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RHINITIS AND ITS RELATIONSHIP WITH HYPOTHYROIDISM

ENT

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ABSTRACT

Aim:
- To compare the nasal mucosa change of hypothyroid patients during hypothyroid and euthyroid periods.
- To determine the co-relation(if any) between patients with rhinitis and hypothyroidism.

Methodology: A total of 50 hypothyroid patients were selected from the OPD of Department of ENT and HNS of Swaroop Rani Nehru Hospital,Prayagraj ,U.P.All the cases were evaluated for features of rhinitis using nasal parameters like MCT, NOSE score and PNIF. The patients were then given thyroxine supplement and were followed up in the OPD with repeat thyroid profiles every month until they attained a euthyroid state.Re-evaluation of all nasal parameters were done in euthyroid state.Observation was made using statistical analysis and conclusion was drawn. **Results:** It was observed that the change in MCT and NOSE score post treatment(on attainment of euthyroid state) was significant($p=0.005$ and $p=0.018$ respectively) while the change in PNIF remained insignificant($p=0.302$).A significant decrease in S. TSH ($p<0.001$) ,significant increase in f.T4($P<0.001$), and no significant change in fT3($p=0.016$) was also noted in the thyroid profiles pre and post- treatment. **Conclusion:** The findings of the study are indicative of a possible relationship between hypothyroidism and nasal mucosa changes which tend to normalize following treatment and attainment of euthyroid state.

KEYWORDS

MCT – mucociliary clearence time, NOSE – nasal obstruction symptom evaluation scale, PNIF-peak nasal inspiratory flow, hypothyroidism, rhinitis

INTRODUCTION

The thyroid is the largest endocrine organ, weighing 10-25g.The highly vascular gland is located infront of the trachea in the anterior neck and consists of a left and a right lobe, connected by isthmus.[1] Thyroid gland produces two hormones, thyroxine or T4 (3,5,3',5' L-tetraiodothyronine) and triiodothyronine or T3 (3,5,3' L-triiodothyronine). In addition, the thyroid gland secretes small amounts of biologically inactive 3,3',5' L-triiodothyronine (reverse T3[rT3]) and minute quantities of monoiodotyrosine (MIT) and diiodotyrosine (DIT) which are the precursors of T3 and T4.[2] Thyroid disease can be both (i) physical-presence of localized or generalized physical changes in the gland resulting in swelling of the gland (*viz.* diffuse goiter, multinodular goiter, or single thyroid nodule). These changes may be inflammatory, benign or malignant in nature, as well as (ii)physiological- physiological or functional changes resulting in increased or decreased plasma concentrations of thyroid hormones (T3, T4 and TSH) and are termed as thyroid dysfunction.[3] Thyroid dysfunction encompasses both deficiency and excess of thyroid hormone production, respectively hypothyroidism and hyperthyroidism[4]. Depending on this clinical condition, thyroid hormone deficiency can have various ENT manifestations like hearing loss(mostly sensorineural), sleep apnoea, hoarseness of voice, nasal obstruction and discharge from nose etc.[5,6]

Rhinitis is an inflammatory disease of the nasal mucous membranes which is characterized by one or more of the following nasal symptoms: sneezing, itching, rhinorrhea , and/or nasal congestion. Rhinitis is broadly classified into two types based on duration of symptoms: Acute rhinitis (symptoms less than 12 weeks) and chronic rhinitis (symptoms more than 12 weeks)[7].Further rhinitis patients are clinically divided into following categories : Allergic rhinitis and non-allergic non-infectious rhinitis (NARES).

Diagnosis of allergic rhinitis is based on the correspondence between the history of induction of symptoms by allergen contact and positive results of skin prick test or allergen specific IgE in the blood.[8] . Approximately 50% of all cases of rhinitis are caused by allergy.[9]According to some studies in India , the prevalence of allergic rhinitis alone in India is around 20-30%.[10]

Non-allergic Non-infectious Rhinitis (NARES): Subgroups of nonallergic rhinitis types may include, hormonal including pregnancy induced[11], drug-induced, rhinitis of elderly[12]etc.

