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The Spectrum of Tuberculosis in BCG-Vaccinated and Unvaccinated Children

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Abstract---Introduction: Tuberculosis remains a very important communicable disease in many parts of the world and a major health problem in developing countries. The international controversy surrounding the use and effectiveness of the Bacillus Calmette-Guérin vaccine. The aim the study is to evaluate the spectrum of tuberculosis among Bacillus Calmette-Guérin vaccinated and non-vaccinated children's. Method: A retrospective study depending on data from flow sheet of each patient which include: age, sex, weight, residence, date of diagnosis, Bacillus Calmette-Guérin vaccination status ,the presence of scar or not, intra or extra familial contact, pattern of disease (pulmonary or extra pulmonary), investigations and associated risk factors. Results: 74 (46.8%) patients were males and 84 (53.2%) were females, they were divided into 2 groups: - group 1 those equal or less than 5 years old who 70 (44.3%) patients, and group 2 those more than 5 year old who 88 (55.7%) patients. The BCG vaccinated patients were 124 (78.5%),9 (7.3%) of them were not developed scar. Distribution of total 158 of TB patients according to the years as following: in 2007 were 46 (29.1%) patients, in 2008 were 51 (32.3%) patients, and in 2009 were 61 (38.6%) patients. 60 (38%) patients, Hashimiyah 43 (27.2%) patients, Mahaweel 31 (19.6) patients andMussayab were 24 (15.2%) patients. Most common site of TB were lungs 104 (65.8%) patients, then lymph nodes 23 (14.6%) patients, pleura 14 (8.9%) patients, meninges 9 (5.7%) patients, bone 6 (3.8%) patients, skin 1 (0.6%) patient, and finally pericardium 1 (0.6%) patient. Only 16(10.1%) of patients with positive sputum for acid-fast bacilli. Patients with positive family history of tuberculosis were

111(70.3%), 66.5% were living in rural area, 124 (78.5%) patients from crowded families and 90 (57%) of them from low social class. Conclusion: All types of TB occur in BCG vaccinated and non-vaccinated children, and there are many risk factors that play a role in patient's diagnosis with TB and start treatment..

Keywords---Spectrum, Tuberculosis, BCG-vaccinated, Unvaccinated Children.

Introduction

Scientists know it as an infection caused by *M. tuberculosis*. In 1882, the microbiologist Robert Koch discovered the tubercle bacillus, at a time when one of every seven deaths in Europe was caused by TB ⁽¹⁾. During the last decade of the 20th century, the number of new cases of tuberculosis increased worldwide. A 95% of tuberculosis cases occur in developing countries where HIV/AIDS epidemics ⁽²⁾. The World Health Organization (WHO) estimates that >8 million new cases of tuberculosis occur and approximately 3 million people die of the disease worldwide each year. Almost 1.3 million cases and 450,000 deaths occur in children each year ^(3, 4). There are 5 closely related mycobacteria in the *M. tuberculosis* complex: *M. tuberculosis*, *M. bovis*, *M. africanum*, *M. microti*, and *M. canettii* ⁽⁴⁾. Transmission of *M. tuberculosis* is person to person, usually by airborne mucus droplet nuclei. The chance of transmission increases when the patient has an acid-fast smear of sputum, upper lobe infiltrate or cavity, copious production of thin sputum, and severe and forceful cough. Environmental factors, especially poor air circulation, enhance transmission ⁽⁵⁾. The lung is the portal of entry in >98% of cases. The tissue reaction in the lung parenchyma and lymph nodes intensifies over the next (2–12 weeks) as the organisms grow in number and tissue hypersensitivity develops. The parenchymal portion of the primary complex (Ghon complex) often heals completely by fibrosis or calcification after undergoing caseous necrosis and encapsulation ⁽⁶⁾. Tuberculosis control programs involve case finding and treatment, which interrupts secondary transmission of infection from close contacts ⁽⁷⁾. Bacille Calmette-Guérin (BCG) vaccine is a live strain of *Mycobacterium bovis* developed by Calmette and Guérin for use as an attenuated vaccine to prevent tuberculosis and other mycobacterial infections. The vaccine was first administered to humans in 1921 and remains the only vaccine against tuberculosis in general use, named for the 2 French investigators responsible for its development and used after World War II ⁽⁷⁾. The route of administration and dosing schedule for the BCG vaccines are important variables for efficacy. The preferred route of administration is intradermal injection with a syringe and needle because it is the only method that permits accurate measurement of an individual dose. Local ulceration and regional suppurative adenitis occur in 0.1–1% of vaccine recipients. Local lesions do not suggest underlying host immune defects and do not affect the level of protection afforded by the vaccine ⁽⁴⁾. The official recommendation of the WHO is a single dose administered during infancy, including in asymptomatic HIV-infected children in populations where the risk for tuberculosis is high. In some countries, repeat vaccination is universal. In others, it is based on either tuberculin skin testing or the absence of a typical

scar ⁽⁸⁾. The aim of study is to evaluate the spectrum of tuberculosis infection in BCG vaccinated and non-vaccinated children.

