Prevalence, risks, and comorbidity of thyroid dysfunction: a cross-sectional epidemiological study

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Background
Worldwide, the incidence of individuals with thyroid dysfunction is increasing and represents approximately 30–40% of the patients seen in an endocrine clinic. The undiagnosed thyroid dysfunction may adversely affect the metabolic control and add more risk to already predisposing cardiovascular risk factors. Thus, the objective of the present study was to assess the prevalence of undiagnosed thyroid dysfunction and its association with other comorbidities.
Patients and methods
A cross-sectional study was conducted on 430 patients who attended the outpatient clinic of Diabetes and Endocrinology, the Internal Medicine Department, Zagazig University Hospitals. All patients underwent clinical and laboratory evaluations. A total of 304 patients had normal thyroid function (euthyroid) and 126 patients had thyroid dysfunction, who were stratified into one of the following groups based on the reference of the normal thyroid function test result: hyperthyroidism, subclinical hyperthyroidism, hypothyroidism, and subclinical hypothyroidism. Thyroid-stimulating hormone and free thyroxine were used as the screening tests to diagnose thyroid dysfunction.
Results
Our results show the prevalence of thyroid dysfunction was 29.3%. Among thyroid dysfunction groups, the prevalence of subclinical hypothyroidism was 44.4%, hypothyroidism was 20.6%, hyperthyroidism was 19.2%, and subclinical hyperthyroidism was 15.8%. The prevalence of overall thyroid dysfunction among studied patients with type 2 diabetes mellitus was 27.6%, whereas in type 1 diabetes mellitus, the prevalence of overall thyroid dysfunction was 38.7%. Patients with subclinical hypothyroidism and hypothyroidism had a high prevalence of hypertension compared with those with subclinical hyperthyroidism and clinical hyperthyroidism. Approximately 8% of studied pregnant female patients had subclinical hypothyroidism. Among the 15% of female patients in the postpartum period who had thyroid dysfunction, 10% had clinical hypothyroidism and 5% had clinical hyperthyroidism. Among postmenopausal women, 20% had thyroid dysfunction (12% had subclinical hypothyroidism and 8% had clinical hypothyroidism).
Conclusion
The most frequently undiagnosed thyroid dysfunction was subclinical hypothyroidism. Thyroid dysfunction was common in certain age groups: reproductive age and postmenopausal as well as in patients with diabetes mellitus and hypertension; thus, screening for thyroid disease among those groups of patients should be routinely performed.

Keywords:
diabetes mellitus, hypertension, postmenopausal, postpartum, prevalence, thyroid dysfunction, thyroid-stimulating hormone

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Introduction

Worldwide, the incidence of individuals with thyroid dysfunction is increasing and represents approximately 30–40% of the patients seen in an endocrine clinic; thus, it is one of the leading endocrine disorders [1]. The undiagnosed thyroid dysfunction especially subclinical and clinical hypothyroidism may increase cardiovascular risk factors [2]. In fact, many published studies highlighted the morbidity associated with thyroid dysfunction. The findings of the earliest studies regarding the complications of thyroid dysfunction particularly with hypothyroidism revealed that dyslipidemia is very common; thus, it could contribute to atherosclerosis development and

increase risk of coronary artery disease and cardiovascular mortality [3].

Recently, increased interest has focused on the prevalence of thyroid dysfunction. The results of these studies revealed that hypothyroidism is more common in female than male individuals, and its prevalence increases with age [4]. The prevalence of subclinical hypothyroidism varies and ranges from 1 to 20% [5].

Higher levels of thyroid-stimulating hormone (TSH) define hypothyroidism, and decreased TSH levels define hyperthyroidism. When TSH levels are abnormal, but concentrations of free thyroxine (FT4) fall within the reference range, this is referred to as subclinical thyroid dysfunction. The diagnosis of thyroid dysfunction requires both TSH and FT4 measurements. However, TSH is a sensitive marker of thyroid dysfunction, as small changes in FT4 create large changes in TSH [6].

The prevalence of thyroid disorders depends on various factors such as age, sex, geographical factors, and iodine intake [5]. Thyroid disorders need to be addressed as a priority in certain populations, for example, postmenopausal and pregnant women. In light of the above, the objective of the present study was to assess the prevalence of undiagnosed thyroid dysfunction and its association with other comorbidities. To the best of our knowledge, this is the first epidemiology study of undiagnosed thyroid dysfunction in Egypt.

