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**Principal Contact**

Dr. Robin Maskey

Editor- in- Chief

Journal of Diabetes and Endocrinology Association of Nepal

Address: B.P. Koirala Institute of Health Sciences

Tel : 9852045177

Email : journaldean2017@gmail.com

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Journal of Diabetes and Endocrinology Association of Nepal

EDITORIAL OPEN ACCESS

# DEAN NECON 2023 theme "Empowering endocrine practice in Nepal"

Maskey R[1], Gupta PP[2], Acharya DK[3]
[1] Additional Professor and Head, Internal Medicine, BPKIHS, Dharan, Nepal
[2] Associate Professor, GP and Emergency Medicine, BPKIHS, Dharan, Nepal
[3] Consultant Cardiologist, Kankai Hospital, Biratmod, Jhapa, Nepal

## INTRODUCTION

Empowering in medicine is defined as the ability to effectively motivate and mobilize yourself and others to accomplish positive outcomes in your practice and work environment.[1]

Nepal has a high prevalence of various endocrine diseases, which is a challenge for its endocrinologists,[2] because endocrinologists are few introduced into medical fraternity of Nepal since decade only. Moreover endocrinology is relatively one of the newer super specialties of internal medicine.[3]

The Diabetes and Endocrinology Association of Nepal (DEAN), which has celebrated more than decade since 2008, continues to mature along with its members, the endocrinologists of Nepal. DEAN represents the aspiration and ambition of Nepalese endocrine fraternity, and exists for rights as well as responsibilities and its mission, vision and goal.

DEAN has empowered the endocrine practice in Nepal in following ways:

- unique platform for budding endocrinologists
- meet and interact regarding endocrine problems
- establish consensus statements on diabetes and hypothyroidism
- have conducted various National and International Conferences/CME/
- have conducted PHFI diabetes and thyroid courses regional and national level
- World diabetes day and thyroid day are celebrated with education and health camp
- conducted first ever national endocrine conference (DEAN NECON 2023) in Eastern Nepal motivating young budding endocrinologist and awarded best endocrine clinical case presenter.

**Corresponding Author:**
Dr. Robin Maskey, Additional Professor, Department of Internal Medicine, B.P.Koirala Institute of Health Sciences, Dharan, Nepal.

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Journal of Diabetes and Endocrinology Association of Nepal

ORIGINAL ARTICLE OPEN ACCESS

# Anxiety, Depression and Self-Care Management among Hypothyroidism Patients Attending Chitwan Medical College Teaching Hospital, Chitwan

Khanal D[1], Chapagain S[2], Thapa S[3]
[1]Senior lecturer, School of Nursing, [2]Assistant Professor, School of Public Health, [3]Associate professor, School of Nursing, Chitwan Medical College.

**Abstract**

**Background:** Thyroid dysfunctions have been recognized to cause significant manifestations in physical health as well as mental health.A descriptive cross-sectional research design was used to assess anxiety, depression and self-care management among hypothyroidism attending Chitwan Medical College Teaching Hospital (CMC-TH). **Methods :** A total of 258 patients diagnosed with hypothyroidism were selected by convenience sampling.Data was collected from the date June 6, 2021 to November 17, 2021 using face to face interview schedule. The data was analyzed in SPSS version 20 using descriptive and inferential statistics was used to analyze the data. **Result :** Out of 258 respondents females constituted 64% of the sample. A total of 72.1% of the respondents had different level of anxiety based on GAD-7 among them 43.8% of the respondents had mild anxiety and 9.3% severe level of anxiety. Regarding depression 60.1 % of the respondents had different level of depression based on PHQ-9. Among them 27.1% had mild level of depression whereas 4.7% severe level of anxiety.More than fifty percentages of the respondents (54.3%) had inadequate level of self-care management. Anxiety was significantly associated with sex (0.044), marital status (0.000) and family history of mental illness (0.009) whereas depression was significantly associated with educational status (0.009) and duration of illness (0.002). **Concluion :** It is concluded that anxiety and depression was more prevalent among hypothyroidism patients so, routine screening of hypothyroidism patients for psychiatric disorder and treating by both anendocrinologist and a psychiatrist in liaison with each other is very important to optimize their management and improve quality of life.

**Key Words :** Anxiety, depression, self-care management and hypothyroidism

## Introduction

Hypothyroidism is the most prevalent endocrine disorder worldwide.[1] It can be defined as a disorder of the endocrine system in which there is a deficient production of thyroid hormone by the thyroid gland and can be primary (abnormality in thyroid gland itself) or secondary/central (as a result of hypothalamic or pituitary disease). Primary hypothyroidism is the etiologies in approximately 99% of cases of hypothyroidism.[2] Thyroid dysfunctions have been recognized to cause significant manifestations in physical health as well as mental health. They may lead to disturbances in emotions and cognition.[3]

**Correspondence Author**
Dr. Dina Khanal, Chitwan Medical College, Chitwan, Nepal , Email: khanaldina9@gmail.com

The prevalence of hypothyroidism in the developed world is about 4-5%. The prevalence of subclinical hypothyroidism in the developed world is about 4-15%.[4] In the United States, it was 5% depression among hypothyroidism patients during 2018.[5] Prevalence of hypothyroidism in western part of Nepal is 10.5%[6] and in eastern part of Nepal is 17.9%.[7]

Hypothyroidism patients had many behavioral disturbances among them depressive symptoms, and anxiety are more common and it can impact certain aspects of cognitive functioning, such as slowed information processing, poor learning and

memory, mood disturbance, and problems in verbal fluency. More severe hypothyroidism can mimic melancholic depression and dementia.[8] Similarly, High prevalence of moderate to high level depression, anxiety cause increased stress response and it triggers a cascade which producing a series of changes in human vital physiological functions such as blood pressure, respiratory rate and heart rate which was significantly higher.

The coexistence of hypothyroidism, anxiety and depression results in poor self-care management and reduces overall quality of life so, early screening for psychiatric disorder , recognition and treatment of these conditions and promoting self-care behavior are essential for achieving optimal goals in the management of hypothyroidism. In Nepal, depression and anxiety are usually underdiagnosed and undertreated due to social stigma.Anxiety and depression are common among patients suffering from hypothyroidism and their prevalence has been summarized in a number of studies.[8,12,13,16]Even though limited study has been conducted to assess anxiety and depression among hypothyroidism patients. Hence, this study aimed to assess anxiety, depression and self-care management among hypothyroidism patients attending the Chitwan Medical College Chitwan Nepal.

**Material and Methods**

A descriptive cross-sectional research design was conducted. Population of the study was those clinically diagnosed with hypothyroidism by physician of at least 1 year duration and under medication of hypothyroidism attending endocrinology Out Patients Department of CMC-TH and they were selected by using convenience sampling method. A patients with a history of mental illness or currently diagnosed as a mental illness were excluded from this study. Data was collected from the date June 6, 2021 to November 17, 2021by using face to face interview schedule. Sample size was determined using 60% overall prevalence of depression[8] among hypothyroidism with an allowable error of 6% at 95% confidence interval. The estimated sample size was 258.

Research instruments consist of three parts. Part I which consists of socio-demographic information, Part II:The Patient Health Questionnaire-9 (PHQ-9) and Generalized Anxiety Disorders-7 (GAD-7) were used for the screening of depression and anxiety.[9,10] These two instruments assessed the symptoms experienced by respondents during the 2-week period before they take the survey. Each item of GAD-7 and PHQ-9 was rated from 0 to 3 scores, where 0-not at all, 1-several days, 2-more than half of the days, and 3-nearly every day, with higher scores indicating patients' increased self-report of anxiety and depression.Scores obtained in GAD-7were classified into mild (5–9), moderate (10–14), and severe anxiety (≥15). Likewise, scores of PHQ-9 were divided into mild (5 to <10), moderate (10 to <15), moderately severe (15 to <20), and severe (≥20) depression.The Patient Health Questionnaire PHQ-9 and GAD-7 is a validated tool found to be useful in screening psychiatric illness and had used for different chronic disease worldwide. PHQ-9 had 61% sensitivity and 94% specificity and 89% sensitivity and 82% sensitivity in adult. Part III consists of Self-care management which consists of [1011,14] items generated from extensive review of literature. Each item contains 0-4 score, and total score is calculated by summing all item score and then divided into two categories as adequate (>60%) and inadequate (<60%) 11. Content validity was maintained by consulting with subject experts. Pretesting of the Nepali version instrument was done among 30 hypothyroidismpatients on medical OPD of CMC-TH and they were excluded from the final study.

Ethical clearance was obtained from Institutional Ethical Review, CMC-TH with reference number CMC-IRC/077/078-223. Informed written consent was obtained from each participant. Privacy, confidentiality and anonymity of the respondents were maintained. All the collected data was checked, reviewed and organized for accuracy, consistency and completeness. After that collected data were coded and entered in Statistical Package for Social Science (SPSS) version 20 for analysis. Than the data were analyzed using descriptive statistics and inferential statistics.

