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COMORBIDITY BURDEN DRIVES HYPOTHYROID SEVERITY AND DELAYS BIOCHEMICAL RECOVERY: A PROSPECTIVE OBSERVATIONAL STUDY FROM RURAL TELANGANA

Endocrinology

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ABSTRACT

Hypothyroidism affects approximately 11% of Indian adults — substantially higher than the global estimate of 3–5% — and its clinical management is frequently complicated by co-existing diabetes mellitus, hypertension, chronic kidney disease, anaemia, and dyslipidaemia. The influence of this comorbidity burden on disease severity and six-month treatment outcomes in rural Indian populations has not been prospectively examined. A prospective observational study enrolled 50 consecutive adults (≥18 years; serum TSH >4.5 mIU/L) at the Department of General Medicine, Kamineni Institute of Medical Sciences, Narketpally, Telangana, from January 2024 to December 2025. All patients were admitted as inpatients for management of associated acute illnesses; hospital length of stay (LOS) represents all-cause inpatient LOS. The cohort was 76% female; 38% were aged 35 years or below. Anaemia, diabetes mellitus, and hypertension each affected 38% of patients. When comorbidity burden was assessed across five major systemic conditions (diabetes mellitus, hypertension, dyslipidaemia, CAD, CKD), 38% had two or more co-existing conditions (multimorbidity). Every multimorbid patient had moderate or severe hypothyroidism, with 68.4% reaching the severe category ($p<0.001$). Severe disease was associated with a significantly longer mean hospital stay (4.31±1.93 days vs 1.92±1.61 days; ANOVA $p<0.001$). Clinical symptom resolution reached 94% at six months; however, biochemical normalisation (TSH ≤4.5 mIU/L) was attained in only 53.8% of severe versus 100% of mild cases at six months ($p=0.001$). Comorbidity burden strongly predicts hypothyroid severity, prolongs hospitalisation, and delays biochemical recovery. Intensified TSH monitoring and proactive dose escalation are warranted in multimorbid patients.

KEYWORDS

Hypothyroidism; Comorbidities; TSH Severity; Levothyroxine; Rural India; Treatment Outcomes

INTRODUCTION

Hypothyroidism carries a substantially higher burden in India (10.95%) than in Western populations (3–5%), attributed to iodine deficiency, genetic predisposition, and limited diagnostic reach in rural areas.[1,2] The disease rarely presents in isolation: diabetes mellitus, hypertension, coronary artery disease, CKD, anaemia, and dyslipidaemia cluster alongside hypothyroidism through bidirectional pathophysiological mechanisms. Thyroid hormone deficiency worsens insulin resistance, drives atherogenic dyslipidaemia, impairs renal haemodynamics, and suppresses erythropoiesis; each comorbidity, in turn, delays biochemical normalisation despite adequate levothyroxine dosing.[3–6]

How this comorbidity burden shapes hypothyroid severity and six-month treatment outcomes has not been prospectively examined in rural India. This study, conducted at a rural tertiary care centre in Nalgonda District, Telangana, aimed to evaluate this relationship and its clinical implications.

