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Prevalence and associated Risk Factors for Obesity among Adult Patients with Thyroid Nodules

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Abstract

Background: Obesity and thyroid nodules (TNs) are a growing medical health problem globally. Hence, the current study was performed to evaluate the prevalence and associated predictors for obesity among adult patients with TNs in the Royal Commission Hospital, Kingdom of Saudi Arabia (KSA).

Methods: A retrospective study was conducted between January 1, 2015 and December 31, 2021. Patients with documented TNs based on the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) were recruited. Then, the prevalence and associated risk factors for obesity were assessed.

Results: Three hundred and ninety-one patients with documented TNs were enrolled in the study. The median (IQR) age was 46.00 (20.0) years, and 332 (84.9%) of the patients were female. The median (IQR) BMI was 30.27 (7.71) kg/m^2, and most participants were euthyroid (64.0%) or exhibited hypothyroidism (28.6%), while a few had hyperthyroidism (7.4%). The outcome of thyroid ultrasound reports among the patients based on ACR TI-RADS was: ACR TI-RADS-1 (2.6%), ACR TI-RADS-2 (18.4%), ACR TI-RADS-3 (40.7%), ACR TI-RADS-4 (36.3%), and ACR TI-RADS-5 (2%). There was a high prevalence of obesity (51.66%) among the participants. In the univariate analysis, there was a significant association between obesity in these patients and age, gender, diabetes mellitus, hypertension, bronchial asthma, thyroid-stimulating hormone (TSH), free thyroxine (FT4), total cholesterol, and the finding of an ultrasound based on TI-RADS. In the multivariate analysis, older age (OR = 1.029 (95.0 % CI: 1.009–1.048) and female gender (OR = 3.806 (95.0% CI: 1.975–7.334) were significantly associated with obesity in adult patients with TNs.

Conclusion: There was a high prevalence of obesity among patients with TNs. Older age and female gender were significantly associated with obesity and TNs.

Keywords: Prevalence; Obesity; Thyroid nodules; Predictors

Abbreviations

KSA: Kingdom of Saudi Arabia.

TNs: thyroid nodules.

IQR: interquartile range.

AOR: Adjusted odds ratio;.

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BMI: Body mass index;

CI: confidence interval;

SD: Standard deviation.

FNAC: Thyroid fine-needle aspiration cytological

TI-RADS: Thyroid ultrasound reports based on thyroid imaging reporting and data system.

Introduction

The American Thyroid Association (ATA) defines a thyroid nodule (TN) as an abnormal lesion within the thyroid gland tissue [1]. TNs have become markedly prevalent during the last two decades: 2000–2011 (21.53%) versus 2012–2022 (29.29%) [2]. A recently published study identified that the overall worldwide prevalence of thyroid nodules was 24.83%, irrespective of the diagnostic techniques adopted, in addition to being more prevalent among women (36.51%) compared to men (23.47%) [2]. Globally, variation in the prevalence of TNs was demonstrated in different areas: highest in South Africa (79%), high in Denmark 54%, and much lower in the United States and Canada (around 30%) [3]. Despite the fact that most thyroid nodules are benign (72.5–80%) [4,5], the risk of malignancy should be assessed, as earlier intervention is associated with a high cure rate and a better prognosis [6,7]. Improvement in the management of TNs reflects the diagnostic tools available today, which refine the risk of malignancy, reduce the rate of unnecessary thyroid surgeries, and influence the prognosis. Examples of these tools include a thyroid ultrasound that enhances the ability to diagnose even non-palpable thyroid nodules [8,9], sonography-guided fine needle aspiration cytology (FNAC), which improves the accuracy and safety of the technique [9,10], scoring systems for thyroid ultrasound [10], thyroid FNAC [11], and genetic and molecular testing [12].