## Results

**Table 1: General Characteristics of Respondents**

| General Characteristics | | Frequency | Percentage |
|---|---|---|---|
| Age (in years) | ≤ 52 | 132 | 51.2 |
| | >52 | 126 | 48.8 |
| **Mean age of the respondent 52.22±12.61 years** | | | |
| Sex | Male | 93 | 36.0 |
| | Female | 165 | 64.0 |
| | | | |
| Marital status | Married | 167 | 64.7 |
| | Unmarried | 67 | 26.0 |
| | Divorce | 24 | 9.3 |
| Religion | Hindu | 189 | 73.3 |
| | Buddhist | 65 | 25.2 |
| | Others | 4 | 1,6 |
| Educational Status | Illiterate | 105 | 40.7 |
| | Literate | 153 | 59.3 |
| | informal educational | 25 | 9.7 |
| | basic level | 21 | 8.1 |
| | secondary level | 86 | 33.3 |
| | bachelor and above | 21 | 8.1 |
| Occupation | Service | 94 | 36.4 |
| | Business | 48 | 18.6 |
| | Farmer | 40 | 15.5 |
| | house maker | 70 | 27.1 |
| | Other | 6 | 2.3 |
| Economic status (yearly income sufficiency) | enough for less than 1 year | 162 | 62.8 |
| | enough or sufficient for 1 year | 96 | 37.2 |
| Duration of illness (in years) | 1-4 years | 169 | 65.5 |
| | ≥ 5 years | 89 | 34.5 |
| Co morbid condition | Yes | 70 | 27.1 |
| | No | 188 | 72.9 |
| Family History of mental illness | Yes | 97 | Yes |
| | No | 160 | No |

Table 1 depicts that Mean age of the respondents was 52.22+12.61 years. More than half of the hypothyroid patients (64.0%) were female and 64.7% of the respondents were married. Regarding religion more than half of the respondents (73.3%) were Hindu. More than half (59.3%) of the respondents were literate among them only 8.1% of the respondents had completed bachelor and above level. Regarding occupation 36.4% of the respondents were services holder followed by business, house maker, and farmer. Only 37.2% income were enough or sufficient for 1 year. Regarding duration of illness most (78.3%) of the respondent had hypothyroidism of 1-5 years duration and among them 27.1% of respondents had comorbid condition and only 37.6% had family history of mental illness.

**Table2: Respondents Level of Anxiety and Depression**

| Level of Anxiety and Depression | Frequency (n=258) | Percentage |
|---|---|---|
| **Level of Anxiety (GAD-7)** | | |
| **Mild anxiety** | 113 | 43.8 |
| **Moderate anxiety** | 49 | 19.0 |
| **Severe anxiety** | 24 | 9.3 |
| **Overall anxiety** | 186 | 72.1 |
| **Level of Depression (PHQ-9)** | | |
| **Mild depression** | 70 | 27.1 |
| **Moderate depression** | 41 | 15.9 |
| **Moderately severe depression** | 32 | 12.4 |
| **severe depression** | 12 | 4.7 |
| **Overall depression** | 155 | 60.1 |

Table 2 shows that 72.1% of respondents had different level of hypothyroidism among them 43.8% of respondents had mild and 9.3% had severe level of anxiety. Whereas regarding depression 60.1% of respondents had different level of depression among them 27.1% had mild and 4.7% had severe level of depression.

**Table 3: Respondents Level of Self-care Management**

| Level of Self-Care Management | Frequency (n=258) | Percentage |
|---|---|---|
| **Adequate(≥60%)** | 118 Frequency (n=258) | 45.7 |
| **Inadequate (<60%)** | 140 | 54.3 |

Table 3 shows that more than half of the respondent had inadequate level of self - care management and 45.7% had adequate level of self-care management.

**Table 4: Association between Levels of Anxiety and Selected Variable of Respondents**

| Characteristics | | No anxiety | Anxiety | Value | chi-square |
|---|---|---|---|---|---|
| Age in years | ≤52 | 37 | 94 | 0.015 | 0.902 |
| | > 52 | 35 | 92 | | |
| Sex | Male | 19 | 74 | 4.041 | 0.044* |
| | Female | 53 | 112 | | |
| Marital Status | Married | 33 | 133 | 16.23 | 0.000* |
| | Unmarried | 31 | 37 | | |
| | Divorce | 8 | 16 | | |
| Religion | Hindu | 57 | 132 | 1.781 | 0.182 |
| | Other | 15 | 54 | | |
| Educational Status | Illiterate | 32 | 73 | 0.581 | 0.446 |
| | Literate | 40 | 113 | | |
| Economic status (yearly income sufficiency) | enough for less than 1 year | 41 | 121 | 1.461 | 0.227 |
| | enough or sufficient for 1 year or more | 31 | 65 | | |
| Comorbid condition | Yes | 17 | 53 | 0.626 | 0.429 |
| | No | 55 | 133 | | |
| Family history of mental illness | Yes | 18 | 79 | 6.755 | 0.009* |
| | No | 54 | 107 | | |
| Duration of illness | 1-4 years | 51 | 118 | | 0.263 |
| | ≥5 years | 21 | 68 | 1.255 | |

* Significant level at $<^{0.05}$ where p value computed from chi-square test

Table 6 shows there is statistically significant association of anxiety level with sex, marital status and family history of mental illness and depression.

## Discussion

A cross-sectional descriptive study was conducted to assess anxiety, depression and self-care management among hypothyroidism patients attending Chitwan Medical College-Teching Hospital, Chitwan.Out of 258 respondents more than half of the respondents (64.0%) were female.[12,13] Majority (72.1%) of the respondents had different level of anxiety based on GAD-7 among them 43.8% of the respondents had mild anxiety whereas 19% and 9.3% had moderate and severe level of anxiety respectively. Where as in the study conducted in India 63% of the respondents had some level of anxiety among hypothyroid patient.8In contrast to this study, study conducted at India observed 46.1% had severe level of anxiety.[14]

Regarding depression 60.1 % of the respondents had different level of depression based on PHQ-9 among them 27.1% had mild level of depression whereas 15.9%, 12.3% and 4.7% of the respondents had moderate, moderately severe and severe level of depression respectively. This finding is supported by study conducted in Saudi Arabia where prevalence of depression among hypothyroid patients was 70% based on PHQ-9.[15] Similar finding were observed on the study conducted by Bathla et al in india8 where 60% of the respondents had some level of depression. Whereas study conducted in Nepal 42.2% of the thyroid dysfunction disorder respondents had depression.[16] As this study revealed that 4.7% of the respondents had severe level of depression nearly Similar finding was identified on study conducted at India where 4.6% subjects had severe depression.[14]

As this study revealed anxiety and depression was highly prevalent among hypothyroidism this might be the reason that in hypothyroidism there is decrease in CNS-TH which promotes alteration in neurotransmission leading in mood disorder such as anxiety and depression.

More than fifty percentage of the respondents (54.3%) had inadequate level of self-care management similar finding was noted on the study conducted at Kerala where 52.8% of the respondents had inadequate level of self-care management.[14]

Anxiety was significantly associated with sex (0.044), marital status (0.000), family history of mental illness (0.009) whereas depression was significantly associated with educational status (0.009) and duration of illness (0.002) whereas in the study conducted by Gorkhali et al revealed statistical significant of anxiety and depression with sex and economic status.[16]

In this current study even respondents had comorbid conditions, different level of economic status, religion and occupation. It showed no statistical significant association between this condition with anxiety and depression. This indicates that patients who were having anxiety and depression are more likely to be due to hypothyroid-related causes rather than other confounders.

## Conclusions

Based on finding of the study it is concluded that majority of the respondents had anxiety and more than half of the respondent had depression whereas regarding self-care management more than half of the respondents had inadequate level of management. As this study revealed anxiety and depression were common among hypothyroidism. Thus, the relation between hypothyroidism and psychiatry disorder is a major area of concern. So, routinescreening for psychiatric disorder and those patients' presenting with such sign and symptoms should be treated and managed by both an endocrinologist and a psychiatrist in liaison with each other. Beside this awareness about self-care management of hypothyroidism should be addressed to optimize their management and improve quality of life.

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An analysis of Clinical, Ultrasonological and Cytopathological findings of thyroid swellings at a teaching hospital in eastern Nepal
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# An analysis of Clinical, Ultrasonological and Cytopathological findings of thyroid swellings at a teaching hospital in eastern Nepal

Thakur SK[1], Thakur R[2], Nepal N[3], Khanal T[4], Adhikari A[4], Yadav RK[4], Ghimire N[5]

[1]Associate Professor, Department of ENT, Nobel Medical College, Biratnagar, Nepal, [2]Lecturer, Department of ENT, Nobel Medical College, Biratnagar, Nepal, [3]Associate Professor, Department of Pathology, Nobel Medical College, Biratnagar, Nepal, [4]Resident, Department of ENT, Nobel Medical College, Biratnagar, Nepal, [5]Associate Professor, Department of Physiology, Nobel Medical College, Biratnagar, Nepal.