Patients and methods

Patients

A cross-sectional study was conducted among 430 patients. Of the studied patients, 304 patients had normal thyroid function (euthyroid) and 126 patients had thyroid dysfunction, who were recruited from diabetes and endocrinology outpatient clinic of the Internal Medicine Department of Zagazig University Hospitals. Patients were stratified into one of the following four groups based on the reference of the normal thyroid function test. Subclinical hypothyroidism was defined as TSH between 4.50 and 19.99 mU/l and FT4 within the reference range. Overt hypothyroidism was defined as TSH more than or equal to 20 mU/l or TSH between 4.50 and 19.99 mU/l and FT4 below the reference range [7,8]. Hyperthyroidism was defined as TSH under 0.45 mU/l, and FT4 measurements allowed us to differentiate between overt hyperthyroidism (FT4 above the reference level) and subclinical hyperthyroidism (FT4 within the reference range). Notably, the American Thyroid Association recommends the combined use of TSH and FT4 as the most efficient combination of blood tests for diagnosis and follow-up of both ambulatory and hospitalized patients [9].

All patients were subjected to thorough history taking and full clinical assessment, including BMI. Blood pressure was recorded as the mean of three consecutive measurements in the sitting position taken 5 min apart. Hypertension was defined according to the current guidelines as BP levels more than or equal to 140/90 mmHg or the use of anti-hypertensive drugs. Exclusion criteria included patients with a history of thyroid disease, stroke, respiratory disease, heart failure, cancer, severe hepatic, renal diseases, acute illness, hormonal therapy, and active inflammatory diseases. The ethical committee of the Faculty of Medicine, Zagazig University, approved our study protocol, and all participants signed written informed consent.

Blood sampling

Blood samples were obtained from all women after an overnight fast and divided into three portions: 1 ml of whole blood was collected into EDTA-treated tubes, for glycated hemoglobin; 1 ml of whole blood was collected into sodium fluoride-treated tubes for fasting plasma glucose and 2-h postprandial plasma glucose (2-h plasma glucose). Serum was separated from the remaining part of the sample and stored at -80°C until analysis.

Laboratory measurements

Fasting plasma glucose and 2-h postprandial plasma glucose levels were measured by enzymatic method-based kit (Spinreact, Girona, Spain). Glycated hemoglobin was estimated by cation-exchange resin-based assay kit (Stanbio Laboratory, Boerne, Texas, USA). Total cholesterol, high-density lipoprotein cholesterol, and triglycerides levels were determined by colorimetric commercial kits (Spinreact). Friedewald formula was used for calculation of low-density lipoprotein cholesterol level [10]. The thyroid function tests including FT4 and TSH were measured using the chemiluminescence immunoassay assay kit provided by Immunospec Corporation (Canoga Park, California, USA). Gestational age has a major effect on thyroid function tests; thus, in pregnant women, we used trimester cutoffs to define thyroid disorders.

Statistical analysis

Data were expressed using descriptive statistics (mean ±SD) and were analyzed. One-way analysis of variance

test was done to compare different parameters between more than two groups. The statistical significances of differences in the frequencies of variants between the groups were tested using the χ^2 test. Multiple stepwise linear regression analysis was performed to detect the main predictors of TSH levels. *P* values were considered significant if less than 0.05. Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows (version 20.0; SPSS Inc., Chicago, Illinois, USA).

Results

This is the first study conducted in Egypt in an attempt to assess the prevalence of thyroid disorders among adult people; of 430 patients randomized, 126 (29.3%) had thyroid disorders.

Among the various varieties of thyroid disorders, our study reported the prevalence of clinical and subclinical hypothyroidism at 44.4 and 20.6%, respectively. Regarding hyperthyroidism, our results revealed that the prevalence of clinical and subclinical hyperthyroidism was 19.2 and 15.8%, respectively.

The clinical and laboratory characteristics of participants

Patients with thyroid dysfunction compared with those with normal thyroid function were older and more frequently women (Table 1). They had higher FT4 and TSH. Patients with thyroid dysfunction had more frequent type 1 diabetes mellitus (T1DM), type 2 diabetes mellitus (T2DM), and hypertension compared with the euthyroid group.

