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Original Research Article

Anemia and its effect on thyroid profile in pregnant women in tertiary care centre

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ABSTRACT

Background: According to WHO, highest incidence of anaemia is seen in Asia with about half of the anaemic women present in Indian subcontinent only. Various studies in the past have reported that iron deficiency hampers thyroid function. The thyroid hormones are essential for both foetal and maternal well-being. Our aim was to study anemia among pregnant women and its effect on thyroid profile.
Methods: In this prospective observational cohort study 200 women were enrolled (100 anemic and 100 non anemic) and subsequent thyroid profile was done. Confounders like high risk pregnancy, chronic diseases like coronary heart disease, renal failure/insufficiency, liver disease, Astro-intestinal diseases, known cases hypothyroidism was excluded. The women were followed up till delivery. The data was be tabulated and analysed using Chi square test in case of qualitative data and student t test in case normally distributed quantitative data.
Results: Four percentages of pregnant women had overt hypothyroidism in anemic group as compared to 3% in non-anemic group. 35% in anemic group had sub-clinical hypothyroidism as compared to 16% in non-anemic group and the difference was statistically significant. The comparison of TSH values in anemic and non anemic women was statistically significant (p=0.002). There was no association found with severity of anemia with TSH, ft3, ft4 values.
Conclusions: The present study found a significant association between anemia and hypothyroidism. However thyroid dysfunction was not associated with the severity of anemia. Further studies are warranted to directly identify the causal relationship between the two.

Keywords: Anemia, Pregnancy, Hypothyroidism

INTRODUCTION

As per WHO highest incidence of anemia is seen in Asia with about half of the anemic women present in Indian subcontinent only, among which 88% are seen in pregnancy.[1]

The WHO divides anemia into the normocytic, microcytic, as well as the macrocytic anemia according to the form of red blood cells (RBC). The major causes of anemia are inadequate supply of iron, folic acid as well as the vitamin B12.[2]

Anemia causes a number of feto-maternal complications in antepartum, intrapartum and in postnatal period including the decreased ability of mother to cope up with bleeding that occur during delivery, low birth weight of the fetus, growth retardation and increased perinatal mortality.[3] About 56% of maternal deaths are directly or indirectly related to anemia.[4]

Nutrient requirement of pregnant women is higher and they are at increased risk of iron deficiency. The importance of minerals, such as selenium and iron, to thyroid function has been extensively studied. Iron

deficiency has multiple adverse effects on thyroid metabolism. It decreases circulating thyroid hormone concentrations, likely through the impairment of the hem dependent thyroid peroxidase {TPO} enzyme. Iron deficiency may influence iodine deficiency disorders through alterations of the central nervous system control of thyroid metabolism or through modification of nuclear triiodothyronine {T3} binding. The thyroid hormones are very important for both foetal and maternal well-being.[5] Lower maternal iron level causes increase in TSH and decrease in total T4 level.[6]

In India, reports on the prevalence of maternal hypothyroidism ranged between 1.2% and 67.0% in various studies (7) Globally, the leading cause of hypothyroidism in pregnancy is iodine deficiency, and in iodine sufficient areas most common cause is autoimmune thyroiditis.[5,8]

Maternal thyroid hormone levels are critical to the fetus, especially in the first trimester due to its inability to produce iodothyronines before ten weeks of gestation. This is the period when neurodevelopment of fetus can potentially be hampered due to deficiency of iodothyronine.[9]

Some studies have noted that anemia can weaken thyroid dysfunction by reducing TPO activity.[10] Various other studies have shown that women with thyroid dysfunction are more likely to have anemia than euthyroid women. Females are more prone to the development of thyroid disorders and/ or anemia, especially during the reproductive age and pregnancy. Therefore, this study was conducted to find out the prevalence of anemia in pregnant women and its effect on the thyroid function.

METHOD

The study was a prospective study conducted at Subharti medical college a tertiary care hospital in North India over 2 years duration between Oct 2020 to August 2022, 200 antenatal women attending the outpatient department during study period was enrolled in the study. High risk pregnancy, chronic diseases like coronary heart disease, renal failure/insufficiency, liver disease, gastro-intestinal diseases, known case of hypothyroidism were excluded. All pregnant women willing to take part in the study were included after taking written and informed consent. Anemia and thyroid profiles were done.

This study participants (n=200) were grouped in 100 anemic pregnant women and 100 non-anemic pregnant women to compare thyroid profiles in 2 groups.

The demographic details of each participant was collected.

The women were categorized into four groups depending upon the hemoglobin level as recommended by the ICMR.[11]

Normal; >11 gm/dl, mild anemia:10-10.9 gm/dl, moderate anemia:7-9.9 gm/dl, severe anemia: <7 gm/dl and very severe anemia: <4 gm/dl.

