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RESEARCH ARTICLE **OPEN ACCESS**

MEASUREMENT OF THYROID BIOMARKERS AS PART OF A MALAYSIAN COMMUNITY HEALTH PROJECT

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ABSTRACT

Introduction: Non-communicable diseases (NCDs), including thyroid disease, are prevalent in Malaysia. A community health project was undertaken to improve community awareness of the risks of NCDs, and the benefits of screening for disease prevention and early detection. **Methods:** Community health screening was conducted during the 2016 KembaraMahkota community event in Johor, Malaysia. Blood samples were taken from willing participants who attending the event. Samples were tested for a range of biomarkers, including thyroid stimulating hormone (TSH) and anti-thyroid peroxidase antibodies (anti-TPO). Individuals identified as high risk were referred for specialist follow-up. **Results:** A total of 2744 individuals participated in biomarker screening. Based on TSH levels, hyperthyroidism and hypothyroidism were present in 1.5% and 0.95% of the population, respectively, and 11% of participants were positive for anti-TPO, indicating a risk of autoimmune thyroid disease. **Conclusion:** Community health projects such as ours are required to raise awareness of the risks of common preventable diseases, and to encourage individuals to participate in health checks and disease screening programmes.

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INTRODUCTION

Thyroid dysfunction is the most common endocrine disorder in Malaysia.[1] Although many patients with thyroid dysfunction experience no or only mild symptoms, the clinical consequences of abnormal thyroid function can be diverse. Abnormal thyroid hormone levels are associated with dyslipidaemia,[2] impaired bone strength,[3], and may contribute to development of epilepsy.[4] Even subclinical thyroid dysfunction is associated with an increased risk of cardiovascular disease and mortality.[5-9] In addition, the children of women with thyroid disease during pregnancy are at risk of impaired cognitive and physical development.[1] The presence of goitre, which is endemic in some parts of Malaysia,[10-12] may increase the risk of developing thyroid cancer.[13]

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Because of the potential public health consequences, and the lack of specific symptoms of undiagnosed thyroid disease, population-based screening may help to identify people with this condition, and then to begin appropriate treatment and/or make relevant lifestyle and dietary changes. However, screening for non-communicable diseases (NCDs) in Malaysia is mainly performed opportunistically by healthcare providers or is initiated by the individual, and the uptake of health checks is low.[14-16] Population screening programs can also help individuals to better understand the risks of NCDs, including thyroid disease, and motivate them to undergo future health checks for NCDs. We took advantage of a major state-wide public event to conduct a community health screening project, using blood-based biomarkers to screen for risk of a range of health conditions, including thyroid disease, in the general population of Johor, Malaysia. The aim of this project was to improve community awareness of the risks of the common NCDs, and the benefits of screening for disease prevention and early detection. This report describes the results of the thyroid screening assessment; results of the other screening programs have been reported elsewhere.

MATERIALS AND METHODS

Study population: Community health screening was conducted during the Kembara Mahkota event, which took place from the 14th to the 17th of May 2016. The Kembara Mahkota is a royal "meet the people" tour that covers the 10 districts of the state of Johor. During the Kembara Mahkota event, members of the Johorian public aged ≥18 years were offered free blood-based biomarker tests to screen for risk of cardiovascular disease (CVD), type 2 diabetes, cancer, and thyroid disease. A total of 2744 individuals participated in biomarker screening. They were briefed by district healthcare personnel, and asked basic questions regarding their medical, surgical and family disease history. Collected blood samples were transported to Johor Specialist Hospital for analysis. This study was approved by the Johor State Health Department. All participants gave informed consent.

Biomarker assay methods: Blood sample analyses were performed daily at Johor Specialist Hospital. All analyses were performed on the Abbott ARCHITECT system. A number of biomarkers indicating risk of CVD, diabetes, cancer, and thyroid disease were measured. Thyroid-stimulating hormone (TSH) levels and anti-thyroid peroxidase (anti-TPO) antibodies were measured to screen for thyroid dysfunction.

Biomarker levels and disease risk: Biomarker cut-off levels interpreted as being indicative of high risk of disease were based on Abbott biomarker assay sensitivities and evidence-based reference values. An anti-TPO antibody reading >6.8 IU/mL was considered abnormal, indicating autoimmune thyroid disease. A TSH level of between 0.45 and 4.5 mIU/L was considered to indicate normal thyroid function. Hyperthyroidism was defined as a TSH level of ≤0.44 mIU/L, and further subcategorised as probable hyperthyroidism at levels of <0.1 mIU/L and subclinical hyperthyroidism at levels of 0.01 to 0.44 mIU/L. Similarly, hypothyroidism was defined as aTSH level≥4.6 mIU/L, with subclinical hypothyroidism at levels of 4.6–10 mIU/L and probable hypothyroidism at >10.0 mIU/L(Abbott Diagnostics, Data on file).

