Knowledge, Awareness and Practice of Patient with Primary Hypothyroidism Among the Patient Attending at Endocrinology Care Center: A Pharmacist Intervention

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Abstract

Hypothyroidism is a common endocrine disorder with a prevalence of 1-2% in the world. The symptoms of hypothyroidism includes, cardiac dysfunction, dyspnea and reduced exercise tolerance, overt cardiovascular diseases, and diabetes mellitus. The aim of the study was to access Knowledge, awareness and, the practice of patient with primary hypothyroidism among the patient attending at endocrinology care center. In this study, most of the female patients were seen hypothyroid than males. Out of a total of 164 respondents, 5.5% were age group of 15-24, 52.4% were age group 25-44, 39% were from the age group 45-64 and 3% were above 65. Among the studied population, 93.9% were male and other were female. The majority of the respondent was in the age group of 25-44 years (52.4%). Major differences were seen after the intervention regarding the Knowledge about thyroid and hypothyroidism. Before intervention respondent was more unknown towards the test required for treatment and similarly after the intervention improved the understanding level of patients towards hypothyroidism. Hence this study suggested advantages of intervention by pharmacist in improving knowledge, attitude and practice of patients towards management of disease.

Keywords: Awareness, Knowledge, Practice, Primary hypothyroidism

1 Introduction

The thyroid gland is butterfly-shaped and sits on the trachea, in the anterior neck which is the largest endocrine gland in the body. Thyroid hormones (THs) produced by the thyroid gland are involved in metabolic hemostasis in the body. Thyroxine (T4) and triiodothyronine (T3) are the two major types of TH present in the body which involves in regulating metabolic functions1,2.

Hypothyroidism indicates inadequate production of thyroid hormone by the thyroid gland which can be primary (abnormality in the thyroid gland itself) or secondary/central (as a result of hypothalamic or pituitary disease). Approximately 99% of cases of hypothyroidism is the etiology cases of primary hypothyroidism3. The worldwide prevalence of spontaneous overt hypothyroidism is between 1% and 2% and ten times more common in women than in men while approximately 8% of women and 3% of men have subclinical hypothyroidism4.

Patient’s knowledge and awareness about diseases and its treatment is very important for good long term outcomes and compliance in any chronic diseases5. It has also been observed that faulty practices prevail among these patients. There is an inadequate of data regarding knowledge and practices among treated hypothyroid patients. It has been recognized that general awareness about hypothyroidism is poor and is associated with inadequate knowledge, wrong beliefs, and practices in a significant proportion of patients. The knowledge and practices amongst the hypothyroid patients have resulted in several misconceptions, poor compliance, and suboptimal management. Lack of qualified physicians for treating hypothyroidism. Inadequate time spent by doctors for patient education is another contributing factor. Patient-related factors include inadequate education, social beliefs, and incorrect information acquired from the internet. Previous studies have consistently shown that
knowledge, awareness, and practices in hypothyroidism patients are impaired.

In Nepal paucity of awareness programs regarding hypothyroidism like Diabetes exists. The common problem observed in hypothyroidism is misleading signs and symptoms and ignorance of monitoring thyroid level regularly. To reduce this problem patient education should be provided by health care providers. So, this study aims to pharmacist intervention on Knowledge, awareness and, the practice of patients with primary hypothyroidism among the patients attending at endocrinology care center.

2 Materials and Method

2.1 Study design

It was a prospective, interventional interview which was carried out in outpatient’s department (OPD) of endocrinology care center situated in New Road, Pokhara, Kaski, Nepal. Total one hundred and sixty-four patients were interviewed with the questionnaire prepared regarding knowledge, awareness and practice of hypothyroidism, it was correlate it with the gender, education level, age and ethnic group of patients, intervention was given by using informative leaflet with poster presentation, after intervention compare was done by Knowledge, Awareness and Practice (KAP) scores before and after an educational intervention. After the one-month interval, they have given the same questionnaire and their KAP scores was compared before and after the one-month period of time.

The sample size was calculated by using the formulae where,

$$\text{Sample Size} = \frac{Z^2 \cdot \sigma^2}{d^2} \times \frac{1}{p(1-p)}$$

where,

$Z$ = standard normal variate (at 5% type I error (p<0.05), it is 1.96)

$P$ = Expected proportion in population-based on previous studies

$d$ = absolute error (Charan et al., 2013)

As per Yadav R et al.9 Overall prevalence of hypothyroidism in the western part of Nepal was 12%. So, taking this value, we get a sample size of 163 patients.

