

Compliance of Post Thyroidectomy Patients to Thyroid Replacement Therapy

Soheir M. Weheida⁽¹⁾ Marwa Khalil Hafez⁽²⁾, Yasmine Fathy⁽³⁾, Ahmad Shaaban⁽⁴⁾, Naglaa Abd Allah Abd El Hafeez⁽⁵⁾

(1) Prof. of Medical-Surgical Nursing. Faculty of Nursing, Alexandria University, Egypt.

(2,3,5) Assistant professor of Medical-Surgical Nursing. Faculty of Nursing, Alexandria University. Egypt.

(3) Assistant professor of Surgery. Medical Research Institute. Alexandria University. Egypt.

Abstract

Background: Patients post thyroidectomy might fail to reach normal levels of Thyroid Stimulating Hormone (TSH). Compliance to lifelong hormonal replacement therapy is greatly necessary to prevent deficiency of thyroid hormone and complications as hypothyroidism. **Aim:** the study aimed to identify compliance of post thyroidectomy patients to thyroid replacement therapy. **Setting:** The study was conducted at the endocrine outpatient clinic of the Main University Hospital, Alexandria University, Egypt. **Materials and method:** A descriptive research design was utilized. Data was collected from 100 adult patients post thyroidectomy for at least 6 months. **Tools:** Bio-socio-demographic data structured interview schedule, post thyroidectomy signs and symptoms of hypothyroidism observational checklist, medication compliance questionnaire and factors associated with compliance of patients' to thyroid replacement medication structured questionnaire are tools were utilized for data collection. **Results:** More than half of the studied patients had low level of compliance. They had signs of hypothyroidism such as dyspnea, hypotension, anorexia and weight gain, all these signs were significantly associated with low level of compliance to therapy where $p = (<0.001, 0.002, <0.001 \text{ and } <0.001)$ respectively. Statistically significant relations were found between low level of compliance to replacement therapy and several associated factors such as patients did not know how to read or understand what is written on the medication labels, did not understand why they need to take this medication, and they just forgot where $p = (<0.001, <0.001, \text{ and } <0.001)$ respectively. **Conclusion:** Identification of patients' compliance to thyroid replacement therapy and its associated factors is highly needed to achieve appropriate lifelong health outcomes. **Recommendation:** Replication of the study on large sampling.

Keywords: Compliance, Post Thyroidectomy Patients, Thyroid Replacement Therapy.

Introduction

A thyroidectomy refers to surgically removing the thyroid gland which is recommended for patients with goiter, Graves' disease, thyrotoxicosis, and thyroid cancer. There are several surgical forms of thyroidectomy such as partial, subtotal, or complete removal of thyroid gland which might be performed depending on the reason of surgery Abd Elazeem et al. (2020) & Mansy et al. (2023). Unfortunately, post thyroidectomy hypothyroidism is the most frequent complication especially following a complete removal of the gland. Therefore, thyroid hormone replacement therapy is greatly necessary Al-Janabi et al. (2022) & Karunarathna et al. (2024).

Thyroid hormone replacement therapy means administering medication aims to restore thyroid function, so it must be taken as lifelong

therapy post thyroidectomy in order to replenish missing thyroid hormones and prevent postoperative thyroid hypo function. Levothyroxine (LT4) medication is the widely used lifelong treatment for thyroid hormones replacement; doses are adjusted based on circulating levels of Thyroid Stimulating Hormone (TSH). Failure of post thyroidectomy patients' compliance to take the prescribed doses of LT4 could lead to appearance of signs and symptoms of hypothyroidism. It includes hypothermia, hypotension, bradycardia, fatigue, lack of energy, feeling of coldness, weight gain, constipation, hair loss, and dry skin Wilson et al. (2021) & Kilit et al. (2022).

In this particular context, hypothyroidism presenting mainly as the lack of compliance to replacement therapy, can lead to an increased risk of various secondary diseases, including cardiovascular problems, obesity, low blood pressure, reduced physical ability, diminished

quality of life and even cause an emergency which might be life threatening **Bocale et al. (2022) & Feldt-Rasmussen et al. (2024) & Ryu et al. (2024)**.

In terms of therapy, compliance is the degree to which a patient adheres to the actual treatment plan that has been prescribed by their medical providers. This encompasses every facet of the patients' conduct, ranging from punctual medicine intake to adjusting their dietary patterns to bring about lifestyle modifications **Kumar & Shaukat (2019)**. In addition, it's thought of as a dynamic process that might have an immediate impact on patients' progress and the results of therapy **Yavuz et al. (2022)**. Notably, in low- and middle-income countries, compliance to lifetime treatment is lower than in high-income countries; approximately half of patients are believed to be compliant with therapy **Bocale et al. (2022) & Khoiry et al. (2023)**.

Patients who have no or lower levels of compliance to hormonal replacement therapy might show major consequences, such as worsened clinical outcomes, increased hospitalization rates, higher costs of health care, and shorter life spans with higher rates of morbidity and mortality **El Helou et al. (2019) & Stewart et al. (2023)** Therefore, improved levels of compliance to thyroid replacement medication must be confirmed in order to enhance the health outcomes for patients who have had thyroidectomy. Education regarding the consequences of not taking their prescribed therapy as instructed could improve their compliance to therapy. Additionally, for the nurse to improve medication compliance, they must be aware of the contributing variables that may lead to a patient's inability to comply with thyroid replacement therapy. **Kumar & Shaukat (2019) and Aremu et al. (2022)**.

Indeed, there could be a number of reasons behind poor drug compliance rates. According to **Ge et al., (2023)**, the causative factors can be broadly classified into five dimensions: patient-related, health condition-related, health-care system-related, therapy-related, and socio-economic-related. The latter category includes various items like the cost of medications, accessibility to health insurance, and support from social or familial networks **Srivalli & Pereira (2020) & Basim et al. (2021) &**

Gudeta et al. (2023). In order to monitor patients' compliance to hormonal replacement therapy, reviewing direct patient reports, applying patients' physical assessment, and monitoring blood laboratory investigations of thyroid hormones should be ensured **Khoiry et al. (2023)**.

Low compliance to thyroid replacement therapy continues to be a major health problem, despite the fact that hypothyroidism is a chronic illness. Nurses have to reinforce significance and impact of higher levels of compliance to thyroid replacement therapy on patient's quality of life **Kumar & Shaukat (2019) & Sulaiman & Al-Saigh (2020) & Reizian et al. (2023)**.

In recent years, there isn't much information available about post thyroidectomy patients' compliance to thyroid replacement **El Helou et al. (2019) & Aqeeli & Hassan (2022)**. Limited number of studies has evaluated patients' compliance to thyroid replacement therapy in different clinical situations and with different methodological approaches **Bocale et al. (2022)**. No sufficient research has been done to yet to size the issue in Egypt. So, the present study highlights compliance of patients toward hormonal replacement therapy post thyroidectomy.