**Abstract**

**Background:** Thyroid swelling can be benign or malignant. It is evaluated by clinical examination, Ultrasonography(USG) and Fine Needle Aspiration Cytology (FNAC).This study was conducted with the aim of comparing discrepancy of diagnosis by USG, considering FNAC as gold standard. **Methods:** A prospective observational study of thyroid swellings with convenient sampling was carried out over a year (20 October 2020 to 19 October 2021) at Outpatient department of Nobel Medical College, Biratnagar, eastern region of Nepal. Clinical, ultrasonological and cytological parameters were recorded. Sensitivity, Specificity, Positive predictive value (PPV) and negative predictive value (NPV) were calculated. **Results :** Out of 120 study population,with a mean age of 45.37 years, there was female preponderance, 110(91.66%).The commonest age group was 30-40 years, 28(23.33%). On Ultrasonography, non neoplastic lesions diagnosed were in 104 (86.7%) cases, as compared to FNAC, 113(94.2%). While, malignancy was diagnosed in 16 (13.7%) cases, by USG, only 7(5.8%) cases were . malignant on FNAC. The Sensitivity of USG for malignancy detection was 100 %, Specificity was 92 %, Positive predictive value (PPV) was 43.75 % and Negative Predictive value (NPV) was 100 % as compared to FNAC. Accuracy was 92.5%. **Conclusions:**Ultrasonography has an excellent diagnostic sensitivity , specificityand accuracy compared to that of FNAC.

**Key words:** Thyroid, Cytology, Nodule, Neoplasm, Benign, Malignant.

## Introduction

Thyroid disease is a common endocrine disorder, worldwide and in Indian subcontinent1. The world's biggest goiter belt is the Himalayan goiter belt. Thyroid disease usually presents as a palpable midline neck swelling, with altered thyroid function. Thyroid nodules (TNs) are common and are found in 20% to 76% of the population[2].The prevalence of TNs has been reported to be 2-6% with palpation, 19-35% with ultrasonography (USG), and 8%-65% on autopsy[3].Incidence of TNs is higher in females than in males and increases with age[4].

The most common cause of thyroid swelling is deficiency of iodine[5]. Thyroid diseases can be varied with various developmental, inflammatory and neoplastic disorders [6].

Thyroid swelling can be benign or malignant. Thyroid disease include nodular abnormalities like diffuse goitre, multinodular goitre and tumors which include thyroid adenoma, papillary carcinoma, follicular carcinoma, medullary carcinoma etc. In middle age women Hashimoto's disease, follicular carcinoma and thyroid adenoma with toxic features is common. In young girls papillary carcinoma is more common. In later ages anaplastic carcinoma occurs[7].

Among all thyroid carcinomas, papillary carcinoma is most common accounting for 81%, followed by follicular carcinoma,10%, medullary carcinoma,5%, anaplastic carcinoma,3%, and lymphoma,1% incidence[7].

The importance of TNs lies in need to exclude

**Correspondence Author**
Sanjeev Kumar Thakur, Department of ENT, Nobel Medical College and Teaching Hospital, Biratnagar, Nepal. Email ID : sanjeevkr055@gmail.com, Contact Number: 9842089844

thyroid cancer, which occurs in 7-15% of cases[8].

Diagnostic modalities for thyroid swellings include detailed history, clinical examination, thyroid function test, radiological examination, surgical intervention and microscopic examination.

Ultrasonography (USG) is safe and cost effective investigation of choice for determining the extent and to characterize the thyroid nodule. It will help to differentiate between benign and malignant nodules. Thyroid USG is more sensitive than clinical palpation in identifying multiple nodules[9,10].

Fine Needle Aspiration Cytology (FNAC) is a widely accepted diagnostic modality of thyroid nodules. It is the most sensitive, rapid, safe, precise, and economical procedure than sonlogical studies to evaluate thyroid nodules from neoplastic and non-neoplastic lesion. In preoperative evaluation of thyroid swelling, FNAC has replaced other Investigation[9].

Benign TNs are grouped according to cytological features into adenomatous nodules (nodular goiter), colloid nodules, and cystic nodules[11].

This study was intended to study clinically, the relative occurrence of various pathological conditions presenting as thyroid swelling and the ultrasonological and cytopathological analysis of examination findings of the swelling.

The objective of this study is to diagnose the nature of thyroid swelling clinically and perform ultrasonography and Fine needle aspiration cytology of the swelling and to find out the sensitivity, specificity, positive predictive value, negative predictive value and accuracy of ultrasonography (USG) to diagnose the malignancy as compared against the diagnosis by fine needle aspiration cytology (FNAC).

## Methods

A prospective observational study was carried out over a year (20 October 2020 to 19 October 2021) at Outpatient department of Nobel Medical College, Biratnagar, eastern region of Nepal.

Convenient sampling method was applied. All the cases presenting to Outpatient Department, with midline neck, thyroid swelling were included in the study. Informed consent was obtained from all the patients, after ethical clearance from Institutional review board. The cases underwent detailed history taking and physical examination. They were subjected to ultrasonography (USG) of the neck. The needy cases, underwent further fine needle aspiration cytology (FNAC) examination. All the cases who underwent both USG and FNAC, were included in the study. Patients with non thyroid swelling and those who refused informed consent were excluded. Patients with incomplete data were also excluded.

Ultrasonography was done using 8–12 Mega Hertz linear probe which is adjusted to operate at clinically highest appropriate frequency along with real time Color Flow Doppler technology. Patients in which deeper penetration is needed low frequency probe was used. Ultrasound neck was done to know the anatomy and nodularity of gland and to look for findings suggestive of malignancy like hypoechoic, calcification, irregular margins, solid component, taller than wider[12].

With all aseptic precautions , FNAC was done in all patients, in the pathology department by using 23 gauge needles. Smears were prepared from aspirated material and were stained with Haematoxylin and Eosin. A cytological diagnosis was made[13].

The data obtained were tabulated and analysed. SPSS software version 16.0 was used. The observations were expressed in number and percentage. Mean age was calculated. Sensitivity, Specificity, Positive predictive value (PPV) and negative predictive value (NPV) were calculated to compare the diagnosis of malignancy by USG against the FNAC diagnosis of malignancy.

## Results

Out of a total of 120 study subjects, with midline neck thyroid swelling, 110 (91.66%) were females, which outnumbered the male, 10(8.3%), as shown in table 1. The mean age was 45.37 years, with an age range of 11-76 years. The maximum number of patients were in the age group of third to fourth decade, 28(23.33%) followed by fifth to sixth decade, 26(21.66%). 21(17.5%) cases were in the age group of fourth to fifth decade.

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**Table 1. Age and Gender distribution of study population**

| Age range (years) | Male number (percentage) | Female number (percentage) | Total number (percentage) |
|---|---|---|---|
| 10-20 | 1 (0.83) | 3 (2.5) | 4 (3.33) |
| 21-30 | 3 (2.5) | 15 (12.5) | 18 (15) |
| 31-40 | 3 (2.5) | 25 (20.83) | 28 (23.33) |
| 41-50 | 2 (1.6) | 19 (15.83) | 21 (17.5) |
| 51-60 | 0 | 26 (21.66) | 26 (21.66%) |
| 61-70 | 0 | 14 (11.66) | 14 (11.66) |
| 71-80 | 1 (0.83) | 7 (5.83) | 8 (6.66) |
| 81-90 | 0 | 1 (0.83) | 1 (0.83) |
| Total | 10 (8.3) | 110 (91.66) | 120 (100) |

All of the patients complain was swelling in the neck, which was for 2 to 4 years duration in maximum number of patients, 92 (76.7%), as shown in table 2. 18(15%) cases presented early, less than 24 months, while, 10(8.3%) cases had duration of more than 48 months.

**Table 2. Duration of neck swelling**

| Duration in months | Number | Percentage |
|---|---|---|
| Less than 24 | 18 | 15 |
| 24-48 months | 92 | 76.7 |
| More than 48 months | 10 | 8.3 |

The comparative table of diagnosis by clinical,ultrasonological and cytoathological (fine needle aspiration cytology, FNAC) is given in the table 3.

**Table 3. Comparative table of Clinical diagnosis, USG(Ultrasonography) and FNAC (Fine needle aspiration Cytology).**

| Clinical Diagnosis | Number | Percentage | USG | Number | Percentage | FNAC | Number | Percentage |
|---|---|---|---|---|---|---|---|---|
| Diffuse Goitre | 34 | 28.3 | Adenomatous Nodule | 10 | 8.3 | Adenomatous nodule | 5 | 4.2 |
| Multinodular goitre | 69 | 57.5 | Multinodular goitre | 48 | 40 | Colloid nodule | 53 | 44.2 |
| Solitary Nodular Goitre | 12 | 10 | Indeterminate | 9 | 7.5 | Follicular neoplasm/Suspicious of Neoplasm | 8 | 6.7 |
| | | | Cystic lesion | 24 | 20 | Colloid Goitre | 21 | 17.5 |
| | | | Thyroiditis | 13 | 10.8 | Thyroiditis | 26 | 21.7 |
| Malignancy | 5 | 4.2 | Malignancy | 16 | 13.3 | Malignancy | 7 | 5.8 |

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On clinical examination, non- neoplastic lesions were diagnosed in 115 (95.83%) cases, while, malignancy was suspected in 5(4.27 %) cases. Out of non neoplastic lesions, most of the patients were diagnosed to have multinodular goitre,69(57.5%), followed by diffuse goitre,34(28.3%) and solitary nodular goitre, 12 (10%).

