

## Factors contribute to Tuberculin Skin Test (TST) Positive among Urban Islander, Malaysian Borneo

Malezya Borneosu, Kentssel Adalılar'da Arasında Tüberkülin Deri Testi (TST) Pozitifliğine Katkıda Bulunan Faktörler

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### ABSTRACT

**Introduction:** Latency and the identification of risk groups have become a challenge and a priority to achieve the control and eradication of the TB disease. The objective of this study is to determine the prevalence and risk factors of tuberculin skin test (TST) positive in Pulau Gaya, Sabah, Malaysian Borneo.

**Methods:** A cross-sectional study was conducted among 197 from Pulau Gaya residents by using non-probability convenient sampling method from March to May 2017. Questionnaire on socio-demographic and risk factors of TB was used to assess the risk factors for TST positive. The data was collected by trained health personnel. TST was administered and measured after 72 hours by a trained lab technician. The standardised cut-offs of  $\geq 10$  mm are defined as reactive positive TST. TST positive cases were referred to Luyang Health Clinic for further investigations and management. SPSS version 24 was used to analyse the associated factors.

**Results:** The response rate was 100% (197) and the Prevalence of TST positive was 46.2%, which is considered high compare to other areas in Malaysia. The significant risk factors in bivariate analysis for TST positive were old age ( $p < 0.005$ ), increase BMI ( $p < 0.033$ ), marriage ( $p < 0.001$ ), employment ( $p < 0.05$ ), closed contact with TB patient ( $p < 0.005$ ), and Bacillus Calmette-Guerin (BCG) scars ( $p < 0.005$ ). In multivariate analysis, all the significant variables were entered, resulting in variables of employment (aOR 2.327 (95% CI: 1.175-4.609)) and no BCG scar (aOR 2.473 (95% CI: 1.175-4.446)).

**Conclusion:** The risk factors for positive TST were unemployment and no BCG scar. These high-risk group individuals need to be screened and monitored to detect the latent TB or early symptoms of active PTB. A health facility needs to be built in Pulau Gaya to improve TB vaccination activity and management programme.

**Key Words:** Risk factors, tuberculin skin test, tuberculosis, Borneo

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### ÖZET

**Amaç:** Risk gruplarının gecikmesi ve tanımlanması, TB hastalığının kontrolünü ve ortadan kaldırılmasını sağlamak için bir zorluk ve öncelik haline gelmiştir. Bu çalışmanın amacı, Pulau Gaya, Sabah, Malezya Borneo'da tüberkülin deri testi (TST) pozitif olan prevalans ve risk faktörlerini belirlemektir.

**Yöntem:** 197 Pulau Gaya sakinleri arasında Mart-Mayıs 2017 arasında olasılıksız uygun örnekleme yöntemi kullanılarak kesitsel bir çalışma gerçekleştirildi. TST pozitif risk faktörlerini değerlendirmek için TB'nin sosyodemografik ve risk faktörleri anketi kullanıldı. Veriler eğitimli sağlık personeli tarafından toplanmıştır. TST, eğitimli bir laboratuvar teknisyeni tarafından 72 saat sonra uygulandı ve ölçüldü.  $\geq 10$  mm'lik standartlaştırılmış kesme değerleri reaktif pozitif TST olarak tanımlanır. TST pozitif vakalar, daha fazla araştırma ve yönetim için Luyang Sağlık Kliniğine sevk edildi. İlişkili faktörleri analiz etmek için SPSS versiyon 24 kullanıldı.

**Bulgular:** Yanıt oranı% 100'dü (197) ve TST pozitif prevalansı% 46.2 idi, bu da Malezya'daki diğer bölgelere göre yüksek kabul ediliyor. TST pozitif için iki değişkenli analizde önemli risk faktörleri yaşlılık idi ( $p < 0.005$ ), VKİ ( $p < 0.033$ ), evlilik ( $p < 0.001$ ), istihdam ( $p < 0.05$ ), TB hastasıyla kapalı temas ( $p < 0.005$ ) ve Bacillus Calmette-Guerin (BCG) skarlarını ( $p < 0.005$ ) artırın. analizde, tüm önemli değişkenler girilerek istihdam değişkenleri (aOR 2.327 (% 95 CI: 1.175-4.609)) ve BCG izi yok (aOR 2.473 (% 95 CI: 1.175-4.446)).

