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Original Research Article

## Association and correlation of thyroid dysfunction with anemia types in pregnant women of northern Andhra Pradesh, India

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### ABSTRACT

**Background:** Thyroid dysfunction is a common disorder in pregnancy along with anemia. But no study has evaluated the association between them. To estimate the prevalence of thyroid dysfunction and its association with anemia types in pregnant women during 1<sup>st</sup> trimester.

**Methods:** Three hundred and eighty pregnant women with <12 weeks of gestational age were selected for the study with no history of thyroid dysfunction and anemia. All the pregnant women were classified into A, euthyroid and B, thyroid dysfunction groups. The B group was again subdivided into hypothyroid, subclinical hypothyroid (SCH), hyperthyroid according to nature of dysfunction. 5 ml of blood sample was collected from all subjects to analyse thyroid hormones and erythrocyte indices.

**Results:** Out of 380 subjects, euthyroid was found to be 77.9%, and rest 22.1% were with thyroid dysfunction. Out of 84 thyroid dysfunction, hypothyroid was found to be 7.9%, SCH 13.9% and hyperthyroid was 0.3%. Out of 296 euthyroid women, anemia was identified in 97 pregnant women (32.8%) whereas in thyroid dysfunction women it was 43 women out of 84 (51.2%) which is a statistically significant. Significantly higher frequency of microcytic hypochromic anemia and normocytic normochromic anemia types were also found in thyroid dysfunction groups compared to euthyroid group ( $p < 0.05$ ). However, no significance between the thyroid dysfunction groups, Statistically significant difference was observed in the Hb concentration, RBC count, MCV, MCH and PCV between euthyroid and different thyroid dysfunction conditions ( $p < 0.05$ ). A statistically significant positive correlation was found between fT4 and erythrocyte indices.

**Conclusions:** As fT4 and TSH correlated with erythrocyte indices, it is advisable to screen for thyroid dysfunction and vice versa so as to prevent the complications associated with anemia and thyroid dysfunction.

**Keywords:** Anemia, Pregnancy, RBC indices, Thyroid dysfunction

### INTRODUCTION

In developing countries, the anemia during pregnancy remains the major public health problem and associated with increased risk of maternal and perinatal mortality.<sup>1</sup> The incidence of anemia is found to be about 10% in females of child-bearing age and elderly women as well.<sup>2</sup> According to WHO about 38% of antenatal mothers were anemic worldwide.<sup>3</sup> In developing countries the causes of anemia in pregnancy are multifactorial, which includes micronutrient deficiencies, parasitic infestations and chronic infections.<sup>4</sup> In addition, several socio-

demographic factors such as age, parity, economic status, literacy, frequent child birth and late booking (3<sup>rd</sup> trimester) also contribute for anemia.<sup>5</sup>

Both thyroid dysfunction and anemia are common disorders of clinical practice. The association between anemia and thyroid disorder in experimental animal studies have been well documented.<sup>6</sup> In spite of the fact, the anemia and thyroid dysfunction often occur at the same time, the relation between them remains ill-defined. There are several human studies on the association

between anemia and thyroid dysfunction, however the results are in conflicting nature with less sample size.<sup>7,8</sup>

Thyroid hormones play an important role in the process of hematopoiesis particularly in erythropoiesis. They directly influence erythroid precursor proliferation and also increases the erythropoiesis by inducing erythropoietic gene expression.<sup>9,10</sup> Thyroid dysfunction increases the risk of complications in pregnancy such as anemia, miscarriages, postpartum bleeding, preeclampsia, placental abruption and low birth weight.

Thyroid abnormalities are often associated with hematological findings such as erythrocyte indices, hemoglobin (Hb) concentration, iron, TIBC etc. The anemia is more prevalent in hypothyroid patients rather than in patients with hyperthyroidism.<sup>10-12</sup>

Anemia and thyroid dysfunction are two common medical disorders in females of reproductive age group including pregnancy.<sup>13-15</sup> There are no clinical studies performed about the incidence of thyroid dysfunction and its association with various types of anemia in south Indian population. Hence the present study was designed to measure the prevalence of thyroid dysfunction and to study their association with anemia types in pregnant women of northern Andhra Pradesh.

## METHODS

The present cross sectional study was conducted in the department of Obstetrics Gynecology in association with department of Biochemistry at NRI Institute of Medical Sciences, Sangivalasa between July 2018 and December 2019.

