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Frequency of BCG vaccine among children with chest infection

A THESIS
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Table of Contents

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Dedication

To my beloved parents,
Who were there for me with their support and encouragement,
I dedicate this work to all their loving tears and beautiful smiles.

To all my respectable teachers,
Who enlightened me with their knowledge and understanding

To all my fellow students, friends, and colleagues
For their unconditional Support and love.

To all patients out there, hoping this little work will do something to help them more in their sufferings.

ABSTRACT

BACKGROUND:
The bacille Calmette–Guérin (BCG) vaccine was first given to humans in 1921, and came into common use in many countries during the 1930s. The vaccine protects against tuberculosis (TB) and leprosy, but the effi- cacy against TB varies a lot between countries. Recent research has provided support for the hypothesis that the variation in BCG vaccine efficacy can be ascribed to prior 5ensitization with environmental mycobacteriae.

PATIENTS AND METHOD:
A total of [60] cases, (30) of them with chest infection were reviewed with clinical manifestations of Pneumonia, or Bronchiolitis that received at pediatrics floor.
The other (30) were control cases reviewed at the outpatient clinic as well as in the ward as relatives to patients.
For every patient medical evaluation conducted included: history, examination of BCG scar presence and growth chart assessment.

RESULTS:
60 patients within pediatric age groups was involved in this study, with mean age of 17.8 mo., males were more common, Statistical growth parameters show a mean weight of 13.8 kg, the social status of the involved sample, findings were 33 (55%) of them were in good social status, with 20% of moderate status, 50% percent of patients with chest infections of a total 30 patients
These results of chest infections were correlated to the BCG vaccination status, and this relation was found to be significance, indicates a relationship between chest infections and BCG scars, with pneumonia being the most common type in 21 (70%) of patients

CONCLUSION:

Bacille Calmette-Guerin (BCG) vaccines represent one of the most widely used forms of childhood immunization in the world and in this study, BCG scar found to be associated with no protective effect against lower respiratory tract infections in BCG-vaccinated children.

Chapter one: introduction & aim

Introduction

BCG:

The bacille Calmette–Guérin (BCG) vaccine was first given to humans in 1921 [1], and came into common use in many countries during the 1930s [2,3]. The vaccine protects against tuberculosis (TB) [4] and leprosy [5], but the effi- cacy against TB varies a lot between countries [6]. Recent research has provided support for the hypothesis that the variation in BCG vaccine efficacy can be ascribed to prior sensitisation with environmental mycobacteriae [7].

BCG vaccination is known to stimulate cell-mediated im- munity, and BCG immunotherapy has for many decades been used in the treatment of bladder cancer resulting in im- proved survival [8]. Several studies investigated the effect of BCG vaccination on other cancer forms, but results in terms of survival have been contradictory [9]. In West Africa we found BCG vaccination of infants to be associated with a Th1-biased immune response [10], increased antibody re- sponse to unrelated antigen [11], less atopy [12], less anergy [13] and a reduction in childhood mortality [14]. Cutaneous anergy to tuberculin and panels of antigens has been asso- ciated with decreased survival in adults [15,16].

If the difference in mortality between BCG-vaccinated and BCG-unvaccinated children [14] is due to the vaccine and not a result of selection bias between vaccinated and un- vaccinated children, we hypothesise that the strongest ben- eficial effect should be found among children with a BCG scar or a positive tuberculin reaction. In connection with a vaccine trial in Guinea-

Bissau, we obtained data on BCG scar status and tuberculin reaction in BCG-vaccinated in- fants and their subsequent childhood mortality. Since TB is also studied in this community, we examined whether the effect of BCG was related to better protection against house- hold exposure to TB.

