http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v7i10.145

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

**Original Article**

# RDW is Useful Predictor of Cardiovascular and Renal Disease of Patients Suffering from Subclinical Hypothyroidism Attending at Tertiary Care Hospital of NBMCH

Authors
**Ashoke Kr Saha[1], Rajarshi Kayal[2*], Saheli Kayal[3], Krishanu Banik[4]**
[1]Assistant Professor, Department of Biochemistry, North Bengal Medical College, West Bengal, India
[2]Researcher, Ph.D in Biochemistry, Mritwika Appartment, P30 Gabtala Lane, West Bengal, Kolkata 700060
[3]Assistant Teacher, Birla Bharati, Taratolla, Santoshpore New Road, Near Nature Park, P.O.- Bidhangarh, Kolkata, West Bengal- 700 066, India
[4]Assistant Professor, Department of General Medicine, COM & amp; JNMH, The WBUHS, Kalyani, Nadia-741235, West Bengal, India
*Corresponding Author
**Rajarshi Kayal**
Researcher, Ph.D in Biochemistry, Mritwika Appartment, P30 Gabtala Lane, , West Bengal, Kolkata 700060

**Abstract**

**Background:** *Deficiency of thyroid hormones causes red cell disorder in our body. Anaemia is a common sign. Hypothyroid disorder patients have a decreased RBC mass due to reduction plasma volume. On routine examination such as hemoglobin estimation it may be missed because of increased RBC mass is observed in other causes of anaemia. Thyroid hormones have significant effects on renal haemodynamics and suspected cardiovascular diseases.*

1. *To know the effect of SCH on 1) erythrocyte indices (HB, HCT, MCV & RDW-cv)*
2. *Renal function parameters( urea, creatinine and e-GFR)*
3. *Cardiovascular parameters (triglycerides, total cholesterol, HDL, LDL )*
4. *Inflammatory marker i.e CRP*

*In our study ie hospital based observational study for one year. HB, HCT, MCV, RDW, FT4, TSH, TOTAL CHOLESTEROL, TRYGLYCERIDES, LDL, HDL, CRP, UREA, CREATININE were estimated and eGFR was calculated using modification of diet in renal disease study equation. Higher RDW measurement have been strongly associated with low HDL cholesterol and an inverse and graded association between renal function was reported in our study.*

## Introduction

Thyroid hormones have long been recognized as important role in hematopoiesis in our body[(1&2)]. Hematopoiesis occur in young sac and then in the liver and finally in the bone marrow ie permanent area of the production. Common thyroid disorders are hypothyroidism, hyperthyroidism and goiter. Hypothyroidism (subclinical and clinical) is the most prevalent type throughout the world[(3&4)]. From different studies, it is seen that erythrocyte abnormalities are frequently associated with hypothyroidism[(5,6&7)]. Several types of anemia have been reported wit thyroid disorder which may be normocytic normochromic, microcytic

and macrocytic hypochromic[8]. Macrocytic anemia may be unresponsive to vit B12 or folate. It has been shown thyroid hormones deficiency may lead to bone marrow suppression or decrease in in erythropoietin production due to reduction of O2 requirement or low levels of micronutrients like iron, folic acid, and vit B12 etc[9&10]. Alteration in other hematological parameters such as leucopenia and neutropenia are common in hypothyroidism due to hypoplasia of myeloid cell lines[11]. Hyperthyroidism is rare associated with anemia[12].

Subclinical hypothyroidism may impair left ventricular diastolic dysfunction, alter endothelial function, increase CRP level and thus increase the risk of atherosclerosis[13]. Therefore, screening for subclinical hypothyroidism has been suggested to prevent cardiovascular disease[14&15&16].

The interplay between thyroid and kidney functions has long been known[17]. Thyroid hormones have significant effects on renal hemodynamics, control of salt and water and active tubular transport process of ions. Hypothyroidism including subclinical hypothyroidism increases systemic vascular resistance as well as vascular resistance of afferent and efferent arterioles of kidney. This increased vascular resistance lowers the effective renal plasma flow and Egfr[18]. Therefore we assumed that RDW may be associated with subclinical hypothyroidism. The goal of this study was to evaluate the relationships between subclinical hypothyroidism and (HB, HCT, RDW levels, CRP &HDL, LDL,TOTAL CHOLESTEROL, TRYGLYCERIDES levels) with a healthy euthyroid sample with same parameters.

Because of high prevalence of both thyroid dysfunction (subclinical hypothyroidism) and anaemia in Indian population, a few studies have been conducted on these problems in the subhimalayan region. Our study was conducted to estimste and to compare anaemia, kidney functions, cardiovascular problems among the patients of thyroid disorders with special emphasis on subclinical hypothyroidism patients.