A total of 380 pregnant woman between the age group 20-35 years with gestational age <12 weeks were included for the study with their written informed consent. Detailed medical and obstetrical history was taken along with clinical examination. 2.5 ml of whole blood was collected from all the pregnant woman in a plain vacutainer to measure fT3, fT4 and TSH and 2.5 mL was collected in EDTA vacutainer for the measurement of Hb concentration, RBC count, packed cell volume (PCV), mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH) using Sysmex XN-330 haematology analyzer. Serum fT3, fT4 and TSH levels were measured by fully automated electrochemiluminescent immunoassay using commercially available kits from bioMerieux SA with Vidas analyser. The reference range used in the study was based on the manufacturer's manual for diagnosis of thyroid dysfunction during 1<sup>st</sup> trimester of pregnancy (fT3 1.93-5.89 pg/ml, fT4 0.94-1.52 ng/ml and TSH 0.6-5.0  $\mu$ IU/ml). Anemia was defined by hemoglobin level <11 gm/dl and microcytosis by MCV <80 fl and macrocytosis by MCV >100 fl and hypochromic anemia by MCH <25 pg.<sup>16-18</sup>

The pregnant woman with current or past history of acute illness within at least 3 months, past history of/current chronic medical condition like haemorrhoids, patients with bleeding disorders, using medication for medical conditions, and taking iron were excluded from the study. In addition, patients with multiple pregnancies and threatened miscarriage were also excluded from the study.

All the subjects were divided into two groups mainly basing on their thyroid function. The 'A' group consisting of pregnant woman with normal thyroid profile which is served as 'control group' whereas 'B' group with abnormal thyroid profile. The B group was further subdivided into hypothyroid, subclinical hypothyroid (SCH) and hyperthyroid groups depending on their nature of thyroid dysfunction. The RBC indices were compared between these groups.

Statistical analysis of the results was done using SPSS version 16 (SPSS Inc., Chicago, USA). Student's t test was used to compare two groups. One way analysis of variance (ANOVA) was used to make comparisons between more than two groups. Correlations were measured using Pearson's correlation coefficient test and the p value of <0.05 was considered to be significant.

## RESULTS

The mean $\pm$ SD age (in years) and body mass index BMI (kg/m<sup>2</sup>) of all the subjects recruited was 24.6 $\pm$ 6.8 and 22.1 $\pm$ 1.3 kg/m<sup>2</sup> respectively. Out of 380 pregnant women, primigravida 39.5%, second pregnancy 31.6%, third pregnancy 16.3% and more than three pregnancy was 12.6% (Table 1).

**Table 1: Demographic characteristics of studied pregnant women.**

Characteristics	Mean $\pm$ SD
<b>Maternal age (in years)</b>	24.6 $\pm$ 6.8
<b>Body mass index (kg/m<sup>2</sup>)</b>	22.12 $\pm$ 1.3
<b>Gestational age at screening, n (%)</b>	
<12 weeks	380
<b>History of previous pregnancy (%)</b>	
None (primi)	150 (39.4)
Gravida 2	120 (31.6)
Gravida 3	62 (16.3)
>3 pregnancy	48 (12.6)

Distribution of cases according to thyroid dysfunction was depicted in Table 2. The mean $\pm$ SD fT3 for all subjects, euthyroid, hypothyroid and subclinical hypothyroid (SCH) pregnant women was 2.14 $\pm$ 1.05, 2.0 $\pm$ 1.02, 1.75 $\pm$ 1.10 and 3.03 $\pm$ 0.45 respectively. Similarly, mean $\pm$ SD of fT4 for all subjects, euthyroid, hypothyroid and SCH pregnant women was 1.18 $\pm$ 0.27, 1.22 $\pm$ 0.19, 0.66 $\pm$ 0.44 and 1.21 $\pm$ 0.11 respectively (Table 2). And, the mean $\pm$ SD TSH for all subjects, euthyroid,

hypothyroid and SCH pregnant women was 3.59±1.87, 2.78±0.84, 5.6±0.35 and 7.0±1.82 respectively. Out of 380 subjects, euthyroid was found to be 77.9%, and rest 22.1% were with thyroid dysfunction. Out of 84 thyroid dysfunction, hypothyroid was found to be 7.9%, SCH 13.9% and hyperthyroid was 0.3% (Table 2).