For the knowledge and self-care measures regarding Hypothyroidism, a questionnaire from Kumar P et al.6 was used. Consent was taken to use the questionnaire.

2.2 Inclusion and Exclusion criteria

Hypothyroid patients of age range 18-75 years visiting the endocrine department as OPD patients were included in the study. Similarly, Psychiatric patients and Hospitalized patients with thyroid dysfunction were excluded from this study.

2.3 Ethical approval

The study was approved by Institutional Review Committee (IRC), Pokhara University Research Centre Kaski, Nepal and data collection approval were obtained from endocrinology care center, Pokhara, Nepal. The data were collected in a structured pro forma, which include the validated KAP questionnaires and follow up was carried after one month.

2.4 Statistical Analysis

After collection of the data, data was entered and analyzed in Excel and the latest version of SPSS (Statistical Package for Social Sciences)16. Data was represented as tables and figures and statistical tool as appropriate was used. Microsoft excel 2012 was used to analyzed the results descriptively. Descriptive indexes, including frequency, percentage, mean and standard deviation were used to express data for all variables. Association between variable were analyzed using chi-square test. A p-value of <0.05 was considered as statistically significant throughout the study.

3 Results

3.1 Socio-demographic characteristics of the study population

The detail of socio-demographic characteristics is given in Table 1. Out of a total of 164 respondents, 5.5% were age group of 15-24, 52.4% were age group 25-44, 39% were from the age group 45-64 and 3% were above 65. Among the studied population, 93.9% were male and the rest other was female. The majority of the respondent was in the age range of 25-44 years (52.4%).

Among the respondent, based on caste, 47% were of upper caste group followed by relatively advantage Janajati 18.3%. It was found that 7.9% of respondents were illiterate and only 11% of respondents had studied bachelor degrees or above. Similarly, 70.1% were unemployed and the rest of others were employed. Overviewing the residence (85.4%) were of town residence, (16.6%) were village residential people.

3.2 Respondent on medication

Among the respondent, 163 were on medication and rest was not on medication. Similarly, the respondent who uses alternative medicine was less than those who don’t use it. Certain modifications were made in respondent life for a healthy life which is given in Table 2.

3.3 Knowledge about thyroid and hypothyroidism

Table 3 represents the knowledge about thyroids and hypothyroidism before and after the knowledge was given. It was observed that before the intervention thyroid definition was a disease (54.9%), swelling on neck (26.2%) and a normal gland in the body (18.9%).
| Socio demographic characteristics of study population | Total Number(N=164) | Frequencies(n) | Percentage (%) |
|------------------------------------------------------|----------------------|----------------|----------------|
| Sex                                                  |                      |                |                |
| Male                                                 | 10                   | 6.1            |                |
| Female                                               | 154                  | 93.9           |                |
| Age Group                                            |                      |                |                |
| 15-24                                                 | 9                    | 5.5            |                |
| 25-44                                                 | 86                   | 52.4           |                |
| 45-64                                                 | 64                   | 39             |                |
| 65+                                                  | 5                    | 3              |                |
| Ethnic Group                                         |                      |                |                |
| Dalit                                                | 11                   | 6.7            |                |
| Disadvantage Janajati                                | 18                   | 11             |                |
| Religious Minorities                                 | 13                   | 7.1            |                |
| Disadvantage non dalit terai                         | 15                   | 9.1            |                |
| Relatively advantage Janajati                        | 30                   | 18.3           |                |
| Upper Caste                                          | 77                   | 47             |                |
| Socio economic Status                                |                      |                |                |
| Education                                            |                      |                |                |
| Illiterate                                           | 14                   | 7.9            |                |
| Read and write                                       | 49                   | 29.9           |                |
| Primary                                              | 57                   | 34.8           |                |
| Secondary                                            | 16                   | 9.8            |                |
| Higher Secondary                                     | 11                   | 6.7            |                |
| University or more                                   | 18                   | 11             |                |
| Occupation                                           |                      |                |                |
| Job                                                  | 25                   | 15.2           |                |
| Business                                              | 22                   | 13.4           |                |
| Foreign Employment                                    | 2                    | 1.2            |                |
| Unemployed                                            | 115                  | 70.1           |                |
| Residence                                            |                      |                |                |
| Town                                                 | 140                  | 85.4           |                |
| Village                                               | 24                   | 16.6           |                |

