The value of red blood cell distribution width in subclinical hypothyroidism

O valor da amplitude de distribuição de eritrócitos no hipotireoidismo subclínico

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ABSTRACT

Objective: Therefore, we evaluated the relationship between the subclinical hypothyroidism and red cell distribution width (RDW) levels in a healthy population. **Subjects and methods:** The medical records of 23,343 consecutive health subjects were reviewed. Subjects were classified into four thyroid stimulating hormone (TSH) groups to determine the correlation between TSH and other variables in detail (0.3 to < 2.5 mU/L, 2.5 to < 5 mU/L, 5 to < 7.5 mU/L, and ≥ 7.5 mU/L). **Results:** In the multivariate linear regression analysis, RDW was associated with TSH levels, and e-GFR was inversely associated with TSH levels, respectively (standardized beta coefficient = 0.102, -0.019; p < 0.001, p < 0.001). After adjusting for age and sex, in the four groups, TSH levels were significantly correlated with RDW, estimated glomerular filtration rate (e-GFR), and free thyroxine (fT4) levels in all groups. Furthermore in the 4th group, RDW levels were more strongly associated with TSH levels than in the other groups (p = 0.006). **Conclusions:** RDW levels are correlated with euthyroid and subclinical thyroid status. Notably, RDW is more correlated with subclinical hypothyroidism than the euthyroid status. This study presents the relationship between the RDW levels and thyroid function using TSH level in a large healthy population. Arq Bras Endocrinol Metab. 2014;58(1):30-6

Keywords

Red blood cell distribution width; subclinical hypothyroidism; thyroid stimulating hormone

RESUMO

Objetivo: Avaliamos a relação entre o hipotireoidismo subclínico e os níveis de distribuição do tamanho dos eritrócitos (RWD) em uma população saudável. **Pacientes e métodos:** Foram revisadas as fichas médicas de 23.343 sujeitos saudáveis consecutivos. Os sujeitos foram classificados em quatro grupos de nível de hormônio tireoestimulante (TSH) para se determinar a correlação entre o TSH e outras variáveis, em detalhe (0,3 a < 2,5 mU/L; 2,5 a < 5 mU/L; 5 a < 7,5 mU/L; e ≥ 7,5 mU/L). **Resultados:** Na análise de regressão linear múltipla, a distribuição do tamanho dos eritrócitos (RWD) foi associada aos níveis de TSH, e a taxa estimada de filtração glomerular (e-GFR) foi inversamente associada aos níveis de TSH, respectivamente (coeficiente betapadronizado = 0,102; -0,019; p < 0,001; p < 0,001). Depois do ajuste para idade e sexo, nos quatro grupos, os níveis de TSH se correlacionaram significativamente com os níveis de RDW, e-GFR e tiroxina livre (fT4) em todos os grupos. Além disso, no quarto grupo, os níveis de RDW estiveram mais fortemente associados aos níveis de TSH do que nos outros grupos (p = 0,006). **Conclusões:** Os níveis de RDW estão correlacionados com o estado eutiroide e com o hipotireoidismo subclínico. Notavelmente, a RDW é mais correlacionada com o hipotireoidismo subclínico do que com o estado eutiroide. Este estudo apresenta uma relação entre os níveis de RDW e a função tiroidiana por meio da concentração de TSH em um grande número de indivíduos saudáveis. Arq Bras Endocrinol Metab. 2014;58(1):30-6

Descritores

Amplitude de distribuição do tamanho dos eritrócitos; hipotireoidismo subclínico; hormônio tireoestimulante

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INTRODUCTION

Red cell distribution width (RDW) is a quantitative measure of variation of circulating red blood cell size, and is routinely assessed in the differential diagnosis of anemias, especially in the microcytic category. In addition to aiding the diagnosis of anemia, RDW levels have been associated with cardiovascular and renal disease in recent studies (1). Higher RDW measurements, even within a normal reference range, have been strongly and independently linked with cardiovascular mortality in patients with cardiovascular disease and in a community-based population (2,3). RDW has also been associated with an increased risk of new cardiovascular events in patients with previous myocardial infarction (4). Additionally, an inverse and graded association between RDW and renal function was reported in a large cohort of adult outpatients (5). These data support the hypothesis that RDW is a useful predictor of disease associated with cardiovascular or renal disease (3,6).