On Ultrasonography, non neoplastic lesions diagnosed were in 104 (86.7%) cases, while malignancy was diagnosed in 16 (13.7%) cases. Out of non neoplastic lesions, maximum number of cases were diagnosed with multi nodular goitre, 48 (40%). 10 (8.3%) cases had adenomatous nodule, while, 9 (7.5%) cases had indeterminate features. Also, 24 (20%) cases had cystic lesions and 13 (10.8%) cases were those of thyroiditis.

FNAC diagnosed most of the cases to be non neoplastic in nature, 113(94.2%) , while 7 (5.8%) cases were of malignant in nature. Most of the cases were those of colloid nodule, 53 (44.2%). Other diagnosis were adenomatous nodule, 5(4.2%), follicular neoplasm ,8(6.7%), and colloid giotre, 21(17.5%). There were 26 (21.7%) cases of thyroiditis.

The sensitivity of ultrasonography for malignancy detection was 100 %, as compared to FNAC, as shown in table 4.s The specificity was 92 %, Positive predictive value (PPV) was 43.75 % and Negative Predictive value (NPV) was 100 %.The accuracy was 92.5%.

**Table 4. Sensitivity, Specificity, Positive predictive value (PPV) and Negative Predictive value (NPV) calculation of diagnosis by Ultrasonography (USG) compared against Fine Needle aspiration Cytology(FNAC) diagnosis.**

| | |
|---|---|
| Sensitivity | 100 % |
| Specificity | 92 % |
| PPV | 43.75 % |
| NPV | 100 % |
| Accuracy | 92.5% |

**Discussion:**

There are several radiological and pathological methods of diagnosing the nature of thyroid swellings. The most important point is to exclude malignancy. Among them, Ultrasonography(USG) is an important modality for the diagnosis. The fine needle aspiration cytology (FNAC) remains the gold standard for confirming the diagnosis. Our findings confirm a strong compatibility for the diagnosis by USG and confirmation by FNAC.

Our study finds thyroid swelling to be more common in female (91.66% vs 8.3%) than male. Previous studies have also shown the disease occurring predominantly in females[14,15].This was due to the fact that females have higher hormonal requirement especially during puberty, lactation, and during menopause. The Estrogen and Progesterone may contribute to this difference in incidence.

The mean age was 45.37 years, with an age range of 11-76 years, in our study. This result is in accordance to the previous studies by Cesur M et al. and Ram N and co-authors, who reported a mean age of 43±9.4 and 43±13 years, respectively[11,16].

The maximum number of patients were in the age group of third to fourth decade, 28(23.33%) followed by fifth to sixth decade, 26(21.66%), in our study. A study conducted by Santosh and co authors found a maximum number of patients in 21–30 years (37.4%)[17]. Another study done by Kumari and Mrudula also found the commonest

incidence to be in third and fourth decade of life with an age range of 31–40 years (44.4%)18. This was because the thyroid swellings are more common in reproductive and perimenopausal age group women due to increased hormonal requirements[12].

All of the patients complaint was that of swelling in the neck, which was for 2 to 4 years duration in maximum number of patients, 92 (76.7%). 18(15%) cases presented early, less than 24 months, while, 10(8.3%) cases had duration of more than 48 months. Similar study conducted by Santosh and co authors found that 63.3% patients presented with neck swelling of 1 year. Swelling of 1 and 5 years duration was seen in 26% patients. The remaining 10% patients had swelling from 5 to 10 years[17].

On clinical examination, non- neoplastic lesions (benign) were diagnosed in 115 (95.83%) cases, while, malignancy was suspected in 5(4.27 %) cases, in our study. Saeed et al., in their study reported that benign lesions were in 87.4% in females and 12.6% in males, while malignant lesions were found in 87.5% in females and 12.5% in males[19].

Out of the non neoplastic lesions, diagnosed on clinical examination, most of the patients were diagnosed to have multinodular goitre in 69(57.5%)., followed by diffuse goitre,34(28.3%) and solitary nodular goitre, 12 (10%). Rathod and co authors found in their study, that the patients had solitary thyroid nodule (29%), diffuse thyroid swelling (38%), multi-nodular goiter (20%), cystic lesion (10%) and malignant thyroid lesion (3%)[20].

Tyagi and Chatterji in their study found that, the clinical diagnosis revealed multinodular goiter (60%) followed by solitary thyroid nodule in (34%) and diffuse goiter (6%)[21].

On Ultrasonography, non neoplastic lesions diagnosed were in 104 (86.7%) cases, while malignancy was diagnosed in 16 (13.7%) cases, in our study. Out of non neoplastic lesions, maximum number of cases were diagnosed with multi nodular goitre, 48 (40%). 10 (8.3%) cases had adenomatous nodule, while, 9 (7.5%) cases had indeterminate features. Also, 24 (20%) cases had cystic lesions and 13 (10.8%) cases were those of thyroiditis.

Our study is similar to study done by Gupta and co authors in which 90 (90%) nodules were benign, 10 (10%) were malignant[22].

In a study by Persichetti A and co authors, they reported a malignancy rate of 2.8% among benign US-appearing thyroid lesions[23].

FNAC diagnosed most of the cases to be non neoplastic in nature, 113(94.2%), while 7 (5.8%) cases were of malignant in nature, in our study. Most of the cases were those of colloid nodule, 53 (44.2%). Other diagnosis were adenomatous nodule, 5(4.2%), follicular neoplasm ,8(6.7%), and colloid giotre, 21(17.5%). There were 26 (21.7%) cases of thyroiditis.

Padmawar and co authors, on performing FNAC on 57 patients with thyroid swelling, 51 cases (89.47%) were benign and 6 cases (10.52%) were malignant[24]. Hariprasad and co authors conducted a study on 159 patients with thyroid swelling, out of which 51 cases (73.58%) were benign and (26.42%) were malignant[25].

The sensitivity of ultrasonography for malignancy detection was 100 %, as compared to FNAC. The specificity was 92 %, Positive predictive value (PPV) was 43.75 % and Negative Predictive value (NPV) was 100 %.in our study.The accuracy was 92.5%.

In a study conducted by Shin et al the sensitivity, specificity, positive predictive value, negative predictive value and accuracy for overall malignancy were 94.5%, 26.8%, 27.5%, 94.3% and 42.2% respectively[26].Another study revealed that USG had a sensitivity of 98.38% in determining the nature of thyroid lesions. It had 98.38% PPV and 55.55% NPV for benign thyroid lesions, with 71.42% specificity[27].

In a study by Manikantan and co authors, it was reported that ultrasonography is very effective in determining the nature of thyroid lesions, with an accuracy rate of about 84.5%[28].The results also consistent with a study by Popli MB et al., who reported 87.2% diagnostic accuracy using US for diagnosis of benign and malignant thyroid lesions[29].

The specificity and sensitivity of FNAC has shown a wide variation in different studies. It could be because of performance bias of the clinician performing the FNAC procedure, also that multiple nodules may harvest benign and malignant disease

at the same time in a single goiter. It is suggested that USG guided FNAC can yield a better and accurate results for diagnosing malignant nodules[13].

**Conclusions :**

Females between third to fourth decades of age suffered from thyroid swelling, more commonly. Most of them had swelling of neck for two to four years duration before seeking medical help. Most of them suffered from multi nodular goitre. Ultrasonography is a highly valuable mode of investigation to differentiate benign from malignant thyroid lesions and can almost always predict the true nature of thyroid lesions with excellent diagnostic sensitivity and specificity. Ultrasonography revealed a consistent diagnostic capacity comparable to that of FNA cytology for predicting malignant thyroid lesions.

**List of Abbreviations**

USG- Ultrasonography
FNAC- Fine needle aspiration cytology
TNs- Thyroid nodules

**Ethics approval and consent to participate**

Our study was conducted after obtaining institute ethical approval ( IRC-NMCTH: 384 /2020), Nobel Medical College and Teaching Hospital. Participants were explained about the research detail, its significance, the benefit and harm in Nepali language before obtaining the consent. A statement indicating that the participants has understood all the information and is willing to participate voluntarily was obtained. The confidentiality of participants were assured and not mentioned anywhere.

**Competing interests**

The authors declare that they have no competing interests.

**Authors' contribution**

SKT- Conceptualized, collected data, analyzed and wrote the manuscript. RT,NN,TK,AA,RKY,NG- Involved in the study from the beginning and critically reviewed the manuscript.