Similarly, after intervention, the respondent answer the definition as a disease (0.6%) and a normal gland in the body (99.4%). Major differences were seen before and after the intervention.

| Table 2: Respondent on medication | Participants(N)=164 | Frequencies (n) | Percentage (%) |
|-----------------------------------|----------------------|----------------|----------------|
| Are you on Medication             |                      |                |                |
| Yes                               | 163                  | 99.4           |                |
| No                                | 1                    | 0.6            |                |
| Use of any herbal/Ayurveda/homeopathic |              |                |                |
| Yes                               | 4                    | 2.4            |                |
| No                                | 160                  | 97.6           |                |
| Modification of lifestyles        |                      |                |                |
| Diet                              | 3                    | 1.8            |                |
| Exercise                          | 9                    | 11.6           |                |
| Others                            | 142                  | 86.6           |                |

| Table 3: Knowledge about thyroid and hypothyroidism | Participants (n=164) | Knowledge of terminologies n % | Before | After |
|----------------------------------------------------|----------------------|--------------------------------|--------|-------|
| Thyroid Meaning                                    |                      |                                 |        |       |
| A disease                                           | 90                   | 54.9                           | 1      | 0.6   |
| Swelling on neck                                   | 43                   | 26.2                           | 0      | 0     |
| A normal gland in the body                         | 31                   | 18.9                           | 163    | 99.4  |
| Hypothyroidism                                     |                      |                                 |        |       |
| Increased secretion of thyroid hormone              | 6                    | 3.7                            | 0      | 0     |
| Decreased secretion of thyroid hormone              | 81                   | 49.4                           | 164    | 100   |
| Swelling on neck                                   | 77                   | 47                             | 0      | 0     |

3.4 Knowledge about symptoms of hypothyroidism

Table 4 represents the concept of the respondent regarding symptoms of thyroidism and major differences were seen before and after the intervention.

3.5 Common Misconception regarding hypothyroidism

The common misconception regarding hypothyroidism improved after the intervention as shown in table 5.

3.6 Medication Practice and beliefs
The medication practice and belief regarding the interval between thyroid medicine and food, the correct response was seen in 87.8% incorrect response in 7.3% and 4.9% were unknown.

Table 4: Knowledge about symptoms of hypothyroidism

| Question                                | Total Number (N=164); N, % | Before Intervention | After Intervention |
|-----------------------------------------|----------------------------|---------------------|--------------------|
|                                         | Yes | No | Don’t Know | Yes | No | Don’t Know |
| Sore throat, neck pain, joint pain      | 122(74.4) | 34(20.7) | 8(4.9) | 152(92.7) | 12(7.3) | 0 |
| Weight gain                             | 102(62.2) | 55(33.5) | 7(4.3) | 164(100) | 0 | 0 |
| Depression                              | 89(54.3) | 67(40.9) | 8(4.9) | 152(92.7) | 12(7.3) | 0 |
| Irregular menstrual cycle               | 65(39.6) | 63(38.4) | 36(22) | 160(97.6) | 4(2.6) | 0 |
| Voice change                            | 91(55.5) | 67(40.9) | 6(3.7) | 131(79.9) | 33(20.1) | 0 |
| Hair fall                               | 123(75) | 34(20.7) | 7(4.3) | 164(100) | 0 | 0 |
| Infertility                             | 61(37.2) | 2(1.2) | 101(61.6) | 152(92.7) | 9(5.5) | 3(1.8) |
| Constipation                            | 63(38.4) | 89(54.3) | 12(7.3) | 127(77.4) | 35(21.3) | 2(1.2) |
| Skin problems                           | 72(43.9) | 76(46.3) | 16(9.8) | 144(87.8) | 19(11.6) | 1(0.6) |
| No symptoms require: as a part of routine health screen | 6(3.7) | 4(2.4) | 154(93.9) | 1(0.6) | 2(1.2) | 161(98.2) |