TB:

Tuberculosis (TB) is an infectious disease usually caused by Mycobacterium tuberculosis (MTB) bacteria.[17] Tuberculosis generally affects the lungs, but can also affect other parts of the body.[17] Most infections do not have symptoms, in which case it is known as latent tuberculosis.[17]About 10% of latent infections progress to active disease which, if left untreated, kills about half of those affected.[17] The classic symptoms of active TB are a chronic cough with blood-containing sputum, fever, night sweats, and weight loss.[17] It was historically called "consumption" due to the weight loss.[21] Infection of other organs can cause a wide range of symptoms.[22]

Tuberculosis is spread through the air when people who have active TB in their lungs cough, spit, speak, or sneeze.[17][23] People with latent TB do not spread the disease.[17] Active infection occurs more often in people with HIV/AIDS and in those who smoke.[17] Diagnosis of active TB is based on chest X-rays, as well as microscopic examination and culture of body fluids.[24] Diagnosis of latent TB relies on the tuberculin skin test(TST) or blood tests.[24]

Prevention of TB involves screening those at high risk, early detection and treatment of cases, and vaccination with the bacillus Calmette-Guérin (BCG) vaccine.[18][20][19] Those at high risk include household, workplace, and social contacts of people with active TB.[19] Treatment requires the use of multiple antibiotics over a long period of time.[17] Antibiotic resistance is a

growing problem with increasing rates of multiple drug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB).[17]

Pneumonia:

Pneumonia is the leading cause of death among young children in developing nations, responsible for about 1.2 million early childhood deaths annually.(25,26) Undernutrition is a known risk factor for developing and dying from pneumonia,(27) but much recent research has focused on the effects of wasting or under-weight,(28–29) which primarily reflects acute undernutrition.

Chronic undernutrition is best reflected by stunting, or low height (or length)-for-age.(30) Stunting affects 162 million children (26.7% of all children) worldwide, 92% of whom live in Asia or Africa.(31) For children with pneumonia, stunting may have harmful effects that are distinct from those related to nutritional deficiency, since height is the major determinant of lung size and pulmonary function.(32,33) Stunting is independently associated with an increased risk of parent-reported acute respiratory infection,(34) WHO-defined pneumonia, (35) radiographically-confirmed pneumonia,(36) with increased risk of RSV-related lower respiratory tract infection (but not upper respiratory infection),(37) and with increased risk of hospitalization for pneumonia.(38)

Beyond increasing the risk of developing severe pneumonia, the restricted lung growth associated with stunting may make children less able to tolerate severe pulmonary infection, more prone to develop hypoxemia and respiratory failure, and may impair recovery from pneumonia.(39,40) 1 To better understand the effect of stunting on pneumonia outcomes, we

evaluated the effect of stunting on the risk of failing treatment and time to recovery from pneumonia, using data from the previously completed Severe Pneumonia Evaluation Antimicrobial Research (SPEAR) study (41) and Amoxicillin Penicillin Pneumonia International Study (APPIS).(42) These studies were multinational randomized clinical trials of antibiotic regimens for pneumonia among children in low and middle-income countries, settings with high rates of both stunting and pneumonia. We hypothesized that (25) stunted children would have an increased risk of failing treatment of their episode of pneumonia, and that (26) stunted children would take longer to recover from pneumonia.

Aim of present study

To assess the frequency of BCG vaccine among children with chest infection.

Chapter two: Patients and methods

Design:

Through the period extending from October 2018 to April 2019. Hospital based case-control study at pediatrics floor at Imamin ALKhadimmian city hospital.

Method:

A total of [60] cases, (30) of them with chest infection were reviewed with clinical manifestations of Pneumonia, or Bronchiolitis that received at pediatrics floor. The other (30) were control cases reviewed at the outpatient clinic as well as in the ward as relatives to patients.

For every patient medical evaluation conducted included: history, examination of BCG scar presence and growth chart assessment.

Inclusion criteria:

This study included any patients who had chest infection.

Exclusion Criteria

- Age above 3 years
- Children with comorbidities
- Preterm children

Statistical analysis

Data was calculated and tabulated using Microsoft Excel 2016 and SPSS inc. Version 24, P value < 0.05 was considered to be significant, mean and standard deviation were calculated.

Chapter three: Results

60 patients within pediatric age groups was involved in this study, with mean age of 17.8 mo., males were 35 (58.3%), and females 25 (41.7%) and male:female ratio was found to be 1.4:1, as shown in fig. (1)

