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# Association of hypothyroidism in patients with migraine and tension-type headache disorders in Kashmir, North India

Hamed B Khan *MD*, Parvaiz A Shah *MDDM*, M Hayat Bhat *MDDM*, Ali Imran *MD*

*Neurology Division (Postgraduate Department of Medicine), Govt. Medical College &associated S.M.H.S. Hospital, Srinagar, Kashmir. J & K, India*

### *Abstract*

*Objective:* This case control study was undertaken to ascertain the frequency of subclinical and overt hypothyroidism in patients with various types of primary headache disorders in Kashmir, North India. *Methods:* The study was conducted in a tertiary care (university of Kashmir) hospital of North India. The study subjects consisted of 250 patients with primary headache disorders. This was compared with an age-sex matched control of 500 subjects. Thyroid function tests were performed by new automated immunochemiluminometric assay. *Results:* Among patients with primary headache disorders, subclinical hypothyroidism was present in 22% and overt hypothyroidism in 7.2%. On the other hand, subclinical hypothyroidism was observed in 11.2% and overt hypothyroidism in 1.2% of cases in the control group, the differences between primary headache and control group was statistically significant ($p<0.05$). Frequency of hypothyroidism was more in chronic headache disorders (chronic tension-type headache and migraine). The frequency of hypothyroidism in patients with primary headache disorders was higher among females than males, but this was not statistically significant ($p> 0.05$).
*Conclusion:* Hypothyroidism is found to be a co-morbidity or predisposes to the development of chronic headache (tension-type headache and migraine) in this North Indian study.

## INTRODUCTION

Hypothyroidism as a cause of headache is known for over six decades.[1-3] Singh reported migraine in 25% of hypothyroid patients.[4] Moreau *et al*. observed improvement in headache in 30% of hypothyroidism patients after initiation of thyroid hormone replacement.[5] Similarly, a strong correlation has been found between hypothyroidism and new daily persistent headache.[6] On the other hand, some of the investigators could not find any significant relationship between hypothyroidism and headache disorders.[7-9] The aim of present study was to ascertain frequency of hypothyroidism in headache patients to determine the relationship between hypothyroidism and primary headache disorders in a North Indian clinic population.

## METHODS

This case control study was conducted in the S.M.H.S. Hospital, Srinagar, an associated teaching hospital of the Government Medical College Srinagar, University of Kashmir. Patients with history of headache attending neurology outpatient clinic were enrolled in the study. The headache of the patient was assessed based on a headache questionnaire. The questionnaire was pretested in a group of 125 cases of primary headache disorders. The questionnaire was interpreted in local vernacular by the resident doctor wherever necessary. After informed consent, patients were asked about their history of headache, its duration, clinical features, frequency of attacks, duration of each attack, associated features, response to treatment, aggravating factors and other relevant features. Attention was taken to rule out any co-morbid illness or any drug intake which is known to affect thyroid status of the patient. Responses to the questionnaire were evaluated by the resident in charge. The patients were also subjected to careful examination, particularly the neurological system. Patients who fulfilled the criteria for primary headache disorders, migraine and tension-type headache (TTH) according to International Classification of Headache Disorders - 2nd Edition (ICHD-2) were enrolled in the study.[10] The diagnosis of all the study patients was confirmed by a neurologist.

Control group comprised of patients reporting

*Address correspondence to*:Dr.Parvaiz.AShah (Neurologist), H.No:35,Mominabad,Hyderpora Bye-Pass, Near Asif Filling Station, Srinagar, Kashmir. J&K. India 190014. E-mail: parvaizshah11@rediffmail.com, parvaizshah11@gmail.com

to medical outpatients department for complaints other than the headache. History was taken from the control group to rule out any co- morbid illness or any drug intake which is known to affect thyroid status of the patient. Patients with history of essential hypertension, diabetes mellitus, coronary artery disease, dyslipidemia and respiratory tract infection with no complaint of headache were included in the control group. The exclusion criteria were: 1). Patients with any form of thyroid disease prior to enrolment in the study as revealed by clinical examination or past medical records; 2). Patients < 16 and > 55 years of age; 3). Patients with abnormal neurological examination; 4). Pregnancy; 5). Any chronic illness known to affect thyroid hormone levels, e.g. chronic kidney disease or other systemic illness; 6). Chronic drug intake known to affect thyroid status of the patient like lithium carbonate, amiodarone, and antithyroid drugs.

