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EPIDEMIOLOGICAL STUDY OF THE ASSOCIATION OF HYPOTHYROIDISM WITH ANAEMIA IN NON-PREGNANT WOMEN OF REPRODUCTIVE AGE GROUP IN A TERTIARY CARE HOSPITAL IN KOLKATA

Joya Ghosh[1], Mriganka Baruah[2]

[1]Associate Professor, Department of Biochemistry, ESIC Medical College, Joka, Kolkata, India; [2]Assistant Professor, Department of Biochemistry, ESIC Medical College, Joka, Kolkata, India.

ABSTRACT

Objectives: Many studies suggest that hypothyroidism should be suspected in patients who have anaemia with an unknown aetiology. Thus the study was conducted to find out the proportion of hypothyroidism in both anaemic and non-anaemic women of reproductive age group and to determine the association between anaemia and hypothyroidism, if any.

Methods: A cross sectional study with case control design was carried out in 100 non-pregnant women of reproductive age group in a hospital in eastern India for a period of one year. The proportion of hypothyroidism in both the groups was estimated by measuring TSH. The association between anaemia and hypothyroidism were ascertained in both the groups by Pearson's Chi-Square test. Data analysis was also done using logistic regression.

Results: The mean haemoglobin was 12.85 gm/dl in the non-anaemic population and 10.57 gm/dl in the anaemic population. The mean TSH was 2.81μIU/ml in the non-anaemic population and 2.61μIU/ml in the anaemic population. But there was no significant association between anaemia and hypothyroidism, which was one of the objectives. Logistic regression analysis showed that with increasing number of living issues, the risk of anaemia increases and the mode of delivery had a hazard ratio of 2.6.

Conclusion: In our study, hypothyroidism did not show any significant association with anaemia thus, thyroid profile test may not be made mandatory in all anaemic women of reproductive age group to rule out hypothyroidism as its cause. In our study, risk factors for anaemia were found to be younger age group, caesarean mode of delivery and parity.

Key Words: TSH – Thyroid stimulating hormone, Hb– Haemoglobin, Menarche, Parity

INTRODUCTION AND BACKGROUND

Anaemia is defined as a condition in which there is a deficiency of red cells or of haemoglobin in the blood, resulting in pallor and weakness. It is a global public health problem affecting both developing and developed countries with major consequences for human health as well as social and economic development. In a study conducted by WHO, worldwide prevalence of anaemia (1993–2005), showed that globally, anaemia affects 1.62 billion. Of this 468.4 million non-pregnant women are affected.[1] In India, anaemia affects an estimated 50 per cent of the population.[2] The low dietary intake of iron and folic acid coupled with poor bioavailability of iron is the major factor responsible for very high prevalence of anaemia in the country.[3]

Hypothyroidism i.e, under activity of the thyroid gland, affects 1% of general population.[4] Primary hypothyroidism is the aetiology in approximately 99% cases of hypothyroidism. Anaemia is often the first sign of hypothyroidism. In a study, that looked at the frequency of anaemia in overt hypothyroidism, clinical hypothyroidism and control groups, the frequency of anaemia in patients with subclinical hypothyroidism was as high as that in patients with overt hypothyroidism. The prevalence of anaemia was 43% in the overt hypothyroid group and 39% in the subclinical hypothyroid group. Anaemia prevalence was 26% in the control group. They concluded that anaemia of chronic disease is the most common type of anaemia in patients who have hypothyroidism, whether it's overt hypothyroidism or subclinical

Corresponding Author:
Joya Ghosh, Associate Professor, Department of Biochemistry, ESIC Medical College, Joka, Kolkata, India.
Mobile: 08100021634; E-mail: joya_ghosh@yahoo.com

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hypothyroidism. They also suggest that hypothyroidism must be ruled out in patients who have anaemia with an unknown etiology.[5]