Method

A retrospective study in which (158) patients with a diagnosis of TB were enrolled. Their age was ranging between (1 month to 14 years) old age they were attending TB center in Babylon city from January 2007 to December 2009. Data were collected depending on flow sheet of each patient that documented in TB center and included the following:- Age, sex, address, the date of diagnosis, the date of starting treatment, BCG vaccination status, presence of scar or not, intrafamilial or extrafamilial contact with TB patients. The clinical presentation of patients which include:- Prolonged fever, night sweating, loss of weight, unresolving pneumonia, chronic cough, shortness of breath, rapid breathing, loss of appetite, fits and disturb level of consciousness, lymph nodes enlargement, bone pain or fracture, soft tissue swelling and skin lesion. The physical examination includes:- Poor air entry; crepitation; bronchial breathing; abnormal heart sound; lymph adenopathy; hepatosplenomegaly; neck stiffness; coma and edema. The investigations for each patient which were done in TB center or other hospitals or private laboratory includes:- Complete blood count and erythrocyte sedimentation rate. Chest radiograph (some of them associated with reports). Tuberculin test not done because it was not available Sputum and gastric aspirate for acid fast bacilli which was done by doing a film from the sample and fixating it by strong carbol fuchsin and add H₂SO₄ after 5minute then wash it many times and add methylene blue and see the bacilli under microscope after dryness (Diagnostic Microbiology Bailey and Scotts 12edition page 491 procedure 45-2). Fluid aspirate (cerebrospinal, pleural and pericardial fluid) and examine it for cytology, gram stain, biochemistry, culture and sensitivity. Tissue sample (lymph nodes, bone tissue, pleura, skin). Brain CT scan and abdominal ultrasound. Other information's obtained include the preexisting condition that increase the risk of tuberculosis like history of recurrent respiratory disease, failure to thrive, gastrointestinal tract disease, and diabetes mellitus. The socioeconomic state of each patient includes if the patient live in rural area or urban, crowded family or not and the economic state (high, middle or low class) as mentioned in case file of patient. The data are collected, organized and tabulated by using computer software Statistics Package for Social Science (SPSS) version 17. The results expressed in form of numbers, percentages and Pearson Chi-square, which was statistically significant at p-value less than 0.05. The figures are done by using Microsoft office excel 2007.

Results

Distribution of patients according to the years, in 2007 they were 46 (29.1%) patients, 36 (78.3%) were vaccinated and 10 (21.7%) were not vaccinated, in 2008 they were 51 (32.3%) patients, 40 (78.4%) were vaccinated and 11(21.6%) were not vaccinated and in 2009 they were 61 (38.6%) patients, 48 (78.7%) were vaccinated and 13 (21.3%) were not vaccinated (table 1). Those patients were from different towns of Babylon province, from Hilla center 60 (38%) patients, 54(90%) patients were vaccinated and 6 (10%) were not vaccinated, from Hashimiyah 43 (27.2%) patients, 30 (69.7%) patients were vaccinated and 13 (30.3%) patients were not, from Mahaweel 31 (19.6%) patients, 25 (80.6%)