Besides, a relationship between cardiovascular and thyroid disease has been shown in several studies, some of which also linked cardiovascular disease to subclinical hypothyroidism (7-10). Renal disease has also been associated with thyroid disease, because thyroid hormone affects the regulation of volume status and vascular resistance (5,11). Hypothyroidism, including subclinical hypothyroidism, increases systemic vascular resistance as well as vascular resistance of afferent and efferent arterioles of the kidney. This increased vascular resistance lowers the effective renal plasma flow and glomerular filtration rate (GFR) without increasing blood urea nitrogen (BUN) or creatinine (Cr) levels, although reversible elevation of serum Cr may occur (12-14).

Therefore we assumed that the RDW may be associated with subclinical hypothyroidism. The goal of this study was to evaluate the relationship between subclinical hypothyroidism and RDW levels in a large healthy sample.

MATERIALS AND METHODS

Study design and subjects

This study utilized a cross-sectional analysis and included the review of medical records from 25,192 (14,889 male and 10,303 female) consecutive patients who completed the routine Health Investigation at the Eulji University Hospital Health Screening Center in Korea, from January 1st, 2007 to December 31st, 2008. Participants comprised healthy subjects with no known systemic diseases and who were not taking any medication that may affect thyroid function, and were not pregnant or within the first year of the postpartum period. Subjects with history of thyroid dysfunction (hyperthyroidism or hypothyroidism) were excluded from the study. The number of subjects excluded from the study due to disease state, medication use, or improper condition was 1,711. A total of 138 subjects (48 male and 90 female) who were diagnosed with thyroid disease in advance based on written informed consent, even though having normal thyroid function and who had abnormal thyroid function level (TSH < 0.3 or abnormal fT4 level) were also excluded. There were a total of 1,849 patients (662 males and 1,187 females) excluded from the study, resulting in the enrollment of 23,343 patients. Written informed consent for data collection was obtained from all participants. The study was approved by the institutional review board at the Eulji University Hospital.

Demographic and clinical data

Basic demographic information (age, sex) and physical data including height, bodyweight, body mass index (BMI), and systolic and diastolic blood pressures (BP) were collected. History of pregnancy, alcohol or tobacco use, family and personal history of thyroid disease, diabetes, dyslipidemia, and hypertension were obtained. Due to the fact that RDW can be influenced by recent illnesses or other stressors, information on recent treatment for anemia (including blood transfusions) or acute illnesses, including cold, flu, diarrhea, vomiting, pneumonia, or ear infections within the past 4 weeks were collected using a standardized questionnaire.

Laboratory data were collected in the morning and fasting blood samples were obtained from each participant. Laboratory tests performed included thyroid function tests (TSH, T3, free T4), CBC (WBC, RBC, Hemoglobin, Hematocrit, MCV, MCH, RDW), lipid profile (total cholesterol, triglyceride, HDL cholesterol, LDL cholesterol), blood chemistry (total protein, albumin, BUN, Cr, uric acid), iron, vitamin B_{12}, folate, erythrocyte sedimentation rate (ESR), high sensitivity C-reactive protein (hs-CRP), and rheumatoid factor (RF). Serum TSH, free T4, and T3 concentrations were measured with chemiluminescent

immunoassays with an ADVIA Centaur XP analyzer (Diamond Diagnostics, USA). Hematological tests were performed on the ADVIA 2120i (Siemens Health Care Diagnostic, USA). Chemistry was measured on the ADVIA 1800 (Siemens Medical Solution Diagnostic, USA). Blood specimens were drawn from an antecubital vein in all patients.

BMI was calculated as weight (kg) divided by height squared (m^2). Systolic and diastolic BP readings were obtained after the participant rested for 5 min. To obtain the most accurate blood pressure readings, 3-4 consecutive measurements were taken on the same arm using a mercury sphygmomanometer, and an average value was calculated. Kidney function was defined by estimated glomerular filtration rate (e-GFR) using the formula developed and validated in the Modification of Diet in Renal disease (MDRD) study, because a number of factors such as age, ethnicity, and sex can influence serum creatinine concentrations. The MDRD formula is as follows: e-GFR (ml/min/1.73 m^2) = 175 x (serum creatinine)$^{-1.154}$ x (age)$^{-0.203}$ x 0.742 (if the participant is female) x 1.212 (if the participant is black).

