

A Cross-Sectional Study on Motor and Sensory Nerve Functions in Women Newly Diagnosed and Untreated for Hypothyroidism in a Tribal Area of Odisha, India

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ABSTRACT

Introduction: Altered levels of thyroid hormones can impact various body systems, including the nervous system. Hypothyroidism may disrupt nerve conduction due to pathophysiological changes associated with hormone deficiency. The tribal population, characterized by distinct lifestyles and dietary habits, may experience unique influences on their growth and development.

Aim: This study aimed to compare nerve conduction in newly diagnosed and untreated tribal women affected by hypothyroidism with euthyroid tribal women.

Method: A cross-sectional study was conducted in southern Odisha, India, spanning from April 2020 to January 2021. Forty-five newly diagnosed hypothyroid tribal women were enlisted from the outpatient department of general medicine as the case group. Additionally, 45 age-matched apparently healthy euthyroid tribal women were included as the control group. The subjects' height and weight were measured by an expert clinician. Nerve conduction (motor and sensory) study on both extremities (left and right side) were conducted for all participants in the human physiology laboratory.

Results: The mean age of participants was 48.13 ± 12.12 years in the case group and 47.18 ± 12.2 years in the control group. In hypothyroid tribal women, a significant decrease in conduction velocity was observed in the majority of motor nerves (right median [$p = .03$], left median [$p = .02$], left ulnar [$p = .04$], right posterior tibial [$p = .001$], left posterior tibial [$p = .0001$]) and sensory nerves (right median [$p = .005$], right ulnar [$p = .02$], right sural [$p = .001$], and left sural [$p = .02$]).

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Conclusion: *In newly diagnosed cases of hypothyroidism in tribal women, there is a risk of neuropathy that impacts both motor and sensory neurons. Therefore, it is crucial to initiate early diagnosis and immediate treatment to prevent additional neurological damage.*

Keywords: hypothyroidism, hormones, India, motor neurons, neural conduction, thyroid hormones, tribal women.

INTRODUCTION

Thyroid hormones (triiodothyronine [T3], thyroxine [T4], and calcitonin) exert a significant impact on an individual's proper growth and development (1). Hypothyroidism, a disorder where the synthesis and secretion of thyroid hormones is deficient, may not cause immediate damage to the body. However, with longstanding deficiency, if not detected and treated, it can lead to a wide range of physical and mental health issues, including fatigue, weight gain, depression, etc. Overall, there is a drastic drop in body metabolism (2). In India, approximately one in ten individuals suffers from hypothyroidism, with females experiencing it more frequently than males (3). Despite the fact that a decrease in thyroid secretion affects nearly all systems of the body, patients with hypothyroidism frequently present with symptoms and signs of neuromuscular dysfunction, sensorimotor axonal neuropathy and other neurological disorders (4).

As the symptoms of hypothyroidism are generalized and non-specific, they often do not prompt immediate attention from patients, leading to delayed healthcare seeking (5). Among the 8.6% of the total tribal population in India, healthcare-seeking behavior is still not optimal due to several factors such as cultural barriers and poor accessibility (6). Consequently, there is a burden of both communicable and non-communicable diseases, along with poor nutritional status and mental health issues (7). Nutritional factors may contribute to hypothyroidism. A recent study reported a high prevalence of sub-clinical hypothyroidism in the tribal population, with iodine deficiency identified as one of the causes in sub-Himalayan region of India (8).

The healthcare-seeking behavior of tribal women remains low, with approximately 35% of that population seeking treatment only when

symptoms first appear, and gender playing a role in the early detection and treatment of diseases (9, 10). It is important to note that this finding is based on studies conducted in different parts of India, and the percentage may vary across regions. Hence, there may be the presence of sub-clinical hypothyroidism damaging neurons for an extended period before tribal women seek medical attention.

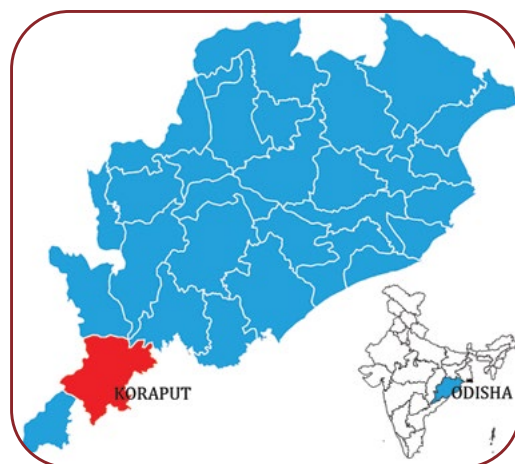
Given this context, the aim of this study was to assess the prevalence and severity of motor and sensory nerve function alteration in newly diagnosed hypothyroid tribal patients before the commencement of their treatment. The findings of the present study aim to enhance our understanding of the patterns of motor and sensory deficiency among the tribal population at the time of diagnosis. □