Aim of the Study

The present study aimed to:

- Identify compliance of post thyroidectomy patients to thyroid replacement therapy.

Research questions:

- What is the level of compliance of post thyroidectomy patients to thyroid replacement therapy?
- What are the factors associated with compliance of post thyroidectomy patients to thyroid replacement therapy?

Materials and Method

Materials:

Research design:

A descriptive research design was utilized to conduct the study.

Setting:

The study was carried out at the endocrine outpatient clinic of the Main University Hospital, Alexandria University, Egypt.

Subjects:

A convenient sample of 100 post thyroidectomy patients was selected from patients showing up at the above mentioned setting.

Sample size calculation: The G*Power Windows 3.1.9.7 A program was used with the following parameters to estimate the participants: Power ($1-\beta$ err prob) = 0.95, effect size = 0.25, α err prob = 0.05, number of groups examined = 1, and a dropout rate of approximately 20% **Kang (2021)**. The program identified the minimum sample size as 100 patients.

The patient inclusion criteria:

1. Male and female Adults between the ages of 20 and 60.
2. Post thyroidectomy for at least 6 months and treated with prescribed thyroid replacement therapy.
3. Free from uncontrolled chronic diseases.

Tools of the study:

In order to fulfill the aim of the study, four tools were used for data collection.

Tool I: Bio-Socio-Demographic Data Structured Interview Schedule: It was developed by the researchers based on review of the recent relevant literature **Wilson et al., (2021)** & **Al-Janabi et al., (2022)** to obtain information about bio-socio-demographic data of the studied patients. It consisted of two parts as the following:

Part I: Patients' socio-demographic characteristics: this part was used to collect data about the patient's socio-demographic characteristics such as; age, gender, residence, marital status, level of education, and occupation.

Part II: Patients' clinical data: This part was utilized to obtain data about the clinical history of the patients such as; post-thyroidectomy duration (in Years), thyroid replacement therapy related data (such as

timing of taking medication either in the morning or not and before or after meal), serum levels of T3, T4 and TSH, associated medical disease and family history of thyroid disorders.

Tool II: Post Thyroidectomy Signs and Symptoms of Hypothyroidism

Observational Checklist: It was developed by the researchers based on review of the relevant literature **Bocale et al., (2022)** & **Snyder et al., (2022)** to obtain data about the signs and symptoms of hypothyroidism among the studied patients. It included data such as assessment of vital signs, tenderness of joints, fatigue, dermatologic disorders such as skin dryness, hair loss, cold intolerance, menstrual changes in females, weight changes and GIT disturbances such as anorexia and constipation.

Scoring system:

Each sign and symptom if present was given (1 score), whereas if absent was given (zero score). After then the total score was calculated and converted into number and percentage scores.

Tool III: Medication Compliance Questionnaire (MCQ):

This questionnaire was adapted from **Mendorf & Schöenberg, (2022)** to assess level of patients' compliance to thyroid replacement therapy and it consisted of 8 questions regarding the patient's experience concerning medication taking behavior. These questions were such as asking patients if sometimes forget to take medication, cut back or stopped taking medication, if did not take medication over the past two weeks, forgetting to bring medication when travelling and whether sometimes stop taking medication when feeling better health.

Scoring system:

The MCQ included eight categories; each category of them had response either no=zero or yes=1 and was coded according to a specified rule and used to determine the overall scores, which varied from 0 to 8. Participants answering "no" to all items of the MCQ (score = 0) were identified as highly compliant, while participants with (score = 1-4) were identified as moderately compliant", and (score = 5-7) were identified as poorly or low compliant as well as score 8 or more were identified as non-compliant.

Tool IV: Factors Associated with Compliance of Patients' to Thyroid Replacement Medication Structured Questionnaire:

This tool was adapted from Ge et al., (2023) to assess factors associated with patients' compliance to thyroid replacement medications. It included a total of 17 questions which were categorized in five main dimensions as follows; patient related factors (5 questions), condition related factors (3 questions), therapy related factors (5 questions), social and economic related factors (2 questions), and Healthcare system related factors (2 questions).

Scoring system:

The five dimensions covered a total of 17 statements in the form of questions with Yes = 1 or No = zero answer and the total score of patients' answers was calculated as number and percent.

Method:

The study was accomplished as follows:

- An approval from The Research Ethics Committee, the Dean of the Faculty of Nursing and the Head of the Endocrine Disorders Department at Alexandria Main University Hospital after explaining the study purpose and assuring the privacy, anonymity, and confidentiality of the collected data.
- To carry out the study, formal written consent was acquired from the faculty of nursing and presented to the hospital administrative personnel and directors of nursing services department of the chosen setting.
- Tool I and II were developed by the researchers after review of recent relevant literature Wilson et al., (2021) & Al-Janabi et al., (2022) & Bocale et al., (2022) & Snyder et al., (2022); while tools III and IV were adapted from Mendorf & Schöenberg (2022) & Ge et al. (2023).
- Tools of the study were revised by jury of five experts in the fields of Medical Surgical Nursing and General Surgery for testing tools for content validity, completeness and clarity of the items, and then the necessary modifications were carried out accordingly.
- Reliability of the developed tools was estimated using the Cronbach's Alpha test to measure its internal consistency. It indicated that tools of the study have a reliability $r = 0.75, 0.78, 0.89$ & 0.84 respectively.
- A pilot study was carried out by the researcher on 10 patients to test the clarity and the applicability of the tools and to identify the difficulties that might be faced during the application of the tools. Those patients were excluded from the study sample.

Data collection

Data was gathered over the course of five months, beginning at the end of January and ending at the end of May 2024 and the following steps were considered:

- It was conducted throughout patient's personal interview schedule during the patients' visits for follow up at the study setting.
- The researchers collected data using the study tools during scheduled interview for two times of patients' follow up visits with every patient of the study sample on an individual base in the waiting room of the out-patient clinic for 30-45 minutes.
- The studied patients' socio-demographic and clinical data was initially obtained using tool I.
- Comprehensive assessment of the studied patients for the presence of signs and symptoms of hypothyroidism using tool II was done through the following:
 - Measuring vital signs.
 - Performing head to toe assessment by using four techniques of physical examination.
 - Estimation of body mass index to assess weight changes through measuring patients' heights in square meter and weight in kilograms using the clinic's scale then BMI was calculated. Comparison of pre-thyroidectomy patients' BMI with present estimation was done subsequently.
 - Reviewing patients' medical records to collect necessary data regarding past and present history, current associated diseases and medications as well as results of laboratory investigations.

- The total score of tool III was calculated for all studied patients accordingly the studied patients' level of compliance to thyroid replacement medication either low, moderate or high compliance was determined.
- The studied patients were assessed using tool IV to determine factors associated with their compliance to thyroid replacement medication then a comparison was conducted to evaluate the differences between them in relation to these factors.