Follow-up and education: When test results indicated high risk of disease, individuals were referred to specialist physicians for follow-up. Brief lectures on cancer, diabetes, heart disease and hypertension were given for the benefit of all visitors of the healthcare booth, irrespective of whether or not they decided to participate in biomarker disease screening.

RESULTS

Subject characteristics: Of the 2744 individuals who took part in biomarker screening, 93% were <60 years old, and 50.6% were female.

Thyroid biomarkers: The distribution of thyroid biomarker levels across the population are shown in Figure 1. Anti-TPO antibody levels were >6.8 IU/mL in 11.3% of the population. TSH levels were ≥4.6 mIU/L (hypothyroid) in 1.7% of the population, and ≤0.44 mIU/L (hyperthyroid) in 3.6%. Overall, 89.5% of the population were classified as having a normal thyroid (Table I). Anti-TPO levels ranged from 0 to 1000.0 IU/mL across the screened population. There was no difference in mean or median anti-TPO levels between men and women (Table II and Figure 2), but there was a small trend of increasing mean anti-TPO levels between the ages of 30 to 79 years (Table I and Figure 3). TSH levels ranged between 0.01 mIU/L and 100 IU/L. There was no difference in mean or median between genders (Table II and Figure 2), although there was more variability among women than men. There was no age-related trend in average TSH levels (Table II and Figure 3). TSH levels were within normal limits in anti-TPO-negative men and women. This was not affected by age (Table III).

Table I. Classification of thyroid status in the general population

Thyroid status	Proportion of the population (n=2663)
Normal	2382 (89.45%)
Subclinical hyperthyroidism	63 (2.37%)
Subclinical hypothyroidism	40 (1.50%)
Probablehyperthyroidism	32 (1.20%)
Probablehypothyroidism	5 (0.19%)
Other	141 (5.29%)

DISCUSSION

The Kembara Mahkota event, which is traditionally well attended by a large cross-section of the community, provided an opportunity to identify individuals at high risk of NCDs, including thyroid disease, and to improve awareness of these common NCDs within the general Johor population. Information offered to people visiting our healthcare booth was aimed at improving awareness of disease and the importance of screening for early detection or prevention of disease. Consequently, 2744 individuals accepted our offer of blood-based biomarker testing to assess their disease risk. We used blood-based biomarkers to identify high-risk individuals, and individuals identified as being at high risk were referred for specialist follow-up, thereby allowing them to begin appropriate therapy and/or adopt lifestyle and dietary changes that could improve long-term outcomes. It is thought that the potential benefits of early detection and treatment of subclinical thyroid dysfunction significantly outweigh any potential adverse effects of early treatment.[17] TSH testing, which can distinguish people with hyper- or hypothyroidism from normal euthyroid individuals, is the best screening tool for thyroid dysfunction.[18,19] Additionally, anti-TPO antibodies, which are detectable in the circulation before there is any abnormality in thyroid function and predict progressive thyroid dysfunction, are the best markers of autoimmune thyroid disease.[17-19]

Although subclinical hyperthyroidism is usually less prevalent than hypothyroidism,[17,18] TSH levels in our study population revealed that hyperthyroidism was slightly more common than hypothyroidism (1.5% vs 0.95%). Based on measurement of anti-TPO antibodies, approximately 11% of our study population was at risk of autoimmune thyroid disease and progressive thyroid dysfunction. All individuals identified as being hypothyroid, hyperthyroid, or at risk of autoimmune thyroid dysfunction were referred for further assessment, monitoring and potential therapeutic intervention. Internationally, there is no consensus on the use of routine screening for thyroid dysfunction in asymptomatic individuals in the community,[17] and the low prevalence of hypo- or hyperthyroidism in our community sample would appear to support this ambivalence. Nevertheless, there is agreement for "aggressive case-finding" of thyroid dysfunction, in which

Table II. Mean and median thyroid biomarker values in specific population subgroups