As per American thyroid association [ATA] guidelines 2017, a cut off value of 4 mU/l of TSH was taken in all three trimesters.[12] Complete blood count along with peripheral smear, fT_3, fT_4 and TSH was done.

All participants were be followed up and details of patient will take like, mode of delivery, baby details etc., will be noted. The data was analyzed using Chi square test in case of qualitative data and student t test in case normally distributed quantitative data.

RESULTS

The demographic data like age, weight, height BMI were compared and there was no statistically significant difference ($p<0.05$) found between the groups. Residence, religion, gravidity and period of gestation were compared and there was no significant statistical difference in between the groups (Anemic and non-anemic). Four% of pregnant women had overt hypothyroidism in anemic group as compared to 3% in non-anemic group. 35% in anemic group had sub-clinical hypothyroidism as compared to 16% in non-anemic group with statistically significant with p value 0.007. There was no significant statistical difference between S. TSH, FT3, FT4 and severity of anemia with a $p>0.05$.28% women in anemic group were having microcytic anemia. The 70% women were having normocytic anemia. Only 1% woman had macrocytic anemia. There was no significant difference in TSH, fT3, fT4 range values and type of anemia.

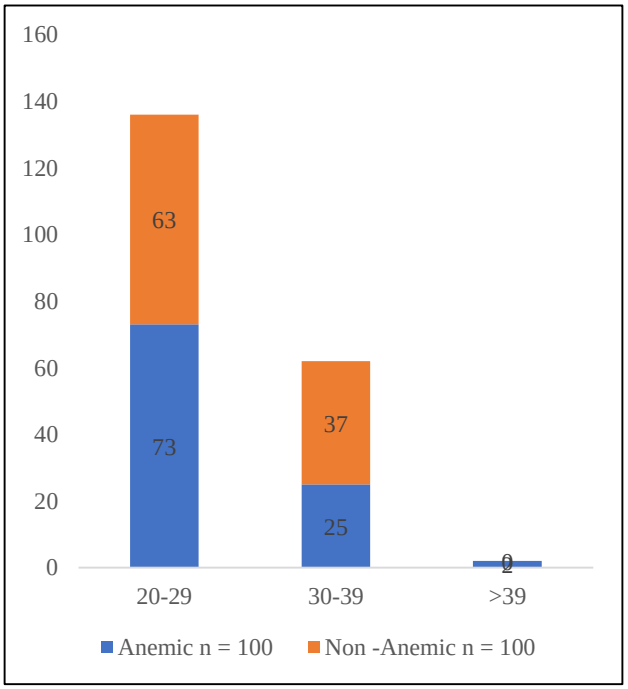

Figure 1: Distribution of women in anemic and non-anemic group according to age.

Table 1: Thyroid status of women in two groups, (n=100).

Thyroid status	Anemic, n (%)	Non-anemic, n (%)	Chi square	P value
Euthyroid	61 (61)	81 (81)	3.589	0.007
Overt hypothyroid	4 (4)	3 (3)		
Subclinical hypothyroidism	35 (35)	16 (16)		

Table 2: Comparison of TSH, FT3, FT4 with severity of anemia.

Variables		Mild anemia, n (%)	Moderate anemia, n (%)	Severe anemia, n (%)	Chi square	P value
TSH (mIU/L)	0.5-2.5	25 (64.1)	14 (25.9)	0 (0.0)	4.614	0.594
	2.5-4	11 (50.0)	11 (50.0)	0 (0.0)		
	4-10	17 (48.5)	18 (51.4)	0 (0.0)		
	>10	2 (50)	1 (25)	1 (25)		
FT3 (nmol/l)	<3.5	2 (50)	1 (25)	1 (25)	5.938	0.204
	3.5-6.5	53 (55.2)	43 (44.7)	0 (0.0)		
	>6.5	0 (0.0)	0 (0.0)	0 (0.0)		
FT4 (pmol/)	<11.5	2 (50)	1 (25)	1 (25)	5.938	0.204
	11.5-22.7	53 (55.2)	43 (44.7)	0 (0.0)		
	>22.7	0 (0.0)	0 (0.0)	0 (0.0)		

Table 3: Correlation of MCV with TSH within anemic group.

MCV	TSH (mIU/L), n (%)				Chi square	P value
	0.5-2.5	**2.5-4**	**4-10**	**>10**		
Less than 80	10 (25.6)	5 (22.7)	12 (34.3)	1 (25)	4.282	0.639
80-100	28 (71.8)	17 (77.3)	22 (62.8)	3 (75)		
More than 100	1 (50)	0	1 (50)	0		

Table 4: Correlation of MCV with FT4 within anemic group.