Table (1): Gender distribution

Gender	Frequency	Percent
Female	25	41.7
Male	35	58.3
Total	60	100.0

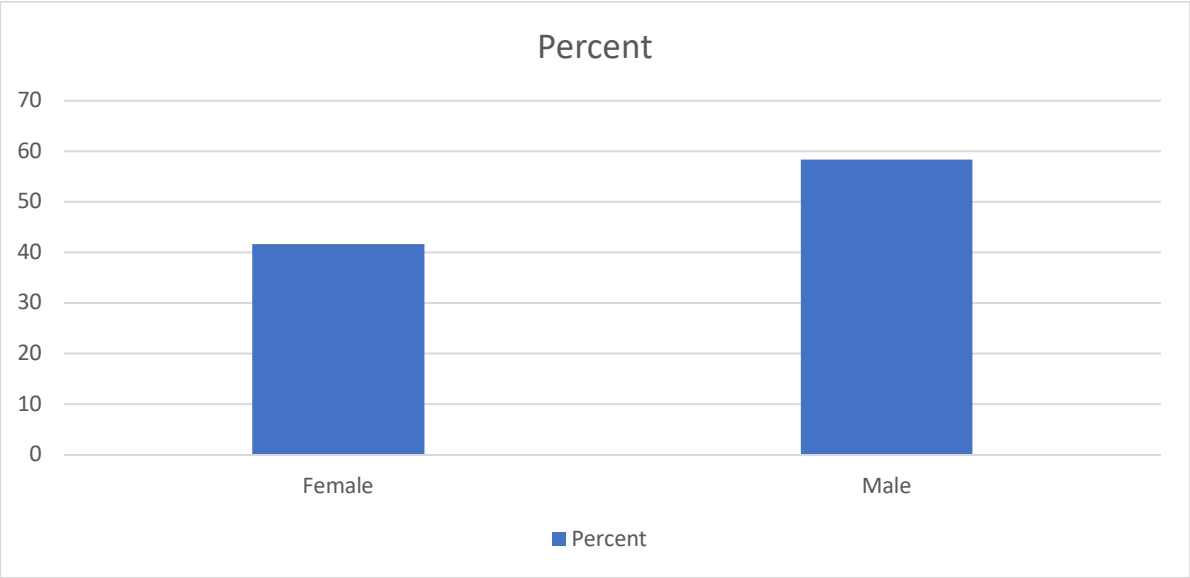

Figure (1): Gender distribution

Statistical growth parameters show a mean weight of 13.8 kg, mean height of 73 cm and mean head circumference of 43.8 cm, with their standard deviations as shown in table (2)

Table (2): statistical growth parameters

Parameters	N	Minimum	Maximum	Mean	Std. Deviation
Age	60	0.5	36.0	17.8	11.6
Weight	60	3.7	14.5	13.8	22.7
Height	60	50xx.3	96.0	73	18.0
Head Circumference	60	32.0	50.0	43.8	5.1

T-Test had been done for equality of means in correlation to chest infections in term of age, weight, height and head circumference, that showed a great significance with P value < 0.05, emphasizing the correlation of these parameters to chest infection, as shown in fig. 2

Table (3): T-test for Equality of Means in correlation Chest infection

	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference
Age	2.938	58	.005	8.35000	2.84162
Weight	2.108	52	.040	12.70292	6.02739
Height	7.105	52	.000	25.23333	3.55155
OFC	9.357	52	.000	8.21000	.87742