MATERIALS AND METHODS

Ethics This study involved adult participants (age >18 years) who willingly provided their written consent for voluntary participation. Since the research focused on a tribal population, special efforts were made to recruit participants by clearly explaining the study aim and nature together with the associated risks and benefits in their vernacular language. Participants capable of signing the consent form did so, while those unable to sign provided a fingerprint in the presence of a witness.

All participants were explicitly informed that they had the option to withdraw from the study without affecting their treatment process in the hospital. The recruitment process commenced only after obtaining formal permission from the Institutional Ethics Committee (reference number 03/V IEC SLNMCH). We affirm that the present study was conducted in strict adherence to

FIGURE 1. Study state on the map of India and district where the study was conducted



the WMA Declaration of Helsinki, updated in 2013.

Type and settings

This case-control study was conducted in the Department of Physiology, Saheed Laxman Nayak Medical College and Hospital in Koraput, Odisha, India (Figure 1). Participants were selected from the outpatient department of the tertiary care hospital. The study spanned a period of 10 months, running from April 2020 to January 2021.

Minimum sample size

A study by Mahadule *et al* found that the mean motor nerve conduction velocity on the right median nerve in controls was 58.12 (SD 4.21) and the number of hypothyroid patients was 55.59 (SD 4.55) (11). With this reference data and expected standard deviation (SD) of 4.21 (SD of control), $\alpha = .05$ and $\beta = .2$ (power of the study 80%), the minimum sample size was 87. However, to equalize the control and study groups, we have taken 90 as the final sample size, with 45 in each group.

Sampling method and recruitment

For this study we used a convenience sample with fixed inclusion and exclusion criteria. Adult female patients belonging to the tribal community aged between 18 and 60 years, who were diagnosed with hypothyroidism and not yet initiated on any treatment, and did not suffer from diabetes, hypertension (12) or neuromuscular disorders (such as muscle hypertrophy, carpal tunnel syndrome, amyotrophic lateral sclerosis,

Guillain-Barré syndrome, Lambert-Eaton myasthenic syndrome, diabetic neuropathy) were included after obtaining written consent from each of the selected subjects.

Exclusion criteria encompassed individuals with acute or chronic diseases, those under medication affecting nerve conductions like calcium or methylcobalamin, individuals with vitamin B12 deficiency or undergoing treatment with methylcobalamin, those with a history of smoking (13) or alcohol consumption, and women in any trimester of pregnancy. Also, patients taking drugs that might have influenced thyroid tests, such as diclofenac, dopamine, glucocorticoids, phenytoin, and carbamazepine, were excluded (14).

Cases were enlisted from the general medicine outpatient department, while controls were selected from patients' families, friends or accompanying individuals. We recruited age, height and weight-matched tribal women residing in the same area with similar food habits and lifestyles, adhering to the same inclusion and exclusion criteria, except for the presence of hypothyroidism.

Anthropometry and blood test

The height and weight of study participants were measured by an experienced clinician with over five years of clinical anthropometry expertise. Weight was assessed using a digital weighing scale with a sensitivity of 100 gm, while height was measured with a portable stadiometer to the nearest mm. All measurements were conducted with participants wearing light clothing and in the presence of a same-sex attendant.

At the regional diagnosis center affiliated with the hospital, the thyroid profile was analyzed using the chemiluminescent immunoassay (CLIA) method (Immulite, Diagnostic Products Corp, Los Angeles, CA, USA). The report included serum total T3, total T4 and TSH levels. Cases were recruited after undergoing thyroid profile testing and subsequently underwent anthropometric measurements and nerve function assessments in the Physiology laboratory.

For the control group, anthropometric measurements were conducted first, followed by thyroid profile testing. A single expert measurer recorded anthropometric parameters to minimize interobserver variation. Participants' comfort and privacy were prioritized and measure-

ments were performed by a female doctor in the presence of another female attendant.