METHODS

A prospective observational study enrolled 50 consecutive adults (≥18 years; serum TSH >4.5 mIU/L) at the Department of General Medicine, KIMS, Narketpally, Telangana, from January 2024 to December 2025. Patients with post-thyroidectomy or radiotherapy-induced hypothyroidism and pregnant patients were excluded. All enrolled patients were admitted as inpatients for management of an associated acute medical illness or comorbid condition; hypothyroidism was identified as a known diagnosis or on workup during the same admission. Hospital LOS represents all-cause inpatient LOS. Disease severity was stratified as mild (TSH 5.0–9.9 mIU/L), moderate (10.0–19.9 mIU/L), or severe (≥20.0 mIU/L), consistent with the Colorado Thyroid Disease Prevalence Study[16] and AACE/ATA clinical guidelines.[17] Comorbidities were assessed using standard diagnostic criteria. Comorbidity burden was stratified as: no comorbidity, single comorbidity, or multimorbidity (≥2 co-existing conditions), counting diabetes mellitus, hypertension, dyslipidaemia, coronary artery disease, and chronic kidney disease. Anaemia was tracked and analysed as a separately associated finding — frequently a downstream consequence of hypothyroidism-driven erythropoietic suppression — and was therefore not included in the comorbidity burden classification. All patients received weight-adjusted levothyroxine with concurrent comorbidity management. Clinical outcome (symptom resolution) and biochemical outcome (TSH ≤4.5 mIU/L) were assessed at three and six months. Sample size was estimated using Cochran's formula as a planning estimate ($n=Z^2pq/d^2$; $p=0.11$,[2] minimum n=38; enrolled n=50; subgroup comparisons are hypothesis-generating). Statistical analysis used chi-square, Fisher's Exact test, and one-way ANOVA (SPSS v25.0; $p<0.05$). Written informed consent obtained; Ethics Committee approval received (IEC, KIMS).

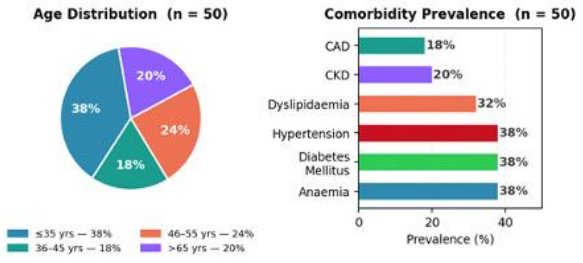

Figure 1: (A) Age distribution of the study cohort (n = 50). (B) Prevalence of comorbidities. Anaemia, diabetes mellitus, and hypertension each affected 38% of patients; 38% had ≥2 comorbidities.

RESULTS

Demographic and Clinical Profile

The cohort was 76% female (n=38) and notably young, with 38% of patients aged 35 years or below. All patients above 65 years were male. Moderate hypothyroidism predominated (48%), with mild and severe cases each comprising 26%. The most common presenting symptoms were fatigue (26%), constipation (22%), cold intolerance (20%), and dry skin (20%). Across five major systemic conditions (diabetes mellitus, hypertension, dyslipidaemia, CAD, and CKD), comorbidity burden was absent in 50% of patients, single in 12%, and two or more (multimorbidity) in 38%. Diabetes mellitus and hypertension co-occurred in the same 19 patients, consistent with metabolic syndrome clustering in this rural referral cohort.

Comorbidity Burden and Disease Severity

Not a single multimorbid patient had mild hypothyroidism, and 68.4% had severe disease (Fisher's Exact, $p<0.001$). No patient with zero or one comorbidity reached the severe category. Age and gender were significantly associated with severity ($\chi^2=6.11$, $p=0.047$ and $\chi^2=17.11$, $p<0.001$, respectively). All comorbidities were significantly associated with more severe hypothyroidism (all $p<0.05$): CKD (80.0% severe, $p<0.001$), CAD (77.8%, $p<0.001$), diabetes mellitus and hypertension (68.4% each, $p<0.001$), dyslipidaemia (31.3%, $p=0.041$), and anaemia (42.1%, $p=0.031$). See Figure 2 and Table 1.

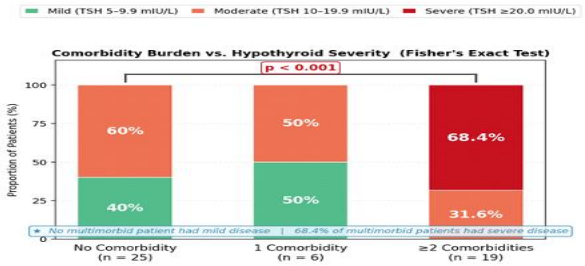

Figure 2: Comorbidity burden and hypothyroid severity (Fisher's Exact Test, p<0.001). No multimorbid patient had mild hypothyroidism; 68.4% had severe disease. No patient with zero or one comorbidity reached the severe category.