Table 1 Clinical, anthropometric, and laboratory characteristics of all studied patients

Characteristics	Euthyroid group (*N*=304)	Thyroid dysfunction group (*N*=126)	*P*
Age (years)	46.38±15.9	49.5±15.2	0.195
Male [*n* (%)]	69 (46.6)	32 (50.8)	0.313
BMI (kg/m^2)	26.7±2.5	26.7±3.0	0.411
FT4 (ng/dl)	0.9±0.3	1.0±1.1	0.400
TSH (μIU/ml)	2.4±1.9	5.6±4.1	0.975

FT4, free thyroxine; TSH, thyroid-stimulating hormone.

Association of thyroid disorders with clinical and biochemical characteristics

The prevalence of undiagnosed thyroid dysfunction among diabetic patients

Regarding the prevalence of diabetes, T2DM frequencies were common in all studied thyroid dysfunction groups than T1DM (Tables 2 and 3).

The prevalence of undiagnosed thyroid dysfunction among hypertensive patients

Patients with subclinical hypothyroidism and hypothyroidism had high prevalence of hypertension compared with those with subclinical hyperthyroidism and clinical hyperthyroidism, as according to our results, we did not find any hypertensive patients among patients with subclinical hyperthyroidism and clinical hyperthyroidism (Table 4).

The prevalence of thyroid dysfunction in pregnant women

Regarding the prevalence of thyroid dysfunction in pregnant women, approximately 8% of studied pregnant women had subclinical hypothyroidism (Fig. 1).

The prevalence of thyroid dysfunction in women during the postpartum period

The present study investigated the prevalence of thyroid dysfunction among women in the postpartum period and found that 15% of women in the postpartum period had thyroid dysfunction, of whom 10% of patients had clinical hypothyroidism and 5% of patients had clinical hyperthyroidism (Fig. 2).

The prevalence of thyroid dysfunction in postmenopausal women

Our study found that 20% of postmenopausal women had thyroid dysfunction, of whom 12% had subclinical

Table 2 Clinical, anthropometric, and laboratory characteristics of thyroid dysfunction groups

Characteristics	Subclinical hypothyroidism (*N*=26)	Clinical hypothyroidism (*N*=56)	Subclinical hyperthyroidism (*N*=24)	Clinical hyperthyroidism (*N*=20)	Euthyroid group (*N*=304)
Age (years)	53.3±12.0	49.8±15.1	49.9±15.5	41.3±12.0	46.38±15.9
Male [*n* (%)]	5 (38.5)	11 (39.3)	8 (66.7)	8 (80)	69 (46.6)
BMI (kg/m^2)	28.5±3.4	26.8±3.2	25.6±1.6	28.5±3.4	26.7±2.5
FT4 (ng/dl)	0.8±0.2	0.3±0.2*	1.0±0.2	2.8±1.2*	0.9±0.3
TSH (μIU/ml)	7.5±2.5*	8.5±2.9*	0.2± 0.1*	0.17±0.08*	1.4±1.9

FT4, free thyroxine; TSH, thyroid-stimulating hormone. **P* value less than 0.05.

Table 3 Prevalence of undiagnosed thyroid dysfunction among both types of diabetic patients

Characteristics	T1DM (*N*=62)	T2DM (*N*=246)	*P* value
Euthyroid group (*n*=304)	38 (12.5)	158 (51.9)	<0.001*
Subclinical hypothyroidism (*n*=26)	2 (7.7)	12 (46.1)	<0.001*
Clinical hypothyroidism (*n*=56)	12 (21.4)	32 (57.1)	<0.001*
Subclinical hyperthyroidism (*n*=24)	2 (8.3)	14 (58.3)	<0.001*
Clinical hyperthyroidism (*n*=20)	8 (40)	10 (50)	<0.001*

T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus.
**P* value less than 0.05.