Definition of subclinical hypothyroidism

Subclinical hypothyroid disease was defined as elevated serum TSH levels with normal fT4 (reference range of 0.8-1.7 ng/dL) concentrations (7,15). Subjects were classified into two groups based on TSH levels representing subclinical hypothyroidism (> 5 mU/L) or a euthyroid state (0.3-5 mU/L). These two groups were further subdivided into four TSH groups to determine the correlation between TSH and other variables. For the purposes of this study, TSH levels were examined as a continuous variable and were divided into quartiles using the following cutoff values: 0.3 to < 2.5 mU/L, 2.5 to < 5 mU/L, 5 to < 7.5 mU/L, and ≥ 7.5 mU/L.

Statistical analysis

With the exception of sex distribution, shown as n (%), all demographic and laboratory data are presented as means ± SD and organized by TSH group. Participant characteristics were studied across TSH subgroups and differences between groups were examined for significance using a univariate linear regression (for continuous variables) and the Pearson chi-square test (for categorical variables) (Table 1). Multivariate linear regression analysis was used to determine factors that were associated with higher TSH levels (Table 2). A partial correlation analysis was performed to identify correlations between TSH levels and variables, including RDW levels in each group after adjusting for age and sex (Table 3). Data were analyzed using the statistical package SPSS version 18.0 (SPSS, USA) and p-values < 0.05 were considered statistically significant.

RESULTS

A total of 23,343 consecutive healthy subjects (14,227 men and 9,116 women) were examined in the Health Investigation Center. All subjects were classified in one of four groups based on baseline TSH levels. There were 16,896 patients in the 1st quartile group (TSH: 0.3-2.5 mU/L), 5079 in the 2nd quartile group (TSH: 2.5-5.0 mU/L), 645 in the 3rd quartile group (TSH: 5.0-7.5 mU/L), and 283 in the 4th quartile group (TSH: ≥ 7.5 mU/L). The euthyroid group included the 1st and 2nd groups, and the subclinical hypothyroid group included the 3rd and 4th groups.

Table 1 presents demographic characteristics and physical/clinical data, as well as a comparison of laboratory results according to the TSH quartile. More elders and more women were included in the subclinical hypothyroid group than the euthyroid group. RDW, ESR, total protein, total cholesterol, HDL, and LDL levels positively correlated with increasing TSH quartiles. In addition, RBC, hemoglobin, hematocrit, uric acid, free T4 levels, and e-GFR decreased with increasing TSH quartiles.

In a multivariate linear regression analysis, RDW was associated with TSH levels (standardized beta coefficient = 0.102; p < 0.001), and e-GFR was inversely associated with TSH levels (standardized beta coefficient = -0.019; p < 0.001) (Table 2). Other factors such as RBC, Hb, Hct, ESR, total protein, total cholesterol, and FT4 were also correlated with baseline TSH levels as shown in table 2. Although other factors except RDW and e-GFR correlate with TSH levels, their variance inflation factor (VIF) shows high levels (not shown in Table 2). In terms of multicollinearity, just two of these factors, RDW and e-GFR, have independent, significant association with TSH levels.

We adjusted variables that were found to be associated with TSH levels. Table 3 presents the correlation of TSH levels with variables in the four groups and in the entire investigated population after adjusting for age and sex. In all four groups, TSH levels

were significantly correlated with RDW, e-GFR, and fT4 levels ($p < 0.001$). Furthermore, in the 4th group, RDW levels have a tendency to be more strongly associated with TSH levels than in the other groups ($p = 0.006$). Other variables that were correlated with TSH levels are shown in table 3.

Table 1. Baseline demographic and physical/clinical characteristics and laboratory examination values across TSH quartiles