Hypothyroidism can cause macrocytic, microcytic hypochromic and normocytic normochromic anaemia. In Hypothyroidism, microcytic anaemia may be due to increased blood loss due to menorrhagia.[6] Macrocytic anaemia is caused by malabsorption of vitamin B12, folic acid, pernicious anaemia and inadequate nutrition. As autoimmune disorders commonly coexist, pernicious anaemia occurs 20 times more frequently in patients with hypothyroidism than generally. Macrocytosis found in up to 55% patients with hypothyroidism and may result from the insufficiency of the thyroid hormones themselves, without nutritive deficit as well as pernicious anaemia.[7] In hypothyroidism, normocytic anaemia is considered to be an adaptation to a decreased basal metabolism. Thyroid hormones through erythropoietin, stimulate erythropoiesis.[8] A study conducted in Eastern India showed that prevalence of anaemia in subclinical and overt hypothyroid groups was 26.6 % and 73.2 % respectively and most common type of anaemia in hypothyroidism was normocytic normochromic.[9] But, they did not take a control group, so the association between anaemia and hypothyroidism cannot be established, The age group selected was also very broad and they included both sexes.

This study also restricts the age and sex under study, since the study population is only non-pregnant women in reproductive age group (15-49 years). We selected this study population because in the 2005-2006 National Family Health Survey (NFHS-3), it was seen that 55% females aged 15–49 years were affected with anaemia. It also estimated that about 20% to 40% of maternal deaths in India were due to anaemia.[10] Thus, if a significant association is found in between hypothyroidism and anaemia in women of reproductive age group, thyroid profile test should be made mandatory in all anaemic women of reproductive age group to rule out hypothyroidism as its cause and accordingly management of hypothyroidism can be started for patients of anaemia.

MATERIAL AND METHODS

A cross-sectional with case-control design study was carried out in the Department of Biochemistry, ESIC Medical College, Joka, Kolkata for a period of one years. The project was started after receiving the IEC clearance bearing letter number: MBBS Project/IEC 2/2016. One hundred non-pregnant women in reproductive age group of 15-49 years attending the OPD of Obstetrics and Gynaecology were included in this study where 50 anaemic cases (Hb<12gm/dl) were compared with 50 non-anaemic controls (Hb>/=12gm/dl). Only untreated cases of anaemia and hypothyroidism were included. The patients did not have any obvious cause of anaemia like chronic diseases, infection, malignancy, haemoglobinopathies and bleeding diathesis. All procedures for the study is followed and informed consent was obtained from all patients and control subjects participating in this study. A detailed history and meticulous physical examination were carried out.

Inclusion criteria- Women of reproductive age group: (15-49) years and haemoglobin :<12 gm/dl.. It was further divided into severe (<8gm/dl), moderate (8.0 – 10.9 gm/dl) and mild (11 -11.9 gm/dl).[11] Age matched control with Haemoglobin: > or = 12 gm/dl were included in our study.

Exclusion criteria – Patients on medications like, iron and folic acid and vitamin B12 supplementation, subjects with history of amenorrhea for more than 6-8wks, known case of hypothyroidism on levothyroxine therapy.

5 ml of blood is drawn from the ante cubital vein under aseptic precautions and then 3 ml of blood samples were dispensed in EDTA vial for estimation of haemoglobin analysis and 2 ml dispensed in clot vial for TSH analysis.

- Haemoglobin was assessed on 5-part automated haematology analyzer (Beckman Coulter). Three levels of control (Beckman and Coulter) was used for the analysis.
- TSH was assessed on Access 2 analyzer (Beckman Coulter). Three levels of controls (Randox) was run with every batch of samples. Calibrator (Beckman Coulter) was run depending on its duration of validity as given on the reagent kit. Primary hypothyroidism cases were defined as cases with TSH >4.0µIU/L (0.4-4.0).

STATISTICAL METHODS

Random sampling procedure was followed to ensure that the selected study participants were representative of NPW (Non-Pregnant Women) of child bearing age group in the population of the study area. The data was compiled in Microsoft Excel Sheet. The results obtained were presented in Mean±SD. Association between hypothyroidism and anaemia was assessed in 2x2 contingency table by Pearson's Chi square test. Odd's Ratio was also calculated to find out the strength of association by using Epi-info software (version 3.2). Fischer's exact was used whenever the assumption of Chi -Square tests were not met. Logistic regression analysis was also used for the data analysis, probability (p) less than 0.05 was considered significant.