Table 4 Prevalence of undiagnosed thyroid dysfunction among hypertensive patients

Characteristics	No-HTN (*N*=340)	HTN (*N*=97)	*P* value
Euthyroid group (*n*=304)	252 (82.8)	52 (14.5)	<0.001*
Subclinical hypothyroidism (*n*=26)	18 (69.2)	8 (30.8)	<0.001*
Clinical hypothyroidism (*n*=56)	26 (46.4)	30 (53.6)	<0.001*
Subclinical hyperthyroidism (*n*=24)	24 (100)	0 (0)	<0.001*
Clinical hyperthyroidism (*n*=20)	20 (100)	0 (0)	<0.001*

HTN, hypertension. **P* value less than 0.05.

hypothyroidism and 8% of had clinical hypothyroidism (Fig. 3).

Linear regression analyses to test the influence of the main independent variables against thyroid-stimulating hormone levels (dependent variable)

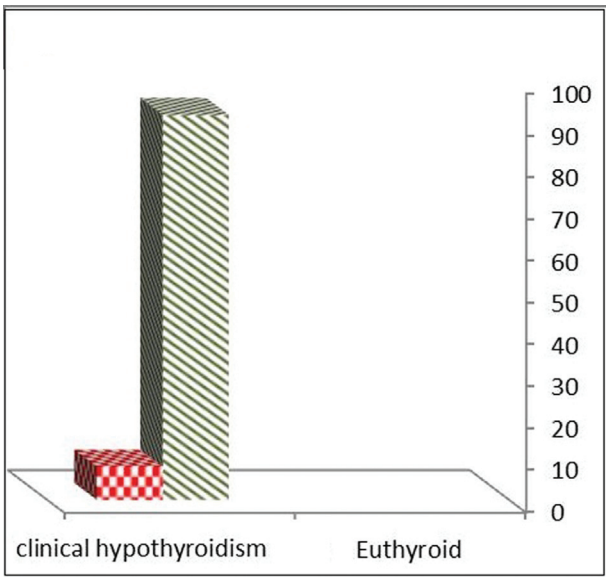
Stepwise linear regression analysis showed that female sex, FT4, and BMI were independent predictors of TSH level ($P<0.001$) (Table 5).

Discussion

Thyroid dysfunction has noteworthy public health consequences. Emerging evidence demonstrated that the prevalence of thyroid dysfunction varies among populations of the same race in different geographical areas. Thereby, this study was carried out to investigate the prevalence of undiagnosed thyroid dysfunction. In addition, we aimed to explore the association of thyroid dysfunction with other comorbidities.

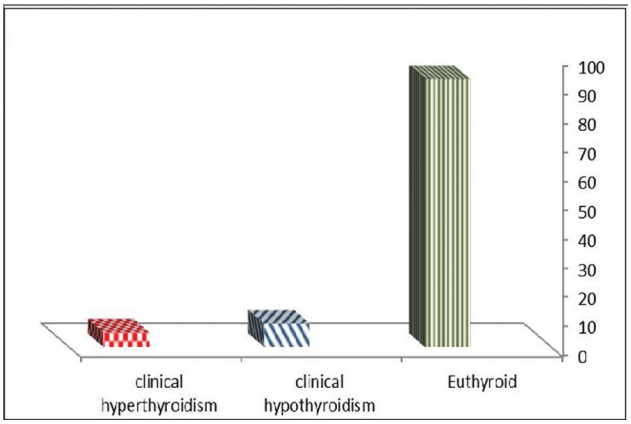
Our study revealed clear evidence that the prevalence of thyroid dysfunction was found in 29.3% of the studied population. Among thyroid dysfunction groups, the most common thyroid dysfunction was subclinical

Figure 1



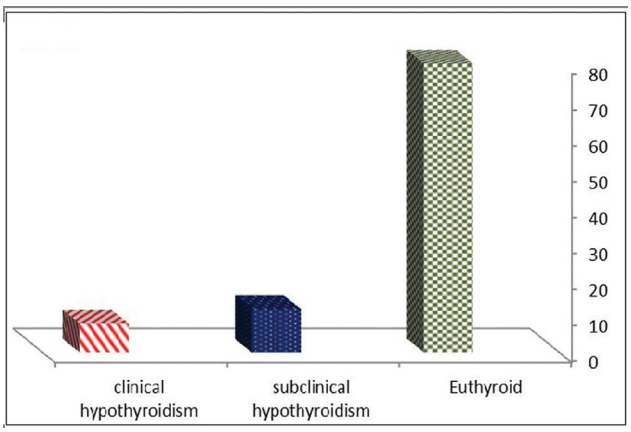
Prevalence of thyroid dysfunction in pregnant women.