Owing to the increased Thyroid Stimulating Hormone(TSH) release in hypothyroidism some histopathological changes are detected in the respiratory mucosa. Hypertrophy of mucous glands and increase in submucosal connective tissue by mucopolysaccharide deposition effect the normal nasal physiology . Cilial loss, submucosal inflammatory cell infiltration, increased acid mucopolysaccharide production in submucosal tissue were detected in nasal and paranasal region[13,14].

There are many studies describing histopathological changes due to hypothyroidism. On the other hand, the number of published clinical studies describing nasal manifestations of hypothyroidism are quite limited in the literature.

Thus the goal of the present study is to evaluate the rhinological changes during hypothyroid and euthyroid periods in patients with hypothyroidism.

AIMS AND OBJECTIVES

- To compare the nasal mucosa change of hypothyroid patients during hypothyroid and euthyroid periods.
- To determine the co-relation (if any) between patients with rhinitis and hypothyroidism.

MATERIALS AND METHODS

This prospective study was conducted in department of ENT and HNS, Motilal Nehru Medical College, Swaroop Rani Nehru Hospital, Prayagraj from December, 2021 to November,2022 after due clearance from Institutional Ethics Committee.

A written informed consent was taken from all the patients participating in the study. Patients were informed about the nature of the disease, the course of treatment and the tentative adverse effects (of both the treatment and no treatment).

A total of 60 newly diagnosed hypothyroid patients were taken in the study out of which 10 were lost to follow up. So, the study was conducted on 50 hypothyroid patients.

The patients included were newly diagnosed patients with hypothyroidism having age group between 20-45 yrs.

Patients excluded were the ones who did not give consent, patients with allergic rhinitis on medication, current upper respiratory tract infection, nasal pathologies like DNS, nasal polyposis etc., H/O nasal or paranasal surgery, immunocompromised state or other comorbid conditions, ciliary dysfunction diseases like kartagener's syndrome, history of smoking, lost to follow up.

METHOD:

The patients with hypothyroidism visiting the OPD in Department of ENT and HNS were screened and then evaluated for nasal changes.

The evaluation was done using the following methodology:

- NOSE (NASAL OBSTRUCTION SYMPTOM EVALUATION) QUESTIONNAIRE SCORE
- PEAK NASAL INSPIRATORY FLOW RATE (PNIF)
- NASAL MUCOCILIARY CLEARANCE TIME (MCT)

All the patients were asked to complete Nasal Obstruction Symptom Evaluation (NOSE) scale, based on 5 questions to evaluate nasal obstruction (Table 1). Sum of five answers were calculated, multiplied (by 5) and noted.

	Not a problem	Very mild problem	Moderate problem	Fairly bad	Severe problem
Nose congestion and stuffiness	0	1	2	3	4
Nose obstruction	0	1	2	3	4
Trouble breathing through my nose	0	1	2	3	4
Trouble sleeping	0	1	2	3	4
Unable to get enough air through my nose during exercise or exertion	0	1	2	3	4

Nasal obstruction of patients were categorised as follow:

- Mild range-5 to 25
- Moderate range-30 to 50
- Severe range- 55 to 75
- Extreme range- 80 to 100

To evaluate the nasal airflow of participants, the measurement of Peak Nasal Inspiratory Flow (PNIF) was done using a nasal inspiratory flow meter. The use of device was explained in detail to all patients. The patients were asked to sit and make a forceful expiration. Thereafter, they held the flow meter mask attachment over the nose and mouth tightly. With the device on their face, they were asked to inspire as forcefully as possible when their lips are firmly closed. Three consecutive recordings (liters per minute [L/min]) were measured, and average of them was accepted as the final value.

Nasal mucociliary clearance time (MCT) was measured by using the saccharin test. The saccharine transit time results was recorded in minutes. Although the patient were sitting in an upright position a 1.5–1.5 mm piece of saccharine tablet was placed on the medial and posterior surface of inferior turbinate via diagnostic nasal endoscopy (DNE). The time to subjective taste sensation in the throat was accepted as mucociliary clearance time (MCT).

Follow -Up:

All the patients were then subjected to standard treatment for hypothyroidism and the dosage of thyroxine was calculated using the formula 1.6ug/Kg body weight per day and were followed at monthly intervals to assess thyroid status. On attaining a euthyroid state, they were again subjected to assessment of nasal changes via NOSE, PNIF and MCT measurements.