Variables	Euthyroid		Subclinical hypothyroidism		*p* value
	Quartiles				
	1st	2nd	3rd	4th	
Number	16,896	5,079	645	283	
TSH (mU/l)					
Unweighted (median)	1.48	3.14	5.8	8.9	
Interquartile range	0.3-2.5	2.5-5	5-7.5	> 7.5	
Age (years)	41.8 ± 10.0	41.5 ± 10.6	42.8 ± 11.6	43.2 ± 11.3	0.956
Female sex (%)	34.5%	49.3%	58.9%	63.3%	< 0.001*
BMI (kg/m^2)	23.6 ± 3.1	23.4 ± 3.2	23.7 ± 3.5	23.5 ± 3.2	0.935
Blood pressure (mmHg)					
Systolic	125.2 ± 15.8	124.5 ± 16.1	125.8 ± 16.3	124.2 ± 16.9	0.015*
Diastolic	73.0 ± 10.8	72.5 ± 10.8	73.2 ± 10.9	71.9 ± 10.2	0.377
WBC (10^3/μL)	6.6 ± 1.7	6.4 ± 1.6	6.4 ± 1.6	6.4 ± 1.6	0.563
RBC (10^6/μL)	4.8 ± 0.5	4.7 ± 0.5	4.6 ± 0.5	4.6 ± 0.4	< 0.001*
Hemoglobin (g/dL)	14.8 ± 1.6	14.7 ± 1.6	14.2 ± 1.6	14.1 ± 1.5	< 0.001*
Hematocrit (%)	42.4 ± 4.1	41.4 ± 4.2	41.0 ± 4.2	40.6 ± 3.9	< 0.001*
MCV (fL)	88.5 ± 4.4	88.2 ± 4.6	88.5 ± 4.6	88.3 ± 4.3	0.534
MCH (pg)	30.9 ± 1.8	30.7 ± 2.0	30.8 ± 2.0	30.7 ± 1.9	0.348
Iron (μg/dL)	118 ± 8.9	116 ± 5.9	121 ± 10.1	117 ± 4.4	0.053
Vitamin B_{12} (pg/mL)	421 ± 95.3	420 ± 99.2	423 ± 91.3	422 ± 92.3	0.096
Folate (ng/mL)	7.1 ± 2.3	7.2 ± 2.1	7.3 ± 2.0	7.2 ± 2.0	0.076
RDW (%)	12.50 ± 0.93	12.51 ± 0.95	12.61 ± 0.95	12.82 ± 1.05	< 0.001*
ESR mm/hr	8.0 ± 8.5	9.3 ± 9.2	11.0 ± 10.9	11.4 ± 10.5	< 0.001*
Total protein (g/dL)	7.5 ± 0.4	7.5 ± 0.4	7.6 ± 0.4	7.6 ± 0.4	< 0.001*
Albumin (g/dL)	4.6 ± 0.2	4.6 ± 0.2	4.6 ± 0.2	4.6 ± 0.2	0.860
BUN (mg/dL)	13.7 ± 3.6	13.4 ± 4.1	13.5 ± 3.5	13.7 ± 3.3	0.084
Creatinine (mg/dL)	1.0 ± 0.2	1.0 ± 0.3	1.0 ± 0.2	1.0 ± 0.1	0.678
e-GFR (mL/min/1.73 m^2)	75.9 ± 9.5	74.5 ± 9.8	72.8 ± 9.9	72.0 ± 9.7	< 0.001*
Uric acid (IU/L)	5.4 ± 1.4	5.2 ± 1.4	5.1 ± 1.5	5.0 ± 1.3	< 0.001*
Total cholesterol (mg/dL)	189.1 ± 33.5	188.5 ± 33.6	189.3 ± 35.0	192.5 ± 37.1	< 0.001*
Triglyceride (mg/dL)	133.2 ± 90.9	128.4 ± 84.7	130.4 ± 85.5	127.7 ± 100.6	0.948
HDL (mg/dL)	55.5 ± 12.4	56.9 ± 12.8	57.0 ± 13.2	57.0 ± 14.1	0.001*
LDL (mg/dL)	106.9 ± 28.8	105.3 ± 28.4	105.5 ± 29.2	108.2 ± 29.5	0.023*
hs-CRP (mg/dL)	0.2 ± 0.4	0.2 ± 0.3	0.2 ± 0.54	0.1 ± 0.3	0.532
Rheumatoid factor (IU/mL)	8.1 ± 13.5	8.0 ± 14.0	7.9 ± 10.0	7.8 ± 13.3	0.657
T3 (ng/dL)	125.0 ± 22.6	122.6 ± 23.7	118.6 ± 15.3	99.0 ± 39.3	0.487
fT4 (ng/dL)	1.3 ± 0.2	1.2 ± 0.2	1.2 ± 0.2	1.1 ± 0.2	< 0.001*

Data were presented as means ± SD except for n (%) for sex. Data between four groups were compared using Pearson chi-square test for categorical variables, simple linear regression for other continuous variables, and Univariate linear regression analysis.* $p < 0.05$, indicates significant correlation with TSH levels. TSH: thyroid stimulating hormone; BMI: body mass index; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; RDW: red cell distribution width; ESR: erythrocyte sedimentation rate; BUN: blood urea nitrogen; e-GFR: estimated glomerular filtration rate; HDL: high density lipoprotein; LDL: low density lipoprotein; hs-CRP: high sensitivity C-reactive protein; T3: triiodothyronine; fT4: free thyroxine.