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# Spectrum of endocrine disorders in a hospitalized patient in a Tertiary University Hospital, Nepal

Yadav G[1], Paudel G[2], Gautam Arun[3], Maskey R[4]
[1,2] MBBS, B.P. Koirala Institute of Health Sciences
[3] PG Resident, Internal Medicine, B.P. Koirala Institute of Health Sciences
[4] Add Professor and Head, Internal Medicine, B.P. Koirala Institute of Health Sciences

## Abstract

**Background:** The epidemiological spectrum of endocrine disorders in hospitalized patients is not much explored in developing countries. Therefore, the spectrum to visualize a complete picture of the endocrine-related disease is still missing. The study aims to find the spectrum of endocrine-related-disorders in a hospitalized patient, characterize demographic variables, and the duration of hospital stay of patients. **Methods:** This was a retrospective study of medical records of admitted cases between January 2014 to December 2018 in the Medicine Ward of BPKIHS. Records were retrieved from the Medical office and were entered into Excel and then transferred to SPSS and were analysed. **Result:** Out of 26,590 admitted cases,1141 (4.3%) had endocrine-related-disease. This includes 565 males and 576 females (1.02: 1 ratio) with an overall mean age of 52.81 ± 16.21 years and median (IQR) age 53 (42-64) years. Among which 904 (79.2%) had Diabetes mellitus, 118 (10.3%) had Metabolic Disorders, 38 (3.3%) had Disorders of Thyroid gland, 38 (3.3%) had Other Nutritional Deficiencies, 29 (2.5%) had Disorders of other endocrine glands, 7 (0.6%) had other disorders of glucose regulation and pancreatic internal secretion, 5 (0.4%) had Overweight, obesity and other hyperalimentation, 2 (0.2%) had Malnutrition. **Conclusion:** Diabetes and Metabolic disorders are the main components of the spectrum of endocrine disorders in admitted cases. Emphasizing the resources essential for further investigation will help both in dealing with and managing the cases of endocrine disorders.

**Key Words:** Endocrine, Disorders, Hospitalized, Diabetes

## Introduction

The spectrum of endocrine disorders in hospitalized patients is not much explored in developing countries. Due to a lack of data and a smaller number of endocrinologists, the burden of endocrine disorders is not well researched[1]. The number of researches done so far in Nepal has tried to visualize the major burden of Diabetes mellitus and Disorders of thyroid gland in the community[2–4]. However, the lack of spectrum to visualize a complete picture of the endocrine-related disorder is still missing. The need for research to highlight the complete picture of endocrine-related disorders is essential. Though most of the research-based on hospital setting is based on ease of access to patients and referrals from doctors, the data recorded can characterize the disease, and its frequency, which could reflect the burden of disease in the community. This study has tried to visualize the spectrum of endocrine-related-disease for over five years. This report would further help in emphasizing the need for the management of endocrine disease in a hospital setting in Nepal. The study aims to find the spectrum of endocrine-related-disorders in a hospitalized patient, characterize relevant demographic variables, the duration of hospital admission, and the disease outcomes on a patient's discharge.

**Correspondence Author**
Dr. Girendra Yadav
BP Koirala Institute of Health Sciences, Dharan, Nepal
Email address: ygirendra@gmail.com, Tel. No. +977 9842123704,
Fax: BPKIHS, Dharan-18, Sunsari, Nepal

## Methodology

This was a retrospective study of medical records of patients admitted in the Medicine Ward of BPKIHS.

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The hospital, established as an autonomous Health Sciences University in 1993 has been continuously providing service as primary, secondary and tertiary level. This teaching University hospital is main referral center in Eastern Nepal with area of 699 acres of land and over 700 beds [5]. The medicine ward has a capacity of over 90 beds.

After the ethical clearance with Ref. No. 156/078/079-IRC and approval from the department, the medical record was retrieved from the Medical record section for 5 years.

All the cases admitted in Medicine Ward between January 2014 to December 2018 were included. Records that were repeated and incomplete were excluded.

**Data entry and analysis:**

Records were then entered into Microsoft Excel 2007. The data were then transferred to SPSS (Statistical Package for Social Sciences) and analyzed. Data were decoded for categorical and class-interval was made for numerical data in variable view. Diagnosis of patient were entered according to ICD 10 coding International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10)-WHO Version for; 20160.

**RESULT**

26,590 adult cases were admitted in Medicine Ward from January 2014 to December 2018. 1141 (4.3%) had endocrine-related-disease (Figure 1). In Year 2014, 2015, 2016, 2017, 2018, a total of 207, 252, 215, 268, 199 new patients were admitted respectively . This includes a total of 565 (49.5%) males and 576 (50.5%) females with a male-to-female ratio of 1.02: 1. The overall mean age of the patients was 52.81 ± 16.21, with a range of 18-99 years. The median (IQR) age of presentation for males was 53 (42-64) years, which was significantly different from that of female 53 (42-65) years, $p< 0.0001$. The modal age for both lies 50-69 years with a peak at 60-69 years.

Out of 1141 patient admitted who had endocrine-related-disease, 904 (79.2%) had Diabetes mellitus, 118 (10.3%) had Metabolic Disorders in which 90 (7.9%) had Other Disorders of Fluid, Electrolyte and Acid-Base Balance, 18 (1.6%) Disorders of Mineral Metabolism, 4 (0.4%) had Other and Unspecified Metabolic Disorders, 2 (0.2%) had Volume Depletion, 2 (0.2%) had Disorders of porphyrin and bilirubin metabolism, 1 (0.1%) had Other Disorders of Carbohydrate Metabolism, 1(0.1%) had Disorders of Lipoprotein Metabolism and other Lipidemias , 38 (3.3%) had Disorders of Thyroid gland, 38 (3.3%) had Other Nutritional Deficiencies in which 6 (0.5%) had Deficiency of other B group of vitamins, 2 (0.2%) had Other Vitamin Deficiency , 29 (2.5%) had Disorders of other endocrine glands, 7 (0.6%) had other disorders of glucose regulation and pancreatic internal secretion in which 7 (0.6%) had hypoglycemia unspecified , 5 (0.4%) had Overweight, obesity and other hyperalimentation, 2 (0.2%) had Malnutrition (Table 1).

| ICD 10 Classification (E00-89) | | Frequency, n (%) |
|---|---|---|
| E00-07 Disorders of the thyroid gland | Hypothyroidism Unspecified | 38 (3.3%) |
| E08-13 Diabetes mellitus | Type 1 DM | 67 (5.9%) |
| | Type 2 DM | 830 (72.7%) |
| | Unspecified DM | 7 (0.6%) |
| E15-E16 Other disorders of glucose regulation and pancreatic internal secretion | Hypoglycaemia Unspecified | 7 (0.6%) |
| E20-E35 Disorders of other endocrine glands | Hypofunction and other disorders of pituitary gland | 10 (0.9%) |
| | Hyperfunction of Pituitary gland | 3 (0.3%) |
| | Cushing's Syndrome | 6 (0.5%) |
| | Hyperaldosteronism | 1 (0.1%) |
| | Other disorders of adrenal gland | 8 (0.7%) |
| | Disease of Thymus | 1 (0.1%) |
| E40-E46 Malnutrition | Protein-Energy Malnutrition | 2 (0.2%) |
| E50-E64 Other nutritional deficiencies | Deficiency of other nutrients elements | 30 (2.6%) |
| | Deficiency of other B group of vitamins | 6 (0.5%) |
| | Other Vitamin Deficiency | 2 (0.2%) |

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| | | |
|---|---|---|
| E65-E68 Overweight, obesity and other hyperalimentation | Obesity Unspecified | 5 (0.4%) |
| E70-E88 Metabolic Disorders | Other Disorders of Fluid, Electrolyte and Acid-Base Balance | 90 (7.9%) |
| | Disorders of Mineral Metabolism | 18 (1.6%) |
| | Other and Unspecified Metabolic Disorders | 4 (0.4%) |
| | Volume Depletion | 2 (0.2%) |
| | Disorders of porphyrin and bilirubin metabolism | 2 (0.2%) |
| | Other Disorders of Carbohydrate Metabolism | 1 (0.1%) |

**Diabetes Mellitus**

Out of 904 Patients with Diabetes, 480 (53.1%) were male and 424 (46.9%) were female with a male: female ratio of 1.1: 1. Among admitted, with diabetes, 830 (91.8%) were Type 2 DM, 67 (7.4%) were Type 1 DM and 7 (0.8%) Unspecified DM. The median (IQR) age of presentation for males was 54 (43-64) years, which was significantly different from that of females 56 (44.2 -66) years, $p<0.0001$. The modal age for male was 50-59 years while for female was 60-69 as shown in figure 1. The median (IQR) age of patients with Type 2 DM, Type 1 DM, and Unspecified diabetes median were 56 (65-45) years, 25 (35-20) years, 47 (60-29) years respectively, with $p<0.0001$. (Kruskal-Wallis test) and the male: female for Type 2 DM, Type 1 DM, and Unspecified diabetes were 1.1: 1, 1.03:1, and 1.3: 1 respectively.