Ethical considerations:

- An official approval was obtained from The Research Ethics Committee of Faculty of Nursing, Alexandria University for carrying out this study.
- All patients who were being studied were informed of the study's aim, and prior to their involvement, their consent and readiness to be included in the study were first acquired.
- Before beginning the study, all patients received assurances regarding their privacy and the confidentiality of their data.
- The recruited patients were informed that participation in the study is voluntary, and they can withdraw at any time.

Statistical analysis of the data

- Data were fed to the computer and analyzed using IBM SPSS software package version 23.0 **Patel (2021) & Turney (2023)**.
- Qualitative data were described using number and percent.
- Significance of the obtained results was judged at the 5% level.
- The used tests were:
 - 1 - **Chi-square test:** For categorical variables, to compare between different groups
 - 2- **Monte Carlo correction:** Correction for chi-square when more than 20% of the cells have expected count less than 5.

RESULTS

Table (1) shows the studied patients' socio-demographic characteristics. It revealed that

the highest percentages of the studied post thyroidectomy patients were in the age group (30 < 40 years), female and illiterate (40.0 %, 63.0%, 57.0%) respectively. In relation to the patients' marital status, occupation and residence, it can be noticed that the highest percentage of them were married, un-employed and from urban (60.0%, 49.0%, 76.0%) respectively.

Table (2) Shows the studied patients' clinical data. The table illustrated that more than half of the studied patients (56.0%) had associated diseases and family history of thyroidectomy (59.0%). Additionally, it can be noticed that nearly half of the studied post thyroidectomy patients (45.0%) had less than year post thyroidectomy period. As regards timing of thyroid replacement therapy, more than two thirds of the studied patients (71.0%) had their medication at any time rather than taking it one hour before breakfast. The table also revealed that nearly half of patients (47.0%) had abnormal laboratory values of thyroid hormones.

Table (3) shows the studied patients' signs and symptoms of hypothyroidism. In relation to signs and symptoms of hypothyroidism, it can be noticed that nearly half of the studied patients had hypothermia, bradycardia, hypotension, anorexia and weight gain as weight changes post thyroidectomy (42.0%, 46.0%, 48.0%, 49.0% and 48.0%) respectively. Also, it illustrates that about two thirds of studied patients had dyspnea and hair loss (66.0% and 69.0%) respectively. In addition, the vast majority of them (90.0%) had joint pain and fatigue.

Table (4) shows the studied patients level of compliance to thyroid replacement therapy .

This table reveals that more than half of the studied post thyroidectomy patients (59.0%) had low level of compliance, while (19.0%) of them had moderate level and only (22.0%) had higher level of compliance to thyroid replacement medication.

Table (5): Presents factors associated with compliance of the studied patients to thyroid replacement therapy. It can be noticed from the table that the majority of

studied patients emphasized that their potential causes of low levels of compliance might be due to several factors related to patients themselves, for example; they did not comprehend or know how to read the information on the labels of the medication, they did not comprehend the necessity of taking this medication or the significance of following the instructions. and just forgot (62.0%, 63.0%, and 70.0%) respectively. Moreover, therapy related factors were such as they had problems with taking medication at specific time, they took many drugs at various intervals throughout the day, and they wanted to avoid side effects (70.0%, 46.0%, and 79.0%) respectively. Regarding the studied post thyroidectomy patients' condition related factors, the table revealed that (63.0 %) of them felt sad, down, or blue. Considerable factors about doctor did not involve patients in their treatment choices and they had run out of medication could be noticed as regards health care related factors (100.0% and 57.0%) respectively. The table also clarifies that (68.0%) of the studied post thyroidectomy patients stated that medication was too expensive in relation to socio-economic factors of non-compliance.

Table (6): Displays relation between the studied patients' level of compliance and their socio-demographic characteristics. The table reveals that the studied patients' age, level of education and marital status were significantly associated with their level of compliance to thyroid replacement therapy, where $p = <0.001$, <0.001 and <0.001 respectively.

Table (7): Shows Relation between the studied patients' level of compliance and their clinical data. The table shows that post thyroidectomy duration, timing of thyroid replacement therapy and laboratory values of

thyroid hormones had statistically significant associations with the studied patients' level of compliance to thyroid replacement therapy, where $p = <0.001$, <0.001 and <0.001 respectively.

Tables (8): Reveals Relation between the studied patients' level of compliance and signs & symptoms of hypothyroidism. The table clarifies that certain signs of hypothyroidism such as dyspnea, hypotension, anorexia, hair loss and weight changes were significantly associated with the studied patients' level of compliance to thyroid replacement therapy, where $p = <0.001$, 0.002 , <0.001 , <0.001 and <0.001 respectively.

Table (9): Presents relation between the studied patients' level of compliance and factors associated with their compliance to therapy. It can be noticed from this table that statistical significant associations were found between level of compliance to thyroid replacement therapy and patient related factors such as they did not comprehend or know how to read the information on the labels of the medication, did not comprehend the necessity of taking this medication or the significance of following the instructions. and just forgot, $p = <0.001$, <0.001 and <0.001 respectively. As regards therapy related causes, there were significant associations between level of compliance and factors such as patients had problems with taking medication at specific time and doctor frequently changed their therapy, where $p = <0.001$ and <0.001 respectively. Other factors such as the studied patients felt sad (condition related causes), they had run out of medication (e.g., did not get refills on time, medication was not available as a health care system related factors) and medication was expensive as a socio-economic causes had statistically significant associations with the studied patients' level of compliance.

Table (1): The Studied Patients' Socio-demographic Characteristics (n= 100)

Patient's socio-demographic data	No.	%
Patient age		
20 < 30	28	28.0
30 < 40	40	40.0
40 – 60	32	32.0
Gender		
Male	37	37.0
Female	63	63.0
Educational level		
Illiterate	57	57.0
Primary	13	13.0
Secondary	9	9.0
Bachelor	21	21.0
Marital status		
Single	40	40.0
Married	60	60.0
Occupation		
Unemployed	49	49.0
Manual work	43	43.0
Sedentary work	8	8.0
Residence		
Urban	76	76.0
Rural	24	24.0

Table (2): The Studied Patients' Clinical Data (n= 100)

Patient's clinical data:	No.	%
Associated diseases		
No	44	44.0
Yes	56	56.0
Family history of thyroidectomy		
No	41	41.0
Yes	59	59.0
Duration post thyroidectomy		
Less than 1 year	45	45.0
1 – 3 year	20	20.0
More than 3 year	35	35.0
Medications Timing		
1 hour before breakfast	29	29.0
any time	71	71.0
Laboratory investigations		
Thyroid hormones tests		
Normal	53	53.0
Abnormal	47	47.0

Table (3): The Studied Patients' Signs and Symptoms of Hypothyroidism (n= 100)