Figure 2



Prevalence of thyroid dysfunction of females in postpartum period.

Figure 3



Prevalence of thyroid dysfunction of postmenopausal women.

Table 5 Multiple stepwise linear regression analysis in thyroid dysfunction group to test the influences of the main independent variables against thyroid-stimulating hormone levels (dependent variable)

Model	Unstandardized coefficients		Standardized coefficients	*t*	*P*	95% CI	
	B	SE	Beta			Lower bound	Upper bound
1							
Constant	−1.635	1.236		−1.323	0.191	−4.110	0.840
Female	3.448	0.794	0.499	4.343	0.000	1.858	5.038
2							
Constant	0.425	1.390		0.306	0.761	−2.359	3.209
Female	2.839	.784	0.411	3.622	0.001	1.269	4.409
FT4	−1.092	.397	−0.312-	−2.749	0.008	−1.887	−0.296
3							
Constant	−8.884	3.462		−2.567	0.013	−15.821	−1.947
Female	1.941	0.799	0.281	2.431	0.018	0.341	3.542
FT4	−1.175	0.374	−0.335	−3.140	0.003	−1.925	−0.425
BMI	0.405	0.139	0.322	2.904	0.005	0.125	0.684

FT4, free thyroxine.

hypothyroidism (44.4%), followed by overt hypothyroidism (20.6%), hyperthyroidism (19.2%), and subclinical hyperthyroidism (15.8%).

Previous studies have also investigated the prevalence of thyroid disorders in a population-based study conducted on Indian populations. The most common thyroid disorders were subclinical hypothyroidism [11].

Regarding the prevalence of thyroid diseases in Arab countries, in a Saudi Arabia study, the researchers revealed clear evidence that the prevalence of thyroid disorders in the Makkah region was very high at approximately 47.34% [12]. The study conducted by Nouh *et al.* [13], in Libya, observed the prevalence of hypothyroidism was 6.18%. Even more interestingly findings from other researchers suggested that the prevalence of subclinical hypothyroidism was 2.3% [14]. Here, the evidence for these studies will be scrutinized and compared to provide a robust analysis of the current knowledge.

These results are in agreement with the results that were obtained in Delhi by Marwaha *et al*. [15], who reported increasing of the prevalence of subclinical hypothyroidism to reach approximately 19.3% of the study populations.

A study by Yang *et al*. [16] found that the prevalence of hyperthyroidism varied between 1.2 and 2%, whereas subclinical hyperthyroidism oscillated between 1.1 and 3.9% depending on iodine intake.

Regarding sex distribution, the present study demonstrated that thyroid dysfunctions were more common in females than males. Notably, our findings revealed that female frequencies were more common in subclinical hypothyroidism and clinical hypothyroidism. On the contrary, males were more common in subclinical hyperthyroidism and clinical hyperthyroidism groups.

These results were supported by Golden *et al*. [17] who reported that the percentage of hypothyroidism was higher for women than for men. Consistent with previous studies, it was demonstrated that women had a higher prevalence of hypothyroidism compared with men [18,19].

In contrary to our results, previous studies suggested that the prevalence of hyperthyroidism is 10 times more common in women than in men [20,21].

To evaluate the prevalence of thyroid dysfunction among diabetics, we found that T2DM frequencies were common in all studied thyroid dysfunction groups than T1DM. Moreover, the prevalence of overall thyroid dysfunction among studied patients with T2DM was 31.1%, whereas in T1DM, the prevalence of overall thyroid dysfunction was 38.7.

These results are in agreement with the results that are explored from studies conducted on patients with T2DM in our region; in Saudi, ~16% of patients with T2DM had thyroid dysfunction [22]. Likewise, researchers from Jordan found the overall prevalence of thyroid dysfunction was 12.5% in patients with T2DM [23].

Several studies have implicated that thyroid hormones have a key role in regulating energy balance,

metabolism of glucose, and lipids [24]. Thyroid hormones have anti-insulin action such as stimulating the hepatic gluconeogenesis and glycogenolysis. They also up-regulate the expression of genes such as glucose transporter type-4 [25].