A total of 250 patients and 500 control subjects were enrolled in the study. All the study subjects were tested for serum TSH and serum T4 by new automated immunochemiluminometric assay (ICMA).

Overt hypothyroidism was defined as elevated TSH (> 10mU/L) with low T4 (T4 < 4.5µg/dl), whereas subclinical hypothyroidism was defined as elevated TSH (TSH : > 4.5mU/L) with normal T4 (normal T4: 4.5 – 13µg/dl).[11,12] The frequency of subclinical and overt hypothyroidism in patients with primary headache disorders was compared with those in control group. Patients with primary headache disorders other than migraine and tension-type headache were not included in final statistical analysis. The study protocol was approved by the institutional review and ethical committee. Statistical analysis was performed by using SPSS and MINITAB statistical packages. All the inferences for intergroup comparison were made by using non-parametric test measures. Chi square test ( $\chi^2$), Yates corrected Chi square ( $\chi^2_{yates}$), Mann Whitney U test were applied for valid inferences.

## RESULTS

The headache group with 250 patients consisted of 140 (56%) females, 110 (44%) males and a mean age of 35.0 ± 10.5years (mean ± SD). The control group with 500 subjects consisted of 280 (56%) females, 220 (44%) males and a mean age of 35.2 ± 10.7 years (mean ± SD).

The headache group consisted of 164 (65.6%) TTH patients and 86 (34.4%) migraine patients. The sex ratio of the TTH patients was 114 (69.5%) males and 50 (30.5%) females, and that of the migraine headache was 36 (41.9%) males and 50 (58.1%) females. Among patients with TTH, 78 (47.6%), 52(31.7%) and 34(20.7%) had infrequent episodic TTH, frequent episodic TTH and chronic TTH respectively. Among patients with migraine, 41 (47.7%), 5 (5.8%) and 40 (46.5%) had migraine without aura, migraine with aura and chronic migraine respectively. In the study group, 55 (22%) and 18 (7.2%) cases had subclinical and overt hypothyroidism respectively and the difference was statistically significant ($p < 0.05$) in comparison to the control group where subclinical and overt hypothyroidism was present in 56 (11.2%) and 6 (1.2%) subjects respectively. Moreover, hypothyroidism was found in 34 and 29 patients with TTH and migraine respectively($p = >0.05$).

Female preponderance of hypothyroidism, both subclinical and overt, though statistically not significant ($p >0.05$) was observed in patients with primary headache disorders. Hypothyroidism was observed in 26(23.4%) males and 47( 34.6%) females in the study group. Frequency of hypothyroidism was more in chronic TTH as compared to either infrequent episodic TTH {$\chi^2$=9.906; p=0.002} (Table 1) or frequent episodic TTH, {$\chi^2$=7.791; p=0.005} (Table 2). Frequency of hypothyroidism was more in patients with chronic migraine as compared with migraine without aura {$\chi^2$=5.843; p=0.016}(Table 3). However, frequency of hypothyroidism in patients of chronic migraine compared to migraine with aura did not show any statistically significant difference {$\chi^2_{yates}$=0.475; p=0.491}(Table 4) .

## DISCUSSION

We have found in this study of 250 primary headache patients, that there was significantly higher proportion with subclinical (22%) and overt hypothyroidism (7.2%), as compared to the control subjects of 11.2% and 1.2 %. This were in conformity with the results from other studies.[4,5,9,10]

The frequency of subclinical and overt hypothyroidism in our patients with primary headache disorders was also higher than that reported in the general population. The prevalence of subclinical hypothyroidism in general population ranges from 4-10%[11-13]and that of overt hypothyroidism is 1-2% in women and 0.1% in men.[14,15]

Although hypothyroidism was more common

**Table 1: Frequency of hypothyroidism in patients with chronic tension-type headache (TTH) and infrequent TTH**

| | Chronic TTH | Infrequent TTH | Results |
|---|---|---|---|
| Hypothyroid | 17 | 16 | $\chi^2$=9.906<br>95% C.I=1.62-9.23 |
| Euthyroid | 17 | 62 | P=0.002 |

