this. TB has many manifestations, affecting bone, the central nervous system, and many other organ systems, but it is primarily a pulmonary disease that is initiated by the deposition of *Mycobacterium tuberculosis*, contained in aerosol droplets, onto lung alveolar surfaces. From this point, the progression of the disease can have several outcomes, determined largely by the response of the host immune system. The efficacy of this response is affected by intrinsic factors such as the genetics of the immune system as well as extrinsic factors. In addition, the pathogen may play a role in disease progression since some M. tuberculosis strains are reportedly more virulent than others, as defined by increased transmissibility as well as being associated with higher morbidity and mortality in infected individuals. Despite the widespread use of an attenuated live vaccine and several antibiotics, there is more TB than ever before, requiring new vaccines and drugs and more specific and rapid diagnostics.

INTRODUCTION

Tuberculosis (TB), one of the oldest recorded human afflictions, is still one of the biggest killers among the infectious diseases, despite the worldwide use of a live attenuated vaccine and several antibiotics. New vaccines and drugs are needed to stem the worldwide epidemic of TB that kills two million people each year. To rationally develop new anti tubercular agents, it is essential to study the genetics and physiology of *M. tuberculosis* and related mycobacteria. It is equally important to understand the *M. tuberculosis*-host interaction to learn how these bacteria circumvent host defenses and cause disease. The approaches described in this review identify *M. tuberculosis* genes that are or are potentially involved in virulence. In the future, some of these genes and the proteins they encode, as well as newly discovered ones, should provide new bacterial targets that can be used for creating vaccines and drugs as well as more selective diagnostic reagents [1].

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EPIDEMIOLOGY :- In 2011, there were 8.7 million new cases of active tuberculosis worldwide 13%of which involved co infection with the human immunodeficiency virus [HIV] and 1.4 million deaths, including 430,000 deaths among HIV-infected patients representing a slight decrease from peak numbers in the mid-2000s.It has been estimated that there were 310,000 incident cases of multidrug-resistant tuberculosis, caused by organisms resistant to at least isoniazid and rifampin, among patients who were reported to have tuberculosis in 2011.More than 60% of these patients were in China, India, the Russian Federation, Pakistan, and South Africa. A total of 84 countries have reported cases of extensively drug-resistant tuberculosis, a subset of multidrug-resistant tuberculosis with added resistance to all fluoroquinolones plus any of the three injectable antituberculosis drugs, kanamycin, amikacin and capreomycin [2].

CLINICAL MANIFESTATIONS -: Pulmonary TB has been variously described as consumption and phthisis, both terms indicating the severe wasting and the coughing of blood associated with later stages of the disease. Pott's disease or spinal tuberculosis, marked by spinal deformity

and other bone defects, was named after an 18th-century English physician, but Hippocrates thought there was a great similarity between this bone disease and pulmonary tuberculosis and possibly a common origin. Scrofula, or cervical lymphadenitis, was a common disease in the middle ages that presented with swelling of lymph nodes in the neck. It was also called "The King's Evil" because of the myth that it could be cured by the touch of a reigning monarch. Villemin (mentioned above) showed in the 1860s that scrofula and pulmonary TB had an identical cause. Tuberculosis also can develop in the central nervous system, in which case meningitis is the predominant form of the disease, and also in the urogenital tract, the digestive system, and cutaneously in the form named lupus vulgaris. The incidence of these various extrapulmonary forms of tuberculosis varies from country to country, such that on the average between 1964 and 1989, 20% of the 20,000 new cases of TB in the United States were extrapulmonary while 5 to 10% of the approximately seven million new cases each year in the developing countries were extrapulmonary [3].