The mean±SD RBC indices has been given in Table 3. The mean±SD of Hb, RBC count, PCV, MCV and MCH were significantly lower in thyroid dysfunction group women particularly in hypothyroid and SCH women as compared to euthyroid women (p<0.05). Statistically significant difference was observed in the Hb concentration, RBC count, MCV, MCH and PCV

between euthyroid and different thyroid dysfunction groups (p<0.05) (Table 3).

**Table 2: Status of thyroid hormone levels in different groups.**

	ft3	ft4	TSH
<b>All subjects (n=380)</b>	2.14±1.05	1.18±0.27	3.59±1.87
<b>Euthyroid (n=296)</b>	2.0±1.02	1.22±0.19	2.78±0.84
<b>Hypothyroidism (n=30)</b>	1.75±1.1	0.66±0.44	5.6±0.35
<b>SCH (n=53)</b>	3.03±0.45	1.21±0.11	7.0±1.82

ft3: Free T3 hormone, ft4: Free T4 hormone, TSH: Thyroid stimulating hormone, SCH: Subclinical hypothyroidism

**Table 3: Table showing the erythrocyte indices in thyroid dysfunction women.**

	Euthyroid (n=296)	Hypothyroidism (n=30)	SCH (n=53)	P value
<b>Hemoglobin (g%)</b>	10.9±1.2	10.08±0.98	10.47±0.77	<0.05*
<b>RBC count (×106/μl)</b>	4.0±0.8	3.65±0.64	3.82±0.5	<0.05*
<b>PCV (%)</b>	35.1±5.6	30.7±6.18	33.7±3.05	<0.05*
<b>MCV (fl)</b>	81.5±9.9	74.1±9.91	78.04±4.43	<0.05*
<b>MCH (pg)</b>	27.5±2.23	23.5±4.16	25.8±2.59	<0.05*

Note: p<0.05\* significant. RBC: Red blood cell, PCV: Packed cell volume, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, SCH: Subclinical hypothyroidism.

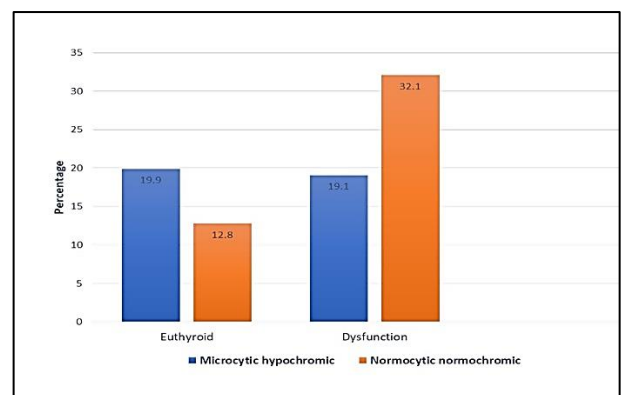
**Table 4: Distribution of anemia types and thyroid dysfunction with their prevalence.**

	Euthyroid (n=296) (%)	Thyroid dysfunction (n=84) (%)		
		Hypothyroidism (n=30)	SCH (n=53)	Hyperthyroidism (n=1)
<b>Non-anemic (n=240)</b>	199 (67.2)	12 (40)*	28 (52.8)*	1 (100)
<b>Anemic (n=140)</b>				
Microcytic hypochromic (n=84)	59 (19.9%)	8 (26.7)*	8 (15.1)*	0 (0)
Normocytic normochromic (n=56)	38 (12.8%)	10 (33.3)*	17 (32.1)*	0 (0)

Note: p<0.05\* compared to euthyroid. SCH: Subclinical hypothyroidism

All the pregnant women were grouped into euthyroid, hypothyroid, SCH and hyperthyroid women based on their thyroid dysfunction. In the present study, 296 pregnant women were presented with no abnormal thyroid function (euthyroid 77.9%). In the present study, the thyroid dysfunction was identified in pregnant women as follows: 7.9% women with hypothyroidism, 13.9% with SCH and 0.3% with hyperthyroidism. Anemia was identified in 140 pregnant women (36.8%) out of 380 total subjects and the prevalence of anemia was significantly higher in thyroid dysfunction group compared to euthyroid group (p<0.05) (Table 4).