Table 5: Common Misconception regarding hypothyroidism

| Question                                | Total Number (N=164); N, % | Before Intervention | After Intervention |
|-----------------------------------------|----------------------------|---------------------|--------------------|
|                                         | Yes | No | Don’t Know | Yes | No | Don’t Know |
| Hypothyroidism causes excessive weight gain | 157(95.7) | 1(0.6) | 6(3.7) | 164(100) | 0 | 0 |
| Cabbage, cauliflowers soya should be avoided | 133(81.1) | 25(15.2) | 6(3.7) | 164(100) | 0 | 0 |
| Thyroid medication should be avoided during pregnancy | 27(16.5) | 37(22.6) | 100(61) | 9(5.5) | 153(93.3) | 2(1.2) |
| Thyroid medication should be stopped once test are normal | 25(15.2) | 127(77.4) | 12(7.3) | 5(3) | 153(93.3) | 6(3.7) |
| Thyroid deficiency can be treated using iodized salt | 67(40.9) | 9(5.5) | 88(53.7) | 161(98.2) | 3(1.8) | 0 |
| Alternative medicine can cure thyroid problems | 14(8.5) | 127(77.4) | 23(14) | 5(3) | 157(95.7) | 2(1.2) |
| Hypothyroidism is heredity               | 51(31.1) | 6(3.7) | 107(56.2) | 163(98.8) | 1(0.6) | 0 |
| Hypothyroidism women can conceive        | 41(25) | 12(7.3) | 111(67.7) | 162(98.8) | 1(1.6) | 1(1.6) |
Similarly, tests for monitoring treatment correct response (74.4%), incorrect response (6.7%), and 18.9% were unknown. After the intervention, all the respondents respond to the correct answer (interval between thyroid medicine and food) and 99.4% correct response for test for monitoring treatment as shown in table

### 3.7 Knowledge of basis of treating hypothyroidism

The reason for treatment was seen to stimulate the thyroid gland to work (82.3%) for intervention while after intervention all the respondents respond to stimulate the thyroid gland to work as shown in Table 7.

#### Table 6: Medication Practice and beliefs

| Question                                      | Total Number(N) = 164 | Correct response | Incorrect response | Don’t Know |
|----------------------------------------------|------------------------|-------------------|--------------------|------------|
| **Before Intervention**                      |                        |                   |                    |            |
| Interval between thyroid medicine and food   | 144(87.8)              | 12(7.3)           | 8(4.9)             |            |
| Test for monitoring treatment               | 122(74.4)              | 11(6.7)           | 31(18.9)           |            |
| **After Intervention**                      |                        |                   |                    |            |
| Interval between thyroid medicine and food   | 164(100)               | 0                 | 0                  |            |
| Test for monitoring treatment               | 163(99.4)              | 1(0.6)            | 0                  |            |

#### Table 7: Knowledge of basis of treating hypothyroidism

| Question                                      | Total Number(N) = 164 | Correct response | Incorrect response | Don’t Know |
|----------------------------------------------|------------------------|-------------------|--------------------|------------|
| **Before Intervention**                      |                        |                   |                    |            |
| Interval between thyroid medicine and food   | 144(87.8)              | 12(7.3)           | 8(4.9)             |            |
| Test for monitoring treatment               | 122(74.4)              | 11(6.7)           | 31(18.9)           |            |
| **After Intervention**                      |                        |                   |                    |            |
| Interval between thyroid medicine and food   | 164(100)               | 0                 | 0                  |            |
| Test for monitoring treatment               | 163(99.4)              | 1(0.6)            | 0                  |            |

#### 3.8 Test required for treatment

Before the intervention respondent was more unknown towards the test required for treatment and similarly after the intervention the respondent has responded to the correct answer which can be clearly seen in table 8.

#### 3.9 Time to have medicine

It was seen that before intervention the time to have the medicine was at empty stomach (93.9%), empty stomach and an interval of at least 30 min before taking coffee or tea in the morning (0.6%), with food, milk or juice (5.5%) while after intervention time was empty stomach (98.8%) and the rest were empty stomach and an interval of at least 30 min before taking coffee or tea in the morning as shown in table 9.

#### 3.10 Percentage of levothyroxine prescribed

Different dose of levothyroxine has been prescribed for treating different conditions. Levothyroxine 25mcg with 37.20% has been prescribed more among the respondent while the least prescribed was levothyroxine 125mcg with 1.2% as given in figure 1.