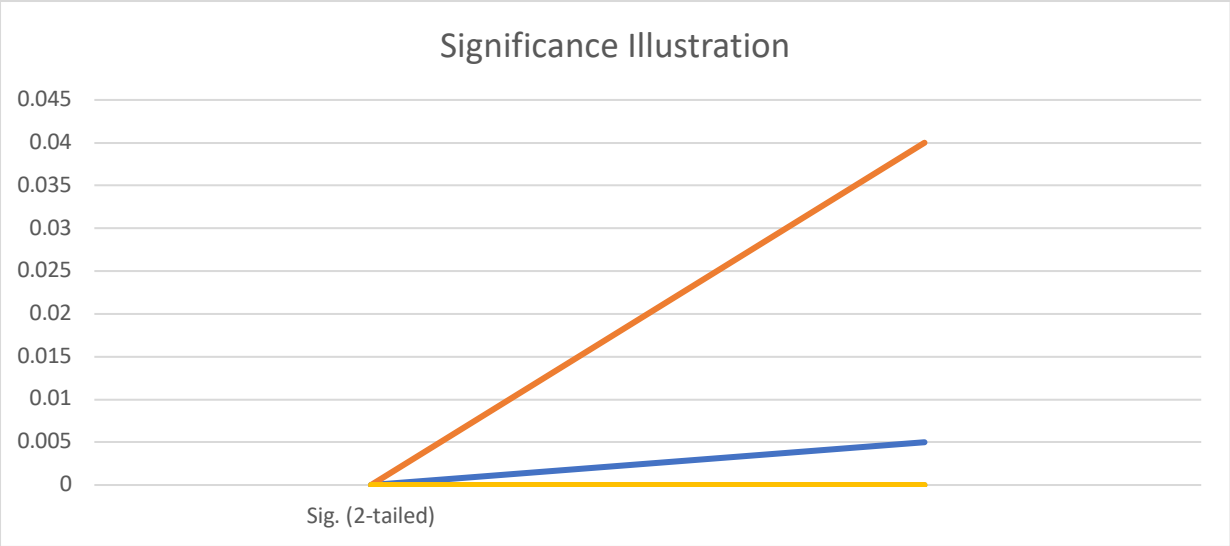

Figure (2): T-test for Equality of Means in correlation Chest infection

In this study, we reviewed the social status of the involved sample, findings were 33 (55%) of them were in good social status, with 20% of moderate status, and 25% were living with poor social status, as showen in fig. 4

Table (4): Social status of the involved sample

Social Status	Frequency	Percent
Good	33	55.0
Moderate	12	20.0
Poor	15	25.0
Total	60	100.0

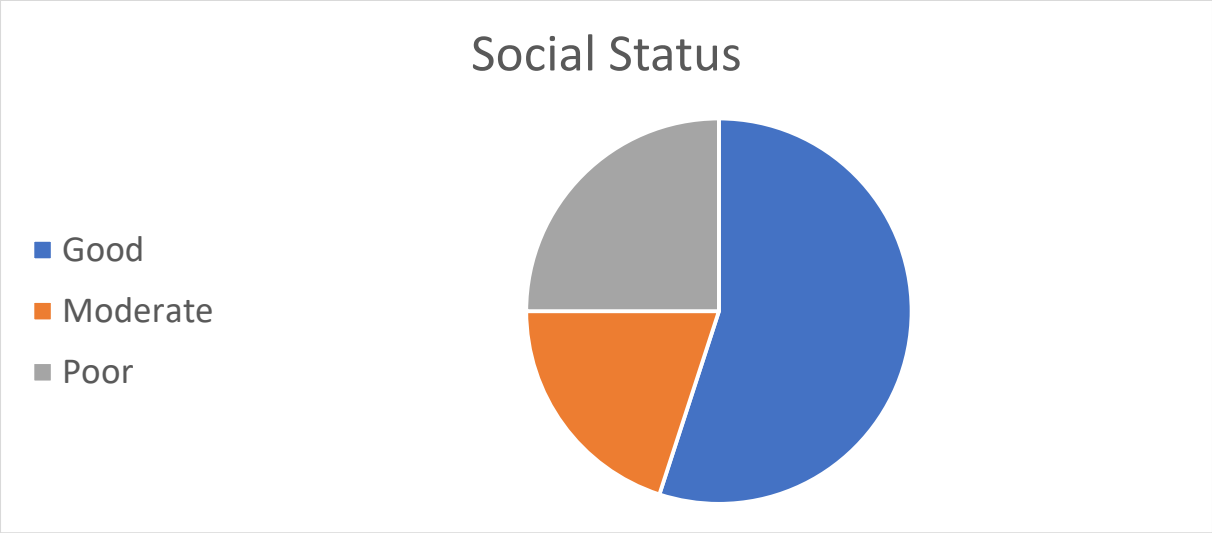

Figure (3): Social status of the involved sample

Regarding the BCG vaccination status, in this study, 44 (73.3%) were vaccinated, while the remaining 16 (26.7%) were unvaccinated, as shown in fig. (4)

Table (5): BCG vaccination status

BCG Vaccine	Frequency	Percent
unvaccinated	16	26.7
vaccinated	44	73.3
Total	60	100.0