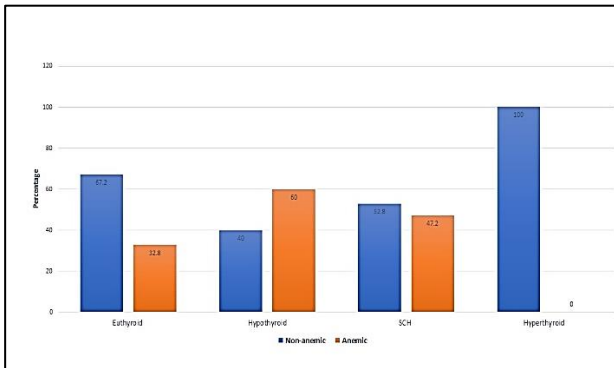
Frequency of anemia types according to thyroid dysfunction in study population: Out of 296 euthyroid women, anemia was identified in 97 pregnant women (32.8%) whereas in thyroid dysfunction, 43 (51.2%) women were found to be anemic and was statistically significant (p<0.05) (Table 4). In euthyroid subjects, the microcytic hypochromic anemia was found to be 19.9% whereas normocytic normochromic anemia was 12.8%.



**Figure 1: Types of anaemia according to thyroid status.**

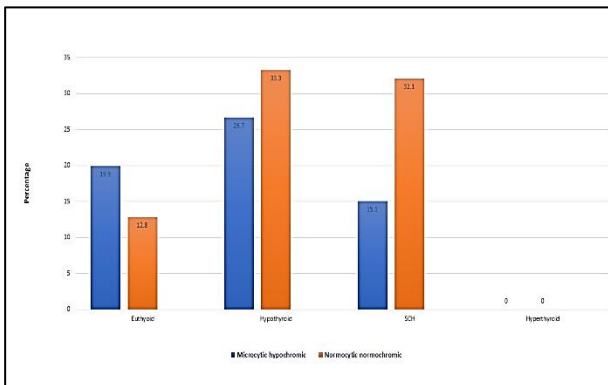
In thyroid dysfunction, anemia was found in 43 (51.2%) pregnant women and anemia types detected were 16 (19.1%) with microcytic hypochromic anemia and 27 (32.1%) with normocytic normochromic anemia. A

higher prevalence of normocytic normochromic anemia was observed in thyroid dysfunction group compared to euthyroid pregnant women though it is not significant (Table 4 and Figure 1).



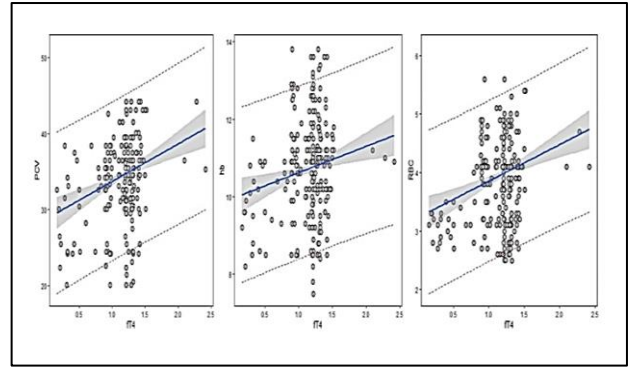
**Figure 2: Percentage of anaemia among thyroid dysfunction compared to euthyroid.**

In euthyroid group, 32.8% were anemic whereas 67.2% were non-anemic. In the present study, 60% of hypothyroid pregnant women were anemic and whereas in SCH group, 47.2% had anemia. However, no anemia cases were found in hyperthyroid pregnant women (Figure 2). A significantly higher prevalence of anemia was found in hypothyroid and SCH groups compared to euthyroid pregnant women ( $p < 0.05$ ) (Figure 2).