Signs and symptoms of hypothyroidism	No.	%
Vital signs:		
Hypothermia		
No	58	58.0
Yes	42	42.0
Dyspnea		
No	34	34.0
Yes	66	66.0
Bradycardia		
No	54	54.0
Yes	46	46.0
Hypotension		
No	52	52.0
Yes	48	48.0
GIT manifestations:		
Abdominal distension		
No	79	79.0
Yes	21	21.0
Constipation		
No	84	84.0
Yes	16	16.0
Anorexia		
No	51	51.0
Yes	49	49.0
Dermatological manifestations:		
Cold intolerance		
No	68	68.0
Yes	32	32.0
Skin Dryness		
No	90	90.0
Yes	10	10.0
Hair loss		
No	31	31.0
Yes	69	69.0
Musculoskeletal manifestations:		
Joints pain		
No	10	10.0
Yes	90	90.0
Fatigue		
No	10	10.0
Yes	90	90.0
Menstrual changes (for females)		
No	43	43.0
Yes	20	20.0
Weight changes:		
No	32	32.0
Gain	48	48.0
Loss	20	20.0

Table (4): The Studied Patients Level of Compliance to Thyroid Replacement Therapy (n= 100)

	Items	Yes		No	
		No.	%	No.	%
1	Forget to take medications.	68	68.0	32	32.0
2	Did not take medication for any reason other than forgetting during the past two weeks.	68	68.0	32	32.0
3	Stop taking medication because of feeling worse with taking it without telling doctor.	54	54.0	46	46.0
4	When travelling or leaving home, sometimes forget to bring medication.	67	67.0	33	33.0
5	Yesterday, did you take your medication ?	98	98.0	2	2.0
6	Stop taking medication when feeling better health and lab tests of thyroid hormone values is normal.	2	2.0	98	98.0
7	Taking medication every day is a real inconvenience and very boring.	59	59.0	41	41.0
8	How often do you have trouble remembering to take all of your medications?				
	Never	32		32.0	
	Once	0		0.0	
	Sometimes	9		9.0	
	Usually	31		31.0	
	All the time	28		28.0	
Total level of compliance					
	Low compliance	59		59.0	
	Moderate compliance	19		19.0	
	High compliance	22		22.0	

Table (5): Factors Associated with Compliance of the Studied Patients to Thyroid Replacement Therapy (n= 100)

	Factors associated with medication compliance	No		Yes	
		No.	%	No.	%
1- Patient-related					
1	Did not see any benefit in taking the medication.	89	89.0	11	11.0
2	Did not comprehend or know how to read the information on the labels of the medication ?.	38	38.0	62	62.0
3	Did not comprehend the necessity of taking this medication or the significance of following the instructions.	37	37.0	63	63.0
4	Fearful of being dependent on drugs or concerned about the long-term consequences of my prescription drugs.	60	60.0	40	40.0
5	Just forget.	30	30.0	70	70.0
2- Therapy-related					
6	Problems with taking medication at certain times (e.g., on an empty stomach, early in the morning).	30	30.0	70	70.0
7	Taking several medications several times a day.	54	54.0	46	46.0
8	Medication regimen is too complex (e.g., cut tablets, still fasting for an hour after taking medication).	100	100.0	0	0.0
9	Want to avoid side effects.	21	21.0	79	79.0
10	Doctor frequently changes medication.	56	56.0	44	44.0
3- Condition-related					
11	Feeling sad, down, or blue.	37	37.0	63	63.0
12	Physical difficulty in opening / administering medications.	98	98.0	2	2.0
13	It is hard to swallow the medication.	100	100.0	0	0.0
4- Healthcare system-related					
14	Doctor did not involve patient in treatment choices.	0	0.0	100	100.0
15	Run out of medication (e.g., did not get refills on time, medication was not available, need substitute).	43	43.0	57	57.0
5- Social/economic					
16	Feeling embarrassed when other people knows about taking medication.	100	100.0	0	0.0
17	The medication is too expensive.	32	32.0	68	68.0

Table (6): Relation between The Studied Patients' Level of Compliance and Their Socio-demographic Characteristics (n= 100)

1) Patient's socio demographic data	Level of compliance						χ^2	MCp
	Low (n=59)		Medium (n=19)		High (n=22)			
	No.	%	No.	%	No.	%		
Patient age								
20 – 30	24	40.7%	0	0.0%	4	18.2%	26.913*	<0.001*
30 – 40	27	45.8%	8	42.1%	5	22.7%		
40 – 60	8	13.6%	11	57.9%	13	59.1%		
Gender								
Male	18	30.5%	10	52.6%	9	40.9%	3.202	0.202
Female	41	69.5%	9	47.4%	13	59.1%		
Educational level								
Illiterate	51	86.6%	3	15.7%	3	13.6%	47.023*	<0.001*
Primary	4	6.7%	8	42.2%	1	4.5%		
Secondary	0	0.0%	1	5.3%	8	36.3%		
Bachelor	4	6.7%	7	36.8%	10	45.6%		
Marital status								
Single	18	30.5%	3	15.8%	19	86.4%	26.612*	<0.001*
Married	41	69.5%	16	84.2%	3	13.6%		
Occupation								
Unemployed	30	50.8%	11	57.9%	8	36.4%	3.817	0.921
Manual work	29	49.2%	0	0.0%	14	63.6%		
Sedentary work	0	0.0%	8	42.1%	0	0.0%		
Residence								
Urban	48	81.3%	17	89.4%	11	50.0%	1.966	0.286
Rural	11	18.7%	2	10.6%	11	50.0%		

 χ^2 : Chi square test

MC: Monte Carlo

*: Statistically significant at $p \leq 0.05$ **Table (7):** Relation between the Studied Patients' Level of Compliance and Their Clinical Data (n= 100)

2) Patient's clinical data:	Level of compliance						χ^2	MCp
	Low (n=59)		Medium (n=19)		High (n=22)			
	No.	No.	No.	No.	No.	No.		
Associated diseases								
No	26	44.0%	9	47.4%	9	40.9%	2.995	0.446
Yes	33	56.0%	10	52.6%	13	59.1%		
Family history								
No	21	35.5%	8	42.1%	12	54.5%	0.736	0.378
Yes	38	64.5%	11	57.9%	10	45.5%		
Duration post thyroidectomy								
Less than 1 year	22	37.2%	8	42.1%	15	68.1%	43.115*	<0.001*
1 – 3 years	10	16.9%	6	31.5%	4	18.1%		
More than 3 years	27	45.9%	5	26.4%	3	13.8%		
Medications Timing								
1 hour before breakfast	3	5.1%	8	42.1%	18	81.8%	47.781*	<0.001*
any time	56	94.9%	11	57.9%	4	18.2%		
Laboratory investigations								
Thyroid hormones tests								
Normal	21	35.6%	10	52.6%	22	100.0%	26.687*	<0.001*
Abnormal	38	64.4%	9	47.4%	0	0.0%		