Patients were followed monthly with respect to thyroid profiles until attainment of euthyroid state.

RESULTS:

Age of patients enrolled in the study ranged from 20 to 45 years. Maximum number of cases were aged <30 years (n=19; 38%) followed by those aged 31-40 years (n=17; 34%) and 41-50 years (n=14; 28%) respectively. Mean age of patients was 33.86±9.53 years.

Majority of patients (n=32; 64%) were females and 18 (36%) were males. The sex-ratio (M:F) of the study was 1:1.77.

At baseline (hypothyroid state) NOSE symptom scores ranged from 0 to 30. Most of the cases (n=43; 86%) did not have any symptom (Symptom score 0). There were 5 (10%) cases having mild symptoms (score 5-25) and 2 (4%) had moderate symptoms (score 30-50). None of the patients had symptom score in severe and extreme range. Mean symptom score was 2.70±7.71(Table 1)

After treatment and attainment of euthyroid state, NOSE symptom scores ranged from 0 to 15. All the cases excepting one (n=49; 98%) had no symptoms. There was 1 (2%) case having mild symptoms (symptom score 15). None of the patients had symptom score in severe and extreme range. Mean symptom score was 0.30±2.12(Table 1)

Table 1

S. no.	NOSE Category	Hypothyroid state		Euthyroid state	
		No. of patients	Percentage	No. of patients	Percentage
1.	No symptom (Score 0)	43	86	49	98
2.	Mild (Score 5-25)	5	10	1	2
3.	Moderate (Score 30-50)	2	4	0	0
TOTAL		50	100	50	100
Mean NOSE±SD (Range)		2.70±7.71 (0-30)		0.30±2.12 (0-15)	

At baseline, MCT ranged from 14 to 28 minutes. Mean MCT was calculated as 18.76±3.60 minutes. There were 13 (26%) cases having MCT >20 minutes (Table 2).In euthyroid state, MCT ranged from 14 to 22 minutes. Mean MCT was calculated as 17.72±1.94 minutes. There was only 1 (2%) case having MCT >20 minutes.(Table 2)

Table 2

S. no.	MCT (in minutes)	Hypothyroid state		Euthyroid state	
		No. of patients	Percentage	No. of patients	Percentage
1.	≤20 minutes	37	74	49	98
2.	>20 minutes	13	26	1	2
TOTAL		50	100	50	100
Mean MCT±SD (Range) in minutes		18.76±3.60 (14-28)		17.72±1.94 (14-22)	

Baseline PNIF in hypothyroid state ranged from 126.66 to 150 L/min with a mean of 136.50±5.43 L/min.Mean PNIF of males was 138.9±4.89 L/min. and that of females was 135.10±5.28 L/min. (Table 3)

Baseline PNIF in euthyroid state ranged from 126.66 to 150 L/min with a mean of 135.92±4.84 L/min. (Table 3). Mean PNIF of males was 138.79±4.45 L/min. and that of females was 134.31±4.32 L/min. (Table 3)

Table 3

S. no.	PNIF	Hypothyroid state		Euthyroid state	
		No. of patients	Mean PNIF±SD (Range) in L/min	No. of patients	Mean PNIF±SD (Range) in L/min
1.	Males	18	138.9±4.89	18	138.79±4.45
2.	Females	32	135.10±5.28	32	134.31±4.32
Total (n=50)		136.50±5.43 (126.66-150.00)		135.92±4.84 (126.66-150.00)	

At baseline, free triiodothyronine (fT_3) levels ranged from 1.07 to 3.71 pg/ml with a mean value of 2.34±0.68 pg/ml. Median fT_3 level was 2.19 with an interquartile range from 1.94 to 2.82 pg/ml(Table 4). Free thyroxine (fT_4) levels ranged from 0.40 to 1.45 ng/ml with a mean of 1.04±0.26 ng/ml. Median fT_4 was 1.10 ng/ml with an interquartile range from 0.86 to 1.21 ng/ml (Table 4).TSH levels ranged from 4.80 to 150 µIU/ml with a mean of 21.80±31.13 µIU/ml. Median TSH was 8.86 µIU/ml with interquartile range from 5.75 to 16.79 µIU/ml (Table 4).