TABLE – 1 INDIVIDUAL COMORBIDITIES AND HYPOTHYROID SEVERITY

Comorbidity	n	Mild n(%)	Moderate n(%)	Severe n(%)	p value
Anaemia	19	4 (21.1)	7 (36.8)	8 (42.1)	0.031*
Diabetes mellitus	19	0 (0.0)	6 (31.6)	13 (68.4)	<0.001*
Hypertension	19	0 (0.0)	6 (31.6)	13 (68.4)	<0.001*
Dyslipidaemia	16	3 (18.8)	8 (50.0)	5 (31.3)	0.041*
Coronary artery disease	9	0 (0.0)	2 (22.2)	7 (77.8)	<0.001*
Chronic kidney disease	10	0 (0.0)	2 (20.0)	8 (80.0)	<0.001*

* p < 0.05 (Fisher's Exact test). ‡ Diabetes mellitus and hypertension co-occurred in the same 19 patients; listed separately for comparability with published literature.

Hospital Stay and Treatment Outcomes

Severe hypothyroidism was associated with a mean hospital stay of 4.31±1.93 days, significantly longer than mild (1.92±1.61 days) and moderate disease (1.71±1.78 days; ANOVA p<0.001). Multimorbid patients had the longest mean stay (3.16±2.50 days) versus those without comorbidities (2.20±1.58 days; p=0.034). Levothyroxine therapy produced high clinical symptom resolution: 96% at three months and 94% at six months. Biochemical normalisation showed a steep severity gradient (Figure 3): 100% in mild, 91.7% in moderate, and only 53.8% in severe disease at six months (p=0.001). Among multimorbid patients, TSH normalisation was achieved in only 68.4% versus 92.0% in those without comorbidities at six months (p=0.04).

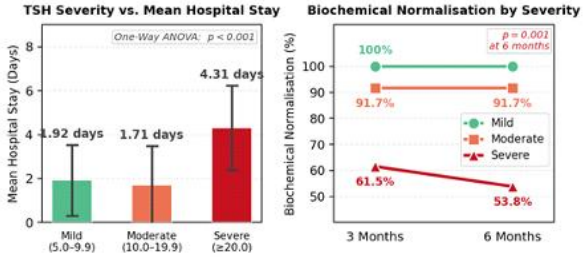

Figure 3: (A) Mean hospital stay (±SD) by hypothyroid severity (ANOVA p<0.001). Values shown above error bars. (B) Biochemical normalisation (TSH ≤4.5 mIU/L) at 3 and 6 months by disease severity (p=0.001 at 6 months). Exact normalisation rates labelled.

DISCUSSION

The age distribution was skewed toward younger adults (38% aged ≥35 years), in contrast to the elderly predominance in NHANES III[8] and the Whickham Survey.[9] Indian data show broader age distribution,[1,7] and the young skew likely reflects early-presenting autoimmune hypothyroidism in females. The complete gender-by-age inversion — all patients ≤35 years female, all above 65 male — suggests two aetiological currents: Hashimoto's thyroiditis in younger women and non-autoimmune disease in elderly men. Dense cardiometabolic co-occurrence (DM and HTN in the same 19 patients) reflects late-presenting metabolic syndrome in this rural referral population. The absolute nature of these distributions warrants acknowledgment as a limitation of this small single-centre sample (n = 50): while each pattern is individually consistent with the pathophysiology described above, their simultaneous absolute expression is mathematically more probable at small n and likely amplified by the referral dynamics of a rural tertiary centre; these proportions should be interpreted in that context rather than as universal epidemiological constants.

The near-complete separation between multimorbidity and severe disease — 68.4% of multimorbid patients had severe hypothyroidism and no multimorbid patient had mild disease — is explained by established bidirectional mechanisms. CKD reduces thyroid hormone clearance through altered deiodination,[4] DM amplifies insulin resistance,[5] hypothyroidism accelerates atherogenic CAD,[6] and erythropoietic suppression drives anaemia.[13] Each comorbidity sustains the metabolic environment that delays TSH normalisation; uncorrected hypothyroidism worsens each comorbidity in return.