patients were vaccinated and 6 (19.4%) patients were not and from Mussayab they were 24 (15.2%) patients 15 (62.5%) patients were vaccinated and 9 (37.5%) patients were not vaccinated (table 2). From the total 158 of TB patients, 70 (44.3%) patients were ≤ 5 years, 56 (80 %) patients were vaccinated and 14 (20 %) were not vaccinated, and 88 (55.7%) patients > 5 years old, 68 (77.3 %) of them were vaccinated and 20 (22.7%) patients were not vaccinated. Males were 74 (46.8%) patients and females were 84 (53.2%) patients and male to female ratio of 0.88. Patients who lived in rural area were 105 (66.5%) patients and in urban area were 53 (33.5%) patients p value more than 0.05 (table 3). The number of patients who were BCG vaccinated were 124 (78.5%) patients and 34 (21.5%) patients were not vaccinated. From 124 vaccinated patients 115 (92.7%) patients had BCG scar with P-value < 0.001 . (Table 4). The patients were distributed according to the site of infection as following:-the lungs in 104 (65.8%) patients , 86 (69.3%) of them were vaccinated and 18 (52.9%) patients were not vaccinated with P-value 0.074, lymph nodes in 23 (14.6%) patients , 17 (13.7%) of them were vaccinated and 6 (17.6%) were unvaccinated patients with P-value 0.564, pleura in 14 (8.9%) patients , 8 (6.4%) of them were vaccinated and 6 (17.6%) were unvaccinated patients with P-value 0.052, meninges in 9 (5.7%) patients, 7 (5.6%) of them were vaccinated and 2 (5.9%) were unvaccinated patients with P-value 0.958, bone in 6 (3.8%) patients, 4 (3.2%) of them were vaccinated and 2 (5.9%) were unvaccinated patients with P-value 0.473, and 1 (0.6%) patients had skin and 1 (0.6%) patients had pericardium both of them were vaccinated patients (0.8%) with P-value 0.599 (table 5). The methods of diagnosis of those patients were as following:- 88 patients were diagnosed by signs and symptoms only, chest radiograph were done to all patients but only 18 films had positive finding. Only 47 patients had high ESR. 26 patients were diagnosed by pleural fluid analysis and 5 by pleural biopsy. The sputum was taken from 58 patients and send for AFB and only 16 patients had positive result, gastric aspirate were done to 13 patients all of them had negative results. 23 patients were diagnosed by lymph node biopsy and 9 patients were diagnosed by cerebrospinal fluid analysis. 6 patients were diagnosed by bone biopsy and 1 patient was diagnosed by skin biopsy and 1 by pericardial aspirate. Abdominal ultrasound done to 63 patients and brain CT scan done to 14 cases with no abnormal finding (table 6). The patients were distributed according to the presence of the pre-existing risk factors as following:- positive family history of TB infection was mentioned in 84 (67.7%) vaccinated patients and 27 (79.4%) unvaccinated patients with P-value 0.187, recurrent respiratory tract infections were noticed in 38 (30.6%) vaccinated and 12 (35.3%) unvaccinated patients with P-value 0.606 , failure to thrive in 31 (25%) vaccinated and 7 (20.6%) unvaccinated patients with P-value 0.594, asthma in 27 (21.8%) vaccinated and 8 (23.5%) unvaccinated patients with P-value 0.827, recurrent gastrointestinal tract infections in 22 17.7% vaccinated and 9 (26.5%) unvaccinated patients with P-value 0.256 and DM in 6 (4.8%) vaccinated and 3 (8.8%) unvaccinated patients with P-value 0.374 (table 7). Regarding the socioeconomic status:-from 124 BCG vaccinated patients, 93 (75%) patients were living in crowded family and 31 (25%) patients were living in not crowded, while 34 BCG not vaccinated patients, 31 (91.2%) patients were lived in crowded family and 3 (8.8%) not crowded with P-value (0.042), for the economic state, from 124 BCG vaccinated patients, 60 (48.4%) were lived with middle economic class and 64 (51.6%) were lived with low economic class while

34 not vaccinated patients 8 (23.5%) were lived with middle economic class and 26 (76.5%) were lived with low economic class with P-value (0.01) (table 8).

Table 1: distribution according to years

year	total	vaccinate	non vaccinate
2007	46 (29.1%)	48 (78.7%)	13 (21.3%)
2008	51 (32.3%)	36 (78.3%)	10 (21.7%)
2009	61 (38.6%)	40 (78.4%)	11 (21.6%)

Table 2: distribution according to place

year	total	vaccinate	non vaccinate
Hilla	60 (38%)	54 (90%)	6 (10%)
Hashimiyah	43 (27.2%)	30 (69.7%)	13 (30.3%)
Mussayab	24 (15.2%)	15 (62.5%)	9 (37.5%)
Mahaweel	31 (19.6%)	25 (80.6%)	6 (19.4%)

Table (3): Distribution of TB patients according to the different variables: age, sex, residence

		TB patients		P-value*
		vaccinated	unvaccinated	
Age group	Less than 5 years	56 (80%)	14 (20%)	0.679
	More than 5 years	68 (77.3%)	20 (22.3%)	
Sex	Males	59 (79.7%)	15 (20.3)	0.72
	Females	65 (77.4%)	19 (22.6%)	
Environment	Urban	46 (86.8%)	7 (13.2%)	0.071
	Rural	78 (74.3%)	27 (25.7%)	

* P-value > 0.05 is not significant.