At follow-up, free triiodothyronine (fT_3) levels ranged from 1.22 to 3.21 pg/ml with a mean value of 2.17±0.52 pg/ml. Median fT_3 level was 2.14 with an interquartile range from 1.87 to 2.45 pg/ml (Table 4).Free thyroxine (fT_4) levels ranged from 0.74 to 2.52 ng/ml with a mean of 1.30±0.38 ng/ml. Median fT_4 was 1.22 ng/ml with an interquartile range from 1.02 to 1.42 ng/ml (Table 4).TSH levels

ranged from 2.94 to 4.80 µIU/ml with a mean of 3.89±0.34 µIU/ml. Median TSH was 3.98 µIU/ml with interquartile range from 3.67 to 4.11 µIU/ml (Table 4).

Table 4

S No	Thyroid function hormone	Hypothyroid state				Euthyroid state			
		Mean	SD	Median (IQR)	Range	Mean	SD	Median (IQR)	Range
1.	Free triiodothyronine (fT_3) pg/ml	2.34	0.68	2.19 (1.94-2.82)	1.07-3.71	2.17	0.52	2.14 (1.87-2.45)	1.22-3.21
2.	Free thyroxine (fT_4) ng/ml	1.04	0.26	1.10 (0.86-1.21)	0.40-1.45	1.30	0.38	1.22 (1.02-1.42)	0.74-2.52
3.	Thyroid stimulating hormone (TSH) µIU/ml	21.80	31.13	8.86 (5.75-16.79)	4.80-150.0	3.89	0.34	3.98 (3.67-4.11)	2.94-4.80

Statistically , there was a significant decrease in S.TSH ($p<0.001$) and a significant increase ($p<0.001$) in Ft4. However, no significant change was found in Ft3.(Table 5). Statistically, there was a significant decrease in MCT ($p=0.005$) and NOSE ($p=0.018$) score . However , there was no significant change in PNIF ($p=0.302$).(Table 5).

Table 5

SN	Parameter	Before treatment (hypothyroid state)	After treatment (euthyroid state)	Significance of change (Paired 't'-test)
1.	fT_3 (pg/ml)	2.34±0.68	2.17±0.52	t=1.43; p=0.160
2.	fT_4 (ng/ml)	1.04±0.26	1.30±0.38	t=4.86; p<0.001
3.	TSH (µIU/ml)	21.80±31.13	3.89±0.34	t=4.06; p<0.001
4.	NOSE	2.70±7.71	0.30±2.12	z=2.38; p=0.018
5.	MCT (min)	18.76±3.60	17.72±1.94	t=2.92; p=0.005
6.	PNIF (L/min)	136.50±5.43	135.92±4.84	t=1.04; p=0.302

DISCUSSION

The relationship of thyroid disorders with rhinitis and nasal mucosal changes have been studied previously in a variety of studies including experimental animal studies as well as in human beings. **Eyigor *et al.*[15]** and **Başal *et al.*[16]** carried out their experimental study in rats. Among human studies too, there is wide variation in age and sex profile of the patients. Age of patients enrolled in this study ranged from 20 to 45 years and mean age of patients was 33.86±9.53 years.There was a female dominance with M:F ratio being 1:1.77.

Uysal *et al.*[17] reported the mean age of patients as 44.7 years and a dominance of females (80.4%). **Demir *et al.*[18]** on the other hand carried out their study in hypothyroidism patients who had a mean age of 39.6 years and a dominance of women (90.3%) as in the present study. The relationship has been looked upon in inverse order too.

Akkoca *et al.*[19] carried out their study in a set of AR patients with mean age 43.20±18.5 years and dominance of females (54.4%) and compared the thyroid function profile between the AR cases and controls. Similarly, **Degirmenci *et al*[20]** too carried out their study in AR patients and compared the prevalence of thyroid disorders with controls without AR. **Ozturk *et al.*[21]** similar to the present study assessed hypothyroidism patients but with a relatively older age profile (mean age 48.6 years) and dominance of females (85%). In the present study, we made an attempt to replicate the research model projected by **Ozturk *et al.*[21]** to explore this relationship. However, we did not include the patients above 45 years of age as older age might be associated with degenerative changes and primarily focussed on young adults only to minimize the confounding effect of age.

