RESEARCH PAPER

The relationship between BCG scar size and socioeconomic status on the severity and mortality of COVID-19 patients, "as indicators of the immunity"

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Abstract

Background: The severity and mortality by COVID-19 vary among countries. This may be related to the underlying immunity**.** Response to the vaccine effect is immunologically related to several factors like vaccination, infestation with parasites and nutrition. Socioeconomic status is an important factor in health problems**.**

Objectives: The purpose of the study is to understand the effect of the BCG scar size and the socioeconomic status as indicators of underlying immunity on the severity and mortality of COVID-19 patients.

Method: A comparative study of PCR-confirmed COVID-19 patients were done in Basrah, Teaching Hospital. The patients were divided into two groups: Severe and mild to moderate cases. All confirmed cases during April and May 2020 in Basrah Teaching Hospital were included. The BCG scar size and socioeconomic status were studied and related to the severity and mortality of COVID-19 cases.

Results: Patients who had small BCG scar size and high socioeconomic status were significantly associated with higher severity and mortality due to COVID-19 infection.

Conclusion: BCG scar size and socioeconomic class can be used as good indicators for immune response against infection and the extent of their severity and mortality.

Keywords BCG scar; socioeconomic status; COVID-19; Immunity

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Introduction

COVID-19 disease can pass to severe pneumonia and associated with high morbidity and mortality. Long lasting immunity by certain live vaccines like BCG can induce protection against severe infections.[1,2] Bacillus-Calmette-Guérin (BCG) is a tuberculosis vaccination that is used early after birth in tuberculosis endemic countries, such as Iraq. Some countries do not vaccinate BCG routinely.[3] The incidence and mortality of patients with COVID-19 vary among countries. Some suggested that this might be related to the different policies regarding BCG vaccination[4,5] The incidence and mortality due to COVID-19 is around 10 times higher in countries where BCG vaccination is not recommended.[6] Immunological responses to vaccination are mainly affected by certain factors like vaccination, infestation with parasites and nutrition.[7,8] Other studies show that there was no evidence that BCG vaccination protects against infection with COVID-19 virus.[9] A previous study by the author suggested that small size or negative BCG scars are significantly higher among children with cancer.[10] Several studies indicate that the mean scar size was 4.6 mm in boys and 4.5 mm in girls with 3.5 mm is considered as a cut point

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for good immune response or as the vaccination is not failed.[11] The socioeconomic status (SES) is an important factor that affect health in general. The SES is mainly detected by several variables where occupation, income and education are important determinants.[12]

Methods

Ethics statement

This study was approved by the Ethical Committee, College of Medicine, University of Basrah, Iraq, and also by Basrah General Directorate. Patient consent had been taken before measurement of the scar size.

Study population

Study population included all patients with PCR confirmed COVID-19 infection admitted to Basrah Teaching Hospital, during the period of April and May 2020. The patients were divided into two groups. Mild to moderate cases as first group compared with the second group who are severely ill as indicated by tachypnea (30 or more breaths per minutes), oxygen saturation (93% or less), CT scan changes of the lung & need for admission to the emergency room.[13] The modified Kuppuswamy scale was used for calculating the social status depending on the information of family income, education and occupation.[14] The patients were then divided into three socioeconomic classes (low: 1-10 score, moderate: 11-25, and high: 26-29).

BCG vaccination and scar size measurement

Iraq's programme of vaccination mandate that every infant must have BCG vaccination within the first week of age. The BCG scar size was measured by the author using a plastic ruler. The largest diameter of scar size was measured. The information was collected using a questionnaire. Statistical analysis was carried out using the SPSS computer package. Chi-squared test was used to compare data. P-value < 0.05 was considered as statistically significant.

Results

During April & May 2020, the Basrah Teaching Hospital received a total of 752 PCR-confirmed COVID-19 patients. About one half of them aged 46 to 60-year-old. BCG scar size distribution did not significantly differ between age groups (Tables-1). There were also no significant differences in relation to sex, address or previous medical history.