 χ^2 : Chi square test

MC: Monte Carlo

*: Statistically significant at $p \leq 0.05$

Table (8): Relation between the Studied Patients' Level of Compliance and Signs and Symptoms of Hypothyroidism (n= 100)

Signs of hypothyroidism	Level of compliance						χ^2	MCp
	Low (n=59)		Medium (n=19)		High (n=22)			
	No.	No.	No.	No.	No.	No.		
Vital signs								
Hypothermia								
No	39	66.1%	10	52.6%	9	40.9%	1.810	0.439
Yes	20	33.9%	9	47.4%	13	59.1%		
Dyspnea								
No	2	3.4%	10	52.6%	22	100.0%	72.281*	<0.001*
Yes	57	96.6%	9	47.4%	0	0.0%		
Bradycardia								
No	34	23.7%	8	42.1%	12	54.5%	0.867	0.094
Yes	25	76.3%	11	57.9%	10	45.5%		
Hypotension								
No	20	33.9%	10	52.6%	22	100.0%	12.787*	0.002*
Yes	39	66.1%	9	47.4%	0	0.0%		
GIT manifestations								
Abdominal distension								
No	47	79.7%	10	52.6%	22	100.0%	0.672	0.511
Yes	12	20.3%	9	47.4%	0	0.0%		
Constipation								
No	47	79.7%	17	89.5%	20	90.9%	0.743	0.904
Yes	12	20.3%	2	10.5%	2	9.1%		
Anorexia								
No	21	35.6%	10	52.6%	20	90.9%	34.996*	<0.001*
Yes	38	64.4%	9	47.4%	2	9.1%		
Dermatological manifestations								
Cold intolerance								
No	39	66.1%	17	89.5%	12	54.5%	0.530	0.602
Yes	20	33.9%	2	10.5%	10	45.5%		
Skin Dryness								
No	49	83.1%	19	100.0%	22	100.0%	2.781	0.279
Yes	10	16.9%	0	0.0%	0	0.0%		
Hair loss								
No	0	0.0%	17	89.5%	14	63.7%	92.478*	<0.001*
Yes	59	100.0%	2	10.5%	8	36.3%		
Musculoskeletal manifestations								
Joints pain								
No	0	0.0%	10	52.6%	0	0.0%	3.730	0.418
Yes	59	100.0%	9	47.4%	22	100.0%		
Fatigue								
No	0	0.0%	10	52.6%	0	0.0%	3.730	0.418
Yes	59	100.0%	9	47.4%	22	100.0%		
Menstrual changes								
No	21	35.6%	9	47.4%	13	59.1%	1.661	0.721
Yes	20	33.9%	0	0.0%	0	0.0%		
Not applicable	18	30.5%	10	52.6%	9	40.9%		
Weight changes								
No	0	0.0%	10	52.6%	22	100.0%	89.378*	<0.001*
Gain	39	66.2%	9	47.4%	0	0.0%		
Loss	20	33.8%	0	0.0%	0	0.0%		

 χ^2 : Chi square test

MC: Monte Carlo

*: Statistically significant at $p \leq 0.05$

Table (9): Relation between level of compliance of the studied patients and factors associated with their compliance to therapy (n= 100)

Factors associated with medication compliance	Level of compliance						χ^2	MC p
	Low (n=59)		Medium (n=19)		High (n=22)			
	No.	No.	No.	No.	No.	No.		
Patient-related								
1 Did not see any benefit in taking the medication.								
No	59	100.0%	8	42.1%	22	100.0%	1.167	0.982
Yes	0	0.0%	11	57.9%	0	0.0%		
2 Did not comprehend or know how to read the information on the labels of the medication ?								
No	7	11.9%	9	47.4%	22	100.0%	53.708*	<0.001*
Yes	52	88.1%	10	52.6%	0	0.0%		
3 Did not comprehend the necessity of taking this medication or the significance of following the instructions.								
No	7	11.9%	8	42.1%	22	100.0%	53.663*	<0.001*
Yes	52	88.1%	11	57.9%	0	0.0%		
4 Fearful of being dependent on drugs or concerned about the long-term consequences of my prescription drugs.								
No	34	57.6%	17	89.5%	9	40.9%	3.188	0.642
Yes	25	42.4%	2	10.5%	13	59.1%		
5 Just forget.								
No	0	0.0%	8	42.1%	22	100.0%	77.945*	<0.001*
Yes	59	100.0%	11	57.9%	0	0.0%		
Therapy-related								
6 Problems with taking medication at specific time (e.g., on an empty stomach, early in the morning).								
No	0	0.0%	8	42.1%	22	100.0%	25.468*	<0.001*
Yes	59	100.0%	11	57.9%	0	0.0%		
7 Taking several medications several times a day.								
No	27	62.7%	10	52.6%	17	77.2%	1.154	0.238
Yes	32	37.3%	9	47.4%	5	22.8%		
8 Medication regimen is too complex (e.g., cut tablets, still fasting for an hour after taking medication).								
No	59	100.0%	19	100.0%	22	100.0%	0.231	0.425
Yes	0	0.0%	0	0.0%	0	0.0%		
9 Want to avoid side effects.								
No	21	35.6%	0	0.0%	0	0.0%	1.817	0.811
Yes	38	64.4%	19	100.0%	22	100.0%		
10 Doctor frequently changes medication.								
No	26	44.1%	8	42.1%	22	100.0%	22.184*	<0.001*
Yes	33	55.9%	11	57.9%	0	0.0%		
Condition-related								
11 Feeling sad, down, or blue.								
No	7	11.9%	8	42.1%	22	100.0%	53.663*	<0.001*
Yes	52	88.1%	11	57.9%	0	0.0%		
12 Physical difficulty in opening / administering medications.								
No	59	100.0%	17	89.5%	22	100.0%		

Factors associated with medication compliance	Level of compliance						χ^2	MCp
	Low (n=59)		Medium (n=19)		High (n=22)			
	No.	No.	No.	No.	No.	No.		
13 It is hard to swallow the medication.	0	0.0%	2	10.5%	0	0.0%	0.412	0.533
No	59	100.0%	19	100.0%	22	100.0%		
Yes	0	0.0%	0	0.0%	0	0.0%	2.945	0.157
Healthcare system-related								
14 Doctor did not involve patient in treatment choices.								
No	0	0.0%	0	0.0%	0	0.0%		
Yes	59	100.0%	19	100.0%	22	100.0%	0.593	0.956
15 Run out of medication (e.g., did not get refills on time, medication was not available, need substitute).								
No	21	35.6%	0	0.0%	22	100.0%		
Yes	38	64.4%	19	100.0%	0	0.0%	44.817*	<0.001*
Social/economic								
16 Feeling embarrassed when other people knows about taking medication.								
No	59	100.0%	19	100.0%	22	100.0%		
Yes	0	0.0%	0	0.0%	0	0.0%	0.189	0.205
17 The medication is too expensive.								
No	0	0.0%	10	52.6%	22	100.0%		
Yes	59	100.0%	9	47.4%	0	0.0%	78.231*	<0.001*

 χ^2 : Chi square test

MC: Monte Carlo

*: Statistically significant at $p \leq 0.05$

Discussion

Many patients following total thyroidectomy may fail to obtain normal Thyroid Stimulating Hormone (TSH) levels and may be affected with hypothyroidism, the most common consequence following thyroidectomy **Al-Janabi et al. (2022)**. Management guidelines for patients following thyroidectomy advise constant lifelong thyroid hormone replacement treatment. Identifying barriers and factors influencing patient compliance to replacement treatment can improve the effectiveness of treatment and prevent further complications **Kilit et al. (2022)**. So, the aim of this study was to assess compliance of post thyroidectomy patients to thyroid replacement therapy.