Table 2. Factors associated with higher levels of TSH in multivariable linear regression

	1% increase in TSH	95% CI	*P* value
RBC	-0.343	-0.493 to -0.193	< 0.001*
Hb	-0.187	-0.212 to -0.109	< 0.001*
Hct	-0.175	-0.247 to -0.092	< 0.001*
RDW	0.102	0.049 to 0.154	< 0.001*
ESR	-0.009	-0.015 to -0.002	0.007*
T. protein	0.576	0.441 to 0.711	< 0.001*
e-GFR	-0.019	-0.024 to -0.014	< 0.001*
UA	0.001	-0.044 to 0.046	0.964
TC	0.002	0.001 to 0.003	0.006*
HDL	-0.003	-0.007 to 0.002	0.236
LDL	-0.001	-0.004 to 0.003	0.710
fT4	-0.088	-0.125 to -0.032	< 0.001*

Positive coefficients indicate a direct relation between the characteristic and higher levels of TSH. * $p < 0.05$, indicates significant correlation with TSH levels. CI: confidence interval; TSH: thyroid stimulating hormone; Hb: hemoglobin; Hct: hematocrit; RDW: red cell distribution width; ESR: erythrocyte sedimentation rate; T. protein: total protein; e-GFR: estimated glomerular filtration rate; UA: uric acid; TC: total cholesterol; HDL: high density lipoprotein; LDL: low density lipoprotein; fT4: free thyroxine.

Table 3. Correlation of TSH levels and variables by TSH groups and all subjects after adjusting for age and sex

Variables	All (n = 23,343)		1st (n = 16,896)		2nd (n = 5,079)		3rd (n = 645)		4th (n = 283)	
			Euthyroid				Subclinical hypothyroidism			
	r	*P* value	r	*P* value	r	*P* value	r	*P* value	r	*P* value
RBC	-0.013	0.058	0.008	0.319	-0.012	0.409	-0.049	0.211	-0.123	0.039*
Hb	-0.003	0.688	-0.010	0.207	0.000	0.972	-0.012	0.752	-0.039	0.515
Hct	-0.009	0.188	-0.011	0.159	-0.003	0.840	-0.027	0.496	-0.094	0.115
RDW	0.024	< 0.001*	0.019	0.014*	0.028	0.045*	0.082	0.038*	0.166	0.006*
ESR	0.018	0.010*	0.012	0.158	0.027	0.069	-0.016	0.705	-0.063	0.324
T. protein	0.058	< 0.001*	0.042	< 0.001*	0.029	0.04*	0.003	0.938	0.124	0.039*
e-GFR	-0.063	< 0.001*	-0.054	< 0.001*	-0.039	0.006*	-0.087	0.027*	-0.144	0.017*
UA	0.019	0.005*	0.026	0.001*	0.015	0.273	-0.071	0.073	0.038	0.532
TC	0.03	< 0.001*	0.010	0.194	-0.02	0.149	0.052	0.192	0.144	0.017*
HDL	-0.004	0.595	-0.002	0.792	0.017	0.239	0.089	0.024*	-0.003	0.966
LDL	0.024	< 0.001*	-0.007	0.372	-0.03	0.041*	0.042	0.3	0.198	0.001*
fT4	-0.076	< 0.001*	-0.074	< 0.001*	-0.053	< 0.001*	-0.89	0.031*	-0.477	< 0.001*

Results were presented as the coefficient (r) of partial correlation analysis after adjusting for age and sex for each group. * $p < 0.05$, indicates significant correlation with TSH levels. TSH: thyroid stimulating hormone; Hb: hemoglobin; Hct: hematocrit; RDW: red cell distribution width; ESR: erythrocyte sedimentation rate; T. protein: total protein; e-GFR: estimated glomerular filtration rate; UA: uric acid; TC: total cholesterol; HDL: high density lipoprotein; LDL: low density lipoprotein; fT4: free thyroxine.