**Materials and Methods**

This was an institutional facility based, noninterventional, epidemiological study with observational design. The study was conducted on the patients attending department of Biochemistry and Department of Pathology of North Bengal Medical College and Hospital, Darjeeeling during Jan 2018 to June 2019.

**Inclusion Criteria**

Patients (male and female agd 20 to 50 years) attending Department of Biochemistry, first time for thyroid function tests and voluntarily given consent to participate.

**Exclusion Criteria**

A) Patients suffering from any thyroid disease, on antithyroid therapy or any thyroid function modifying drug
B) Known anaemic.
C) On prolong drug therapy such as antitubercular, chemotherapy, anti psychotic, hormones (oral contraceptive for female), vitamins and iron supplements.
D) Acute illness
E) Suffering from malignancy or anticancer therapy.
F) Pregnancy
G) Drug abuse or habitual alcoholic

Total 90 participants were chosen by systematic sampling method a interviewed with a predesigned, pretested questionnaire.10ml venous blood was collected from each participant after taking written consent, following standard protocol of blood colletion under aseptic precaution and kept in EDTA and plain vial. serum was separated by centrifugation for estimating FT4 and TSH by enzyme linked immunosorbent assay (ELISA) method at Biochemistry Department. clotted vial was used to estimate total cholesterol, triglycerides, LDL, HDL, CRP, urea and creatinine and EDTA blood was used to estimate Haemoglobin, haematocrit, MCV, RDW, RBC count by blood coulter (Sysmax xs-800) at Central Pathology Department. EGFR was calculated 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.

Anaemia was considered when HB was <11gm% (veinous blood).

Subclinical hypothyroidism was considered when FT4 was within reference range (0.5-2.0 ng/dl) but concentration of serum TSH is greater than 5.5miu/ml.

**Reference Range**

HG: 12-16gm%

MCV: 80-96fl

HCT: 35-50%

RDW-cv (red cell distribution width-coefficient of variation):11.5-14.5%

RBC: 4-5.5 trillion cell/L

Elevated RDW is known as anisocytosis

Subclinical hypothyroidism was considered when FT4 was within reference range (0.5-2.0 ng/dl) but concentration of serum TSH is greater than 5.5miu/ml.

FT4: 0.5-2.0ng/dl

CRP: less than 6gm%

UREA: 20-40mg%

CREATININE: 0.4- 1.1mg%

**Total cholesterol:** less than 200mg%

TRIGLYCERIDES: less than 160mg%

LDL: less than 100mg%

HDL: 35-60mg%

Results and Analysis

**Results and Analysis**

Statistical analysis are done by using SPS VERSION:

**Table 1** Comparison between RBC indices in SCH patients

| RBC INDICES | SCH AND CONTROL | MEAN | STD. DEVIATION | P VALUE |
|---|---|---|---|---|
| MCV | HYPOTHYROIDISM | 93.51 | 5.75 | |
| | CONTROL | 83.77 | 2.62 | <0.05 |
| HCT | HYPOTHYROIDISM | 26.17 | 4.06 | <0.05 |
| | CONTROL | 41.42 | 3.84 | |
| HB | HYOTHYROIDISM | 9.5 | 0.98 | <0.05 |
| | CONTROL | 11.6 | 0.60 | |
| RBC | HYPOTHYROIDISM | 3.86 | 0.16 | |
| | CONTROL | 4.82 | 0.37 | <0.05 |
| RDW | HYPOTHYROIDISM | 16.93 | 1.32 | <0.05 |
| | CONTROL | 0.00 | 0.00 | <0.05 |

Hypothyroid patients are selected among participants. Most of the patients were within age 35 to 50 year. Anaemia was detected in all female patients. Females are more prone to the develop thyroid disorder i.e subclinical hypothyroidism with abnormal lipids parameters (TC, TG, LDL, HDL), higher levelof CRP& renal parameters (UREA, CREATININE,). Normochromic Normocytic anemia was mostly detected. Present study shows hypothyroidism should be ruled out while investigating anaemia.

The low plasma erythropoietin is found in hypothyroid- anaemia. MCV increases rapidly in connection with hypothyroidism. On replacement therapy with thyroxine, MCV was found to be reduced gradually. In a study by Geetha j and Srikrishna R in 2012,[19] revealed that RDW and MCV in patients with hypothyroidism and hyperthyroidism in comparison to euthyroidism individuals have stastical significant difference but other parameters like HB and PCV did not show any significant difference in comparison with control group.

The present study showed increased MCV and RDW and decreased RBC count in untreated coexisting complicated hypothyroidism as compared in euthroidism. Hypothyridism should always therefore be considered as a possible cause of unexplained and unexpected anaemia.