To diagnose hypothyroidism, the following reference ranges for euthyroid status were applied based on the test method: serum total T3 = 0.60–1.81 ng/mL, total T4 = 3.2–12.6 µg/dL and TSH = 0.55–4.78 µIU/mL. Blood tests were conducted under 12-hour fasting conditions, with venous blood collected from the antecubital vein using a commercial vacutainer and immediately transferred to the laboratory for testing. A diagnosis of hypothyroidism was established if there was either elevated TSH with normal total T4 or total T3, or elevated TSH with subnormal T4 and T3 (15).

Nerve conduction test

Motor nerve conduction studies (MNCS) on median, ulnar and posterior tibial nerves as well as sensory nerve conduction studies (SNCS) on median, ulnar and sural nerves of both limbs were conducted (antidromic method) using the RMS-EMG EP MARK II device (Recorders & Medicare Systems Private Limited, Haryana, India) (16). Participants received a detailed explanation and a test demonstration to mitigate apprehensions. All tests were performed in a controlled departmental laboratory environment from 10 am to 12 pm. The device settings for upper limb tests included a duration of 100 µs, sweep speed of 5 ms/D and a filter between 2 Hz to 5 kHz. Lower limb tests had a duration of 200 µs, sweep speed of 5 ms/D and a filter between 2 Hz to 10 kHz.

Statistical analysis

The data were subjected to descriptive statistics and assessed for normality using the Shapiro-Wilk test (17). To compare parameters between the case and control groups, either an unpaired t-test or the Mann-Whitney U test was selected based on data distribution. Categorical data were compared using the Chi-square test. Analyses were performed using SPSS 16 (SPSS Inc., Chicago, USA) and statistical significance was set at $p < 0.05$. □

RESULTS

The data did not adhere to a normal distribution. The case group comprised 45 tribal women with an average age of 48.13 ± 12.12 years,

TABLE 1. Age, height, weight, BMI, and thyroid profile of cases and controls

Parameter	Case (n = 45)	Control (n = 45)	p
Age (years)	48.13±12.12	47.18±12.2	.712
Height (cm)	163.11 ± 6.92	162.64 ± 4.11	.696
Weight (kg)	63.96±6.56	65.30±6.13	.319
BMI (kg/m ²)	24.05 ± 2.24	24.64 ± 2.08	.199
Total T3 (ng/mL)	0.62±0.31	0.99±0.22	<.0001*
Total T4 (µg/dL)	3±0.87	8.64±1.51	<.0001*
TSH (µIU/mL)	7.54±1.43	2.91±0.99	<.0001*

*Statistically significant p value was of Mann-Whitney U test

BMI: body mass index; T3: triiodothyronine; T4: thyroxine;

TSH: thyroid stimulating hormone

TABLE 2. Nerve conduction test result of the motor nerves

Nerve	Parameters	Case (n = 45)	Control (n = 45)	p
Right median	Latency (ms)	3.42±0.33	3.30±0.50	.18
	Amplitude (mV)	14.08±4.33	13.96±4.96	.9
	NCV (m/s)	52.79±3.72	54.86±4.07	.01*
Left median	Latency (ms)	3.04±0.46	3.43±0.58	.0007*
	Amplitude (mV)	14.38±3.80	13.87±4.95	.59
	NCV (m/s)	53.26±3.83	55.21±5.29	.04*
Right ulnar	Latency (ms)	2.43±0.36	2.38±0.45	.56
	Amplitude (mV)	14.79±4.10	12.92±3.17	.02*
	NCV (m/s)	52.87±2.53	56.31±4.07	.0001*
Left ulnar	Latency (ms)	2.53±0.38	2.38±0.46	.95
	Amplitude (mV)	13.99±4.30	14.2±3.15	.79
	NCV (m/s)	53.77±3.61	54.79±4.88	.26
Right posterior tibial	Latency (ms)	4.37±0.71	4.00±0.73	.02*
	Amplitude (mV)	16.17±7.16	20.03±7.32	.01*
	NCV (m/s)	45.19±2.60	49.80±5.53	.001*
Left posterior tibial	Latency (ms)	4.48±0.81	3.74±0.67	.07
	Amplitude (mV)	18.55±7.57	20.22±6.39	.26
	NCV (m/s)	45.25±3.46	46.98±4.10	.03*