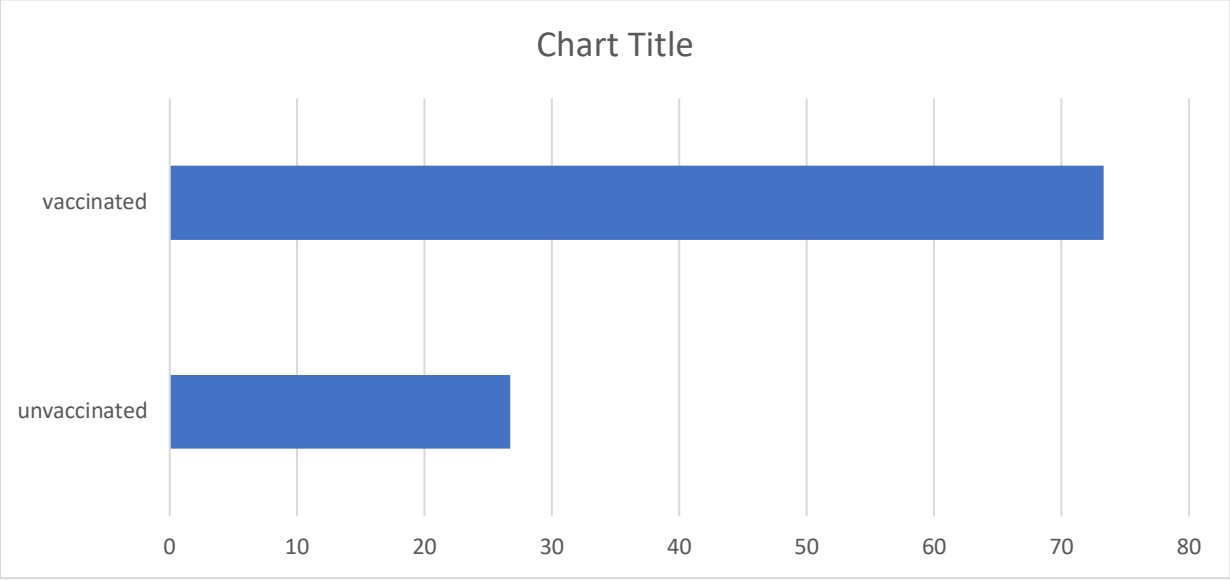

Figure (4): BCG vaccination status

The frequency of chest infections in our sample regardless of the vaccination status was (30) 50% percent of patients with chest infections of a total 30 patients as shown in fig. 5

Table (6): Frequency of chest infections

Chest Infections	Frequency	Percent
No	30	50.0
Yes	30	50.0
Total	60	100.0

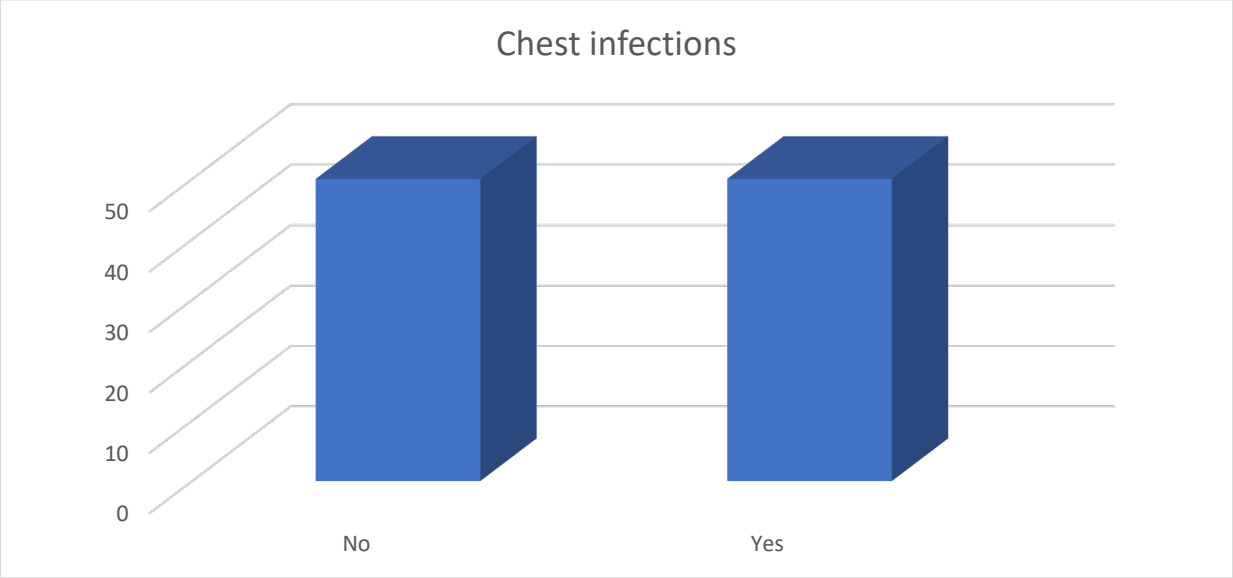

Figure (5): Frequency of chest infections

These results of chest infections were correlated to the BCG vaccination status, and this relation was found to be significant with P value < 0.05, indicates a relationship between chest infections and BCG scars as shown in fig. 6