Nevertheless, obesity remains a major global health problem. The worldwide prevalence of obesity has nearly tripled since 1975, and in the Eastern Mediterranean region, it increased from 6.4% in 1980 to 17.4% in 2019, mainly as a result of increasingly sedentary lifestyles and the consumption of unhealthy diets [13]. Moreover, obesity is more prevalent in women than in men of any age and is associated with comorbidities and mortality [13]. Several studies have documented the higher prevalence and significant association of thyroid nodules among obese individuals and females [4,14,15]. Moreover, obesity has been identified as a risk for thyroid nodular diseases, increased thyroid gland volume, and thyroid malignancy [14-16]. Obesity is also associated with many chronic metabolic disorders, such as stroke, diabetes mellitus, chronic kidney disease, ischemic heart disease, hypertensive heart disease, and low back pain [17]. In addition, it causes a considerable financial burden on patients and health systems [4]. Hence, recommendations for screening this subgroup of patients are of paramount value. Such screening is generally cost-effective and likely to decrease morbidity and mortality in those with a more aggressive disease [18]. Recently published clinical studies reported many factors associated with the occurrence of thyroid nodules in obese patients: female gender, advanced age, central obesity, hypertension, diabetes mellitus [14,16], higher economic level, non-consumption of alcohol, hyperinsulinemia, and lower vitamin D3 levels [14]. Data from Saudi Arabia have demonstrated that TNs are a growing medical problem, more prevalent among females, with considerable malignancy risk (27.5%) [4] and financial burden, especially for those with thyroid cancer [6]. Likewise, studies conducted in the KSA have reported that thyroid cancer is the second most common cancer among females [19], with an increase in the thyroid cancer rate (9–11.7%) in 2012[20,21]. Moreover, a significant geographical variation has been reported in different areas of the KSA [20,22-24]. The prevalence of obesity in KSA, has increased markedly in the last three decades, and in particular among females (35.6%–41%), with notable variations in geographic regions [25,26]. Additionally, some studies from the KSA have revealed a significant association between thyroid nodular diseases and obesity, which can predict the risk of malignancy [27,28]. While there are many clinical studies addressing thyroid nodular diseases among obese individuals, very few published studies have focused on obesity among patients with thyroid nodules. Hence, the current study evaluates the prevalence and associated risk factors of obesity among patients with TNs.

Methods

A retrospective study was conducted at the Royal Commission Hospital from January 1, 2015 to December 31, 2021. The files of adult patients (men and women) aged 18 years and older were retrieved. Those with documented TNs, according to the findings of an ultrasound procedure performed in the hospital, were recruited for the study. The ultrasound procedures were done in the radiology department of the hospital. Medical files with incomplete data or thyroid ultrasound reports for ultrasounds performed outside the Royal Commission Hospital were excluded. The sociodemographic data, including each patient's age, gender, weight, height, thyroid status [euthyroid, hypo or hyperthyroidism] and common comorbidities [DM, hypertension, and bronchial asthma], were obtained using a data collection sheet. Similarly, laboratory tests that were performed during the time of assessing the TNs were obtained: complete blood count (white blood cell counts, hemoglobin, and platelet counts) thyroid function [thyroid-stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4)], lipid profile [total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides] and vitamin D levels. Each thyroid ultrasound

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procedure was performed by a radiology specialist, and each report was reviewed and approved by a radiology consultant. The hospital adopted and released the final thyroid ultrasound reports based on the American College of Radiology Thyroid Imaging Reporting and Data System (ACR TI-RADS) for evaluating TNs (Table 1)[29].

Definition of variables

TNs – TNs were diagnosed based on the definition of the American Thyroid Association (ATA) Guidelines for assessing TNs [1].

Body Mass Index (BMI) – BMI is computed as the body mass divided by the square of the body height; it is expressed in units of kg/m^2, resulting from mass in kilograms and height in meters.

Vitamin D deficiency – Vitamin D deficiency is determined by a 25-hydroxyvitamin D [25(OH)D] level of < 30 ng/mL; levels equal to or above this cutoff point indicate normal levels [30].

Diabetes mellitus – A diagnosis of DM was considered for those who had documentation of DM (types 1 and 2), whether they were on diet control or on glucose-lowering drugs, during the assessment of TNs.

Hypertension – This variable includes patients diagnosed with hypertension and receiving treatment during the assessment of TNs.

Bronchial asthma – This variable includes individuals diagnosed with bronchial asthma based on the documentation of their medical records.