*Statistically significant p value of Mann-Whitney U test

NCV: nerve conduction velocity

TABLE 3. Nerve conduction test result of sensory nerves

Nerve	Parameters	Case (n = 45)	Control (n = 45)	p
Right median	Latency (ms)	3.34 ± 0.41	3.06 ± 0.63	.01*
	Amplitude (mV)	12.46 ± 4.94	16.15 ± 4.95	.001*
	NCV (m/s)	42.15 ± 6.1	46.81 ± 6.16	.005*
Left median	Latency (ms)	2.91 ± 0.74	3.07 ± 0.33	.19
	Amplitude (mV)	9.77 ± 3.83	11.15 ± 3.35	.07
	NCV (m/s)	41.22 ± 3.8	42.7 ± 4.08	.08
Right ulnar	Latency (ms)	3.58 ± 0.75	3.64 ± 0.13	.6
	Amplitude (mV)	8.21 ± 3.83	9.37 ± 3.46	.13
	NCV (m/s)	44.1 ± 8.4	47.7 ± 5.22	.02*
Left ulnar	Latency (ms)	4.04 ± 0.38	3.8 ± 0.71	.05
	Amplitude (mV)	11.31 ± 4.79	12.14 ± 4.23	.39
	NCV (m/s)	46.1 ± 8.4	48.3 ± 5.22	.14
Right sural	Latency (ms)	3.2 ± 0.49	3.71 ± 0.21	.0001*
	Amplitude (mV)	7.47 ± 4.83	7.34 ± 3.24	.88
	NCV (m/s)	38.22 ± 4.8	41.76 ± 4.08	.001*
Left sural	Latency (ms)	2.73 ± 0.22	3.42 ± 0.41	.0001*
	Amplitude (mV)	8.4 ± 4.83	9.16 ± 2.29	.34
	NCV (m/s)	39.71 ± 3.8	41.76 ± 4.08	.02*

*Statistically significant p value of Mann-Whitney U test

NCV: nerve conduction velocity

Nerve	Control		Case		Statistics		
	Within normal limit	Beyond normal limit	Within normal limit	Beyond normal limit	Odds ratio	95% confidence interval	p
Right median	41	4	21	24	11.71	3.59 to 38.2	<.0001*
Left median	32	13	19	26	3.37	1.4 to 8.08	.007*
Right ulnar	31	14	16	29	4.01	1.67 to 9.66	.002*
Left ulnar	32	12	23	22	2.55	1.05 to 6.18	.04*
Right posterior tibial	28	17	19	26	2.25	0.97 to 5.24	.06
Left posterior tibial	27	18	18	27	2.25	0.97 to 5.23	.06

*Statistically significant p value

For categorization, we fixed the normal range of NCV ≥ 45 m/s for the upper limb and ≥ 40 m/s for the lower limb.

NCV: nerve conduction velocity

Percentage was not used as the number of samples does not cross 100.

TABLE 4. Distribution of participants in normal range and beyond normal motor nerve test parameters in case and control groups

Nerve	Control		Case		Statistics		
	Within normal limit	Beyond normal limit	Within normal limit	Beyond normal limit	Odds ratio	95% confidence interval	p
Right median	31	14	29	16	1.22	0.51 to 2.94	.65
Left median	33	12	28	17	1.67	0.68 to 4.08	.26
Right ulnar	28	17	19	26	2.25	0.97 to 5.24	.06
Left ulnar	27	18	18	27	2.17	0.93 to 5.05	.07
Right sural	41	4	21	24	11.71	3.59 to 38.2	<.0001*
Left sural	29	16	18	27	2.72	1.16 to 6.38	.02*

*Statistically significant p value

For categorization, we fixed the normal range of NCV ≥ 45 m/s for the upper limb and ≥ 40 m/s for the lower limb.

NCV: nerve conduction velocity

Percentage was not used as the number of samples does not cross 100.

TABLE 5. Distribution of participants in normal range and beyond normal sensory nerve test parameters in case and control groups

who were newly diagnosed with hypothyroidism. The control group, consisting of 45 tribal women with comparable age (47.18 ± 12.2 years, $p = .68$), height and weight, maintained euthyroid status. Table 1 presents the details of age, height, weight and thyroid profile. In both the case and control groups, 42 individuals were right-handed, while three were left-handed.

The majority of motor nerves (except for the left ulnar nerve) and sensory nerves (except for the left median and left ulnar) showed a lower conduction velocity in hypothyroid tribal women. Test parameters, including latency, amplitude and conduction velocity, for motor nerves are presented in Table 2, while sensory nerves are shown in Table 3 for both the case and control groups.