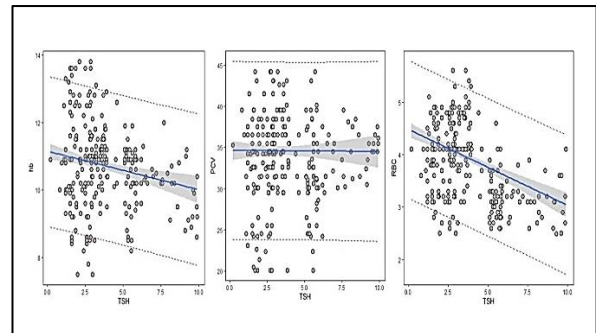
**Figure 3: Types of anaemia according to thyroid dysfunction.**

Out of 30 hypothyroid pregnant women anemia was found in 18 (60%) out of which, 8 (26.7%) with microcytic hypochromic anemia and 10 (33.3%) with normocytic normochromic anemia. The types of anemia identified in SCH women were 8 (15.1%) with microcytic hypochromic anemia and 17 (32.1%) with normocytic normochromic anemia. Significantly higher prevalence of normocytic normochromic anemia was observed in thyroid dysfunction groups as compared to euthyroid group ( $p < 0.05$ ). However, no significant difference in the prevalence of microcytic hypochromic anemia and normocytic normochromic anemia between thyroid dysfunction groups ( $p > 0.05$ ) (Figure 3).



**Figure 4: Correlation of ft4 concentration, RBC count and PCV.**

The correlation of TSH and ft4 with RBC indices was determined by using Pearson's coefficient correlation (Table 5). The ft4 levels were positively correlated with all RBC indices including Hb concentration, RBC count, PCV, MCV and MCH and were statistically significant ( $p < 0.05$ ) (Figure 4). Similarly, TSH levels were found to be negatively correlated with Hb concentration, RBC count, PCV, MCV and MCH with statistical significance ( $p < 0.05$ ). However, no statistically significant correlation was found between TSH and PCV ( $p > 0.05$ ) (Figure 5).



**Figure 5: Correlation of TSH with Hb concentration, RBC count and PCV.**

**Table 5: Correlation between thyroid hormones and RBC indices.**

	RBC count	Hemoglobin	PCV	MCV	MCH	
<b>TSH</b>	r	-0.37	-0.18	-0.004	-0.144	-0.28
	P	<0.05*	<0.05*	0.46	<0.05*	<0.05*
<b>ft4</b>	r	0.23	0.16	0.24	0.19	0.32
	P	<0.05*	<0.05*	<0.05*	<0.05*	<0.05*

Note:  $p < 0.05$ \* significant. RBC: Red blood cell, PCV: Packed cell volume, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, ft4: Free T4 hormone, TSH: Thyroid stimulating hormone.

**DISCUSSION**

The placental hormone, hCG stimulate TSH activity and thereby suppress thyroid hormone secretion.<sup>19,20</sup> At least

2-3% of pregnant women would suffer from thyroid related problems despite the gland has the ability to meet the increased needs during pregnancy.<sup>20</sup> So that early detection and intervention are necessary to prevent maternal and neonatal morbidity.

Thyroid dysfunction was found in 22.1% of studied population and our results were in accordance with previous studies.<sup>21</sup> Out of them, the frequent thyroid disorder observed in pregnancy was SCH 63.1%, followed by hypothyroidism 35.7% and hyperthyroidism 1.2%. Similar results were also claimed by Singh et al, 2020.<sup>22</sup> The frequency of SCH and hypothyroidism in pregnancy were similar to various studies.<sup>23</sup> During early stages of pregnancy the fT4 tends to increase with the suppression of TSH by hCG, whereas fT4 has the ability to decrease during later stages of pregnancy. This would be the possible reason for the higher incidence of SCH and hypothyroidism during pregnancy.<sup>24</sup> In addition, increased iodine intake, deficiency of micronutrients like selenium and iron are few other contributing factors that could be attributed to higher prevalence of hypothyroidism.

The prevalence of anemia in India ranges between 33% and 89%.<sup>25</sup> It was estimated that 87% of Indian pregnant women were anemic.<sup>26</sup> In the present study, anemia was identified in 36.8% pregnant women out of 380 women. Several factors might have contributed for the low prevalence rate such as improved socioeconomic status, public awareness and implementation of various national mother and child care programmes by Government of India.