Table (7): Correlation data between chest infections and BCG scars (vaccinations status) with P value

		BCG		Total
		unvaccinated	vaccinated	
CI	No	10 (33.3%)	20 (66.7%)	30 (100%)
	Yes	6 (20%)	24 (80%)	30 (100%)
Total		16 (26.7%)	44 (73.3%)	60 (100%)
P Value				0.0001

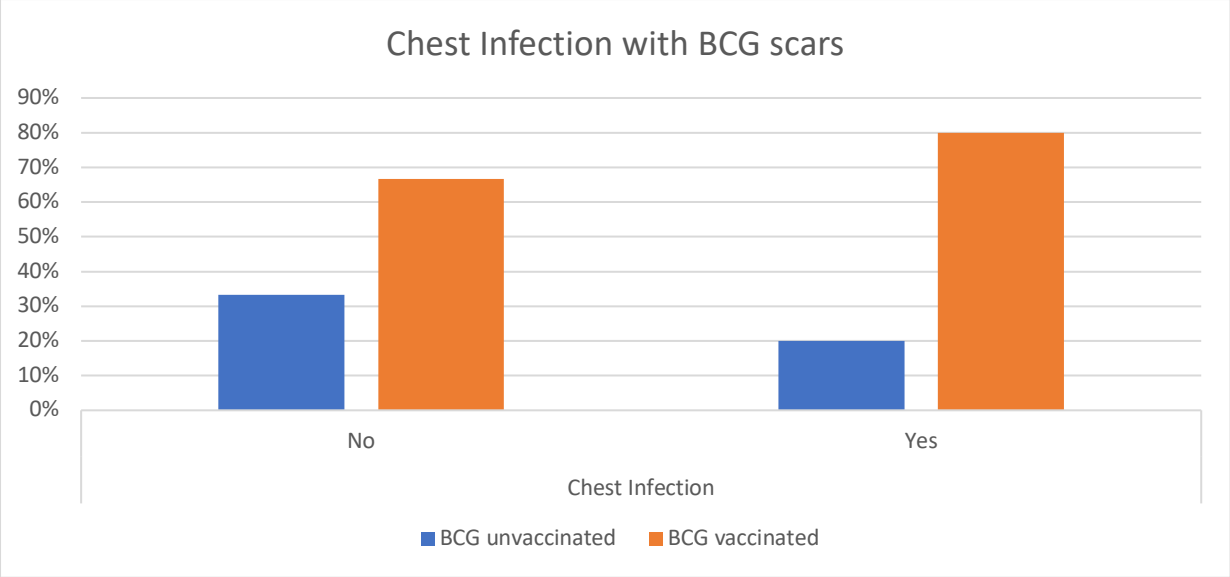

Figure (6): Correlation data between chest infections and BCG scars

The following resultant table (8) shows detailed types of chest infections in our patients, with pneumonia being the most common type in 21 (70%) of patients, as shown in fig. 7

Table (8): Frequency of common types chest infections

Chest Infections	Frequency	Percent
Bronchiolitis	9	30.0
Pneumonia	21	70.0
Total	30	100.0