Statistical analysis

Data were analysed with a computer using SPSS for Windows (version 22.0). Continuous data were checked for normality using the Shapiro–Wilk test, and all were not normally distributed. Data were expressed as applicable: proportions, median (interquartile range [IQR], or number (proportion). Univariate analysis was performed with obesity as the dependent variable. Independent variables were age, gender, thyroid status, diabetes mellitus, hypertension, bronchial asthma, 25-hydroxyvitamin D (25[OH]D) levels, hemoglobin, white blood count, platelets, lipid profile, and

Table 1: (TI-RADS)

TI-RADS -1	Benign
TI-RADS -2	Not suspicion
TI-RADS -3	Mildly suspicion
TI-RADS -4	Moderately suspicion
TI-RADS -5	Highly suspicion

Category definitions: ACR TI-RADS: American College of Radiology Thyroid Imaging Reporting and Data System.

thyroid ultrasound report. Variables were processed by logistic regression analyses if their univariate p was < 0.20, and the backward-stepwise likelihood ratio regression was used for adjustment. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated, and a p value of < 0.05 was considered statistically significant.

Results

Three hundred and ninety-one patients with documented TNs were enrolled in the study. The median (IQR) of age was 46.00 (20.0) years, and 332 (84.9%) were female. The median (IQR) of BMI was 30.27 (7.71) kg/m^2, and the 25-hydroxyvitamin D [25(OH)D] level was 14.5 (12.0) nmol/L. The prevalence of obesity among adult patients with TNs was considerably high (51.66%). The medians (IQRs) for the thyroid function test were thyroid-stimulating hormone (TSH) 1.71 (2.43) mmol/L, free thyroxine (FT4) 1.12 (0.45) ng/dL, and free triiodothyronine (FT3) 2.69 (0.40) nmol/L. The medians (IQRs) of lipid profile, total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglyceride were 5.8 (3.89) mmol/L, 3.76 (0.80) mmol/L, 3.00 (1.71) mmol/L, and 1.78 (1.11) mmol/L, respectively. The median (IQR) of hemoglobin was 12.6 (1.7) gm/dl, of platelets was 276.15 (95.80) 10^9/L, and of white blood cells was 7.01 (2.63) 10^9/L (Table 2).

Most of the participants were euthyroid (64.0%), while 28.6% were diagnosed with hypothyroidism and a lower percentage had hyperthyroidism (7.4%). The outcomes of thyroid ultrasound reports based on (ACR TI-RADS) were ACR TI-RADS-1(2.6%), ACR TI-RADS-2 (18.4%), ACR TI-RADS-3 (40.7), ACR TI-RADS-4 (36.3%), and ACR TI-RADS-5 (2%). In univariate analysis, there was no significant association between obesity in adult patients with TNs and thyroid status, hematological indices (hemoglobin, platelets, and white blood cells), low-density lipoprotein, high-density lipoprotein and triglycerides, free triiodothyronine, and 25-hydroxyvitamin D [25(OH) D] levels. However, there was a significant association between obesity in these patients and age OR = 1.038 (95.0% CI: (1.022–1.054), gender OR = 0.502 (95.0% CI: (0.284–0.888), diabetes mellitus OR = 0.382 (95.0% CI: (0.233–0.626), hypertension OR = 0.360 (95.0% CI: (0.216–0.600), bronchial asthma OR = 0.409 (95.0% CI: (0.183–0.913), thyroid-stimulating hormone (TSH) OR = 1.040 (95.0% CI: (0.983–1.100), free thyroxine OR = 0.837 (95.0% CI: (0.715–0.981), total cholesterol OR = 0.844 (95.0% CI: (0.762–0.934), and the finding of the ultrasound based on TI-RADS: ACR TIRADS-2 (OR = 0.212 (95.0% CI: (0.042–1.066) ACR TIRADS-3, (OR = 0.287 (95.0% CI: (0.059–1.395), ACR TIRADS-4 (OR = 0.250 (95.0% CI: (0.051–1.219), and ACR TIRADS-5 OR = 0.417 26.72 (95.0% CI: (0.051–3.435) (Table 3).