Levothyroxine therapy produced high clinical symptom resolution (94% at six months), consistent with Jabbar et al.[11] The critical observation is the dissociation between clinical and biochemical recovery: only 53.8% of severe patients normalised TSH at six months despite 84.6% achieving symptom resolution. This contrasts with the TRUST trial,[14] which found no benefit in elderly asymptomatic subclinical hypothyroidism — a fundamentally different population. More frequent monitoring and earlier dose escalation are warranted in severe and multimorbid patients.

CONCLUSION

Comorbidity burden strongly predicts hypothyroid severity, prolongs all-cause hospital stay, and delays biochemical recovery in a rural Indian tertiary care population. Clinical symptom resolution is largely preserved with levothyroxine therapy, but TSH normalisation is substantially delayed in severe and multimorbid patients. More frequent TSH monitoring and earlier dose escalation are warranted for this subgroup. Strengthening thyroid screening capacity at primary care levels in rural Telangana remains a clinical priority.

REFERENCES

[1] Unnikrishnan AG, Menon UV, Agarwal AK, et al. Prevalence of hypothyroidism in adults: an epidemiological study in eight cities of India. Indian J Endocrinol Metab. 2013;17(4):647–652.
[2] Biondi B, Cooper DS. The clinical significance of subclinical thyroid dysfunction. Endocr Rev. 2008;29(1):76–131.
[3] Misra A, Sharma R, Gupta V, et al. Rising burden of hypothyroidism in rural India. Indian Heart J. 2023;75(4):410–18.
[4] Ruf JH, Schmidt M, Müller A, et al. Interactions between hypothyroidism and chronic kidney disease. Nephrol Dial Transplant. 2019;34(2):241–8.
[5] Ceresini G, Ceda GP, Lauretani F, et al. Thyroid disease and higher insulin resistance. J Clin Endocrinol Metab. 2015;100(5):1147–54.
[6] Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. N Engl J Med. 2001;344(7):501–9.
[7] Marwaha RK, Tandon N, Ganie MA, et al. Thyroid function in Indian population. Indian J Endocrinol Metab. 2013;17(Suppl 1):S123–7.
[8] Hollowell JG, Staehling NW, Flanders WD, et al. Serum TSH, T4, and thyroid antibodies (NHANES III). J Clin Endocrinol Metab. 2002;87(2):489–99.
[9] Vanderpump MPJ, Tunbridge WMG, French JM, et al. Incidence of thyroid disorders in the community: Whickham Survey 20-year follow-up. Clin Endocrinol (Oxf). 1995;43(1):55–68.
[10] Cooper DS. Subclinical hypothyroidism. J Clin Endocrinol Metab. 2001;86(4):1128–34.
[11] Jabbar A, Pingitore A, Pearce SHF, et al. Thyroid hormones and cardiovascular disease. Nat Rev Cardiol. 2017;14(1):39–55.
[12] Papadopoulou S, Georgiou M, Karagiannis A, et al. Effects of hypothyroidism on insulin resistance. Endocrinology. 2020;161(4):bqaa020.
[13] Turan MI, Celik M, Yilmaz A, et al. Anaemia in hypothyroid patients. J Clin Endocrinol Metab. 2018;103(3):1071–8.
[14] Stott DJ, Rodondi N, Kearney PM, et al. Thyroid hormone therapy in subclinical hypothyroidism (TRUST). N Engl J Med. 2017;376(26):2534–44.
[15] Agarwal G, Sudhakar MK, Singh M, et al. Thyroid dysfunction among type 2 diabetes patients. J Assoc Physicians India. 2018;66(6):25–9.
[16] Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. Arch Intern Med. 2000;160(4):526–34.
[17] Garber JR, Cobin RH, Gharib H, et al. Clinical practice guidelines for hypothyroidism in adults. Endocr Pract. 2012;18(6):988–1028.