Table (4):- Distribution of TB patients according to BCG vaccination status and its scar.

BCG vaccine	No.	%	P-value
Yes	124	78.5%	
No	34	21.5%	
BCG scar			
Yes	115	92.7%	0.001*
No	9	7.3%	-

*P-value < 0.001 is extremely significant.

Table (5):- Clinical spectrum of tuberculosis among BCG vaccinated and unvaccinated groups.

The site of infection	No. & %	BCG vaccine		P-value *
		Vaccinated	Unvaccinated	
Lung	104 (65.8%)	86(69.3%)	18(52.9%)	0.074
LAP	23 (14.6%)	17(13.7%)	6(17.6%)	0.564
Pleura	14(8.9%)	8(6.4%)	6(17.6%)	0.052
Meninges	9(5.7%)	7(5.6%)	2(5.9%)	0.958
Bone	6(3.8%)	4(3.2%)	2(5.9%)	0.473
Skin	1(0.6%)	1(0.8%)	0	0.599
Pericardium	1(0.6%)	1(0.8%)	0	0.599
Total	158	124	34	-

* P-value > 0.05 is not significant.

Table (6):- Distribution of TB patients according to the methods of diagnosis.

The methods of diagnosis	Number
Clinical(history of contact+ symptoms)	88
Lymph node biopsy	23
sputum for AFB	58 +16
Pleural fluid aspiration	26
CSF findings	9
Bone biopsy	6
Pleural biopsy	5
Skin biopsy	1
Pericardial aspirate	1
Gastric aspirate	13
Tuberculin skin test	Not available
Chest radiograph	158
Positive x ray finding	18
Complete blood count +ESR	158
High ESR	47
Abdominal ultrasound	63

Brain CT scan	14
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Table (7):- Distribution of patients according to the presence of risk factors.

The pre-existing risk factors	TB patients		P-value *
	Vaccinated 124	Unvaccinated 34	
Family history of TB infection	84(67.7%)	27(79.4%)	0.187
Recurrent respiratory tract infection	38(30.6%)	12(35.3%)	0.606
Failure to thrive	31(25%)	7(20.6%)	0.594
Asthma	27(21.8%)	8(23.5%)	0.827
Recurrent gastrointestinal infection	22(17.7%)	9(26.5%)	0.256
Diabetes mellitus	6(4.8%)	3(8.8%)	0.374

* P-value > 0.05 is not significant.

Table (8):- Distribution of patients according to socioeconomic aspects

socioeconomic aspects	BCG-vaccinated	unvaccinated	P-value *
Crowded	93(75%)	31(91.2%)	0.042
Not crowded	31(25%)	3(8.8%)	
Total	124(100%)	34(100%)	
Middle class	60(48.4%)	8(23.5%)	0.01
Low class	64(51.6%)	26(76.5%)	
Total	124(100%)	34(100%)	

* P-value < 0.05 is significant.

Discussion

In this study we found an increment in number of patients who recorded in TB center with in last year's (2007,2008, 2009) respectively, in 2009 the number of patients were 61(38.6%) and this goes with results of World Health Organization (WHO) ^(3, 4). This finding may be explained by: increment of total population and crowdedness, travelling to other countries and increase contact with index cases, beside improvement in health care and documentation of cases. The larger