Clinical and laboratory results of patients groups and control group

| PARAMETERS | SUBCLIN HYPOTHYROIDISM | MEAN | STD.DEVIATION | P VALUE |
|---|---|---|---|---|
| TRIGLYCERIDES | SUBCLINHYPOTHYROIDISM | 172.26 | 27.30 | <0.05 |
| | CONTROL | 93.20 | 32.66 | |
| CHOLESTEROL | SUBCLINNHYPOTHYROIDISM | 195.66 | 39.10 | <0.05 |
| | CONTROL | 119.98 | 13.97 | |
| CRP | SUBCLNHYPOTHYROIDISM | 21.00 | 22.22 | <0.05 |
| | CONTROL | 1.29 | 0.40 | |
| HDL | SUBCLINHYPOTHYROIDISM | 31.93 | 4.00 | <0.05 |
| | CONTROL | 50.62 | 7.45 | |
| LDL | SUBCLINHYPOTHYROIDISM | 112.51 | 10.43 | |
| | CONTROL | 91.24 | 7.41 | <0.05 |

More elderly and more women included in the subclinical hypothyroid group than euthyroid group. RDW, CRP, TOTAL CHOLESTEROL, TRIGLYCERIDES, LDL, HDL LEVELS positively correlated with increasing TSH level. In addition, RBC, hamatocrit, haematoglobin and free T4 levels and e-GFR decreased with increasing TSH level.

In our study, an independent association was found between high TSH level in the setting of subclinical hypothyroidism and RDW and e-GFR levels. In addition to reaching statistical significance, we must assume that high level of RDW in the subclinical hypothyroidism patient may show the possibility of coexisiting complications. However, our study also has some limitations ie small sample volume.

| | | MEAN | STDDEVIATION | P VALUE |
|---|---|---|---|---|
| RDW | SUBCLINHYPOTHY | 16.93 | 1.32 | <0.05 |
| | CONTROL | 0.00 | 0.00 | |
| E-GFR | SUBCLINHYPOTHY | 55.71 | 15.15 | <0.05 |
| | CONTROL | 116.95 | 12.5 | |
| TSH | SUBCLINHYPO | 7.8291 | 2.591 | <0.05 |
| | CONTROL | 4.98 | 0.351 | |

**Discussion**

Thyroid disorders are frequently associated with haematological abnormalities among which anaemia is the most prevalent[19]. Females are more prone to the develop thyroid disorders and anaemia[20]. Anaemia was considered when HB less than 11gm%. subclinical hypothyroidism disease was defined as elevated serum TSH levels with normal FT4.Calculating RDW (quantitative measure of variation of circulating red blood cells) requires an inexpensive test and the value is routinely reported by automated laboratory equipment use to perform complete blood count. Recently, highIer RDW levels have been related to cardiovascular morbidity and mortality in several studies[21]. Moreover, an independent association between higher RDW levels and lower e-GFR levels have been demonstrated in a large cohort of adult outpatients[16].

It was reported that dyslipidemia is one of the complications of primary hypothyroidism. In our study, subclinial hypothyroidism patients showed significant higher levels of cholesterol, triglycerides, LDL, and lower level of HDL as compares to euthyroid patients.

Subclinical hypothyroidism may alter endothelial function and increase CRP level and thus increase the risk of atherosclerosis[22]. In our study, subclinical hypothyroidism patients showed significant higher level of CRP.

Thyroid hormones have significant effects on renal haemodynamics. The interplay between thyroid and kidney functions has long been known. Previous studies have shown a close relationship between stage 2-4 chronic kidney disease (CKD) and subclinical hypothyroidism[18]. Thyroid hormones therapy can preserve renal function with subclinical hypothyroidism patients[18].

In our study, subclinical hypothyroidism patients showed significant higher level of serum

creatinine and lower e-GFR levels compared with euthyroid patients.

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 disorder.

In our study, this hypothesis of relationship between subclinical hypothyroidism and RDW was formed based on these abovementioned studies.

Overtly increased RDW may be a consequence of anaemia related nutritional deficiencies or recent blood transfusion. Inflammation may affect RBC half life, RBC deformability, promoting anisocytosis and thus increases RDW.

**Conclusion**

The present study shows that the hypothyroid state is associated with consistent elevation in the serum creatinine level, presumably related to a decrease in the e-GFR. The changes in serum creatinine level may appear to be reversible. It maybe clinically relevant to know of this association in that it could be creatinine elevation in a patient of hypothyroidism. It gives also alert to the clinician to evaluate who has the modest serum creatinine elevation but whose thyroid status is unknown. In the present study the association between TSH level and RDW levels persisted. We identified also other inflammatory marker such as CRP which is related with alter endothelial function of left ventricular dysfunction.