Socio-demographic characteristics of the studied patients and its relation with their level of compliance to thyroid replacement therapy:

The present study showed that the highest percentages of the studied patients were in the age group (30 < 40 years), female, married, illiterate, un-employed and living in urban. These findings were congruent with **Abd Elazeem et al. (2020)** in their study who reported that their studied participants were mostly married women aged 30

to 40. In addition, **El Shafaey et al. (2022)** in their previous study verified that concerning educational level, nearly half of the control group were illiterate compared to less than half of patients in the study group who could read and write. They also found that the majority of patients in both the study and control group were housewives. Additionally, **Machado-Alba & Machado-Duque. (2020)** in their similar study stated that the vast majority of patients were of urban residence.

The current study results also illustrated that the studied patients' age, level of education and marital status all were significantly associated with their level of compliance to thyroid replacement therapy. In this context, findings of the present study indicated that married and illiterate patients aged 30-40 had a low level of compliance. This finding is in agreement with **El Helou et al. (2019)** who confirmed a notable and favorable statistical relationship between the medication adherence score and age. Moreover, **Kilit et al. (2022)** shown in their similar previously conducted study that patients with university education presented significantly higher compliance to medication compared to those who were illiterate.

Moreover, According to the researchers, these results may be attributed to social stressors of marriage especially in this age group that may impair compliance to medication by affecting cognitive abilities and memory. Married patients also could forget to take their medication since they have many responsibility and financial issue. Furthermore, the majority of patients were illiterate i.e. had lack of knowledge about thyroid replacement therapy so; they could not understand either medication's instructions or the importance of taking hormonal replacement medications daily throughout life.

Clinical data of the studied patients and its relation with their level of compliance to thyroid replacement therapy:

According to the current study's findings, over half of the patients had a family history of thyroidectomy and related medical conditions. Furthermore, about half of them saw a recovery period of less than a year following thyroidectomy. These results were consistent with in their study, **El Hefny et al. (2021)** verified that most of the patients they examined had related medical disorders. Also, **Alhemedi et al. (2024)** mentioned that more than half of patients stated that thyroid disorders run in their family. Regarding the timing of thyroid replacement therapy, nearly two thirds of the studied patients had their medication at any time rather than taking it one hour before breakfast. It may be justified by the psychological stress and frustration that patients experience from having family members with the disease, as well as from adequate suffering from other illnesses and regular medicine use.

This result aligned with the findings of a study by **Yavuz (2022)**, who confirmed that nearly all of the patients in the study took their medications just before breakfast without waiting an hour, indicating that they were not compliant to the medication's right timing. As for laboratory values, nearly half of the studied patients had abnormal thyroid hormone levels. This result was supported by **Al-Janabi et al., (2022)** in their study who found that patients with hypothyroidism had markedly higher thyroid-stimulating hormone levels when they were at a hypothyroid stage.

The present study demonstrates statistically significant relationships between the patients'

degree of compliance with post thyroidectomy duration, timing of thyroid replacement therapy and laboratory values of thyroid hormones. This finding was disproved by **Haskard-Zolnierok et al., (2022)** who found no significant difference in the time after thyroidectomy among the patients they examined. Furthermore, according to **Al Kindi et al., (2023)** there were no discernible significant relationships between the degree of medication compliance and clinical or sociodemographic characteristics, including age, gender, education, length of therapy, and family history of thyroid illness.

These findings could be the result of illiteracy, a lack of understanding of the significance of adhering to lifelong treatment, the fact that the patients were less than a year after their thyroidectomy, which indicates that they were only now becoming aware of their conditions, and a lack of familiarity with their treatment plan. Therefore, it was obvious and logical that they had thyroid hormonal disorders, as demonstrated by the results of laboratory tests.

The studied patients signs and symptoms of hypothyroidism and its relation with compliance to thyroid replacement therapy:

According to the study's findings, almost half of the patients had weight gain, anorexia, bradycardia, hypotension, and hypothermia. Additionally, hair loss and dyspnea affected around two-thirds of the patients in the study. **Matsuura et al. (2023)** confirmed this finding, stating that the patient's dyspnea was the most worrisome symptom. Additionally, bradycardia, pericardial effusion, and a little difference between systolic and diastolic blood pressure are common cardiovascular signs of hypothyroidism. In the same context, **Huynh et al. (2021)** in their study displayed that most studies indicate that the majority of patients experience weight gain after total thyroidectomy, with the most significant weight gain happening in the first two years post-surgery.

The current study confirmed that joint pain and fatigue were experienced by the great majority of patients. This finding could be may be connected to the direct role that thyroid hormones play in the cellular development and specialization of bone and cartilage. Additionally, this result was proved by **Garg & Aggarwal (2021)** who mentioned that thyroid hormones are

essential for controlling bone maintenance in adults and for skeletal development. Also, confirmed that hypothyroidism is frequently linked to problems with bones and joints.

The results demonstrated a significant correlation between the investigated patients' degree of compliance to thyroid replacement therapy and specific symptoms of hypothyroidism, including dyspnea, hypotension, anorexia, hair loss, and weight fluctuations. The majority of patients who reported these symptoms did so with lower levels of compliance. **Kebbab et al., (2022)** and **Snyder et al., (2022)** supported this finding by confirming the substantial and positive correlations between hair loss, weight changes, and low therapy compliance. Thyroid dysfunction, decreased serum thyroid hormones, and its impact on metabolism and other bodily systems could be the cause.

The studied patients' level of compliance to thyroid replacement therapy:

According to the results of the current study, over half of the post thyroidectomy patients under investigation had low levels of compliance with thyroid replacement therapy. This finding was supported by similar studies carried out in Lebanon and Oman by **El Helou et al., (2019)** and **Al Kindi et al., (2023)**, who explained that the great majority of their patients had poor adherence to levothyroxine treatment, perhaps as a result of a lack of awareness about the condition and the importance of maintaining a balanced thyroid state. Additionally, **Alofi et al., (2023)** in their research found that most participants nearly two thirds had low adherence to taking thyroid replacement medication.