Table 1. BCG scar size distribution among different age groups of COVID-19 patients

Age (years)	BCG scar size (mm)		Total No. (%)
	0 – 3 No. (%)	> 3 No. (%)	
12-30	9 (5.1)	24 (4.2)	33 (4.4)
31-45	33 (18.8)	122 (21.2)	155 (20.6)
46-60	93 (52.8)	284 (49.3)	377 (50.1)
> 60	41 (23.3)	146 (25.3)	187 (24.9)
Total	**176 (100)**	**576 (100)**	**752 (100)**

x^2 = 1.2, df = 1, P = 0 .75

BCG scar sizes above 3 mm were mostly recognized among patients with mild to moderate COVID-19 infection (80.7%) as compared with sizes of 0-3 mm (19.3%). severe cases were 62.5% associated with BCG scar of 0-3 mm size as compared with 37.5% of severe cases with scars > 3 mm size (Table-2). Mortality were also significantly higher among BCG scar size group of 0-3 mm as compared with those who had more than 3 mm scar sizes (60% versus 40% respectively, p < 0.0001) (Table-3).

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Table 2. BCG scar size in relation to the severity of the cases of COVID-19

BCG scar size (mm)	Severity		Total
	Low-Moderate No. (%)	High No. (%)	
0 – 3	131 (19.3)	45 (62.5)	176
> 3	549 (80.7)	27 (37.5)	576
Total	680 (100)	72 (100)	752

x^2 = 67.9, df = 1, P < 0.0001

Table 3. Mortality frequency of COVID-19 patients in relation to the BCG scar size

BCG scar size (mm)	Mortality		Total
	No	Yes	
0 – 3	164 (22.4%)	12 (60%)	176
> 3	568 (77.6%)	8 (40%)	576
Total	732 (100%)	20 (100%)	752

x^2 = 13.3, df = 1, P <0.0001.

High SES was significantly associated with severe COVID-19 cases (68.1%) as compared with middle (19.4%) and lower (12.5%) SES ($p < 0.0001$) (Table-4). Mortality is also higher among high SES (65%) as compared with middle (20%) and lower (15%) SES ($p < 0.0001$) (Table-5).

Table 4. Severity of COVID-19 patients in relation to their socioeconomic class

Socio-economic status	Severity		Total
	Low-Moderate No. (%)	High No. (%)	
High	109 (16.0)	49 (68.1)	158
Middle	271 (39,9)	14 (19.4)	285
Lower	300 (44.1)	9 (12.5)	309
Total	680 (100)	72 (100)	752

x^2 = 106.9, df = 2, P <0.0001.

Table 5. Mortality of COVID-19 patients in relation to their socioeconomic class

Socio-economic status	Mortality		Total
	No No. (%)	Yes No. (%)	
High	145 (19.8)	13 (65.0)	158
Middle	281 (38.4)	4 (20.0)	285
Lower	306 (41.8)	3 (15.0)	309
Total	732 (100)	20 (100)	752

x^2 = 24.1, df = 2, P < 0.0001.

Discussion

WHO recommended that a single dose of a BCG vaccine should be given to all infants at birth in highly endemic countries.[15] BCG vaccination during infancy in Western Europe, North America and Australia is not obligatory.[6] The BCG vaccination in Iraq is mandatory at the first week of age and before giving a certificate for registration and identity. The vaccine is injected intradermally at the upper left arm. The scar developed after 1-4 weeks and left for life. Most of the studies suggested 3.5 mm as a cut-off point for non-failed vaccination.[11] The 3mm size was taken as the cut-off point in this study for comparing the cases according to the finding of the study results, where the cases subdivided smoothly with comparable numbers around this cut-off point. Although the immune system is complex and depends on several characteristics, but BCG scar size has not been studied before as an indicator of underlying immunity. Previous studies compared the effect of BCG vaccination on the development of infection with controversy about their effect. This study takes to the count that presence of big scar and low SES as indicators to underlying high innate previous immunity regardless of the presence or absence of direct immune effect of the vaccine. The size of the scar may reveal the underlying good immunity that is not related to the effect of vaccination. The scar size response