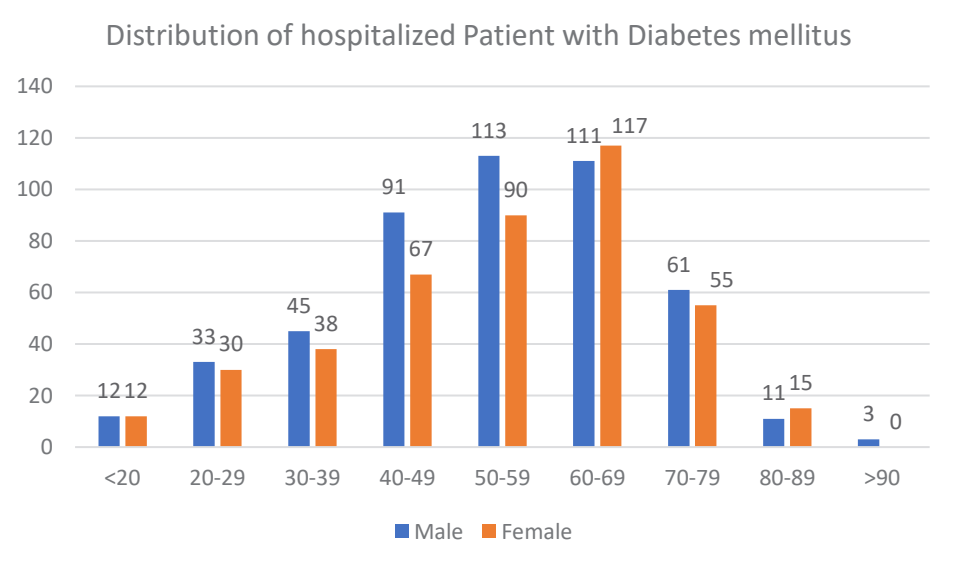

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Figure 1. Distribution of hospitalized Patient with Diabetes mellitus

**Metabolic Disorders**

Out of 118 (10.3%) patients admitted, who had Metabolic Disorders, 69 (58.5%) were female and 49 (41.5%) were male with female to male ratio 1.4: 1. Among them, 90 (76.3%) had Other Disorders of Fluid, Electrolyte, and Acid-Base Balance, 18 (15.3%) had Disorders of Mineral Metabolism, 4 (3.4%) had Other and Unspecified Metabolic Disorders, 2 (1.7%) had Volume Depletion, 2 (1.7%) had Disorders of Porphyrin and bilirubin metabolism, 1 (0.8%) had Other Disorders of Carbohydrate Metabolism and 1 (0.8%) had Disorders of Lipoprotein Metabolism and other Lipedema.

Disorders of Thyroid Glands

Among 38 (3.3%) patients admitted had Hypothyroidism, Unspecified which falls in Disorders of thyroid gland (E00-E07). Out of which 28 (73.7%) were female and 10 (26.3%) were male, with female to male ratio 2.8: 1. The mean age of presentation for males was 45.3± 21.3 years and 46.14± 16.1 years for females. The median (IQR) range of presentation for the male was 40 (69.5-28.2) years, which was not significantly different from 43.5 (35.2-61.7), p=0.85. The modal age for presentation for males is 30-39 years and 40-49 for females.

Other Nutritional Deficiencies

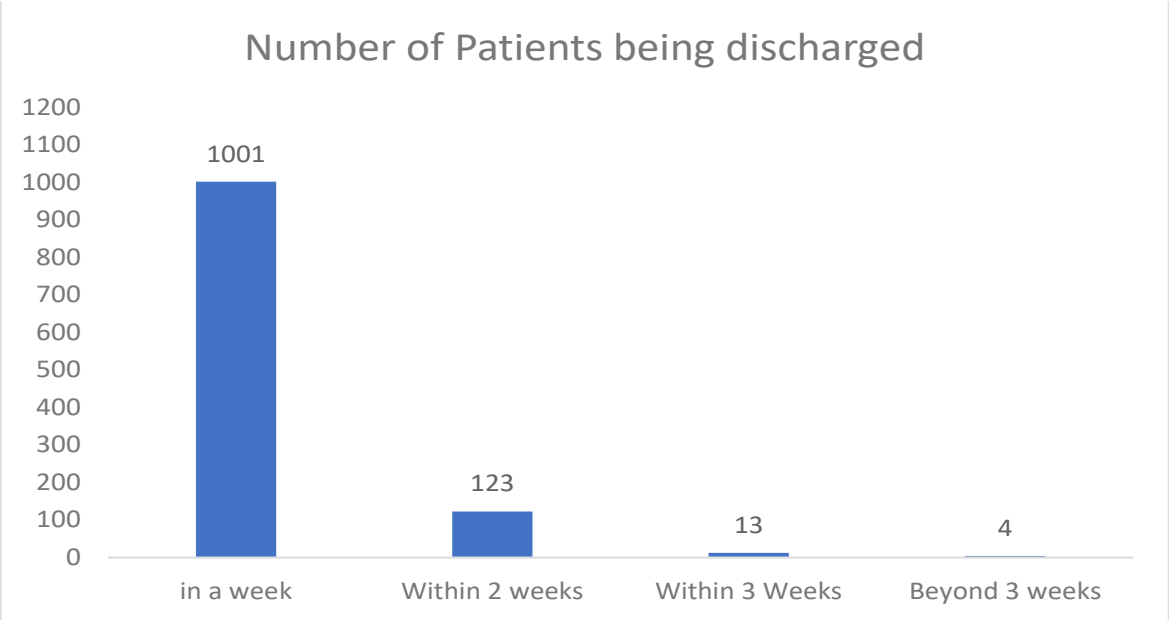
Among admitted, 38 (3.3%) had Other Nutritional Deficiencies, 22 (57.9%) were female and 16 (42.1%) were male giving female: male 1.3: 1. Out of which 30 (78.9%) had Deficiency of other nutrients elements, 6 (15.8%) had Deficiency of other B group vitamins and 2 (5.3%) had Other Vitamin deficiencies.

**Disorders of other endocrine glands**

Among 29 (2.5%) admitted, who had Disorders of other endocrine glands, 23 (79.3%) were female and 6 (20.7%) were male, with a female: male 3.8: 1. Out of which, 10 (34.5%) had Hypofunction and other disorders of the pituitary gland, 8 (27.6%) had Other disorders of adrenal gland, 6 (20.7%) had Cushing's Syndrome, 3 (10.3%) Hyperfunction of pituitary gland, 1 (3.4%) had Hyperaldosteronism, 1 (3.4%) had Disease of Thymus.

**Others**

Among others admitted, 7 (0.6%) were cases who Hypoglycaemia unspecified, 5 (0.4%) had obesity unspecified and 2 (0.2%) were Unspecified Protein-



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Energy Malnutrition.

The mean duration of patients admitted with these disorders in the hospital was 4.4 ± 3.37 days with 1001 (87.7%) being discharged within a week which consist of 791 (79%) patients with DM, 109 (92.4%) with Metabolic disorders,

36 (94.7%) withs Other nutritional deficiencies, 32 (84.2%) with Disorders of Thyroid gland, 20 (69%) with Disorders of Other endocrine glands, 7 (100%) with hypoglycemia unspecified, 4 (80%) with Obesity Unspecified and 2 (100%) with Protein-energy-malnutrition. The number of patients being discharged is shown in figure 2.

## DISCUSSION

In this 5-year study done in Tertiary University Hospital of Nepal, 4.3% patient admitted in the Medicine ward was because of endocrine-related disorders. Diabetes mellitus and metabolic disorder were the major cause of hospital admissions, followed by Disorders of the thyroid gland and Other Nutritional deficiencies.

The number of endocrinologists in Nepal is 47[7]. Endocrinology has been made known to the medical fraternity only a decade ago. Endocrinologists come across 70% of patients with DM, 10-15% of Disorders of thyroid gland, and 15% other endocrine disorders during their practice. The number of endocrine patients treated by surgeons as masses of adrenal gland and pituitary gland and the patient with osteoporosis in the orthopedic clinic, together with masks the actual presentation of endocrine cases[1].

This study included adult cases of 18 years and above and found that the age group of endocrine disorder was 50-69 years with a peak at 60-69 years. The number of DM patients tugged the age group towards the age group of patients suffering DM.

Diabetes mellitus accounts for 80% admitted cases among endocrine-related-disorders. Type 2 DM records for 72.7% cases, and the period prevalence of Type 2 DM comes out to be 3.1%. As of 2014, the prevalence of Type 2 DM in Nepal is 8.4% [2]. The gap in rate is because of the number of patients managed in out-patient clinics that do not sum up in the record. Also, the cases of Gestation DM come in a record of Obstetric ward and out-patient endocrine-clinic. The age of patients admitted with Type 2 DM has a peak in 50-59 years, while Type 1 DM has a peak in 20-29 years, similar to the findings of the age of diagnosis in most studies [8,9].