$\chi^2$ =Chi square, $\chi^2_{yates}$ =Yates corrected chi square, C.I-Confidence interval

**Table 2: Frequency of hypothyroidism in patients with chronic tension-type headache (TTH) and frequent TTH**

| | Chronic TTH | Frequent TTH | Results |
|---|---|---|---|
| Hypothyroid | 17 | 11 | $\chi^2$=7.791<br>95% C.I=1.45-9.60 |
| Euthyroid | 17 | 41 | P=0.006 |

$\chi^2$ =Chi square, $\chi^2_{yates}$ =Yates corrected chi square, C.I-Confidence interval

in females than males with primary headache disorders, it was not statistically significant (p > 0.05.The female preponderance in our study was consistent with the higher prevalence of both subclinical and overt hypothyroidism in the general population as reported in other parts of India. In a multicentre, epidemiological study on prevalence of hypothyroidism in India, prevalence of hypothyroidism was found to be 10.95% with higher prevalence for inland cities.[16,17] In a population-based study done in Cochin on 971 adult subjects, overall prevalence of hypothyroidism was 3.9%, and that of subclinical hypothyroidism being 9.4%.[17] In women, hypothyroidism had gender preponderance for females (11.4%) as compared to males (6.2%). Prevalence of hypothyroidism has been reported to be higher as well, from Kashmir valley than what was generally reported in the literature.[18]Keeping in view the higher prevalence of hypothyroidism in general population in India, cases with established diagnosis of hypothyroidism were excluded from the present study as it was assumed that prior treatment with levothyroxine could have affected clinical profile of headache in such cases.

There was also no statistically significant difference found between frequency of hypothyroidism in tension type headache (TTH) and migraineurs (P>05). This implies that hypothyroidism is a co-morbidity for both forms of primary headache disorders.

We have also found frequency of hypothyroidism was more in chronic TTH when compared with either infrequent episodic TTH{ $\chi^2$=9.906; p=0.002} (Table1) or frequent episodic TTH{$\chi^2$=7.791; p=0.005}(Table2).

**Table 3: Frequency of hypothyroidism in patients with chronic migraine and migraine without aura**

| | Chronic Migraine | Migraine without aura | Results |
|---|---|---|---|
| Hypothyroid | 19 | 9 | $\chi^2$=5.843<br>95% C.I=1.22-8.45 |
| Euthyroid | 21 | 32 | P=0.016 |

$\chi^2$ =Chi square, $\chi^2_{yates}$ =Yates corrected chi square, C.I-Confidence interval

**Table 4: Frequency of hypothyroidism in patients with chronic migraine and migraine with aura**

| | Chronic Migraine | Migraine with Aura | Results |
|---|---|---|---|
| Hypothyroid | 19 | 1 | $\chi^2_{yates}$=0.475<br>95% C.I=0.37-35.30 |
| Euthyroid | 21 | 4 | P=0.491 |

$\chi^2$ =Chi square, $\chi^2_{yates}$ =Yates corrected chi square, C.I-Confidence interval

Again, frequency of hypothyroidism was more in chronic migraine when compared with migraine without aura{$\chi^2$=5.843; p=0.016}(Table 3) but when compared with migraine with aura it was statistically insignificant {$\chi^2_{yates}$=0.475; p=0.491} (Table 4). These observations were consistent with the results of some previous study[6], but not the others.[7-9]

The exact pathogenesis of headache in hypothyroidism is uncertain. Singh[4] proposed a possible pathophysiological link between migraine and hypothyroidism. He suggested that pain threshold is regulated by reciprocal modulation of brain stem serotonergic and noradrenergic nuclei. The failure of one of the two systems implies a compensatory response of the other. Thus, the decreased adrenergic tone in hypothyroidism could up-regulate the serotonergic response which causes headache. The amelioration of headache after achieving euthyroid state could be due to serotonin decreasing effect of thyroid hormone. Thyroid hormone may also be involved in expression of human serotonin transporter (HSERT) gene, the allelic variation of which has been implicated in migraine and depression which again is a common accompaniment of hypothyroidism. Henley *et al*.[19] hypothesised a probable interaction between changes in thyroid status and bulbospinal serotonin (5HT) metabolism. They found that primary hypothyroidism was accompanied by significant increases in 5HT metabolism.