**Sonuç:** Pozitif TST için risk faktörleri işsizlik ve BCG skarının olmamasıydı. Bu yüksek risk grubundaki bireylerin gizli TB'yi veya aktif PTB'nin erken semptomlarını tespit etmek için taranması ve izlenmesi gerekir. TB aşılama faaliyetini ve yönetim programını iyileştirmek için Pulau Gaya'da bir sağlık tesisi inşa edilmelidir.

**Anahtar Sözcükler:** Risk faktörleri, tüberkülin deri testi, tüberküloz, Borneo

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**INTRODUCTION**

Tuberculosis (TB) is an infectious disease that can lead to a global epidemic caused by *Mycobacterium tuberculosis* (MTB) bacteria. Most humans are infected through respiratory infections, which are transmitted from the respiratory tract of an active pulmonary TB (PTB) patient (1). Latent tuberculosis infection (LTBI) is characterized by the presence of immune responses to previously acquired MTB infection without clinical evidence of active TB. Persons with LTBI are not infectious, cannot transmit TB infection to others and have negative sputum test (2).

Latency and the identification of risk groups have become a challenge and a priority to achieve the control and eradication of the TB disease (3, 4). Available evidences suggested that age and comorbidity (such as HIV, steroid user, or chronic kidney disease), are predictors for both LTBI and TB disease (5). However, studies are controversial on whether social factors such as smoking and alcohol abuse should be considered (6).

Data from Kota Kinabalu Health Office, the incident rate of TB in Pulau Gaya is two times higher than the Sabah incident rate in 2015. The incident rate for TB in Pulau Gaya for 2015 is near 234 per 100,000 population, and the incident rate for Sabah is 125.98 per 100,000 population (7). Thus TB is one of the vital health problems among the Pulau Gaya population. In 2016, non-Malaysians contributed 54 per cent of the active TB cases in Pulau Gaya. Previous studies have revealed a high prevalence of LTBI in high-risk groups such as health care workers, prisoners and gold miners (8). In the community, there also vary in the prevalence of LTBI (9). However, it is challenging to find a study on the prevalence of LTBI in the small island community, like Pulau Gaya. The proximity of the island to the city and the geographical factor is a factor of rapid movement in and out of immigrant in Pulau Gaya, especially a country with a high burden of TB like Philippine, which is adjacent to the Sabah. The population of Malaysians, as well as immigrant, contributes to the high incident rate in Gaya (10). Due to the mixture of population, the cultural and the socioeconomic in Pulau Gaya are slightly different from the nearest area.

An estimated one-third of the world population currently presents LTBI, and only between 5 and 10% will develop TB disease during their lifetime (11). Most of these patients develop active TB within the first five years unless they are diagnosed and treated with anti-TB medications (12). Identification LTBI will increase the rate of case detection of active TB. This situation may influence in developing new intervention policies to eliminate the spread of TB (13). Therefore, the present study was done to determine the prevalence and risk factors for positive TST of among residents of Pulau Gaya, Sabah.

**METHODS**

A community-based cross-sectional study was conducted at Pulau Gaya, Kota Kinabalu, Sabah, Malaysia from March to May 2017. A total of 197 subjects were recruited. Non-probability convenient sampling method was utilised to select the study participants. The participants who are i) aged 15 years and over, ii) staying in Pulau Gaya and iii) No previous history of TB disease iv) agreeable to give consent to participate in the study were selected. For the subject under 18 years old, the consent was taken from their parents/guardians. Subjects with cognitive or any others speech impairment and did not meet the inclusion criteria were excluded. The ethical clearance was obtained from University Malaysia Sabah. The permission of conducting this research was obtained by the Institutional Review Board University Malaysia Sabah of Faculty of Medicine and Health Sciences before data collection in Pulau Gaya community.