number of patients recorded were from Hilla 60 (38%) patients and this results may be related to the number of populations in Hilla (estimation done by Babylon Health Directorate in 2010 were 711458 people in Hilla from it 320156 below 14 years old). The male to female ratio was 0.88 and this not agree with study that done in India ⁽⁹⁾. In the current study most of patients were more than 5 years old (55.7%), and the number of BCG vaccinated patients in this age group were (77.3%), other studies were shown the same results of our study ^(9, 10), and this might be explained by that the BCG is time limited ⁽⁴⁾, increase contact of this age group with adults and index case or decrease the immunity of childrens of BCG. More than half cases 66.5% of TB were lived in rural area and this may be related to the crowdedness, bad sanitation, and difficulties to attain health care ⁽⁴⁾. There were no significant difference between these variables and the TB among vaccinated and unvaccinated patients. Most of patients were BCG vaccinated (78.5%), only 9 (7.3%) patients of them did not develop scar, and 34 patients (21.5%) were not vaccinated, and this shows that effect of BCG in prevention of TB is questionable. This result similar to other studies ^(9, 11). The most common site of TB infection in our study were lungs 104 (65.8%) then lymph node 23 (14.6%) and this result differ from other studies that show that the common sites were lungs and meninges as extra pulmonary TB ⁽⁹⁾. Our study shows that there were no significant difference in prevalence of all types of TB in vaccinated and unvaccinated patients and this agree with other studies ^(9, 10). Most of patients (88) were diagnosed by signs and symptoms beside family history of TB infection or contact with index cases because tuberculin test and other sensitive tests such as gamma interferon and nucleic acid amplification not available in our center, while these tests widely used in other countries for diagnosis of TB ⁽⁹⁻¹¹⁾. Sputum was send for detection of acid-fast bacilli and only, 16 patients had positive results, their age was ranging between (9-14 years) this may be due to their ability to induce force cough and expectorate sputum and the nature of disease. There was no patients with positive gastric aspirate for AFB, other studies depend on TST more than sputum ^(9, 10). Chest X –rays was done to all patients but only 18 patients had shown positive radiological finding. 47 patients with high ESR, this go with other researches and authors that show the ESR not a good parameter for diagnosis. There were no significant difference between the pre-existing risk factors (family history of TB infection, recurrent respiratory tract infection, recurrent gastrointestinal tract infection, failure to thrive, asthma and diabetes mellitus) and TB among vaccinated and unvaccinated patients, these results agree with other studies ⁽⁹⁻¹¹⁾. In spite of that there was agreement that these factors play role in transmtion of TB ⁽⁴⁾, but the BCG have no role in protection from these factors. Regarding socioeconomic status (75%) of BCG vaccinated patients and (91.2%) of unvaccinated patients were lived in crowded family and (51.6%) of BCG vaccinated patients and (76.5%) of unvaccinated patients had low economic state, there were significant difference in prevalence of TB between vaccinated and unvaccinated patients and these factors ,this not goes with other studies ^(9, 12), these factor play a role in transmission of disease and effect on immunity of children's.

Conclusion

All types of TB occur in BCG vaccinated and non-vaccinated children, and there are many risk factors that play a role in patient's diagnosis with TB and start treatment.

References

1. Beers, Mark H., MD, and Robert Berkow, MD., editors. "Infectious Diseases Caused by Mycobacteria." In *The Merck Manual of Diagnosis and Therapy*. Whitehouse Station, NJ: Merck Research Laboratories, 2004, ch.4, p33.
2. WHO. Global tuberculosis control. Surveillance, planning, financing. WHO Report . Geneva: World Health Organization, 2005.
3. World Health Organization (2009). "Epidemiology". Global tuberculosis control: epidemiology, strategy, financing. pp. 6–33.
4. Jeffrey R. Starke Flor M. Munoz. Tuberculosis (Mycobacterium Tuberculosis). IN: Behrman RE, Kliegman RM, Jenson HB. Nelson text book of pediatrics, 2007; 212:P1240.
5. Starke JR: Transmission of Mycobacterium tuberculosis from children to adolescents. *Semin Pediatr Infect Dis* 2001; 12:115-123.
6. Zar HJ, Hanslo D, Apolles P, et al: Induced sputum versus gastric lavage for microbiological confirmation of pulmonary tuberculosis in infants and young children: A prospective study. *Lancet* 2005; 365:130-134.
7. Blumberg HM, Burman WJ, Chaisson RE, et al. treatment of tuberculosis. *Am J Respir Crit Care Med*. Feb 15 2003; 167(4):603-62.
8. Novelli V. BCG vaccination gets a boost. *Lancet* 2006; 367:1122-1124.
9. Vishwanath K G1, Siddaraju M L2, Jagannatha P: Spectrum of Tuberculosis in BCG vaccinated and unvaccinated Children in Bangalore, India: *PRIORY MEDICAL JOURNALS* First Published April 28th 2007
10. P. G. Gopi1, R. Subramani1, C. Kolappan2: Estimation of Annual Risk of Tuberculosis Infection Among Children Irrespective of BCG Scar in the South Zone of India: *Indian Journal of Tuberculosis* 2005 31.3. p 23.
11. Anoop Sebastian Pulickal, Gerald Vincent Joseph Fernandez. Comparison of the Prevalence of Tuberculosis Infection in BCG Vaccinated versus Non-Vaccinated School Age Children: *Indian pediatrics* 2007 volume 44 p 344-47 .
12. Mahbubur Rahmana, Miho Sekimoto, Isamu Takamatsub, et al Infectious Disease: Economic evaluation of universal BCG vaccination of Japanese infants: *International journal of epidemiology* 2001;30:380-385.