Similar results were obtained by Smithson [26] who estimated that approximately 10.8% of diabetic patients had thyroid dysfunction. Elegant studies on the association between T2DM and thyroid dysfunction found higher prevalence of thyroid dysfunction in diabetic patients compared with the general population [24,25].

These results agree with those reported in another random cross-section study conducted on diabetic adults by Perros *et al.* [27], which revealed that the prevalence of thyroid dysfunction was found to be 13.4%.

The current study revealed that patients with subclinical hypothyroidism and hypothyroidism had a high prevalence of hypertension compared with subclinical hyperthyroidism and clinical hyperthyroidism. Similarly, Owen *et al.* [28] observed a high prevalence of hypertension among patients with hypothyroidism .

Regarding the prevalence of thyroid dysfunction in pregnant women, approximately 8% of studied pregnant women had subclinical hypothyroidism. Similarly, the study conducted in India by Dhanwal *et al.* [29] suggested that there is a high prevalence of hypothyroidism (13.13%); the majority being subclinical hypothyroidism in pregnant women during the first trimester. These results were supported previously by Klein *et al.* [30] who reported that the prevalence of subclinical hypothyroidism in pregnant was 3%. Moreover, Mandel and Cooper [31] found that endemic iodine deficiency accounts for most hypothyroidism in pregnant women worldwide.

The present study investigated the prevalence of thyroid dysfunction among women in the postpartum period and found that 15% of the women in the postpartum period had thyroid dysfunction: two patients had clinical hypothyroidism and one patient had clinical hyperthyroidism. In line with this, Stagnaro-Green *et al.* [32] reported that the prevalence of postpartum thyroid dysfunctions is between 1.1 and 16.7%. Furthermore, Shahbazian *et al.* [33] revealed that the prevalence of postpartum thyroid dysfunctions was 11.4%. In agreement with our results, Filippi *et al.* [34] found that the prevalence of postpartum thyroid dysfunctions was 18%. In a study conducted in Spain by Stagnaro-Green *et al.* [32], it was observed that the prevalence of postpartum thyroid dysfunctions was 15.9%.To clarify the relationship between menopausal status and thyroid dysfunction, we focused our analyses and found that 20% of postmenopausal women had thyroid dysfunction, of whom 12% had subclinical hypothyroidism and 8% of had clinical hypothyroidism.

These results are in agreement with the results that are shown by Fatourechi [4], who found that the prevalence of subclinical hypothyroidism is 3–8% in postmenopausal women.

Previous studies also have shown the prevalence of clinical hypothyroidism was high in postmenopausal women [35]. Similarly, in a study conducted by Chakera *et al.* [36], the prevalence was approximately 15–18%. Bensor *et al.* [35] revealed that the prevalence of clinical hypothyroidism was 5.9%.

In an effort to better understand the association between TSH and BMI, we further analyzed our results by stepwise linear regression analysis test, which revealed that serum TSH levels were independently correlated with female sex, FT4, and BMI.

Weigh changes are well-known consequences of overt thyroid dysfunction. Bjùro *et al.* [37] observed positive association between change in serum TSH and change in body weight, whereas Kitahara *et al.* [38] found measures of overall and central adiposity were associated with higher circulating levels of TSH and no association with FT4 levels.

In the euthyroid range, excess body weight may induce changes in thyroid hormone levels, as fat tissue could affect thyroid hormones in different ways. In contrast with this study, Manji *et al.* [39] could not confirm the association between body weight and thyroid dysfunction.

Mounting evidence has suggested universal screening for thyroid function, whereas the complications associated with either overt or subclinical thyroid dysfunction cannot be neglected. These complications could be especially severe in patients with cardiovascular diseases, in postmenopausal women, or in pregnant women.

Conclusion

The prevalence of thyroid dysfunction was found in 29.3% of the studied population. The most frequent dysfunction was subclinical hypothyroidism (44.4%), followed by overt hypothyroidism (20.6%). Interestingly, the prevalence was higher in association with other comorbidities such as diabetes and hypertension, and in certain age groups, reproductive age and postmenopausal; thus, the benefits of a screening program should outweigh any potential drawbacks. Further future multicenter studies with a bigger sample size are needed to validate our findings.

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Conflict of Interests

There are no conflicts of interest.

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