After getting the informed and written consent, a validated questionnaire was administered with guided in this study due to some of the participant have a lower educational level. The questionnaire used for the study consists of two parts, including socio-demographic data and individual risk factors towards TB. The information required from the participants included a socio-demographic profile, house conditions, smoking habit, alcohol consumption, TB contact, diabetes mellitus, and end-stage renal failure. BCG scar at the left arm and body mass index (BMI) was examined during the interview. Using the intradermal technique, TST was performed by a trained health personal by administering 0.1 ml of purified protein derivative. The result was obtained after 72 hours by calling the individual participant, and positive TST was measured based on an induration of  $\geq 10$  mm.

Data were analysed using the IBM statistical package for social science (SPSS) Statistics ver. 24.0 (IBM Co., Armonk, NY, USA). The categorical variables were used in frequencies and percentage while the continuous variable was using mean and median in the descriptive analysis of data. Simple logistic regression was performed for bivariate analysis for categorical data and Mann Whitney U test for continuous not parametric data. Multiple logistic regression analysis was used for multivariate analysis. Statistical significance was determined at  $p < 0.05$ .

**RESULTS**

A total of 196 participants from Pulau Gaya were enrolled in the study. Out of these, 91 participants were positive with TST. Hence, the prevalence obtained was 46.2% with a response rate of 100%. Among them, 74 (37.6%) participants were male, and 123 (62.4%) were female. The descriptive data on socio-demographic and individual risk factors have been shown in Table 1. The socio-demographic characteristic of subjects in our study showed that the age of the participants ranged 15-88 years with a mean age of 30.25 and a standard deviation of 16.08 years. In terms of occupation, among 197 participants being interviewed, 45 (22.8%) subjects were working, followed by not working 152 subjects (77.2%). Of the total 197 respondents, only 75 respondents (38.1%) had close contact with who have ever been diagnosed with TB and 122 respondents (61.9%) no known history of close contact with TB patient. Out of a total of 196 interviewees, 120 (60.9%) participants are having BCG scar followed by 79(39.1%) with no BCG scar.

**Table 1:** Descriptive analysis on socio-demographic and individual risk factors

	Overall sample (N = 197)		Frequency (n)	Per cent (%)
	Mean (SD)	Median (IQR)		
Prevalence of TST positive				46.2
Gender				
Male			74	37.6
Female			123	62.4
Age	30.25 (16.8)	21 (24.5)		
< 50 years old			165	83.8
≥ 50 years old			32	16.2
Nationality				
Malaysian			187	94.9
Non-Malaysian			10	5.1
Race				
Bajau			189	95.9
Others			8	4.1
Marital status				
Married			85	43.1
Single / divorced			112	54.3
Family income (RM)	1300.86 (465.65)	1400 (630)		
< RM1500			80	40.6
≥ RM1500			117	59.4
Highest education				
Illiteracy			27	13.7
Primary school			36	18.3
Secondary school			131	66.5
Tertiary			3	1.5
Occupation				
Employed			45	22.8
Unemployed			152	77.2
House condition				
Overcrowded			93	47.2
Not crowded			104	52.8
House windows	5.7 (2.48)	5 (3)		
< 6 windows			139	70.1
> 7 windows			59	29.9
Smoking habit				
Smoker			26	13.2
Not smoker			171	86.8
Alcohol				
Consumer			3	1.5
Non-consumer			194	98.5
TB contact				
Has contact			75	38.6
No contact			122	61.9
BCG scar				
Absent			77	39.1
Present			120	60.9
Diabetes mellitus				
Has diabetes			4	2.0
No diabetes			193	98.0
End-stage renal failure				
Has ESRF			5	2.5
No ESRF			192	97.5
Body mass index	22.43 (5.02)	21.15 (6.12)		
Underweight			39	19.8
Normal			95	48.2
Overweight/Obese			63	32.0

TST: Tuberculin skin test, SD: Standard deviation, IQR: Interquartile Range, ESRF: End stage renal failure,  $\phi$ , showing P-value <0.05

Among sociodemographic variables, only marital status and employment were significantly associated with TST positive in bivariable analysis. Among individual risk factors, the presence of BCG scar and TB contact showed a statistical

difference in bivariate analysis with a p-value of <0.05. The rest of the variables were not statistically significant. It is shown in Table 2.