MCV	T4			Chi square	P value
	<11.5	**11.5-22.7**	**>22.7**		
Less than 80	1	28	0	3.542	0.170
80-100	3	66	0		
More than 100	0	2	0		

DISCUSSION

Majority of women selected for the study in both the groups were between 20-29 years age group which is similar in characteristics with respect to other studies in similar population.[13] Both the groups were similar with respect to educational status (p=0.381), religion (p=0.586) and region (p=0.78). Both the groups were similar in socioeconomic status (p=0.674). A study by Prabhavati et al of 380 pregnant women in Andhra Pradesh, India was having similar characteristics.[14]

In the anemic group 55% patients were having mild anemia 44% had moderate anemia and 1% had severe anemia. This was comparable to a study by Muthulakshmi et al in which 51% patients were having mild anemia 48% had moderate anemia and 1% had severe anemia.[15]

In our study 39% pregnant women in anaemic group and 19% non-anaemic group were having hypothyroidism. Out of them 35% in anaemic group and 16% in non-anaemic group had subclinical hypothyroidism. While 4% pregnant women in anaemic group and 3% in non-anaemic group had overt hypothyroidism. In both the groups subclinical hypothyroidism was more common than overt hypothyroidism which is in accordance with a similar study by Baghel et al who also found subclinical hypothyroidism more common than overt hypothyroidism.[16]

There was statistically significant difference in the in prevalence of hypothyroidism in between the two groups (p=0.007). This was in accordance with the studies by Shaheen et al and Muthulakshmi et al.[15,17] Shaheen et al in a cross-sectional study of 120 pregnant women found 47.5% hypothyroidism in pregnant anemic women. Muthulakshmi et al in their observational study found a significant correlation between anemia and hypothyroidism.[15]

Several animal models have proved association between thyroid dysfunction and anaemia where it was found that

RBC counts were decreased in hypophysectomised mammals and the RBC counts improved with administration of thyroid hormones.[18] Prabhavati et al found that 51.9% of pregnant women with thyroid dysfunction had anaemia.[24] A meta analysis by Yang et al 2020 also concluded increased risk of anemia in untreated overt hypothyroidism in pregnant women (odds ratio=3.14,95% CI 1.95-7.15).

We also found a statistically significant difference in TSH value in between anemic and non anemic groups. However there was no correlation between severity of anemia and TSH values. Similar studies by Kulkarni et al and Anand et al reported a negative correlation between TSH value and severity of anemia which is in contrast to our study.[19,20] In our study we have taken serum TSH values of 4 mIU/L as cut off for diagnosing hypothyroidism as per ATA 2017 guidelines when local specific reference is not available or 0.5 mIU/ml from prepregnancy TSH level. In pregnancy there is increased secretion of human chorionic thyrotropin (HCT) which share near similar molecular structure as well as receptor cross reactivity with TSH.[21] In normal pregnancy a state of physiological thyrotoxicosis caused by high HCG levels.

FOGSI consensus guidelines has upper limit for first trimester and second trimester as 2.5 mIU/L and 3.0 mIU/L repectively. We also campared TSH value ranges with anaemic and non anemic group and found that if cut off of 2.5 mIU/L is considered as per FOGSI guidelines 61% women will have hypothyroidism in anemic group and 51% women in non anemic group would have hypothyroidism. Review by Khadilkar et al has reported that cut off of 2.5mIU/L is too low and may lead to overdiagnosis and overtreatment so cut off sugested by ATA guidelines was taken in our study.[22]

In our study there was no statistically significant difference in free T4 values in between the two groups. Pregnant women in anemic group were not more likley to have low fT4 values than those in non anemic group as per our study. This is in contrast with a similar study by Shaheen et al which have found positive correlation between fT4 and Hb concentration.[17] We did not find any correlation between the severity of anemia and free T4 values.

Different types of anemia are encountered in hypothyroidism. In our study commonest anemia was normocytic (70%) followed by microcytic (28%).This result was in accordance with a similar study by Anand et al where normocytic anemia (53%) was the most common type followed by microcytic anemia (30%).[20] Thyroid dysfunction causes alteration in Hb and MCV values and which is reversible on thyroid medication.[23]

In our study we did not find any correlation between the values of TSH, FT3, FT4 with MCVand Hb values.This was contrary to previous study by Prabhavati et al where FT4 was positively corrrelated with RBC indices and TSH was negatively correlated with MCV and Hb concentration. In another recent study RBC indices and TSH values were not found to have any correlation however they have reported fT4 to have significant correlation with RBC indices.[24]

Since we anemia and thyroid profile was done at same time we could not identify the causal replationship.

CONCLUSION

The present study found a significant association between anemia and hypothyroidism in pregnancy. However, thyroid dysfunction was not associated with the severity of anemia. Further studies are warranted to directly identify the causal relationship between the two.

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