METABOLIC PATHWAYS: From the genome sequence, it is clear that the tubercle bacillus has the potential to synthesize all the essential amino acids, vitamins and enzyme co-factors, although some of the pathways involved may differ from those found in other bacteria. M. tuberculosis can metabolize a variety of carbohydrates, hydrocarbons, alcohols, ketones and carboxylic acids [4-5]. It is apparent from genome inspection that, in addition to many functions involved in lipid metabolism, the enzymes necessary for glycolysis, the pentose phosphate pathway, and the tricarboxylic acid and glyoxylate cycles are all present. A large number (~200) of oxidoreductases, oxygenases and dehydrogenases is predicted, as well as many oxygenases containing cytochrome P450, that are similar to fungal proteins involved in sterol degradation. Under aerobic growth conditions, ATP will be generated by oxidative phosphorylation from electron transport chains involving a ubiquinone cytochrome b reductase complex and cytochrome c oxidase. Components of several anaerobic phosphorylative electron transport chains are also present, including genes for nitrate reductase (narGHJI), fumarate reductase (frdABCD) and possibly nitrite reductase (nirBD), as well as a new reductase (narX) that results from a rearrangement of a homologue of the narGHJI operon. Two genes encoding haemoglobin-like proteins, which may protect against oxidative stress or be involved in oxygen capture, were found. The ability of the bacillus to adapt its metabolism to environmental change is significant as it not only has to compete with the lung for oxygen but must also adapt to the microaerophilic /anaerobic environment at the heart of the burgeoning Granuloma.

REGULATION AND SIGNAL TRANSDUCTION: Given the complexity of the environmental and metabolic choices facing M. tuberculosis, an extensive regulatory repertoire was expected. Thirteen putative sigma factors govern gene expression at the level of transcription initiation, and more than 100 regulatory proteins are predicted. Unlike B. subtilis and E. coli, in which there are >30 copies of different two-component regulatory systems [6]. M. tuberculosis has only 11 complete pairs of sensor histidine kinases and response regulators, and a few isolated kinase and regulatory genes. This relative paucity in environmental signal transduction pathways is probably offset by the presence of a family of eukaryotic-like serine/threonine protein kinases (STPKs), which function as part of a phosphorelay system [7]. The STPKs probably have two domains: the well-conserved kinase domain at the amino terminus is predicted to be connected by a transmembrane segment to the carboxy-terminal region that may respond to specific stimuli. Several of the predicted envelope lipoproteins, such as that encoded by lppR (Rv2403), show extensive similarity to this putative receptor domain of STPKs, suggesting possible interplay. The STPKs probably function in signal transduction pathways and may govern important cellular decisions such as dormancy and cell division, and although their partners are unknown, candidate genes for phosphoprotein phosphatases have been identified.

DRUG RESISTANCE

M. tuberculosis is naturally resistant to many antibiotics, making treatment difficult [8]. This resistance is due mainly to the highly hydrophobic cell envelope acting as a permeability barrier [9], but many potential resistance determinants are also encoded in the genome. These include hydrolytic or drug-modifying enzymes such as β-lactamases and aminoglycoside acetyl transferases, and many potential drug–efflux systems, such as members of the major facilitator family and numerous ABC transporters. Knowledge of these putative resistance mechanisms will promote better use of existing drugs and facilitate the conception of new therapies.

BCG AND NEW VACCINE

M. bovis bacilli Calmette–Guérin (BCG) vaccine continues to be administered in infants at birth in most regions where tuberculosis is endemic. On the basis of a meta-analysis of controlled clinical trials, the vaccine has an estimated overall efficacy of approximately 50% for the prevention of tuberculosis [10]. Since the BCG vaccine can cause fatal disseminated infection in immunosuppressed patients, it should not be administered in HIV-infected newborns. Although the BCG vaccine has never been routinely used in the United States, it is increasingly being considered for use in tuberculin-negative adults who are planning to travel to areas with a high prevalence of

multidrug- resistant tuberculosis in order to provide medical care.Through a major international effort, a range of vaccines, both as primary immune gens to replace BCG and as boosters for BCG, are being studied, with more than 30 vaccines in development. Twelve vaccines have entered clinical trials [11]. A polyantigenic inactivated whole-cell vaccine showed 39% efficacy in a phase 3 trial for the prevention of tuberculosis among HIV-infected adults who had received previous BCG immunization [12].