**Table 2:** Bivariate analysis of socio-demographic and individual risk factors

	Total	Overall sample (N = 197)		P-value	OR	95% CI
		TST Positive, 91 (46.2)	TST Negative, 106 (53.8)			
<b>Gender</b>						
Male	74	36 (48.6)	38 (51.4)	0.592	1.171	0.657-2.088
Female	123	55 (44.7)	68 (55.3)		-	-
<b>Age</b>						
< 50 years old	165	73 (44.2)	92 (55.8)	0.215	-	-
≥ 50 years old	32	18 (56.3)	14 (43.8)		1.62	0.756-3.475
<b>Nationality</b>						
Malaysian	187	86 (46.0)	101 (54.0)	0.804	1.174	0.329-4.192
Non-Malaysian	10	5 (50.0)	5 (50.0)		-	-
<b>Race</b>						
Bajau	189	89(47.1)	100(52.9)	0.0.236	2.67	0.525-13.567
Others	8	2(25.0)	6(75.0)		-	-
<b>Marital status</b>						
Married	85	51(60.0)	34(40.0)	0.001 <sup>†</sup>	2.70	1.510-4.828
Single / divorced	112	40(35.7)	72(64.3)		-	-
<b>Family income</b>						
< RM1500	111	47 (42.3)	64 (57.7)	0.219	-	-
≥ RM1500	86	44 (51.2)	42 (48.8)		1.427	0.810-2.513
<b>Highest education</b>						
Illiteracy	27	15 (55.6)	12 (44.4)	-	-	-
Primary Education	36	20 (55.6)	16 (44.4)	1.000	1.000	0.366-2.730
Secondary Education	131	54 (41.2)	77 (58.8)	0.175	0.561	0.243-1.293
Tertiary Education	3	2 (66.7)	1 (33.3)	0.714	1.600	0.129-19.838
<b>Occupation</b>						
Employed	45	28 (62.2)	17 (37.8)	0.015 <sup>†</sup>	2.327	1.175-4.609
Unemployed	152	63 (41.4)	89 (58.6)		-	-
<b>House condition</b>						
Overcrowded	93	48(46.2)	56(53.8)	0.991	-	-
Not crowded	104	43(46.2)	50(53.8)		1.003	0.573-1.758
<b>House windows</b>						
< 6 windows	139	66 (47.8)	72 (52.2)	0.482	-	-
> 7 windows	59	25 (42.4)	34 (57.6)		1.247	0.674-2.306
<b>Smoking habit</b>						
Smoker	26	15(57.7)	11(42.3)	0.210	1.705	0.740-3.926
Not smoker	171	76(44.4)	95(55.6)		-	-
<b>Alcohol</b>						
Consumer	3	1 (33.3)	2 (66.7)	0.656	-	-
Non-consumer	194	90 (46.4)	104 (53.6)		1.731	0.154-19.405
<b>TB contact</b>						
Has contact	75	25 (33.3)	50 (66.7)	0.005 <sup>†</sup>	-	-
No contact	122	66 (54.1)	56 (45.9)		2.357	1.297-4.285
<b>BCG scar</b>						
Absent	77	46(59.7)	31 (40.3)	0.002 <sup>†</sup>	2.473	1.376-4.446
Present	120	45(37.5)	75 (62.5)		-	-
<b>Diabetes mellitus</b>						
Has diabetes	4	1 (25.0)	3 (75.0)	0.408	-	-
No diabetes	193	90(46.6)	103 (53.4)		2.621	0.268-25.648
<b>End stage renal failure</b>						
Has ESRF	5	2(40.0)	3 (60.0)	0.779	-	-
No ERSF	192	89 (46.4)	103 (53.6)		1.296	0.212-7.932
<b>Body mass index</b>						
Underweight	39	17(43.6)	22(56.4)	-	-	-
Normal	95	38(40.0)	57(60.0)	0.708	0.863	0.406-1.834
Overweight/Obese	63	36 (57.1)	27 (42.9)	0.185	1.725	0.771-3.863