**References**


1. Fein HG, Rivin RS. Anemia in thyroid diseases. Med Clin North Am. 1975:1133-45.
2. Grymula K, Paczkwska E, et al (2007).The influence of 3,3,5-triiodo-L-thyronine on human haematopoiesis. cell prolif,40,302-315.
3. Ambika Gopalakrishnan Unnikrishnan, Usha V. Menon.(2011). Thyroid disorders in India: An epidemiological perspective. Indian journal of Endocrinology and Metabolism,15 (supplement 2).
4. Vanderpump MP. (2011). The epidemiology of Thyroid disease. Br Med Bull,99,39-51.
5. Omar S, Hadj-Taeib S, Kanoun F, Hammami MB, Kamoun S, Ben Romdhane N et al. (2010). Erythrocyte abnormalities In Thyroid dysfunction. Tunis Med,88(11), 783-788.
6. Iddah MA, Macharia BN, Ng'wena AG, Keter A, Ofulla AV.(2013).Thyroid hormones and haematological indices levels in thyroid disorder patients at Moi teaching and referral hospital, Western Kenia.
7. Montagnana M, Lippi G, Salvagno GL, Guidi Gc. The red blood cell distribution width is associated with serum levels of thyroid stimulating hormone in the general population .Int J Lab Hematol.2009:581-2.
8. Bashir H, Bhat MH, Farooq R, Majid S, Shoib S, Hamid R etal., comparison of haematological parameters in unteated and treated subclinical hypothyroidism and primary hypothyroidism patients. Med J Islam Repub Iran.2012;172-8.
9. Christ-Crain M, Meier C, Huber P, Zulewki H, Staub JJ, Muller B, (2003),. Effect of restoration of euthyroidism on peripheral blood cells and erythropoietin in women with subclinical hypothyroidism. Hormones (Athens),2,237-242.
10. Melmed S, Polonsky KS, et al. William's textbook of Endrocrinology,10th ed ,427.
11. Axelord AR, Brman L (1951).The Bone Marrow in Hyperthyroidism and Hypothyrodism. Blood 6 (5),36-453.
12. Perlman JA, Sternthal PM, (1983). Effect of $^{131}$I on the anaemia of Hyperthyroidism. Journal of Chronic Disease, 36(5),405-412.
13. Allen LA, Felker GM, Mehra MR, Chiong JR, Dunlap SH, Ghali JK, et al. validation

and potential mechanism of red blood cell distribution width as a prognostic marker in heart failure.J Card Fail. 2010;16 (3):230-8.

14. Felker GM, Allen LA, Pocock SJ, Shaw LK, Mc Murray JJ, Pfeffer MA, etal.red cell distribution width as a novel prognostic marker in heart failure.J Am Coll Cardiol. 2007;50(1):40-7.
15. Lippi G, Filippozzi L,Montagnana M, Salvagno GL,, Franchini M,Guidi GC, et al. clinical sefulness of measuring red blood cell distribution width on admission in patients with acute coronary syndromes. Clin Chem Lab Med.2009;47(3):353-7.
16. Anderson JL, Ronnow BS, Horne BD, Carlquist JF, May HT, Bair TL, etal. Usefulness of a complete blood count-derived risk score to predict incident mortality in patients with suspected cardiovascular disease. Am J Cardiol. 2007;999(2)169-74.
17. Den Hollander JG, Wulkan RW, Mantel MJ, Berghout A. Correlation between severity of thyroid dysfunction and renal function. Clin Endocrinol 2005 April; 62(4):423-427.
18. Iglesias P, Diez J. Thyroid dysfunction and kidney disease. Eur J Endocrinol 2009 April; 160(4):503-515.
19. Geetha J, Srikrishna R. (2012). Role of red blood cell distribution width(RDW) in thyroid dysfunction. Int J Biol Med Res.3(2).1476-1478.
20. Lippi G, Montagnna M, Salvagno GL and Guidi GC.(2008). Should women with abnormal serum thyroid stimulating hormone undergo screening for anaemia? Arch Pathol Lab Med,132(3),321-322.
21. Li W, Li X, Wang M, Ge X, Li F, Huang B et al. Association between red cell distribution width and the risk of heart events in patients with coronary artery disease .Exp Ther Med.2015:1508-1514.
22. Risal P, Maharjan B, Kozu R, Makaju R, Gautem M. Variation of total serum cholesterol among the patient with thyroid dysfunction .Kathmandu Uni Med J.2010April-jun;8(30):265-268.