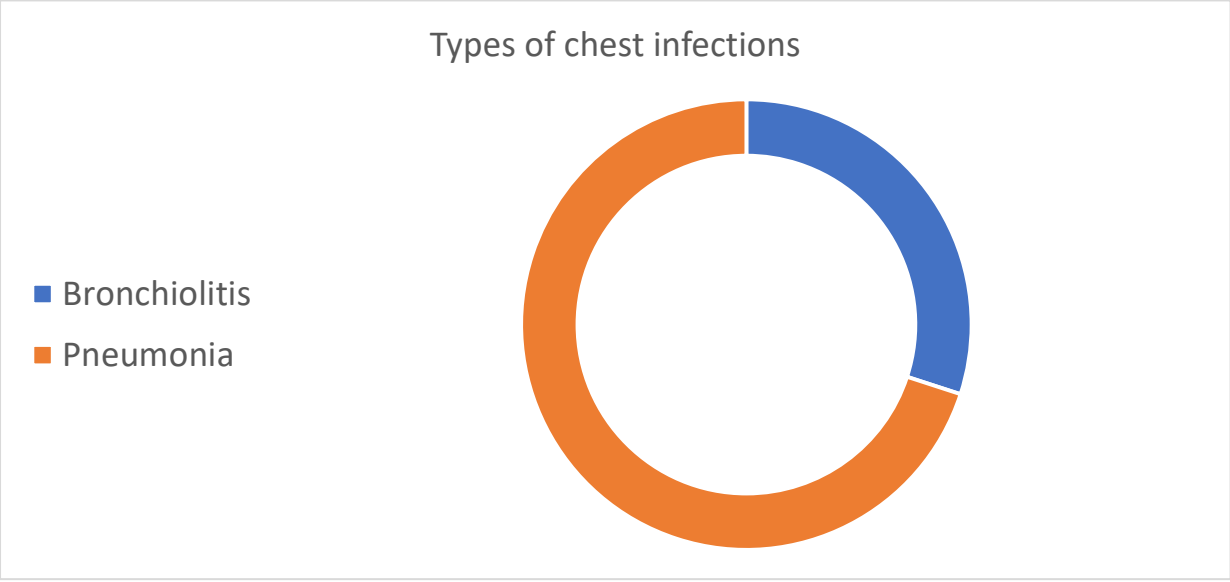

Figure (7): Frequency of common types chest infections

Regarding the common types of chest infection in relation to vaccination status, pneumonia was also found to be the highest with 15 (62%) vaccinated patients, as shown in fig. 8

Table (9): Common types of chest infections in relation to BCG scars

		Chest Infections		
		Bronchiolitis	**Pneumonia**	**Total**
BCG	**unvaccinated**	0	6	6
	vaccinated	9	15	24
Total		9	21	30
P Value				0.072998