The number of participants in the case and control groups were classified into normal and beyond normal categories, with Table 4 showing the result of the motor nerves and Table 5 that of

the sensory nerves along with odds ratio and 95% confidence interval. $\square$

DISCUSSION

In our investigation aiming to observe nerve conduction in tribal women diagnosed with hypothyroidism and to compare them with euthyroid tribal women, we observed that the majority of motor and sensory nerve conduction velocities were lower in hypothyroid patients. This reduction in conduction velocity may be linked to metabolic alterations caused by thyroid hormone deficiency (18). This finding suggests that neuropathy has already set in when hypothyroidism is initially diagnosed, even before the emergence of other complications. Symptoms like generalized weakness, muscular weakness and a history of cramps may indicate hypothyroidism.

We observed a significant reduction in nerve conduction velocity in the majority of motor

nerves (except the left ulnar nerve) and sensory nerves (except the left median and left ulnar) in patients diagnosed with hypothyroidism. Hypothyroidism can lead to neuropathy through multiple mechanisms associated with thyroid hormone deficiency. The reduced production of thyroxine (T4) and triiodothyronine (T3) results in metabolic slowdown, impacting nerve function. Additionally, hypothyroidism diminishes ATP generation, disrupts ATPase activity and ion transport, contributing to axonal degeneration and demyelination. Dysfunction in cellular processes, including the sodium-potassium pump, can compromise nerve conduction. Furthermore, mucinous material deposition around nerves has been observed in hypothyroidism, potentially interfering with nerve function (18, 19). While these mechanisms provide insights, individual variations exist, and further research is needed for a comprehensive understanding of the link between hypothyroidism and neuropathy. If neuropathic symptoms arise in the context of hypothyroidism, consulting a healthcare professional for evaluation and management is essential.

In this study, we found a difference in left and right median nerve conduction. Although handedness may be a potential cause, the precise cause of the discordant finding in the case of the left median nerve and the non-significant difference in the left ulnar nerve requires thorough exploration in future studies.

Asia and Warkar conducted a study on newly diagnosed untreated hypothyroid non-tribal subjects from Maharashtra, India, revealing predominant sensory nerve involvement (20). In contrast, our study on tribal women showed that, for the majority of them, both motor and sensory nerves were involved, possibly due to differences in sample characteristics. Murugiah *et al* from Tamil Nadu indicated a higher incidence of median nerve involvement than ulnar nerve in hypothyroidism (21). Similarly, Gupta *et al* from Nepal reported decreased functions in the sensory and motor components of the median nerve in newly diagnosed hypothyroid patients, supporting our findings (22). Moon *et al* noted lower ulnar nerve latency in hypothyroid patients with carpal tunnel syndrome (23). Our study found significantly higher latencies in the left median and right posterior tibial motor

nerves as well as the right median and right and left sural nerves.

We identified an association between hypothyroidism and reduced nerve conduction velocity (NCV) in median and ulnar motor nerves. The majority of hypothyroid patients exhibited motor neuropathy in the median and ulnar nerves, with no significant association found in the posterior tibial nerve. This suggests a greater involvement of motor nerves in the upper limbs than in the lower limbs in hypothyroidism. Furthermore, in evaluating the association between hypothyroidism and sensory neuropathy, we observed a significant decrease in NCV in the sural nerve on both sides, indicating a higher involvement of sensory nerves in the lower limbs compared to the upper limbs in hypothyroidism. This finding aligns with the study conducted by Waghmare *et al*, which reported a similar effect with involvement of the median sensory and sural nerves, while no significant association was noted in the ulnar sensory nerve (24).

Limitation and novelty of the present study

This hospital-based study utilized a convenience sample, employing a non-probability sampling method. Consequently, the generalizability of the results is limited and cannot be extended to the entire tribal population. Access was confined to patients seeking hospital consultation, restricting the inclusion of diverse age groups. Screening for participants involved various diseases and disorders, with a lack of detailed clinical examination results in the findings. We did not take the history of consanguineous marriage of the participants' parents. The measurement of blood homocysteine levels, indicative of vitamins B12, B6 and folate status, was not feasible due to financial and logistical constraints. However, this case-control study is the first investigation involving tribal women in this area, which recruited an adequate number of participants during the study period to ensure statistical robustness. □

CONCLUSION

In newly diagnosed cases of hypothyroidism in tribal women, there is a potential for underlying neuropathy affecting both motor and sensory nerves. Early diagnosis of hypothyroidism and prompt initiation of treatment should be priori-

tized to prevent further neuronal damage. Given the less-than-optimal healthcare-seeking behavior in the tribal population, it might be beneficial to conduct a screening test among vulnerable women to identify muscular weakness associated with hypothyroidism and potential subclinical neuropathy. 

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