Participant subgroup	Anti-TPO, IU/mL			TSH, mIU/L		
	N	Mean	Median (Range)	N	Mean	Median (Range)
Gender						
Females	1487	53.16	0.4 (0–1000.1)	1507	1.56	1.21 (0.01–100)
Males	1217	27.91	0.5 (0–1000.1)	1231	1.33	1.17 (0.01–9.39)
Age groups						
<20 years	36	28.81	0.4 (0.1–1000.1)	36	1.52	1.425 (0.01–3.33)
20–29 years	491	27.95	0.4 (0.2–1000.1)	497	1.37	1.17 (0.01–8.47)
30–39 years	696	25.94	0.4 (0.2–1000.1)	709	1.40	1.14 (0.01–100)
40–49 years	620	46.93	0.4 (0.3–1000.1)	630	1.43	1.17 (0.01–37.64)
50–59 years	637	55.31	0.5 (0.3–1000.1)	642	1.44	1.22 (0.01–10.87)
60–69 years	198	64.09	0.5 (0.3–1000.1)	198	1.98	1.235 (0.01–100)
70–79 years	21	144.40	0.6 (0.3–1000.1)	21	1.50	1.12 (0.66–5.54)
>80 years	5	31.36	0.7 (0.5–154.3)	5	1.52	1.42 (0.39–2.28)

Anti-TPO, anti-thyroid peroxidase; TSH, thyroid-stimulating hormone

Table III. TSH reference ranges in specific anti-TPO-negative population subgroups

Subgroup	95% reference limit (95% confidence interval)	
	Lower	Upper
Gender		
Females	0.46 (0.44, 0.47)	3.04 (2.89, 3.27)
Males	0.48 (0.45, 0.50)	2.77 (2.66, 3.12)
Age groups		
≤30 years	0.47 (0.42, 0.52)	3.13 (2.83, 3.30)
>30 years	0.47 (0.44, 0.48)	2.90 (2.74, 3.12)
≤40 years	0.47 (0.45, 0.50)	2.90 (2.68, 3.17)
>40 years	0.47 (0.44, 0.49)	3.00 (2.85, 3.45)
≤50 years	0.46 (0.45, 0.49)	2.90 (2.69, 3.12)
>50 years	0.47 (0.44, 0.51)	3.12 (2.89, 3.54)

TSH levels are regularly monitored by physicians if the patient has relevant symptoms, signs, personal history or family history of thyroid disease.[17] Testing for anti-TPO should be undertaken in all patients with abnormal TSH levels in order to identify autoimmune thyroid disease[17].

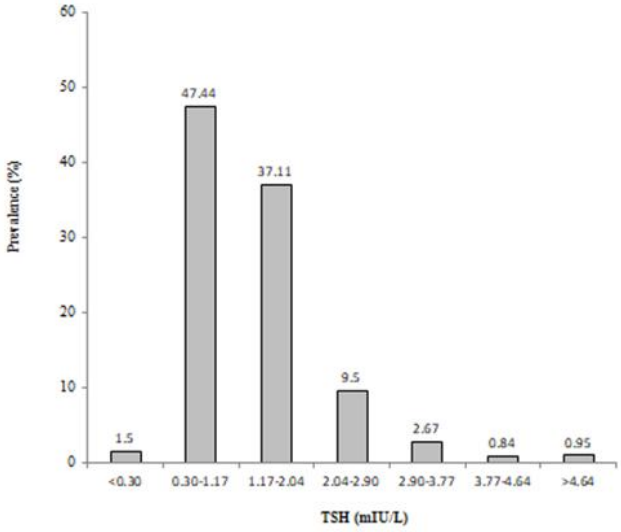


Figure 1. Distribution of thyroid disease biomarker levels in the population: (a) thyroid stimulating hormone (TSH; n=2738) and (b) anti-thyroid peroxidase antibodies (anti-TPO; n=2704)

The prevalence of anti-TPO positivity in our study (11%) is comparable to the prevalence in women of childbearing age reported in the literature (5.4% to 20%),[20] and similar to prevalence among euthyroid pregnant women in a recent study from Singapore and Malaysia (10.3%).[21] However, a higher prevalence (14% to 33%) has been reported in women with a history of miscarriage or infertility.[20] Screening for anti-TPO antibodies in pregnant women is recommended because of the high risk of obstetric complications that can affect the mother and foetus.[22]