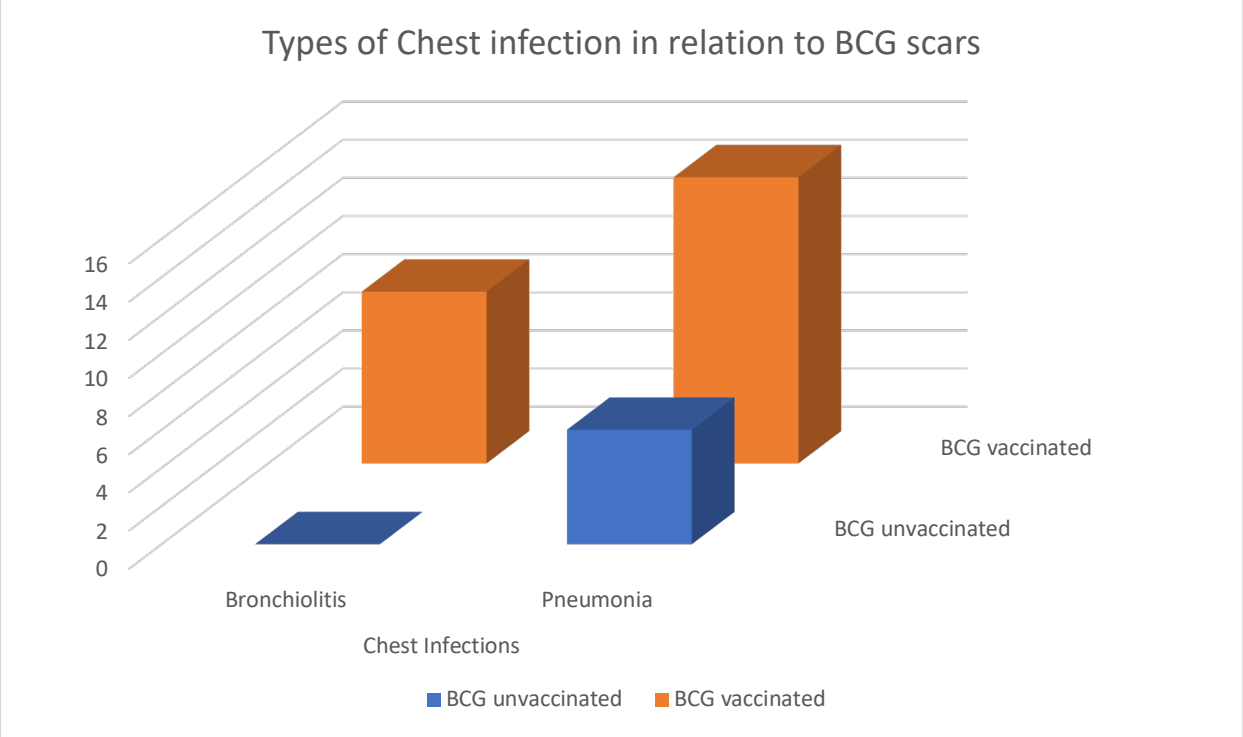

Figure (8): Common types of chest infections in relation to BCG scars.

We had analyzed both gender and social status in relation and chest infection in our sample, with p value was found to be > 0.05, excluding the significance of gender on chest infections as shown in table (10) and p value <0.05 emphasize the relation between good social status and low rates of chest infection as shown in table (11)

Table (10): Gender distribution in relation to chest infections

		Gender		Total
		Female	Male	
CI	**No**	13 (43.3%)	17 (56.7%)	30 (100.0%)
	Yes	12 (40.0%)	18 (60.0%)	30 (100.0%)
Total		25 (41.7%)	35 (58.3%)	60 (100.0%)
P Value				0.241

Table (11): Social status in relation to chest infections

		Social			Total
		Good	Moderate	Poor	
CI	**No**	21 (70%)	3 (10%)	6 (20%)	30 (100%)
	Yes	12 (40%)	9 (30%)	9 (30%)	30 (100%)
Total		33 (55%)	12 (20%)	15 (25%)	60 (100%)
P Value					0.0412

Chapter four: discussion:

Bacille Calmette-Guerin (BCG) vaccines represent one of the most widely used forms of childhood immunization in the world. 1 BCG scar to be associated with better survival in BCG-vaccinated children, and recently been associated with reduction in morbidity and mortality as general [43].

This include associated of BCG vaccination with lower risks of acute lower respiratory infections (ALRI) in children, as studies from Guinea-Bissau. [44]

Presence of scarring at inoculation sites has also been linked to risk reductions in pneumonia-related child mortality in Brazil. [45]

However, determining whether these results are generalizable to children living outside indicated study regions is difficult given established variations in adaptive immune responses to BCG between and within local populations over time. [46,47]

Our population-based analysis included 60 patients revealed that 73.3% of children were vaccinated with BCG with no specific gender predominance, and most cases were in good social status.

In this study, chest infections were correlated to the BCG vaccination status with resultant significance of increased infections in vaccinated children with pneumonia being the most common lower respiratory tract infections, these findings were different from the data reported by Hollm-Delgado et al [48] which stated that BCG vaccination was associated with reduced risk of lower respiratory tract infections, may be due to the Social status of the children as well as the pattern of this effect depended on a child's age at time of vaccination.

Several factors were taken in relation to chest infections, including age, height, weight and head circumference, that were significant in relation to chest infections, with higher rates of chest infections at lower growth parameters, these results were similar to these reported by Hollm-Delgado et al [48] which stated that morbidity and mortality were decreasing with increased growth parameters, that might be predictable factors affecting immune states and their adaptive immunity.

Regarding specific gender involvement compared to children morbidity as chest infections, it was not significant in our results, in contrast to social status findings, that were significant in its relation to chest infection, these findings was similar to these reported by Gary et al [49] and they are affected by different epidemiological distribution.

Chapter five: conclusions and recommendations

Conclusions:

Bacille Calmette-Guerin (BCG) vaccines represent one of the most widely used forms of childhood immunization in the world and in this study, BCG scar found to be associated with no protective effect against lower respiratory tract infections in BCG-vaccinated children.

Recommendation:

Lower respiratory tract infections are common in our population regardless the immune effect of BCG vaccines, other vaccination against lower respiratory tract infections are recommended. Other studies for the relation of BCG vaccination duration in relation to ALRT infections are proposed.

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