DISCUSSION

RDW is calculated by dividing the RBC standard deviation by the mean corpuscular volume (MCV), and reflects the variability in the size of circulating RBCs (16). Calculating RDW requires an inexpensive test, and the value is routinely reported by automated laboratory equipment used to perform complete blood counts. Recently, higher RDW levels have been related to cardiovascular morbidity and mortality in several studies (3,6,17). Moreover, an independent association between higher RDW levels and lower e-GFR levels has been demonstrated in a large cohort of unselected adult outpatients (5).

Subclinical hypothyroidism may impair left ventricular diastolic function, alter endothelial function, increase hs-CRP level, and thus increase the risk of atherosclerosis (7,18). Therefore, screening and treatment for subclinical hypothyroidism has been suggested to

prevent cardiovascular disease. The interplay between thyroid and kidney functions has long been known. Thyroid hormones have significant effects on renal hemodynamics, control of salt and water, and active tubular transport processes of ions (5,11). Previous studies have shown a close relationship between stage 2-4 chronic kidney disease (CKD) and subclinical hypothyroidism (11,19). Thyroid hormone therapy can preserve renal function with subclinical hypothyroidism patients (20). When considering the relationship between RDW and cardiovascular and renal disorders, it seems logical that subclinical hypothyroidism may affect RDW levels because thyroid hormone is associated with cardiovascular and renal disorders. Our initial hypothesis of the relationship between subclinical hypothyroidism and RDW was formed based on these aforementioned studies.

Although the exact mechanisms explaining how RDW is associated with other diseases have not been defined, it is possible that oxidative stress and inflammation play a role in reducing RBC survival (21-23). Overtly increased RDW may be a consequence of anemia or anemia-related nutritional deficiencies (such as vitamin B_{12} or folate deficiencies) or recent blood transfusion. Inflammation may also impact erythropoiesis, erythrocyte circulatory half-life, and erythrocyte deformability, promoting anisocytosis and, thus, increasing RDW levels. In a large unselected outpatient sample, greater RDW values were independently associated with greater CRP levels (21,22). However, in the present study, the association between TSH levels and RDW levels persisted after adjusting for multiple potential confounding factors. Besides, after adjusting for inflammatory markers such as CRP and ESR, we identified an association between TSH and RDW levels.

In our study, an independent association was found between high TSH levels in the setting of subclinical hypothyroidism and RDW, and e-GFR levels. That is, the adjustment for multiple potential confounders attenuated, but did not eliminate, the association between high TSH levels and RDW, and e-GFR levels. In addition to reaching statistical significance, we might assume that high levels of RDW in the subclinical hypothyroidism patient may show the possibility of coexisting complications.

The strengths of our analysis include the large sample size and the use of a central laboratory for all assays. In addition, outcomes were ascertained according to specified criteria from individuals who were unaware of TSH levels. However, our study also has some limitations that should be considered. First, it was limited by its cross-sectional study design, and cause/effect relationships were not shown. The study was not longitudinal, either. Although the incidence of subclinical hypothyroidism in the large study sample of healthy individuals is similar to that observed in the overall population, follow-up was lacking and, therefore, it was not a cohort study, which would have been a preferable study design. Future studies are needed with a large cohort and sufficient patient follow-up to determine the significance of early treatment of subclinical thyroid disease. Second, although we considered several potential confounding factors in the regression models, the relationship between RDW and TSH levels may be influenced by unmeasured residual confounding factors. Third, all variables including RDW and TSH were assessed with a single measurement that might be influenced by biological variability or measurement error, although such errors are likely to attenuate the observed associations between RDW and TSH levels. Fourth, the proportion of male subjects was larger than female subjects. The main reason for this discrepancy is that the social worker-based health check-up is usually performed in male patients devoted to social life. Additionally the proportion of excluded females with abnormal thyroid function tests and thyroid disease was larger than the number of males excluded.

In conclusion, RDW levels and e-GFR are correlated with euthyroid and subclinical hypothyroid status. RDW is especially more strongly correlated with subclinical hypothyroidism. Although there are published reports that examined the relationship between RDW levels and thyroid function (24,25), this study represents the first examination of the relationship between RDW levels and subclinical hypothyroidism using TSH levels in large scale healthy population. The present findings are broadly applicable as RDW is widely available to clinicians as part of the complete blood count and there are no additional costs to obtain these data, in contrast to other novel markers of subclinical hypothyroid disease. Future prospective studies would be useful to provide additional information regarding the mechanisms that correlate RDW with subclinical hypothyroidism.

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