The number of patients admitted with Disorders of thyroid gland 38 (3.3%) is low as compared to the prevalence of Disorders of thyroid gland in Nepal, as most are managed in out-patient-clinics. In addition, there is a female gender preponderance of cases with a ratio of 2.8: 1 similar to findings from other studies[4,10].

The endocrine cases were assessed and managed by a trained endocrinologist in this study. The lack of accessibility to diagnostic resources like Nuclear imaging, CT, and MRI and the patient economic constraints to pay for such investigation has decreased the number of cases of other endocrine-related-disorder.

The complications in endocrine patients with endocrine disorder were not collected, which is the major limitation of this study. Since this was retrospective study of medical records and the height and weight or (BMI) of patients were not mentioned in most of records, thus the result obtained shows very low rate of Overweight, obesity and other hyperalimentation. Also, the study is based on several admitted cases in the medicine ward. The endocrine-disorder seen in the paediatric and adolescent age group were not recorded.

## CONCLUSION

The endocrine cases account for 4.3% of

total cases admitted in the Medicine ward. Diabetes and Metabolic disorder are the main component of the spectrum of endocrine-related-disease. Emphasize on prevention, screening and diagnosing these two spectra will help to minimize the major burden of endocrine diseases.

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CASE REPORT OPEN ACCESS

# "A MASSIVE OVARIAN CYST MASQUERADING AS MALIGNANCY IN UNRECOGNISED PRIMARY HYPOTHYROIDISM"

Sandhya SS [1], Praveen KD [2], Dhananjaya SR[3], Shivaraj G[4]

[1]Consultant, Dept of Obstetrics & Gynaecology, Sarji Hospital, Shivamogga, [2]Professor, Dept of General Medicine, Division of Endocrinol Subbaiah Institute of Medical Sciences, Shivamogga , [3] Medical Director and Senior Consultant Pediatric Generalist, Sarji Hospital, Shivamogga, [4]Professor of Biochemistry, Subbaiah Institute of Medical Sciences, Shivamogga

**Abstract**

We report here probably a huge ovarian cyst of size 7.9x16.4x23 cms which regressed on thyroxine therapy with severe autoimmuneprimary hypothyroidism in a young woman. It is necessary to consider hypothyroidism and other endocrine disorders in the differential diagnosis of adult patients with ovarian multiple cyst formation in order to prevent inadvertent ovarian surgery.

**Key Words:** Ovarian cysts. Juvenile primary hypothyroidism, Oligomenorrhea

## Introduction

Ovarian cysts are a common cause for gynaecological surgery. However, some ovarian cysts arise due to endocrine disorders and hence studies have shown that they do not require any surgical intervention. Primary hypothyroidism is a common endocrine abnormality resulting from thyroid hormone deficiency that in turn may lead to multiple-system impairment. Occasionally, concomitant ovarian cyst formation is reported as Van Wyk and Grumbach syndrome (VWGS) in juvenile primary hypothyroidism [1].

## Case Report

A 17 year old female presented with history of vomiting with pain abdomen. Her age of menarche was 15 years and had irregular menstrual period since then. She gave history of poor scholastic performance. On examination her height was 137 cm (< 3rd percentile), weight 42 kg, BMI 32.4 kg/m2. She had puffiness of face, looked pale and lethargic. Sexual maturity score was B4P2 and absence of axillary hair. There was no goitre. Abdomen was distended with large supra pubic palpable mass up to umbilicus.

The laboratory investigation showed microcytic hypochromic anaemia with normal liver and renal function test. Her thyroid profile showed markedly low T3 (41 ng/dl) (70-210 ng/dL), low T4 3.5 mcg/dl (4.2-12mcg/dL) and free T4 0.42 ng/dl (0.8-1.8 ng/dL) and with very high TSH>100 IU/ml (0.55-4.2 IU/ml). Her TPO antibody was positive and was suggestive of severe autoimmune primary hypothyroidism. LH (0.1 IU/ml) was low with normal FSH. Prolactin was high (100.4 ng/ml).

MRI pelvis was performed to characterise the mass which revealed large cystic lesion of size 7.9x16.4x23 cms with numerous septae arising from right ovary extending to abdominal cavity as shown in Figure 1

**Corresponding Author**
Dr Shivaraj Gowda ,drshivaraj@yahoo.com
Professor of Biochemistry, Subbaiah Institute of Medical Sciences, Shivamogga.

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**Figure 1: MRI pelvis showing the large ovarian cyst**

. Uterus size was normal with thickened endometrium of 16.8 mm. The serum level of CA 125 was normal. Thyroid ultrasound mildly enlarged thyroid lobes with coarse echo texture. X ray hand revealed bone age of 13 years. In view of severe primary hypothyroidism conservative management was planned instead of undergoing for surgical resection and she was initiated on thyroxine replacement therapy. The patient responded well to conservative management, and a significant regression in the size of the cystic lesion was observed at the end of the 6-month follow-up, and complete resolution was observed after 12 months without any need for surgical intervention as shown in Ultrasound abdomen in Figure 2.

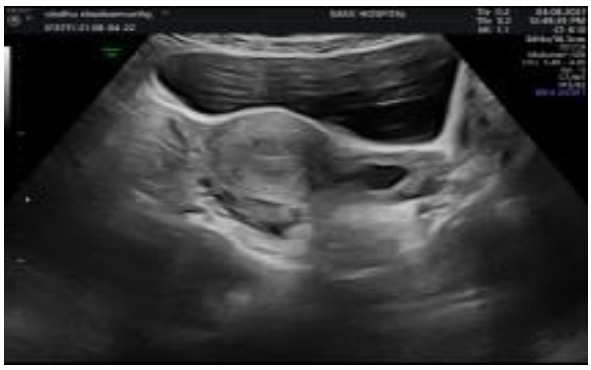

**Figure 2: Ultrasound abdomen showing complete resolution of ovarian cyst**

**Discussion**

Ovarian function, i.e. production of steroid hormones and ova, is subject to regulation by endocrine factors derived from the brain. This brain–gonadal axis is the core unit for the maintenance of endocrine balance and fertility. Hypothyroidism may cause reproductive disorders as well. Occasionally, concomitant ovarian cyst formation is reported as the Van Wyk and Grumbach syndrome [1] in juvenile primary hypothyroidism. It is less commonly seen in adults. Failure to recognize hypothyroidism as aetiology of ovarian cysts could lead to inadvertent oophorectomy.

Hypothyroidism is another endocrine disorder associated with ovarian hyperstimulation, yet it is often ignored during its evaluation. Spontaneous OHSS cases have been reported in pregnant women with hypothyroidism [2]. Van Wyk & Grumbach were first to describe the combination of multicystic ovaries, juvenile hypothyroidism and precocious puberty in 1960, sporadic cases of this syndrome have been reported in prepubertal and adolescent girls [3].

The association of multicystic ovarian disease with hypothyroidism has been described in the literature [4-6]. Various mechanisms have been postulated, which include altered oestrogen metabolism, hypothalamic–pituitary dysfunction and deranged prolactin metabolism. According to Anastiet al [(7)], ovarian enlargement in severe hypothyroidism is probably due to the stimulation of FSHRs by unusually high TSH levels proven to have a weak FSH-like activity. It has been shown that TSH could interact directly with the FSHRs to elicit gonadal stimulation, because TSH has a small FSH- and luteinizing hormone (LH)-like effect.

We report here probably a huge ovarian cyst of size 7.9x16.4x23 cms which regressed on thyroxine therapy. Moreover the thickened endometrium in our patient was probably due to excessive amounts of TSH with amplification of FSH action and release by low LH thus leading to dysfunctional uterine bleeding and anaemia. The FSHR is expressed during the luteal phase in the secretory endometrium of the uterus. Marked clinical improvement was observed in the patient as menstrual cycles became regular, anaemia got corrected and abdominal pain

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got relieved. The regression of the ovarian cyst was observed following administration of thyroid hormone.

**List of Abbreviations:**
VWGS: Van Wyk and Grumbach syndrome
BMI: Body Mass Index
LH: Luteinizing Hormone
FSH: follicle stimulating hormone
TSH: Thyroid stimulating hormone
TPO: Thyroid peroxidase

**Ethics approval and consent to participate**
The study was conducted after the ethical approval from Institutional Review Committee, Sarji Research Centre, Sarji Hospital, Shivamogga, Karnataka, India. Participants were explained about the research detail, its significance, the benefit and harm in local language before obtaining the consent, their queries were answered. A statement indicating that the participants has understood all the information in the consent form and is willing to participate voluntarily was obtained. Participants were able to withdraw from the study at any time without giving any reason during the study period. The confidentiality of participants was assured and code number was used in each interview schedule and name of the participants was not mentioned anywhere.

**Competing interests**
The authors declare that they have no competing interests.

**Authors' contributions**
SSS conceptualized, collected data, analyzed and wrote the manuscript. PKD, DSR and SG supervised and guided throughout the study from the beginning of the study and critically reviewed the manuscript. All authors read and approved the final manuscript.