MATERAL AND METHODS

The present study "Pathogenesis and Effect of BCG Vaccination against Mycobacterium Tuberculosis In Abdomen" was carried out in patients of tuberculosis at dept. Environmental biology of APS university Rewa (M.P).

Criteria for selection were Follows.

1-Patients who presented with chronic abdominal symptoms e.g pain in abdomen, fever, anorexia and bowel symptoms etc.

2- Patients in whom extra abdominal tuberculosis was present along with abdominal symptoms and sings.

3- Known cases of abdominal tuberculosis not responding well to chemotherapy. Who were explored in a planned manner.

METHODS: Patients with acute problem were initially resuscitated with 4 fluid, analgesic and antibiotic. Patients fulfilling criteria for selection were subjected to extensive bio-chemical, pathological and radiological examination. Both prior to and after surgical intervention. Their detailed history of illness together with symptoms and sings were analyzed and patients were grouped in acute, sub -acute and chronic as well as obstructive and non-obstructive groups. Criteria for grouping were as follows.

(A)-Acute

1-Perforation

2-Acute intestinal obstruction.

(B) –Sub Acute

1-Sub Acute intestinal obstruction.

(C) –Chronic

(1) Encysted peritonitis or ascetic.

(2) Lump in Abdomen.

Following were the investigation done to decide the progress in the line of treatment.

(1) Hematological investigation include: Hb levels, total and differential Leukocyte Count.

Erythrocyte Sedimentation Rate, Blood Sugar, Urea, grouping as pre-operative measures.

(2) Sputum for Acid Fast Bacilli: Obtained Smear was prepared and stained with zeihl neelson and examined for presence of acid fast bacilli at DOTS clinic.

(3) Ultra Sound of Abdomen:- To detect the Ascites, Lymphadenopathy, bowel wall thickening etc.

(4) X-Ray Abdomen-: X-Ray Abdomen was taken after suitable preparation in standing position.

OBSERVATION

The present study of "Pathogenesis and Effect of BCG Vaccination against Mycobacterium Tuberculosis In Abdomen" was carried out in 65 patients at A..P.S University Rewa (M.P). During the period of 10th October 2014 to 30thSeptember 2015. Following observation were made.

It is evident from above table-1 that the 65 patients were admitted and 4.18 % of total abdominal cases were reported.

It is evident from the above table-2 that maximum incidence of disease is seen in 16 to50 years age group.

It is evident from the above table-3 that in majority of the patients had one or other constitutional symptoms of tuberculosis like Fever, Sweat and Weight Loss. It is evident from the above table-4 that majority of chronic group (54.68%).

Following graph-1 shows that majority of patient's belonged to the lower economic status (81.25%).

Table 1. Distribution of Cases According to Incidence of Tuberculosis

S.No	Duration	Total Admission	Total Abd.Cases	%	Total Abd.T.B Cases	Percentage (%)
1	Oct. 2014 to Sep. 2015	6439	1552	24.10	65	4.18 (1.09)

Table 2. Distribution of Cases According to Age Incidence

Age Group (In years)	Male		Female		Total	
	NO	%	NO	%	NO	%
O -15	03	7.14	42	17.39	07	10.76
16-50	33	78.14	12	52.17	45	69.23
51-60	04	9.52	02	8.69	06	9.23
'>6O	02	4.76	05	21.23	07	10.76
Total	42	100.00	23	100.00	65	100.00