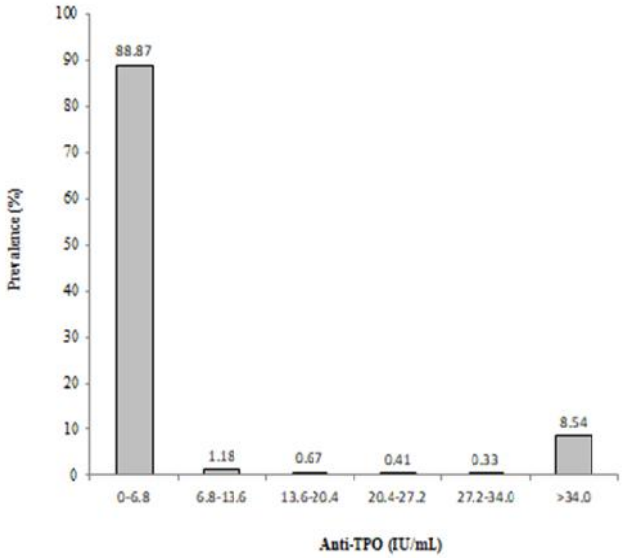
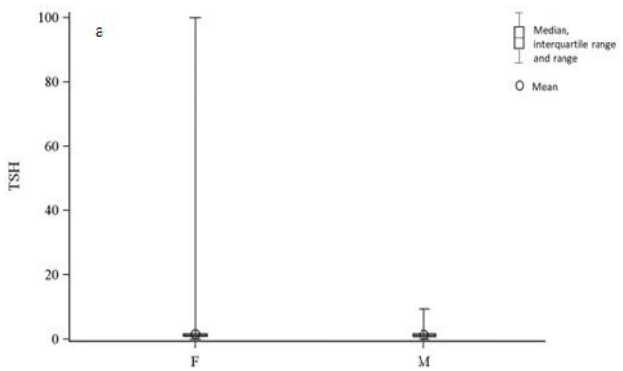
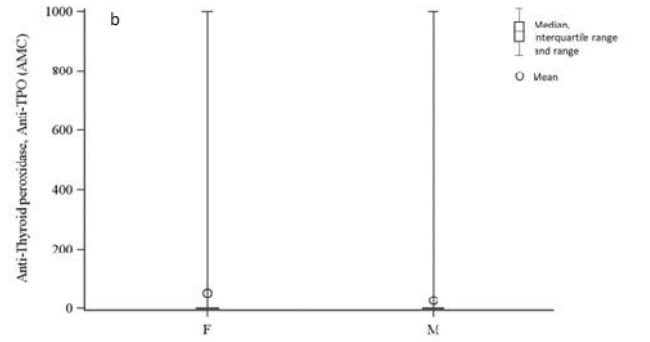


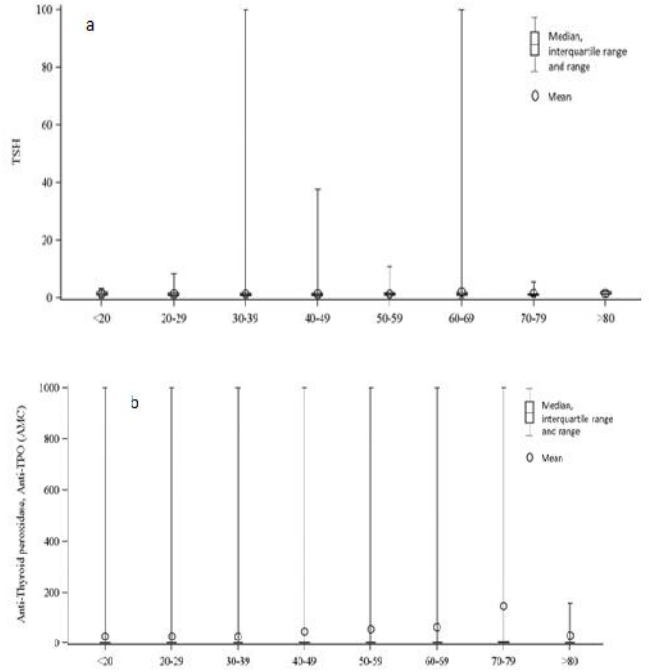
Figure 2. Levels of thyroid biomarkers in men and women: (a) TSH (mIU/L) , and (b) anti-TPO (IU/mL) (a)





TSH, thyroid stimulating hormone; anti-TPO, anti-thyroid peroxidase antibodies

Figure 3. Levels of thyroid biomarkers in different age groups: (a) TSH (mIU/L) and (b) anti-TPO (IU/mL)



TSH, thyroid stimulating hormone; anti-TPO, anti-thyroid peroxidase antibodies

In conclusion, we believe that to effectively implement strategies to reduce the incidence and improve the prognosis of common and preventable NCDs, including thyroid disease, community health projects such as ours are required to raise disease awareness and encourage individuals to participate in health checks and disease screening programmes. Further follow-up is required to determine the nature of interventions and outcomes in the high-risk patients identified and referred for specialist follow-up in our population-based study.

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