OBSERVATIONS AND RESULTS

The anaemic group largely belongs to age group 31-40 years and the non-anaemic group largely belongs to age group 21-

30 years both being 38%. In the anaemic group, 70% belong to age group 21-40 years. Study also showed that 32% of caesarean deliveries were anaemic as compared to 14% being non anaemic. 72% of anaemic women had normal bleeding pattern.

The mean age of the study population is lower in the non-anaemic than anaemic population. Moreover the mean haemoglobin and TSH was higher in the non-anaemic population than the anaemic population. The age of onset of menarche is also lower in anaemic than in non-anaemic population. (Table 1). Anaemia is further classified as Mild, Moderate and Severe Anaemia but there is no significant association with TSH as p>.05 Neither there was any statistical significance between different degrees of anaemia and hypothyroidism as evidence from (Fig.1) Logistic regression analysis showed that with increasing number of living issues, the risk of anaemia increased and the mode of delivery had a hazard ratio of 2.6. Increasing age and higher age of onset of menarche had a protective effect on anaemia.

DISCUSSION

Studies in India and elsewhere shows that iron deficiency is the major cause of anaemia followed by folate deficiency and contribution of B12 deficiency has also been highlighted.[12,13] In India prevalence of iron- deficiency anaemia is high because of poor iron intake and poor bioavailability of iron in phytate and fibre rich diet. Chronic blood loss and hook worm infestation also contribute to this[14] In a study in Ethiopia, a developing country like India it was seen that lower socio-economic. status, illiteracy, mutiparity, intestinal parasitic infestation, menorrhagia etc. were found as risk factors for anaemia in nonpregnant women of child bearing age group[15] In India, a study conducted in women of reproductive age group by Dey et al, in the state of Meghalaya, predictors responsible for anaemia were explored. In their study women of lower socioeconomic status and under nutrition were cited as risk factors, apart from various types of addictions e.g. bidi, gutka, pan etc. Even in their study hypothyroidism was not seen as a risk factor for anaemia corroborating with our study.[16]

The prevalence of hypothyroidism in our study was found to be higher in the non-anaemic group. This further establishes the fact that in our study population there was no relation between the hypothyroid status and Hb levels.

However, this can be accounted to the fact that in hypothyroidism, there is concomitant reduction of plasma volume leading to false high values of haemoglobin in blood. To override this factor, in various studies the actual degree of anaemia were estimated by radioisotopic analysis of red blood cell mass and plasma volume.[17,18,19] We could not use these methods, so that might account for false high values of haemoglobin in the hypothyroid patients and paradoxical results. The small sample size due to the limited time of research work can also suggest that our finding is incidental.

In our study highest percentage of anaemic women were in the age group of (21-40 yrs.). This is accounted by the percentage of parous women in this group which was 70%. Parity itself is a well established risk for the anaemia, due to extra demand by the foetus on the mother as well as blood loss during the process of delivery. In a study in Tehran by Majid et al it was seen that high parity index were associated with higher prevalence of anaemia.[20] While, a study in south India has reported higher rate of anaemia for a parity index more than four. [21]

Increasing age had a protective effect on anaemia as seen by logistic regression analysis in our study. A study in India has assigned the younger women (<30 years old), for the highest prevalence of anaemia.[22] Contrary to our finding, Majid et al have interestingly shown that there was approximately a linear association between increase in prevalence of anaemia with increasing age in individuals aged from 15 to 44 years[23] So the relation of Hb level with age of the patient can vary from population to population.

Logistic regression analysis in our study showed with increasing number of living issues, the risk of anaemia increased and the mode of delivery had a hazard ratio of 2.6.Higher percentage of anaemic women had their delivery by caesarean section in the study.

Age of onset of menarche was lower in anaemic group as compared to the non-anaemic, thus showing that earlier onset and longer duration of bleeding can increase the risk of anaemia. It was also seen that the lower age of onset of menarche affected number of patient having various degrees of anaemia. Though the effect was not significant. Similar finding was shown in a study by Gupta et al that there is no significant effect of age and age of onset of menarche on prevalence of anaemia.[24] Though logistic regression analysis showed higher age of onset of menarche had a protective effect on anaemia. In our study, highest number of cases have mild anaemia and their pattern of uterine bleeding is normal. This clearly indicates that menstrual blood loss is not a risk factor for anaemia in our study. Rather other factors like malnutrition, socioeconomic status parity etc. could be responsible. Bentley et al have pointed out in their study in India that malnutrition and micronutrient deficiency in particular along with lower socioeconomic status are important risk factors for anaemia in Indian women.[25]