Table 2: general characteristics of patients who had documented TNs in eastern region 2015-2021.

Variables		Median	Interquartile range
Age, years		46	20
Body mass index, kg/m^2		30.27	7.71
Haemoglobin, gm/dl.		12.6	1.7
White blood cell, 10^9/L.		7.01	2.63
Platelet, 10^9/L		276.15	95.8
Thyroid-stimulating hormone, mmol/L		1.71	2.43
Free triiodothyronine, nmol/L		2.69	0.4
Free thyroxine, ng/dL		1.12	0.45
Total cholesterol, mmol/L		5.8	3.89
Low-density lipoprotein, mmol/L		3.76	0.8
High-density lipoprotein, mmol/L		3	1.71
Triglyceride, mmol/L		1.78	1.11
25-hydroxyvitamin D (25[OH)]D) levels, nmol/L		14.5	12
		Number	Proportion
Thyroid status	Euthyroid	250	64
	Hypothyroidism	112	28.6
	Hyperthyroidism	29	7.4
Gender	Female	332	84.9
	Male	59	15.1
Bronchial asthma	No	360	92.1
	Yes	31	7.9
Diabetes mellitus	No	297	76
	Yes	94	24
Hypertension	No	303	77.5
	Yes	72	22.5
Ultrasound	ACR TIRADS1	10	2.6
	ACR TIRADS2	72	18.4
	ACR TIRADS3	159	40.7
	ACR TIRADS4	142	36.3
	ACR TIRADS5	8	2

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Table 3: Univariate analysis of the predictors associated with obesity among adult patients with TNs in eastern region, 2015-2021.

Variables		Non-obese (n=189)	Obese (n=202)	OR (95.0 %CI	P
		Median			
Age, years		43.0 (22.0)	50.0 (17.0)	1.038(1.022–1.054)	<0.000
haemoglobin, gm/dl		12.2(2.05)	12.57(1.6)	0.963(0.895–1.036)	0.307
White blood cell, 10^9/L		6.76 (2.16)	7.42(2.97)	0.996(0.986–1.007)	0.492
Platelet, 10^3/dl		276.15 (98.4)	276.15(93.25)	1.001(0.998–1.003)	0.522
Thyroid-stimulating hormone, mmol/L		1.68(2.34)	1.79 (2.65)	1.040(0.983–1.100)	0.174
Free triiodothyronine, nmol/L		1.17(0.47)	1.09 (0.37)	0.916(0.691–1.216)	0.544
Free thyroxine, ng/dL		2.69 (0.46)	2.69(0.38)	0.837(0.715–0.981)	0.028
Total cholesterol, mmol/L		7.10(3.71)	5.40(4.12)	0.844(0.762–0.934)	0.001
Low-density lipoprotein, mmol/L		3.76(0.4)	3.76(1.1)	0.985(0.940–1.033)	0.539
High-density lipoprotein, mmol/L		2.99 (1.1)	2.99(1.74)	1.006(0.985–1.027)	0.578
Triglyceride, mmol/L		2.26 (1.09)	1.6 (1.08)	1.069(0.868–1.317)	0.531
25-hydroxyvitamin D (25[OH)]D) levels, nmol/L		14.47(12.0)	14.6 (10.9)	1.009(0.992–1.027)	0.292
		Number			
Gender	Female	152 (80.4)	180 (89.1)	0.502 (0.284–0.888)	0.018
	Male	37 (19.6)	22 (10.9)	Reference	
Thyroid status	Euthyroid	123 (65.1)	127(62.9)	Reference	
	Hypothyroid	51 (27.0)	61 (30.2)	1.106(0.513–2.388)	0.797
	Hyperthyroid	15(7.9)	14 (6.9)	1.282(0.566–2.903)	0.552
Diabetes Mellitus	No	160 (84.7))	137 (67.8)	Reference	<0.000
	Yes	29 (15.3)	65 (32.2)	0.382(0.233–0.626)	
Hypertension	No	163 (86.2)	140 (69.3)	Reference	<0.000
	Yes	26 (13.8)	62 (30.7)	0.360(0.216–0.600)	
Asthma	No	180 (95.2)	180 (89.1)	Reference	0.029
	Yes	9 (4.8)	22 (10.9)	0.409(0.183–0.913)	
Ultrasound	ACR TIRADS1	2 (1.1)	8 (4.0)	Reference	
	ACR TIRADS2	39 (20.6)	33 (16.3)	0.212 (0.042–1.066)	0.06
	ACR TIRADS3	74 (39).	85 (41.1)	0.287 (0.059–1.395)	0.122
	ACR TIRADS4	71 (37.6)	71 (35.1)	0.250 (0.051–1.219)	0.086
	ACR TIRADS5	3 (1.6)	5(2.5)	0.417 (0.051–3.435)	0.416