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Growth hormone therapy in a girl with Turner syndrome – an experience from Bangladesh
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CASE REPORT OPEN ACCESS

# GROWTH HORMONE THERAPY IN A GIRL WITH TURNER SYNDROME – AN EXPERIENCE FROM BANGLADESH

Nahar J[1], Zabeen B[2], Islam N[3], Azad K[4]
[1]Associate Professor, Department of Paediatrics
[2] Consultant and Coordinator, Department of Paediatrics & CDiC Paediatric Diabetes center
[3] Registrar, Department of Paediatrics
[4] Professor and Project Director, Department of Paediatrics and Perinatal Care Project
Bangladesh Institute of Research & Rehabilitation in Diabetes, Endocrine & Metabolic Disorders (BIRDEM), Dhaka, Bangladesh

**Abstract**
Turner syndrome (TS) is the most common sex chromosome abnormality in females. Short stature and hypogonadism are principal signs of TS. Turner syndrome is well-established. There have been studies that have evaluated the benefits of growth hormone in TS with significant benefit in adult height. A 9-year 11 months-old girl who presented to the Paediatric Endocrinologist, with complaint of not growing according to her age. Her growth was noticed to be slow from early age but her parents initially thought it was normal. They however became worried when she was not growing yet to start pubertal development. Her parents eventually took her to this referral hospital for further evaluation and management.

**Key Words:** Pheochromocytoma, Delirium, Hypertension

## Introduction

Turner syndrome (TS) is the most common sex chromosome abnormality in females. It was first described by Henry Turner and Laurel Thatcher Ulrich in 1938 and is also known as monosomy X or Bonnevie-Ulrich syndrome.[1] It is a condition characterized by monosomy of the X chromosome and complete or partial absence of the second sex chromosome.[2] Short stature and hypogonadism are principal signs of TS[3,4] It has an estimated prevalence of 1/2000 to 1/5000 female live births.[5] Typical stigmata include short stature, primary amenorrhoea, estrogen insufficiency and cardiovascular malformations.[6] Girls with TS universally have short stature (>95%), along with gonadal failure (>90%) and infertility (99%).[7]The mechanism responsible for short stature in patients with Turner's syndrome is unknown. Growth retardation in the syndrome of gonadal dysgenesis is often present in utero; growth velocity after infancy and early childhood is subnormal, and there is no pubertal growth spurt. Clinical incidence suggests that impaired growth is related to resistance of the growing cartilage to growth factors. [8,9] Untreated these girls continue to be short and rarely achieve 150cm of adult height, barring few mosaics. [10]

The effect of growth hormone (GH) on short-to-medium-term growth in girls with Turner syndrome is well-established. There have been studies that have evaluated the benefits of growth hormone in TS with significant benefit in adult height. There is lack of data on effect of GH therapy on TS in Bangladesh. Here we describe a girl with TS who got growth hormone therapy in our hospital.

## Case-Report

A 9-year 11 months-old girl who presented to the Paediatric Endocrinologist, with complaint of not growing according to her age. Her growth was

**Corresponding Author**
Bedowra Zabeen, Consultant and Coordinator, Department of Paediatrics and CDiC Paediatric Diabetes center, Address: Room 309, 1/A Shegunbagicha, BIRDEM 2, Dhaka - 1000, Bangladesh, Cell +8801819259647, Email: bzabeen@hotmail.com, bzabeen@gmail.com

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noticed to be slow from early age but her parents initially thought it was normal. They however became worried when she was not growing yet to start pubertal development. Her parents eventually took her to this referral hospital for further evaluation and management.

She is 2nd issue of a nonconsanguineous parents, birth history was uneventful. She did not have any perinatal problem. Her medical history was unremarkable and did not show any head trauma, seizure, or infections in the central nervous system. No specific family history was found. There was no history of short stature in the family. Her developmental history was normal. She had a history of small Atrial septal defect (ASD), which was closed spontaneously. She also had hiatus hernia and gall stone but was not symptomatic.

On examination, she had depressed nasal bridge, there was no webbed neck but her carrying angle was high. There was no skin lesions or midline defect. Her respiratory system examination was normal. She had no eye signs and the thyroid gland was not enlarged. She was prepubertal. Examination findings in other systems were normal.

She was stunted, short for her age height was 124.6 cm <3rd centile (- 2SD) on CDC and +1SD on Turner chart. Weight was 23 kg <3rd centile (-2SD) percentile on CDC and -1SD on the Turner chart. Her bone age was not delayed. Thyroid function was normal. Karyotype revealed 45XO/ 46 XX(X)($q^{10}$) chromosomes, which indicated TS with mosaicism. Echocardiography showed no abnormality. Pelvic Ultrasound scan showed pre pubescent uterus and ovaries. She was started on Growth hormone therapy at 4.5mg/m2/week 6 days per week. After 2 weeks, she developed headache and we stopped GH therapy. Again GH therapy was started after 2 weeks and gradually it was increased to a maximum dose of 9.5 mg/m2/wk.. After 1 year of the rhGH treatment, her growth velocity increased to 8.2 cm/ year. She has gained 19.4 cm in the past 2 years since starting of GH therapy. She developed puberty after 2 years. The growth hormone treatment was stopped because she gained her final height of 144 cm (+2SD) on Turner chart after 2years and 4 months.

**Discussion**

TS patients are about 20 cm shorter than the average adult female height of that country and considering the fact that the average height of Bangladeshi women is 150.7 cm.[11]Long-term growth and final height after GH therapy in girls with TS are now available from several studies. Some studies have shown only small gain while others claim significant improvement in height. [12,13] This discrepancy is likely to be due to several factors such as age at starting GH, dose of GH, age of sex steroid replacement, use of anabolic steroids, ethnic and genetic differences, sample size of the study, and use of historical or randomized untreated controls, all of which may account for the variation in final height when treated with GH. Apart from the classic clinical phenotypic features, the diagnosis of TS should be suspected in any girl who presents with unexplained short stature even in the first 3 years of life.[14] The average age at diagnosis in a real-world scenario as in an observational study was 12.7 years. Unfortunately, the diagnosis of TS is often delayed, not only because of lack of clinical expertise but also because the girl child is often neglected and brought to the attention of medical help only for evaluation of delayed puberty rather than for short stature. Adding to it is the high cost of GH therapy, and both these factors have significantly affected the use of GH therapy in this country. Short stature and hypogonadism are principal signs of TS. [11,12] Nearly half of the individuals with TS have the typical [45],X karyotype while the rest have various types of chromosomal abnormalities including isochromosome and mosaicism. [3,11,12] Our patient has mosaicism on karyotype. FDA approved recombinant growth hormone for short stature in TS in 1996.[13] The main predictive factor for the best possible response to growth hormone is the age of the patient when she starts treatment. Patients who receive treatment early exhibit better results in terms of final height. [14-17] In this case, the patient began hormonal replacement therapy at around the age of ten years. Although it was started late, this treatment achieved a significant improvement in the patient's skeletal growth. If the therapy had been started earlier, the patient could

possibly have exhibited even better results. But the initial estimation had been a final height far below the average population if she did not receive this treatment.

The dose of GH in TS is higher than the dose for GH deficient patients because as mentioned previously, not many TS patients are GH deficient. However higher doses may be required for better height velocity. Growth response could be poor in patients with TS who had been initially diagnosed with GHD. In this case study, growth velocity increased from 5.7 to 8.2 cm/yr after the rhGH therapy.

Puberty is usually delayed in TS because of gonadal dysgenesis and eventual failure. Though spontaneous puberty and assisted reproduction have been reported in about 5% of TS patients, it is usually in those with the mosaic form. [18,19] The objective of starting oestradiol therapy treatment is development of secondary sexual characteristics and increase and maintenance of bone mass.[20] Timing though has been debated and many suggest that oestradiol should be started as soon as possible. Therefore, at the right time, replacement of estrogen to induce puberty is recommended for the majority of patients. [21] Estrogen therapy is usually started when the girl is between 12 and 13 years old. In this patient, without the need for sexual hormone replacement, she started menarche at 12 years of age. Endocrinological follow-up is a constant necessity, since a hormone insufficiency may arise at any point during the course of the patient's life. Cognitive function in some children with TS is grossly reduced when compared with normal girls. Other reasons for reduced brain growth is GH deficiency, which was clearly demonstrated in different case reports. [22-24] But in our patient, there was no cognition deficit and also she did not have GHD.

## Conclusion

To our knowledge this is one of the report of TS with GH therapy among few published reports in Bangladesh. TS should be an important differential diagnoses while evaluating any girl with short stature. Early diagnosis should be attempted in these girls, keeping in mind that early initiation with high dose GH, as recommended, could result in much improved adult height, which is very unlikely in untreated TS.

## Consent for publication

Consent from parents was taken.

## Competing interests

The authors declare that they have no competing interests.

## Authors' contributions

JN and BZ conceptualized and wrote the manuscript. NI and KA reviewed the manuscript. All authors read and approved the final manuscript.

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