Factors associated with compliance of the studied patients to thyroid replacement therapy:

The majority of the patients in the current study reported that a number of factors with statistically significant relationships could be the cause of their low compliance levels. For instance, patient-related issues include, they did not comprehend or know how to read the information on the labels of the medication, they did not comprehend the necessity of taking this medication or the significance of following the instructions, and just forgot. This might be the consequence of patients not receiving enough

information on the value of their medications and the fact that most of them were illiterate. **Chauke et al., (2022)** concurred with this conclusion, stating that patients' ignorance of and dissatisfaction with their medications are powerful predictors of prescription non-compliance.

Additionally, the current study confirmed that therapy-related factors included patients' inability to take their medication at the appropriate time, their desire to prevent side effects, and the fact that they took multiple medications throughout the day. The same conclusion was supported by **Aljofan., (2023)**, who noted that the higher frequency of medicine taken during the day due to the existence of related medical problems may be one factor contributing to the low level of medication compliance in the populations under study.

Considering patients' condition related factors, the study revealed that more than half of the studied patients felt sad, down, or blue. This result was supported by **Ge et al., (2023)** in their research who clarified that higher risk of experiencing depressive symptoms was consistently associated with low level of medication compliance.

Regarding health care-related factors, the results of the current study showed that patients had run out of medication and that doctors did not involve them in their treatment decisions. This may be linked to inadequate communication between patients and physicians, as well as the infrequent unavailability of thyroid replacement drugs, which may cause physicians to switch to alternative treatments without informing patients. Lastly, the vast majority of patients claimed that the high cost of their medications could be explained by their lack of employment, low socioeconomic standing, and even lack of health insurance.

Accordingly, patient participation in treatment choices is probably going to increase compliance. Healthcare professionals should therefore work with patients to resolve any medication-related issues they may have. **Aljofan et al., (2023)** In conclusion, a variety of strategies are advised to enhance compliance to hypothyroidism treatment. Comprehensive patient education, frequent visits to the same physician, screenings, participation in community health events, and the use of a

multidisciplinary care approach are some of these strategies. **Alhemedi et al., (2024)**

Conclusion

In conclusion, the results of the current study confirmed that more than half of the studied patients showed a decreased degree of compliance to thyroid replacement treatment. Most of them displayed symptoms of hypothyroidism, including weight gain, anorexia, hypotension, dyspnea, and hair loss; these symptoms were all statistically linked to poor therapy compliance. Additionally, there were strong statistically significant correlations between the patients' clinical and socio-demographic characteristics such as age, marital status, education level, medication timing, and thyroid hormone laboratory values and their degree of compliance to replacement therapy. Furthermore, statistically significant relationships were found between low levels of thyroid hormone replacement therapy compliance and a number of related factors, including the high cost of the medication, the fact that the patients simply forgot to take it, and their inability to read or comprehend the information on the medication labels.

Recommendations

In light of the study's findings, the following recommendations are suggested:

The current study should be replicated with a larger statistical sample size drawn from different geographic locations and with a longer follow-up in order to produce more broadly applicable findings.

References

- Abd Elazeem, Y. F., Abdel-Karim, N. E., & Aly, E. F. (2020).** Effect of Perioperative Instructions on Postoperative Discomforts and Satisfaction Level among Patients Undergoing Thyroidectomy. *Evidence-Based Nursing Research*, 2(1), 12-12.
- Al Kindi, R. M., Al Riyami, R. A., Juma, S. Y., & Al Kiyumi, M. I. (2023).** Adherence to levothyroxine treatment among patients with hypothyroidism in Oman: a national cross-sectional study. *Current Medical Research and Opinion*, 39(10), 1313-1319.

- Alhemedi, A. J., Qasaimeh, M. G., Alzoubia, S., Alhallaq, L. S., Alzoubi, N., AlAzzam, R., ... & Naser, A. Y. (2024).** Adherence to thyroid therapy and depressive status among patients with hypothyroidism in the northern of Jordan: A cross-sectional study. *Medicine*, 103(6), e37181.
- Al-Janabi, G., Hassan, H. N., & Al-Fahham, A. (2022).** Biochemical changes in patients during hypothyroid phase after thyroidectomy. *Journal of Medicine and Life*, 15(1), 104.
- Aljofan, M., Oshibayeva, A., Moldaliyev, I., Saruarov, Y., Maulenkul, T., & Gaipov, A. (2023).** The rate of medication nonadherence and influencing factors: A systematic Review. *Electronic Journal of General Medicine*, 20(3).
- Alofi, R. M., Alrohaily, L. S., Jan, R. A., Alsaedi, S. L., Mahrous, F. A., & Alreefi, M. M. (2023).** Adherence to Levothyroxine Treatment Among Patients With Hypothyroidism in Madinah, Saudi Arabia: A Cross-Sectional Study. *Cureus*, 15(6).
- Aqeli, M. J. S., & Hassan, H. S. (2022).** Evaluation of Hypothyroidism Patients' Compliance to Thyroxine Drug in Baghdad City. *Teikyo Medical Journal* ISSN, 3875547.
- Aremu, T. O., Oluwole, O. E., Adeyinka, K. O., & Schommer, J. C. (2022).** Medication adherence and compliance: recipe for improving patient outcomes. *Pharmacy*, 10(5), 106.
- Basım, P., Argun, D., & Özdenkaya, Y. (2021).** Self-reported medication adherence in differentiated thyroid cancer survivors: Role of illness perception and medication beliefs. *Head & Neck*, 43(2), 428-437.
- Bocale, R., Desideri, G., Barini, A., D'Amore, A., Boscherini, M., Necozone, S., & Lombardi, C. P. (2022).** Long-term adherence to levothyroxine replacement therapy in thyroidectomized patients. *Journal of Clinical Medicine*, 11(15), 4296.
- Chauke, G. D., Nakwafila, O., Chibi, B., Sartorius, B., & Mashamba-Thompson, T. (2022).** Factors influencing poor