CONCLUSION

In this study it was seen that in non-pregnant women of reproductive age group, hypothyroidism has no significant

association with anaemia and it is not a risk factor for developing anaemia. This may be due to the fact that in a developing country like India, malnutrition and lower socioeconomic status are the major causes of anaemia. Thus, laboratory tests to detect nutrient deficiency should remain the mainstay to diagnose the cause of anaemia, in non-pregnant females of reproductive age group (15-49 years) than thyroid profile test. Instead our study paradoxically found a higher prevalence of hypothyroidism in the non-anaemic group which may be due to the fact in hypothyroidism there is a concomitant reduction in plasma volume, giving false high values of haemoglobin and hence to diagnose the real degree of anaemia in hypothyroidism, radioisotopic methods should be used. Small sample population and radioisotopic analysis of red blood cell mass and plasma volume to eliminate the effect of haemoconcentration on Hb levels may be considered as a pitfall in our study.

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REFERENCES

1. WHO, Worldwide prevalence of anaemia 1993–2005 : WHO global database on anaemia, Edited by Bruno de Benoist, Erin McLean, Ines Egli and Mary Cogswell.
2. Florentino RF. The burden of iron deficiency and anaemia in Asia: Challenges in prevention and control. Nutrition goals for Asia - vision 2020; Proceedings IX Asian Congress of Nutrition; 2003 p. 313-8.
3. Indian Council of Medical Research, Micronutrient Profile of Indian Population, New Delhi, 2004.
4. Stephen J. Mcphee, Maxine A.P. Endocrine disorders. In: Paul A. Fitzgerald, eds. Current Medical Diagnosis and Treatment. 51st ed. New York, NY: McGraw-Hill; 2012: 182.
5. Erdogan M, Kösenli A, Ganidagli S, Kulaksizoglu M. Characteristics of anemia in subclinical and overt hypothyroid patients. Endocr J. 2012;59(3):213-20.
6. Weeks AD. Menorrhagia and hypothyroidism : Evidence supports association between hypothyroidism and menorrhagia. *BMJ : British Medical Journal*. 2000;320(7235):649.
7. Sims EG Hypothyroidism causing macrocytic anemia unresponsive to B12 and folate. J Natl Med Assoc 1983 75(4): 429-431.
8. Malgor LA, Blanc CC, Klainer E, Irizar SE, Torales PR, Barrios L. Direct effects of thyroid hormones on bone marrow erythroid cells of rats. Blood. 1975;45:671-9.
9. Das C, Sahana PK, Sengupta N, Giri D, Roy M,Mukhopadhyay P. Etiology of anemia in primary hypothyroid subjects in a tertiary care center in Eastern India. Indian J EndocrMetab 2012;16:S361-3.
10. F. Arnold, S. Parasuraman, P. Arokiasamy, and M. Kothari, "Nutrition in India," in National Family Health Survey (NFHS-3) India 2005-06, 2009.
11. WHO, haemoglobin concentration for the diagnosis of anaemia and assessment of severity, Vitamin and nutrition information system. WHO, Geneva ,Switzerland,2011.
12. Yajnik CS, DeshpandeSS, Jackson AA, Refsum H, Rao S, Fisher DJ, et al. Vitamin B12 and folate concentrations during pregnancy and insulin resistance in the offspring: the Pune Maternal Nutrition Study. Diabetologia 2008; 51: 29-38 .
13. Prema Ramachandran, Nutrition in Pregnancy. In: Gopalan C, Kaur S, editors. Women and nutrition in India, Special Publication No. 5. New Delhi: Nutrition Foundation of India; 1989. p. 153-93.
14. Toteja GS, Padam Singh, Dhillon BS, Saxena BN, Ahmed FU, Singh RP . Prevalence of Anaemia among pregnant women and adolescent girls in 16 districts of India. Food Nutr. Bull.,2006 27(4): 311- 315.
15. Yaregal Asres, Tilahun Yemane, and Lealem Gedefaw, Determinant Factors of Anemia among Non pregnant Women of Childbearing Age in Southwest Ethiopia: A Community Based Study, International Scholarly Research Notices Volume 2014 (2014), Page:1-8.
16. Sanku Dey, Sankar Goswami, Madhuchhanda Goswami, Prevalence of anaemia in women of reproductive age in Meghalaya: a logistic regression analysis Turk J Med Sci.2010; 40 (5): 783-789.
17. Antonijević N, Nesović M, Trbojević B, Milosević R. [Anemia in hypothyroidism]. Med Pregl. 1999 Mar-May;52(3-5):136-40.
18. Das KC, Mukherjee M, Sarkar TK, Dash RJ, Rastogi GK. Erythropoiesis and erythropoietin in hypo- and hyperthyroidism. J Clin Endocrinol Metab. 1975Feb;40(2):211-20.
19. Buso R, Olavarrieta ST, Suarez RM. Studies on the pathogenesis of the anemia of hypothyroidism. J Clin Endocrinol Metab 1958, 18: 501–5.
20. MajidSadeghian, M.D., Ali Fatourechi, M.D., and Elham Ahmadnezhad, Ph.D., Sadeghian M, Fatourechi A, Lesanpezeshki M, Ahmadnezhad E. Prevalence of Anemia and Correlated Factors in the Reproductive Age Women in Rural Areas of Tabas. *Journal of Family and Reproductive Health*. 2013;7(3):139-144.
21. Raghuram V, Manjula Anil, Jayaram S. Prevalence of anaemia amongst women in the reproductive age group in a rural area in south india. International Journal of Biological and Medical Research. 2012;3:1482–4.
22. Parashar A, Thakur A, Sharma D Anemia among adolescent girls in Shimla Hills of north India: does BMI and onset of menarche have a role? Indian J Med Sci. 2012 May-Jun;66(5-6):126-30.
23. MajidSadeghian, M.D., Ali Fatourechi, M.D, and Elham Ahmadnezhad, Ph.D., Sadeghian M, Fatourechi A, Lesanpezeshki M, Ahmadnezhad E. Prevalence of Anemia and Correlated Factors in the Reproductive Age Women in Rural Areas of Tabas. *Journal of Family and Reproductive Health*. 2013;7(3):139-144.
24. Kaur S, Deshmukh R, Garg B. Epidemiological Correlates of Nutritional Anemia in Adolescent Girls of Rural Wardha. Indian Journal of Community Medicine. 2006;31:102.