Clinically, particularly in pregnancy, both anemia and thyroid dysfunction occur simultaneously, however, the causal relationship between these disorders remains mysterious. Thyroid hormones play an immense role in erythropoiesis process, although the underlying mechanism by which thyroid hormones modulate red cell production is still ambiguous. The anemia was found to be 32.7% in euthyroid pregnant women. Out of 84 thyroid dysfunction, the anemia was found in 43 women (51.9%). Our results were in agreement with Singh et al, where similar statistics were observed.<sup>22</sup> Anemia contributes about 20-60% in hypothyroidism and is the first sign in majority cases.<sup>27</sup> In the present study, anaemia was found to be 60% of hypothyroid and 47.2% of SCH pregnant women. Our results were in accordance with Omar et al, where the similar results were claimed.<sup>28</sup> However, anemia was not observed in hyperthyroid pregnant women. The anemia in hypothyroidism might result from bone marrow depression, decreased erythropoietin production, concomitant iron or folate deficiency. However, oxidative stress and changes in iron metabolism may contribute to anemia in hyperthyroidism.

Many studies explained the correlation between the thyroid hormones and RBC indices. It has been observed

that a significant correlation between fT4, TSH and Hb concentration in euthyroid patients.<sup>29</sup> In the present study, a positive correlation of fT4 with Hb concentration has been observed, however there was a negative correlation of TSH with Hb concentration.

The association between thyroid dysfunction and anemia has been explained in experimental animals. It has been found that hypophysectomised mammals were found to have decreased RBC counts and are corrected by the administration of thyroid hormones.<sup>30</sup> A significant increase in anemia prevalence was found in thyroid dysfunction pregnant women as compared to euthyroid pregnant women and the prevalence of anemia was found to be 1.5 fold in thyroid dysfunction pregnant women as compared to euthyroids. The higher prevalence of anemia in thyroid dysfunction pregnant women was also associated with decrease in the RBC count, Hb concentration, PCV, MCV and MCH. A significantly decreased Hb concentration and RBC count was found in thyroid dysfunction pregnant women as compared to euthyroid pregnant women.

Different forms of anemia can be encountered during thyroid dysfunction as thyroid hormone stimulate the proliferation of erythrocyte precursors either directly or by increased production of erythropoietin by increased gene expression.<sup>31</sup> Normocytic anemia is the commonest one whereas microcytic and macrocytic anemias occur less frequently.<sup>32</sup> In the present study, it has been observed that the frequency of microcytic and normocytic anemias were 53.6% and 46.4% respectively. Our findings were in accordance with Kapur et al, where normocytic normochromic anemia was common type with a prevalence of 55%.<sup>33</sup> In the present study, microcytic hypochromic anemia and normocytic normochromic anemia were only two types observed. The frequency of both types of anemia were higher in thyroid dysfunction pregnant women as compared to euthyroid pregnant women. In addition, significantly higher incidence of normocytic normochromic anemia and microcytic hypochromic anemia were observed in SCH and hypothyroid groups as compared to euthyroid pregnant women.

Thyroid dysfunction is associated with alteration in RBC indices such as Hb concentration, MCV, MCH and hematocrit (HCT). However, the changes eventually return to normal once thyroid hormone imbalance is corrected.<sup>34</sup>

A very few studies have shown the association between thyroid hormones and RBC indices with conflicting results. In present study, statistically significant lower levels of Hb concentration and RBC indices were found in thyroid dysfunction compared to euthyroid state. Our results were in agreement with the earlier reports where statistically significant difference in MCV was found between thyroid dysfunction and no significance in other RBC indices compared to euthyroid status.<sup>35</sup> In euthyroid

subjects, Bremner et al has observed a significant correlation between fT4, TSH and Hb concentration.<sup>29</sup> On the contrary, in a recent study, no correlation was detected between TSH and RBC indices.<sup>36</sup> Our results were in accordance with the previous study, where there was a positive correlation of fT4 with RBC count and Hb concentration and an inverse relation with MCV and MCH.<sup>28</sup> However, TSH correlated negatively with RBC.<sup>29,37</sup> The significant correlation between fT4, TSH with erythrocyte indices suggest the role of these hormones in erythropoiesis.

## CONCLUSION

Thyroid dysfunction and anemia are commonly associated disorders during pregnancy. According to our study, a significant correlation exists between fT4, TSH with RBC indices. Hence, all the pregnant women with abnormal RBC indices should be screened for thyroid dysfunction and vice versa to avoid the complications of thyroid dysfunction and anemia during pregnancy. Further research is needed to establish a correlation between thyroid dysfunction and anemia types and also the potential causes for anemia and its types during pregnancy.

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