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to BCG vaccination is different from person to another. This difference may indicate the underlying variability and the extent of immune response in general. The differences in immunity might affect the response to infections including viral infection like COVID-19. A previous study is also indicated that large BCG scar size was associated with less risk for cancer which might related to their higher immunity.[10] The study suggests that higher BCG scar sizes that were associated with lower severity and mortality from COVID-19 may be related to their higher immunity as indicated by the large BCG scar size. Previous studies on the effect of socioeconomic status (SES) on BCG scar response are conflicting. Some indicated that low SES is associated with small scar size.[12] In this study the reverse is true. Where the higher severity and mortality were associated with high socioeconomic status and small size BCG scar. High SES patients mean those with high income and education and good job.[14] They live in clean environment as compared with low SES. The dirty environment may be responsible for augmentation of immunity and this may be responsible for the low severity and mortality in this group. The hygiene hypothesis which explained allergic responses in low SES may work here as well. The hygiene hypothesis states that childhood exposure to particular microorganisms protects against allergic diseases by the development of the immune system.[16] The BCG scar size can be used to measure the level of immunity against infection in all age groups. Also, the BCG vaccination can be used for augmentation of the immune system against infection in general. Exposure to the environmental stresses like those who associated with low SES might help in development of immune system perfectly.

In Conclusion, BCG scar size and socioeconomic class can be used as good indicators for immune response against infection and to predict the extent of severity and mortality. The larger scar size at birth indicates good immune response to vaccination. The dirty environment may be responsible for augmentation of immunity. Hygiene hypothesis may explains the reduced severity and mortality that was associated with low SES. Exposure to the environment like those with low SES is indicated for the development of the immune system.

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Data availability

The data is available on request by contacting the author.

Patient consent statement

The patient consent has been taken before the measurement of BCG scar size.

Funding statement

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دراسة تأثير حجم ندبة لقاح BCG والحالة الاجتماعية والاقتصادية على الشدة والوفيات للمصابين بكوفد ١٩

خلفية الدراسة: تختلف حالات الإصابة والوفيات بسبب كوفد ١٩ بين البلدان. بعض الدراسات تشير أن السبب قد يكون مرتبطًا بالسياسات المختلفة المتعلقة بالتطعيم ضد التدرن. إن الاستجابات المناعية للقاحات ترتبط بعوامل متعددة مثل الوضع الاقتصادي وانتشار الطفيليات والتغذية. يعد الوضع الاجتماعي والاقتصادي أحد العوامل المهمة التي تؤثر على الحالة الصحية.

الأهداف: لدراسة تأثير حجم ندبة BCG والفئة الاجتماعية والاقتصادية كمؤشرات للمناعة فيما يتعلق بشدة ووفيات مرضى كوفد ١٩.

طريقة العمل: أجريت دراسة مقارنة بين الحالات الشديدة والحالات الخفيفة إلى المتوسطة من عدوى كوفد ١٩ المؤكدة بفحص PCR في البصرة . تم إدراج جميع الحالات المؤكدة خلال شهري نيسان وأيار ٢٠٢٠ في مستشفى البصرة التعليمي. تمت دراسة حجم ندبة BCG والفئة الاجتماعية والاقتصادية وعلاقتهما بشدة المرض والوفيات لحالات كوفد ١٩.

النتائج: ارتبطت الشدة والوفيات المرتفعة بشكل ملحوظ مع مرضى المصابين بكوفد ١٩ الذين لديهم ندبة BCG صغيرة الحجم وكذلك مع المصابين من ذوي الطبقة الاجتماعية والاقتصادية العالية.

الاستنتاج: يمكن استخدام حجم ندبة BCG والفئة الاجتماعية والاقتصادية كمؤشرات جيدة للاستجابة المناعية ضد العدوى ومدى الخطورة والوفيات.

الكلمات الفتاحية: ندبة BCG ، الحالة الاجتماعية والاقتصادية، كوفيد ١٩، شدة والوفيات، المناعة

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