25. M E Bentley and P L Griffiths, The burden of anemia among women in India, European Journal of Clinical Nutrition (2003) 57, 52–60.

Table 1: Distribution of Study Population(Anaemic and Non-Anaemic groups)

Parameter	Non-Anaemic	Anaemic
Age	30.92±8.24 years	32.75±2.03 years
Age of Onset of Menarche	13.04±1.45 years	12.36±1.17 years
TSH	2.81±1.33ng/ml	2.67±2.03 ng/ml
Hb	12.85±0.79 gm/dl	10.57±1.33 gm/dl

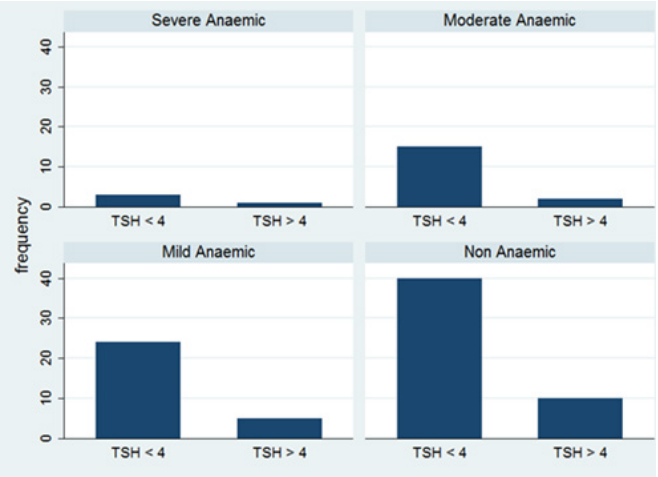

Figure 1: Association between Mild ,Moderate, Severe Anaemia and non- Anaemic population and TSH levels(in µIU/L)