- medication adherence amongst patients with chronic disease in low-and-middle-income countries: A systematic scoping review. *Heliyon*, 8(6).
- Culig, J., & Leppee, M. (2014).** From Morisky to Hill-bone; self-reports scales for measuring adherence to medication. *Collegium antropologicum*, 38(1), 55-62.
- El Helou, S., Hallit, S., Awada, S., Al-Hajje, A., Rachidi, S., Bawab, W., ... & Zein, S. (2019).** Adherence to levothyroxine among patients with hypothyroidism in Lebanon. *EMHJ*, 25(3-2019).
- ELHEFNY, A. M., HASSAN, S. T., HOSSAM, S., AHMED, Y. E., & EMAD, G. (2021).** Early Prediction of Post Total Thyroidectomy Hypocalcaemia: Prospective Study. *The Medical Journal of Cairo University*, 89(March), 145-154.
- Feldt-Rasmussen, U., Effraimidis, G., Bliddal, S., & Klose, M. (2024).** Consequences of undertreatment of hypothyroidism. *Endocrine*, 84(2), 301-308.
- Garg, M., & Aggarwal, D. (2021).** Bone and joint manifestations in 25 hypothyroidism patients: a case series. *Journal of Advanced Medical and Dental Sciences Research*, 9(3), 127-129.
- Ge, L., Heng, B. H., & Yap, C. W. (2023).** Understanding reasons and determinants of medication non-adherence in community-dwelling adults: a cross-sectional study comparing young and older age groups. *BMC Health Services Research*, 23(1), 905.
- Gudeta, D. B., Leta, K., Alemu, B., & Kandula, U. R. (2023).** Medication adherence and associated factors among psychiatry patients at Asella Referral and Teaching Hospital in Oromia, Ethiopia: Institution based cross sectional study. *Plos one*, 18(4), e0283829.
- Haskard-Zolnierok, K., Wilson, C., Pruin, J., Deason, R., & Howard, K. (2022).** The relationship between brain fog and medication adherence for individuals with hypothyroidism. *Clinical Nursing Research*, 31(3), 445-452.
- Huynh, C. N., Pearce, J. V., Kang, L., & Celi, F. S. (2021).** Weight gain after thyroidectomy: A systematic review and meta-analysis. *The Journal of Clinical Endocrinology & Metabolism*, 106(1), 282-291.
- I El Shafaey, M., R Attia, N., A Elnemr, A., & A Salem, F. (2022).** Efficacy of Implementing Pre and Postoperative Protocol of Nursing Care on Postthyroidectomy Patients' Clinical Outcomes. *Egyptian Journal of Health Care*, 13(1), 528-545.
- Kamath, K., Mariam, S., Shifnaz, N. P., & Shabaraya, A. R. (2022).** A COMMUNITY BASED STUDY TO EVALUATE PHARMACIST INTERVENTION IN IMPROVING MEDICATION ADHERENCE AMONG PATIENTS WITH HYPOTHYROIDISM.
- Kang H. Sample size determination and power analysis using the G* Power software. J Educ Eval Health Prof. 2021;18. <https://doi.org/10.3352/jeehp.2021.18.17> .**
- Karunarathna, I., Disanayaka, D., & Kurukulasooriya, P. (2024).** Anaesthetic Challenges and Complications in Thyroidectomy Patients: A Comprehensive Review. *Uva Clinical Lab*. Retrieved from Anaesthetic Challenges and Complications in Thyroidectomy Patients: A Comprehensive Review.
- Kebbab, D. M., El-Naby, A., El-said, S. M., Fouad, S. H., & Hasanin, K. M. E. H. (2022).** Thyroid Functions in Patients with Diffuse Hair Loss. *The Egyptian Journal of Hospital Medicine*, 89(2), 7321-7327.
- Khoiry, Q. A., Alfian, S. D., Van Boven, J. F., & Abdulah, R. (2023).** Self-reported medication adherence instruments and their applicability in low-middle income countries: a scoping review. *Frontiers in public health*, 11, 1104510.
- Kilit, I. T. P., Özyiğit, F., & Onbaşı, K. (2022).** IS DRUG ADHERENCE IN HYPOTHYROIDISM TREATMENT STILL A PROBLEM?. *Nobel Medicus Journal*, 18(1).

- Kumar, R., & Shaukat, F. (2019).** Adherence to levothyroxine tablet in patients with hypothyroidism. *Cureus*, 11(5).
- Machado-Alba, J. E., & Machado-Duque, M. E. (2020).** Adherence to levothyroxine prescription in patients with hypothyroidism. *Rev Med Chil*, 148(6), 740-745.
- Mansy, I., Elsenosy, A. M., Hassan, E. M., & Zakria, M. (2023).** A Clinical Audit of Thyroid Hormonal Replacement After Total Thyroidectomy. *Cureus*, 15(12).
- Matsuura, N., Saitou, K., & Hidaka, H. (2023).** Generalized pitting edema in a patient with dilated cardiomyopathy secondary to hypothyroidism. *CMAJ*, 195(1), E10-E13.
- Mendorf, S., Prell, T., & Schöenberg, A. (2022).** Detecting reasons for nonadherence to medication in adults with epilepsy: a review of self-report measures and key predictors. *Journal of Clinical Medicine*, 11(15), 4308.
- Patel S. (2021).** Medical Statistics Series: Inferential Statistics (Part II). *National Journal of Community Medicine*, 12 (11), 389-393.
- Reizian, A., El Shatby, A., Abo-Elwafa, W. A. H., El-Deeb, H. A., & Mohamed, B. S. (2023).** Effect of Nursing Interventions on Patients' Health Outcomes Post Thyroidectomy. *Alexandria Scientific Nursing Journal*, 25(3), 64-75.
- Ryu, H. J., Choi, M. S., Park, H., Kim, T. H., Chung, J. H., Park, S. Y., & Kim, S. W. (2024).** Adequate dose of levothyroxine for thyroid-stimulating hormone suppression after total thyroidectomy in patients with differentiated thyroid cancer. *Endocrinology and Metabolism*, 39(4), 615-621.
- Snyder, M., Haskard-Zolnierok, K., Howard, K., & Hu, Y. (2022).** Weight stigma is associated with provider-patient relationship factors and adherence for individuals with hypothyroidism. *Journal of Health Psychology*, 27(3), 702-712.
- Srivalli, B. D., & Pereira, P. (2020).** A Study of Medication Compliance and Medication Safety among Geriatric Patients in Rural Areas. *APIK Journal of Internal Medicine*, 8(2), 65-72.
- Stewart, S. J. F., Moon, Z., & Horne, R. (2023).** Medication nonadherence: health impact, prevalence, correlates and interventions. *Psychology & health*, 38(6), 726-765.
- Sulaiman, A. I., & Al-Saigh, T. H. (2020).** Assessment of nurses knowledge towards post thyroidectomy management in Nineveh Governorate Hospitals. *Mosul Journal of Nursing*, 8(1), 25-31.
- Turney, S. 2023. Chi-Square (X^2) Tests | Types, Formula & Examples.** Available at: [https:// www.scribbr.com/statistics/chi-square-tests/](https://www.scribbr.com/statistics/chi-square-tests/) [Accessed on 12-5-2024].
- Wilson, S. A., Stem, L. A., & Bruehlman, R. D. (2021).** Hypothyroidism: Diagnosis and treatment. *American family physician*, 103(10), 605-613.
- Yavuz, D. G., Yazan, C. D., Hekimsoy, Z., Aydin, K., Gokkaya, N., Ersoy, C., ... & Bozkur, E. (2022).** Assesment of attainment of recommended TSH levels and levothyroxine compliance in differentiated thyroid cancer patients. *Clinical Endocrinology*, 97(6), 833-840.