TST: Tuberculin skin test, OR: Odd Ratio, 95% CI: 95% confidence interval

Whitney U test, older age and increasing BMI were statistically significant (Table 3).

There is no significant difference in age and BMI category between people with TST positive and negative. However, for a continuous variable using the Mann

**Table 3:** Analysis of continuous data

TST Results							
Variable	TST Positive		TST negative		U	Z	P-value
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)			
Age (year)	34.19 (16.92)	32.00 (28.00)	26.87 (16.03)	17.00 (18.00)	6361.0	3.907	0.0001
Income (RM)	1318 (423.34)	1400 (650)	1285.47 (500.63)	1300.00 (600.00)	5222.5	1.007	0.314
House Windows	5.59 (2.72)	5 (3)	5.78 (2.27)	6 (3)	4465.5	-0.907	0.365
BMI	23.26 (5.40)	22.23 (6.90)	21.72 (4.56)	20.14 (4.80)	5766.5	2.365	0.018

In multivariable analysis (Table 4), multiple logistic regression analysis was used. All the significant variables in bivariable analysis were entered, which are older age, increase BMI, employment, TB close contact history, BCG scar and

marital status. The variables that had significant results was employment (aOR 2.327 (95% CI:1.175-4.609)) and no BCG scar (aOR 2.473 (95% CI:1.376-4.446)).

**Table 3:** Multivariate analysis

Variable	Crude		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	P-value
Older Age	2.357(1.297-4.285)	0.005	-	-
Increase BMI	1.065 (1.005-1.128)	0.033	-	-
Married	2.700 (1.510-4.828)	0.001	-	-
No known TB contact	2.357 (1.297-4.285)	0.005	-	-
Working	2.327 (1.175-4.609)	0.015	2.309 (1.138-4.687)	0.021 <sup>φ</sup>
No BCG scar	2.473 (1.376-4.446)	0.002	2.153 (1.158-4.003)	0.015 <sup>φ</sup>

<sup>φ</sup>, showing P-value <0.05, OR: Odd Ratio, 95% CI: 95% confidence interval

## DISCUSSION

Research of TB study in Pulau Gaya is still in infancy. TB is a global disease worldwide, even in Sabah, Malaysia. It afflicts the poor and uneducated communities living in congested areas based on a previous study (14). Diagnosis of TB requires certain investigations, namely chest radiography and sputum acid-fast bacilli. Also, TST acts as an adjunct test before going to a definitive investigation modality as described earlier. In this study, the prevalence rate for TST positive is 46.2% which is near half of the subjects. The figure almost the same with the overall rate of LTBI among healthcare worker in Malaysia, which is 46% (15). However, for the community base study, the figure is considered as high compared to other countries (16).

This study did not find a significant difference between people with TST positive and with TST negative in gender but not in the age variable. In this study, older age has more risk of TST positive. In previous studies, TB and LTBI were predominant in a male and elderly population (17-19). Our result also was contradicted with the previously published study showing no significant difference in education, overcrowding and family income between participants with TST positive and TST negative. Other risk factors for TB are smoker, alcohol consumer, IVDU, ex-prisoner, history of closed contact with TB patient, Undernutrition, and some chronic disease (17). In this study, all variables mentioned above were not significant except for the nutritional status (BMI) and history of TB contact. However, for the BMI, the results contradicted with the previous study, which is high or increase BMI were significantly associated with TST positive in the bivariate analysis but not in multivariate analysis.