Compared to the present study, **Dutta *et al.*[22]** in their study on allergic rhinitis patients reported the mean NOSE scores as 64.07 which is much higher than that in the present study (mean NOSE score 2.70±7.71). Compared to these studies, the present study had negligible symptom scores and could not be termed as indicative of rhinitis. With respect to mucociliary clearance time and PNIF rate too, the findings in the present study were within normal range in majority of study population and even among those having values beyond normal range too, they were found to be borderline and did not reflect a clinically significant condition that could be termed as rhinitis.

On comparing the nasal symptom scores (NOSE), MCT and PNIF to the previous study conducted by **Ozturk *et al.*[21]**, who reported the mean NOSE, MCT and PNIF as 3.67, 8.03 min and 72.75 L/min respectively, though, NOSE scores (mean 2.70±7.71) were comparable to their study, however, the MCT (18.76±3.60) and PNIF (136.50±5.43) in the present study were not comparable. In the present study, both MCT as well as PNIF were almost twice as compared to their study. The reason for this difference could be difference in age status and environment. Despite these differences, both the studies do not consider these parameters to be indicative of a clinically diagnosable condition like rhinitis.

Nevertheless, after achievement of euthyroid state following treatment for hypothyroidism, only one patient showed nasal symptom scores (NOSE) of mild order. MCT above 20 minutes was also seen in only one patient. There was a significant change in mean NOSE scores and MCT, however, the change in PNIF was not significant. Consecutively, it may also be noted that these significant changes in nasal symptoms and mucociliary clearance time were accompanied with significant changes in fT_4 and TSH levels and a change in thyroid status from hypothyroid to euthyroid state.

Compared to the present study, where change from hypothyroid state to euthyroid state showed a small positive but statistically significant change in nasal symptom score and MCT, **Ozturk *et al.*[21]** failed to find a significant change in NOSE and PNIF but found a significant change in MCT among those who achieved euthyroid state. The present study differs from their study in the fact that in their study, 32.5% patients failed to achieve euthyroid state as compared to the present study where all the patients achieved euthyroid state. Compared to the present study, in which follow-up assessments were not time-bound and hypothyroidism treatment continued till the achievement of euthyroid state, their study was time-bound spanning over a 4 months' period. It must be noted that **Gunel *et al.*[23]** in their study also found a positive impact of thyroid treatment on nasal symptoms as well as on clearance time and nasal peak flowmetry outcomes. Relatively lower prevalence of nasal symptoms and almost normal MCT and PNIF values in the present study could be owing to the fact that all the patients enrolled in the study were newly diagnosed hypothyroidism patients in whom we did not expect a high symptomatic manifestation in terms of mucosal changes. Correspondingly, in a study population with less pronounced nasal and mucosal symptoms, the treatment effect was almost non-measurable.
The minor yet statistically significant changes in NOSE scores and MCT in the present study are in accordance with the findings of some experimental studies too where aggravation of thyroid hormone activity was able to bring about physiological changes that could trigger the pathogenesis of rhinitis[15,16]. **Uysal *et al.*[17]** also showed that achievement of euthyroid state in thyroid cancer patients was able to reduce the MCT by almost half as compared to that in the hypothyroid state. Although, no such phenomenal change with change from hypothyroid to euthyroid state was seen in the present study, which may be owing to difference in nature of thyroid dysfunction and underlying etiology, however, even in a relatively milder thyroid dysfunction too, the changes in MCT were significant in statistical terms in present study too.

The findings of the present study were interesting, and despite certain limitations were able to highlight the impact of hypothyroidism on nasal symptoms and mucosal abnormalities. Newly diagnosed status, absence of a fixed treatment duration and shorter duration of follow-up were certain factors that might have overlapped with the results of the study. Role of environmental and seasonal factors also needs to be evaluated. Moreover, further studies with inclusion of other variables are recommended on a larger sample size on a diverse study population are recommended.

CONCLUSION

The findings in the study showed that there could be a possible relationship between hypothyroidism and nasal mucosal changes which tend to normalize following treatment and attainment of a euthyroid state. However, no evidence of transformation of these

mucosal changes to clinically diagnosable rhinitis was seen in the study. However all the hypothyroidism cases showing nasal mucosal changes had only borderline changes. Further studies with broader range of thyroid profiles and longer duration of follow up can help us arrive to better and firmer conclusions.

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