Thyroid replacement therapy in patients of migraine with aura with co-morbid hypothyroidism has been found to reduce headache frequency. This is believed to be a result of reduction in cerebral excitability associated with correction of hypothyroidism**.** Innocenzo *et al*. postulated a role for hormone imbalance in the development of chronic migraine especially in patients with chronic migraine and medication overuse headache. They observed significant impairment in both corticotropic and somatotropic functions in these patients.[20]

In conclusion, this study supports the view that chronic TTH and chronic migraine are associated with hypothyroidism, with hypothyroidism a risk factor for primary headache disorders. However further studies are required to clarify further the link between hypothyroidism and primary headache disorders. In the mean time, it seems prudent for primary care physicians to perform thyroid profile in cases with chronic daily headache especially in those not showing satisfactory response to conventional treatment for headache.

## DISCLOSURE

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## REFERENCES

1. Fenichel NM. Chronic headache due to masked hypothyroidism. *Ann Int Med* 1948; 29:456-60.
2. Jones AC Jr. Hypothyroidism as a cause of headache. *AMA Arch Otol* 1955; 62:583-5.
3. Sanders V. Neurological manifestations of myxedema. *NEJM* 1962; 266:599-603.
4. Singh SK. Prevalence of migraine in hypothyroidism. *J Assoc of Phys of India* 2002; 50:1455-56.
5. Moreau T, Manceau E, Giroud-Baleydier F, Dumas R, Giroud M.Headache in hypothyroidism. Prevalence and outcome under thyroid hormone therapy. *Cephalalgia* 1998; 18(10):687-9.
6. Sheftell ME, Rapoport FD, Alan M, Tepper AM, Stewart J, Richard B. Chronic daily headache: Identification of factors associated with induction and transformation. *Headache* 2002; 42 (7):575-81.
7. Amy JR. Tests of thyroid function in chronic headache patients. *Headache* 1987; 27(6):351-3.
8. Iwasaki Y, Kinoshita M, Ikeda K, Takamiya K, Shiojima T. Thyroid function in patients with chronic headache.*Int J Neurosci*1991; 57(3-4):263-7.
9. Larner AJ. Thyroid dysfunction and headache. *J Headache Pain*2006; 7(1):51-2.
10. Olesen J. The International Classification of Headache Disorders, 2nd Edition. *Cephalgia* 2006: 26(12): 1409-10.
11. Bishop ML, Fody EP,Schoeff LE. Clinical Chemistry:

principles, procedures. Liipincott Wiiliams & Wilkins. 2005:730.
12. Gharib H, Tuttle RM, Baskin HJ, Fish LH, Peter A. Singer PA, McDermott MT. Subclinical thyroid dysfunction: A joint statement on management from the American Association of Clinical Endocrinologists, the American Thyroid Association, and the Endocrine Society. *Endocrine Practice* 2005; 10:1:581-5.
13. Nickel SN, Frame B. Neurological manifestation of myxedema. *Neurology (Minneap)* 1958; 8:511-7.
14. TietjenGE, HerialNA, HardgroveJ, Utley C, White L. Migraine comorbidity constellations. *Headache* 2007; 47(6): 857-65.
15. Tunbridge WM, Evered DC, Hall R, *et al*. The spectrum of thyroid the community. Whickham survey. *Clinal Endocrinol* 1977; 7:481-93
16. Unnikrishnan AG, Kalra S, Sahay RK, Bantwal G, John M, Tewari N. Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India. *Indian J Endocr Metab* 2013; 17:647-52.
17. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. *Indian J Endocrinol Metab* 2011; 15(Suppl2): S78-S81
18. Bashir H, Farooq R, Bhat MH, Majid S. Increased prevalence of subclinical hypothyroidism in females in mountainous valley of Kashmir-a signal for advocating sufficient diet. *Indian J Endocrinol Metab* 2013; 17(2):276-80.
19. Henley WN, Bellush LL, Tressler M.Bulbospinal serotonergicactivity during changes in thyroid status. *Can J Physiol Pharmacol* 1998; 76(12):1120-31.
20. RaineroI, Margherita F, Elis R, *et al*. Endocrine function is altered in chronic migraine patients with medication-overuse. *Headache* 2006; 46(4): 597-603.