For the history of TB contact, this study result in the bivariate analysis also was contradicted from previous literature, which is there was no history of closed contact have a higher risk of getting TST positive compared with having a history of close contact with active PTB patient (15, 16). However, in multivariate analysis, the results were not significantly associated. In a subanalysis of the TB contact variable, the majority of the subjects that do not have close contact with PTB patient were associated with the absence of BCG scar, which is significantly associated with TST positive.

The other significant findings in the bivariate analysis were marital status, no BCG scar and employment. For the marital status, marriage subjects showed more risk than single/divorced group. The subjects without BCG scar higher risk of getting TST positive. The results were consistent with previous literature (16). The employed residence also had a higher risk of developed TST positive as compared to unemployed participants in bivariate analysis.

In multivariate analysis among the positive risk factors in this study, two risk factors significantly associated with positive TST, which is employment and absent of BCG scar. The employed participant has risk compared to the unemployed due to they have more contact with the people and exposed to overcrowding environment. Health promotion and health education will improve their knowledge and attitude toward the preventive measure of PTB disease.

In this study, the presence of BCG scar was a protective factor from TST positive. However, only two-third of the participant in Pulau Gaya had not been vaccination of the BCG. This show previous BCG vaccination coverage in Pulau Gaya was low compare to Malaysia policy. Vaccination of BCG is one of the beneficial interventions for the TB control programme. A meta-analysis of BCG trial data also suggested that the protective efficacy of BCG may persist ten years or more after infant vaccination (20). A study showed that BCG vaccination during infancy and adolescence could induce the immunological memory to mycobacterial antigens that are persistent up to 14 years (21). Additionally, a study looking at long term BCG efficacy among American Indians and Alaska natives showed that protection could last up to 60 years (22) and in Brazilians vaccinated as neonates for up to 20 years (23).

The limitations of this study include that majority of previous studies compared TB and non-TB cases as well as latent TB infection and non-latent TB infection. However, in this study, we only managed to make a comparison between positive and negative TST. These happen due to the logistic restriction of the participant, limitation of time and budget constraint. Which is the majority of subjects were unable to go nearest health facility to do further investigation. So, we were unable to proceed with definitive investigations which are sputum acid-fast bacilli and chest radiography for most of the subjects due to Further follow up need to be done to the subject to conform the LTBI and TB status of the TST positive subject.

Another limitation was that we only manage to do a non-probability convenient sampling method to select the study participants. Random sampling was unable to be done due to the logistic challenging to the researcher and the subjects. Most of the Pulau Gaya residence and the subjects were working in the mainland of Kota Kinabalu. This study needs the Mantoux test reading in the 2<sup>nd</sup> follow up. So, we need the subject that contactable and available for the second to follow up that was difficult to choose randomly.

Further research will have found new significant value and can be used in the control of TB cases in Pulau Gaya. It includes as following (1) further research regarding health-seeking behaviour to understand the problems in controlling TB, (2) further proper investigated of TST positive subject for TB confirmation and (3) large sample size with an easy flow for subject doing the further investigation (chest radiography). Treatment of LTBI is an essential component of control and elimination of TB. Knowing the risk factors for LTBI and improving the screening technique will help in the management of LTBI and active TB.

## CONCLUSION

Unemployment and the absence of BCG scar had proven to be the main risk factors of TST positive cases in this study. Health education regarding transmission, risk factors and symptoms of TB need to be emphasis to the high-risk population, specially employed people and no BCG scar groups. Vaccination of BCG is one of the vital interventions for control the spread of TB. Coverage of BCG vaccination needs to be improved in Gaya Island to control the spread of TB. There also need Health facilities to build in the Pulau Gaya to improve TB detection, and vaccination activities need to increase in Pulau Gaya.

## Conflict of interest

No conflict of interest was declared by the authors.

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