#### 3.11 Biochemical Test value

The Biochemical Test values are given in table 10. The thyroid function test was carried out every three months. According to the prescribed dose of a doctor, it was observed most of their thyroid values were normal after having the medicine prescribed by the doctor. Some of their thyroid values were not controlled because of their missing dose.
Table 8: Test required for treatment

| Test     | Total number(N)=164 | Number of response |
|----------|---------------------|--------------------|
|          |                     | Before (%)         | After (%)          |
| T4       | 5(3)                | 163(99.4)          |                    |
| T3       | 11(6.7)             | 163(99.4)          |                    |
| TSH      | 17(10.4)            | 164(100)           |                    |
| Total T3 | 0                   | 1(0.6)             |                    |
| Total T4 | 0                   | 1(0.6)             |                    |
| Don’t know | 131(79.9)       | 0                  |                    |

Table 9: Time to have medicine

| Basis                                                                 | Total number(N)=164 | Number of response |
|-----------------------------------------------------------------------|---------------------|--------------------|
|                                                                        |                     | Before (%)         | After (%)          |
| Empty stomach                                                         | 154(93.9)           | 162(98.8)          |                    |
| Empty stomach and an interval of at least 30 min before taking coffee or tea in the morning | 1(0.6)              | 2(1.2)             |                    |
| With food, milk or juice                                              | 9(5.5)              | 0                  |                    |
| After food                                                            | 0                   | 0                  |                    |

Table 10: Biochemical Test value

| FT3                          | Previous 1(%) | Previous 2(%) | Latest(%) |
|------------------------------|---------------|---------------|-----------|
| Low                          | 8.(15.4)      | 8.(15.4)      | 19(12)    |
| Normal                       | 40(76.9)      | 40(76.9)      | 135(85.3) |
| High                         | 4(7.7)        | 4(7.7)        | 4(2.5)    |
| FT4                          |               |               |           |
| Low                          | 3(5.8)        | 16(13.2)      | 10(6.3)   |
| Normal                       | 39(75.0)      | 98(81.0)      | 134(84.8) |
| High                         | 10(19.2)      | 7(5.8)        | 14 (8.9)  |
| TSH                          |               |               |           |
| Low                          | 2(3.6)        | 3(1.8)        | 5(3.1)    |
| Normal                       | 7(12.5)       | 54(42.9)      | 93(57.1)  |
| High                         | 47(83.9)      | 69(54.8)      | 65(39.9)  |

4 Discussion

About 200 million people in the world have some form of thyroid disease. Thyroid diseases for the most part are treatable; however, untreated thyroid disease can produce serious results sometimes in many other parts of the body\textsuperscript{10}. The diagnosis of thyroid disease can be particularly challenging. In particular, people may not associate the signs and symptoms with the disease process and thus may not bring them to the attention of themselves against thyroid disorder. For these reasons, if early detection of these disorders would be possible then, it would not become any life-threatening problem.

In this study, there were 93.9% of female patients and 6.1% of male patients. Most of the female patients were seen hypothyroid than males. There were 5.5% of patients from the age group 15-24, similarly, there were 52.4% of patients from the age group 25-54, and 39% of patients from age group 45-64, above 65 only 3% of patients were observed. People of various ethnic groups were observed. Among the respondent, based on caste, 47% were of upper caste group followed by relatively advantage Janajati 18.3% and rest other 11%,9.1%, 7.1%, 6.7%, were followed by disadvantage Janajati terai caste,disadvantage nondalit terai, religious minorities, and dalit respectively. In this study it was found that 7.9% of respondent were illiterate and only 11% of respondent had studied bachelor degree or above, a notable proportion can only read and write(29.9%) and had primary level of education (34.85%), secondary level of education (9.8%), higher secondary level education (6.7%). Among 164 respondents (70.1%) were unemployed and the rest of others were employed. Over viewing the occupation (15.2%) were jobholders, (13.4%) were of business, (1.2) were of foreign employment, (70.1%) were unemployed. Over viewing the residence (85.4%) were of town residence, (16.6%) were village residential people.

In a study regarding the meaning of the medical term “thyroid”, only 35.2% participants knew correctly that thyroid is a normal gland in the body, 29.6% considered thyroid as a hormonal disease, 9.2% as a swelling in the neck, and the remaining 26% did not have any idea about it. Only 51% knew that “hypothyroidism” is a clinical term for reduced secretion by the thyroid gland, 11% of participants thought hypothyroidism as a swelling in the neck, and 18% regarded it as an increased secretion by the thyroid gland, and remaining 31% had no idea regarding the same\textsuperscript{5}. Similarly, in another study, 60% of patients knew the correct meaning of the term “thyroid.” Knowledge of disease related to basic terminologies is very important for patients to acquire further knowledge regarding their disease\textsuperscript{11}.