In multivariate analysis, diabetes mellitus, hypertension, bronchial asthma. thyroid-stimulating hormone, free thyroxine, free triiodothyronine, total cholesterol, and the findings of the ultrasound based on TI-RADS were not significantly associated with obesity in patients with TNs. Older age (OR = 1.029 (95.0 % CI: 1.009 –1.048) and female gender (OR = 3.806 (95.0% CI: 1.975 –7.334) were highly significantly associated with obesity in adult patients with thyroid nodules (Table 4).

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Table 4: Multivariate analysis of the predictors associated with obesity in patient with thyroid nodules in eastern region 2015-2021

Variables		OR (95.0 %CI	P
Age, years		1.029 (1.009 – 1.048)	0.004
Gender	Male	Reference	
	Female	3.806 (1.975 –7.334)	< 0.000
Diabetes Mellitus	No	Reference	
	Yes	0.578 (0.325 –1.025)	0.061
Hypertension	No	Reference	
	Yes	0.540 (0.540 – 0.289)	0. 540
Bronchial asthma	No	Reference	
	Yes	0.492 (0.203 – 1.189)	0.115
Thyroid-stimulating hormone, mmol/L		1.058 (0.990 – 1.132)	0.97
Free thyroxine, ng/dL		0.857 (0.731 –1.004)	0.056
Total cholesterol, mmol/L		0.966 (0.852 – 1.094)	0.583
ACR TIRADS Scoring system	ACR TIRADS 1	Reference	
	ACR TIRADS 2	0.198 (.035 – 1.126)	0.068
	ACR TIRADS 3	0.230 (0.042 –1.254)	0.089
	ACR TIRADS 4	0.233 (0.043 – 1.271)	0.092
	ACR TIRADS 5	0.743 (0.072 –7.663)	0.803

Discussion

The main finding of this study is the high prevalence of obesity among adult patients with thyroid nodular diseases, which is slightly higher than that obtained in Riyadh, the capital of KSA (50.3%) [27] and the United States of America (44.%) [31]. Astonishingly, a very low prevalence of obesity among patients with TNs was reported in Korea (3.33%), and obesity was considerably higher among those with malignant TNs compared to those with benign ones [32]. Obesity significantly predicts thyroid nodular diseases, risk of malignancy [2,14,24,33,34], and thyroid gland volume [15,33,34]. Some studies have demonstrated a higher prevalence of TNs among patients with obesity compared to the control group [14,15]. This may reflect the close association between the two medical conditions. Not only was the body mass index (BMI) associated with the presence of thyroid nodules and a highly suspicious sonographic pattern, but with other adiposity markers as well, such as body fat percentage and body surface area, in both men and women [35]. In contrast to this finding, no significant differences were observed in the risk of nodular diseases and obesity [36,37]. While some studies identified a significantly lower prevalence of thyroid nodules in morbidly obese patients [24,38], low weight was associated with significant high-risk thyroid nodules among people ≥ 55 years old [39]. The high prevalence of obesity in this study may be explained by the increase of obesity [25,26] and thyroid nodular diseases over the last few decades [19–21]. Moreover, changes in diet, in particular towards the Western diet, heavy consumption of sugary beverages, and high levels of sedentary lifestyle, are major contributing factors to obesity in the KSA [25]. Additionally, the higher prevalence of obesity may be linked to hypoadiponectinemia, which is a pro-inflammatory state of insulin resistance leading to highly circulating insulin and insulin-like growth factor-1 levels, thus possibly enhancing the risk of developing TNs and thyroid cancer [40]. Likewise, obesity is associated with complex pathological changes in animal models, which induce the formation of TNs and cancer risk: hyperlipidemia, hyperglycemia, hyperinsulinemia, oxidative stress, release of adipokines, and inflammatory responses [41]. Insulin-like growth factor 1 (IGF-1) stimulates protein and DNA synthesis, promotes the proliferation and differentiation of thyroid cells, and enhances the progression of mitosis in many types of cells, leading to cell proliferation, differentiation, and apoptosis [42]. Some studies have documented a significant increase in the frequency and volume of thyroid nodules in patients with higher insulin resistance than in non-insulin resistant subjects [14,15]. Interestingly, metformin use was associated with reductions in thyroid nodule size and improved insulin resistance in patients with thyroid nodules and insulin resistance [43]. Another possible mechanism to explain the significant association between thyroid nodules and obesity is a TSH-dependent mechanism that includes leptin signalling, which directly and indirectly stimulates the secretion of the thyrotropin-releasing hormone and ultimately increases TSH secretion [44]. The current study and several other studies have documented that old age is associated with obesity among patients with thyroid nodular diseases [2,14,16,39,45] and the