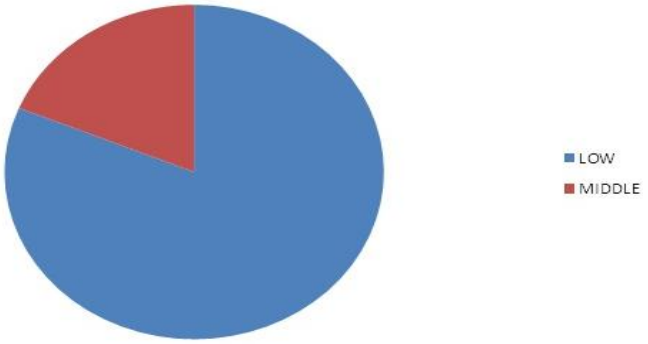
Table 3. Distribution of Cases Constitutional Symptoms like Fever, Sweat, Weight Loss

Constitutional Symptoms	No. of Cases	Percentage (%)
Present	49	76.56%
Absent	16	23.43 %
Total	65	100.00

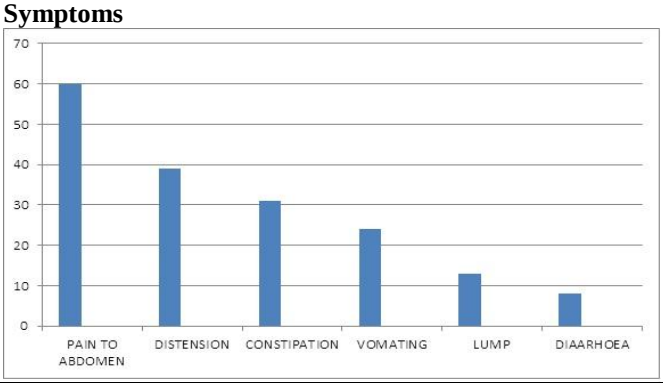
Table 4. Distribution of Cases According to the Type of Presentation

Types of Presentation	No. of Cases	Percentage (%)
Chronic	35	54.68%
Acute or chronic	17	26.56%
Acute	13	18.75%
Total	65	100.00

Graph 1. Distribution of Cases According to Socioeconomic Status



Graph 2. Distribution of Cases According to Presenting Symptoms



RESULTS AND DISCUSSION

The present study "Pathogenesis and Effect of BCG Vaccination against Mycobacterium Tuberculosis In Abdomen" was carried out in 65 patients in A.P.S University, Rewa (M.P). The cases were selected and subjected to extensive clinical biochemical, pathological and Radiological examination prior to and after surgical interventions according to Acute, Acute on chronic and chronic sub type. From the present study following conclusion were drawn. The incidence of abdominal tuberculosis was 1.09% of total hospital admission and 4.18 % of common abdominal cases. Maximum incidence of abdominal Tuberculosis was seen in the age group of 16-50 years age group (69.23%) comprising of 78.14% of total male cases and 52.17% of total female cases.

People of low socioeconomic status (81.25%) and belonging to rural area were more commonly affected. About 55 % Patients presented with symptoms of either acute or sub-acute intestinal obstruction. Constitutional Symptoms like Fever, night sweat and weight loss was present in about 76% of cases. Majority of patients had chronic presentation (54.68%) of more than two month duration. Pain in abdomen was the most common presenting Symptoms (93.75%) followed by abdominal distension (60.93%) and constipation (48.43%).

CONCLUSION

Tuberculosis continues to be a major public health problem in the developing countries of the world like India. Despite tremendous Scientific, socioeconomic and technical advance. This can be attributed to widely prevalent Malnutrition, Poverty and illiteracy in our country. Therefore, identifying infected individuals most likely to progress to disease and treating such subclinical infections to prevent future disease provides a crucial opportunity to interrupt tuberculosis transmission and reduce the global burden of tuberculosis disease. Programmes focusing on single strategies rather than comprehensive programmes that deliver an integrated arsenal for tuberculosis control might continue to struggle. Tuberculosis preventive therapy is a poorly used method that is essential for controlling the reservoirs of disease that drive the epidemic. Comprehensive control strategies that combine preventive therapy for the most high-risk populations and communities with improved case-finding and treatment, control of transmission, and health systems strengthening could ultimately lead to worldwide tuberculosis elimination.

CONFLICT OF INTEREST:

The authors declare that they have no conflict of interest.

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