In this study conducted represented the knowledge about thyroids and hypothyroidism before and after the knowledge was given and it was observed that before the intervention thyroid definition was a disease (54.9%) swelling on neck (26.2%) and a normal gland in the body (18.9%). Similarly, after intervention, the
respondent answers the definition as a disease (0.6%) and a normal gland in the body (99.4%). In another study, 56.9% felt that hypothyroidism is associated with weight gain. Although it is well known that hypothyroidism can cause weight gain, it is seldom more than 2-4 kg. In the same study, 40.98% of patients believed that goitrogens need to be avoided in the diet. Most of the information seemed to be emanating from television and newspapers. No study has however evaluated in detail the effect of goitrogens on the course of hypothyroidism.

In this study, 28.2% believed iodized salt could be used to treat hypothyroidism, while 46.7% of patients believed that alternative forms of medicine can cure hypothyroidism. A notable participants in our study accepted that hypothyroidism can be cured with medications and levothyroxine could be stopped when their thyroid function tests report normalized. Most participants took levothyroxine early morning in the fasting state; however, only a third of the patients gave an adequate gap between taking the tablet and having food or beverages.

In our study, 95% thought hypothyroidism can cause excessive weight gain, 0.6% answered no, 6.1% answered don’t know. 81% thought cabbage, cauliflower should be avoided, 15.2% answered no, 3.7% answered don’t know. 16.5% answered thyroid medicine should be avoided during pregnancy, 22.6 % answered it should not be avoided during pregnancy, 3.7% answered don’t know. Here, 15.2% thought thyroid medication should be stopped once the test is normal. 77.4% answered it should not be stopped, 7.3% answered don’t know. 40.9% answered thyroid deficiency can be treated by using iodized salt whereas 57.3% answered don’t know, 8.5% thought that alternative medicine can treat thyroid, 77.4% answered don’t know, 31.1% answered that hypothyroidism is the hereditary disorder whereas 56.2% answered don’t know. After the intervention, the misconception of the patient about diseases was thoroughly decreased as seen in the result.

As per Maharjan et. al., The clinical manifestation of study subjects was sore throat (41.60%), fatigue (36.40%), voice change (36.40%), neck pain (22.10%), constipation (19.50%), weight gain (20.80%), sleepiness (15.60%), cold intolerance (10.40%), joint pain (10.40%), depression (9.10%), hair fall (9.10%), irregular menstruation (6.50%), difficulty in swallow (7.80%), difficulty in breath (3.90%) and skin problem (1.30%)7.

In the present study, it represented the concept of the respondent regarding symptoms of thyroidism, and major differences were seen before and after the intervention which can be observed in the table i.e sore throat, neck pain, and joint pain 92.7% answered “yes” and 7.3% answered ‘no’. weight gain 100% answered ‘yes’. Depression 92.7% answered ‘yes’ and 7.3 % answered ‘no’.

In a study females had irregular menstrual cycle12 which was also observed in the study conducted by Nimmy N.J et al.13, out of 18 hypothyroidism patients, 13 (72%) were found to have irregularity in menstrual periods which includes heavy menstruation and cessation of periods for 2-3 months. Among hyperthyroid patients, only 3 (25%) were having irregular periods. In the present study (97.6%) answered that there is an irregular menstrual cycle, 38.4% answered ‘no’, 22% answered ‘don’t know’.

5 Conclusion

Patient’s education improved the understanding level of patients towards hypothyroidism. Pharmacist can play a main role in improving patient care by counseling. Hence pharmacist led intervention is improving knowledge awareness and practice of patients towards management of disease.

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Fig 1: Percentage of levothyroxine prescribed

| Levothyroxine Dose | Percentage |
|--------------------|------------|
| 25mcg              | 37.20%     |
| 50mcg              | 24.40%     |
| 75mcg              | 15.90%     |
| 100mcg             | 11%        |
| 125mcg             | 1.20%      |
| 150mcg             | 2.40%      |
| 175mcg             | 7.30%      |
University Research Center (PURC) for the ethical approval for this research works.

7 Conflict of interest
The authors have no current conflict of interest.

8 Author’s contributions
GMK supervised, and draft the manuscript. SP participated in the collection of data, arranged in tabular form, and carried out the literature review. All authors read and approved the final manuscript.

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