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risk of developing thyroid cancer [16]. Elderly patients often have a high rate of multinodular goiter diagnosis and a risk of both hyperfunctioning nodules and hypofunctioning nodules, which may result from high FT3 levels and/or suppressed TSH [46]. Ageing is also associated with an increase in the percentage of body fat by approximately 1% per decade [47]. Moreover, ageing is associated with markedly higher levels of pro-inflammatory cytokines, which are known to affect insulin action [48]. In addition, the reactive oxygen free radicals that are precipitated with aging are linked to changes in the thyroid tissue and an accumulation of harmful changes in the thyroid cells [49], which eventually results in the formation of nodules in the thyroid tissue: hyperplasia of fibrous connective tissue, inflammatory infiltration, filtration in the interstitium of thyroid tissue, and vacuolation of the cytoplasm of the vesicle [50]. The current study found that the female gender is a significant predictor of obesity in patients with TNs. This is in line with similar findings obtained from two recently published studies [16,45]. In addition, females are likelier to have TNs than males [2,4]. On the other hand, gender was not found to be a risk factor for obesity among this group of patients [32]. In contrast to this finding, other studies have revealed that males tend to be obese [2,32]. The possible reasons for this discrepancy may be related to differences in lifestyle, sociodemographic variables, and other genetic or behavioural factors [51]. The significant association between female gender and risk of obesity in patients may be related to the influence of both oestrogen and progesterone as significant contributors in patients with thyroid nodular disease [52]; hence, the fluctuations in reproductive hormone concentrations throughout females' lives are uniquely responsible for excess weight gain. Similarly, the gender differences in TNs may be attributed to the physiology, pregnancy, and oestrogen exposure of females. Oestrogen is a potent growth factor for both benign and malignant thyroid cells, contributing to the gender difference in the prevalence of thyroid nodules and thyroid cancer [53]. In this study, the other variables assessed were not significantly associated with obesity in patients with thyroid nodular diseases, which strongly supports the concept of multi-factorial etiology for the existence of TNs, which includes the influence of genetic, epigenetic, environmental, immune, and inflammatory responses [54,55]. The main limitation of the study is that it was retrospective and collected data from only one centre. Other factors, such as smoking, alcohol consumption, physical activity, thyroid antibodies, iodine levels, nutritional patterns, genetic analysis, and environmental factors were not assessed.

Conclusion

There was a considerably higher prevalence of obesity among adult patients with TNs. Older age and female gender were significant predictors of obesity in this group of patients.

Declarations

Availability of data and material

Data are available upon request.

Ethics approval and consent to participate

The study was approved by the Institutional Review Board of the Royal Commission Hospital, KSA (IB-RCH-012), which waived verbal or written consent from the participants. It was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

Consent for publication

Not applicable.

Conflicts of interest

The author has no conflicts of interest to declare

Disclosure

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