

Medication Adherence to Levothyroxine Therapy among Hypothyroid Patients and their Clinical Outcomes with Special Reference to Thyroid Function Parameters

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ABSTRACT

Background

Non-adherence to medication in hypothyroid patients leads to poor clinical outcome and increased health care costs. Study related to adherence to levothyroxine in hypothyroid patients is limited worldwide.

Objective

To determine the adherence pattern and factors affecting adherence in hypothyroid patients and compare the clinical outcomes among adherent and non-adherent patients.

Method

A cross-sectional study was conducted in Dhulikhel hospital, Kathmandu University hospital. Patients with hypothyroidism on levothyroxine fulfilling the inclusion criteria were enrolled in this study. After obtaining the informed consent from the patients, structured questionnaire was used to interview the patients. Statistical analysis was performed by using SPSS 23.0. P-value < 0.05 was considered as statistically significant.

Result

Among 113 patients enrolled in this study, 85.8% of them were females. Majority (76.10%) of them belonged to the age group of 31-40 years. More than half (51.3%) of the patients were adherent to medication. Non-adherence was significantly associated with literate people following medication ($p=0.003$, $OR=0.305$), missed appointment to follow-up ($p=0.007$, $OR=0.346$) and longer duration of medication ($p=0.019$, $OR=4.385$). However, there was no statistically significant association of clinical outcomes with reference to TSH, ft_4 , ft_3 and patients' age, adherence to medication and concomitant use of other drugs.

Conclusion

More than half of the patients were adhered to the Levothyroxine therapy. Forgetfulness was the main reason for missing the dose and non-specific reasons attributed to discontinuation of medication for these patients. Good adherence was seen among illiterate people. Treatment related factor, patient-provider relationship and patient related factor were determined as the major barrier to medication adherence. Most of the non-adherent patients had uncontrolled TSH.

KEY WORDS

Adherence, Dhulikhel Hospital, Hypothyroidism, Levothyroxine

INTRODUCTION

Hypothyroidism is considered as one of the most prevalent endocrine disorder worldwide.^{1,2} In Nepal it has been one of the commonly encountered clinical conditions.³⁻⁵ Patients with hypothyroidism require lifelong thyroid hormone therapy⁶ in which Levothyroxine is the agent of choice.⁷⁻¹⁰

Levothyroxine is a synthetic hormone which resembles endogenous thyronine.⁹ Although erratic thyroid hormone profile in the hypothyroid patients is maintained by simple monotherapy of Levothyroxine to certain extent, successful clinical outcomes with this regimen still remains a challenging problem.^{6,11} Apparently, non-adherence to medication remains a key factor for treatment failure along with drug-drug interaction, or drug-food interaction, and comorbid conditions.⁶ Medication adherence is influenced by the interplay of five sets of factors: i) Social and Economic factors, ii) Health care team and system-related factors, iii) Condition-related factors, iv) Therapy-related factors, v) Patient-related factors.³⁸ Recognizing various barriers to adherence and motivating patients to adhere to the treatment regimen can lead to good clinical outcomes and improve patients' quality of life.¹³

To date, data on adherence pattern and factors associated with adherence of Levothyroxine is not documented in Nepal. However, it is believed that non-adherence is common among individuals with hypothyroidism and there is an alarming need to explore the ways to improve patient's adherence for better clinical outcomes. Therefore, our study attempted to address the medication adherence pattern among hypothyroid patients and elucidate the factors associated with it along with the clinical outcomes with reference to thyroid function parameters.

METHODS

A cross-sectional study was conducted in the Dhulikhel hospital, Kathmandu university Hospital. This study was carried out among one hundred and thirteen hypothyroid patients. Sample size was calculated by using $Z_{1-\alpha/2}$ as a standard normal variate (196 at 5% type I error ($P < 0.05$) where absolute precision or error (d) was taken as 5% at type I error of 5% and previous prevalence of 8%. Patients with hypothyroidism on levothyroxine medication were enrolled in the study whereas hypothyroid patients without levothyroxine medication did not meet the inclusion criteria. Patients meeting inclusion criteria were interviewed semi-structured questionnaire after taking informed consent.

Questionnaire related to patients' socio-demographics, thyroid dysfunction history, use of concomitant drugs, patients' medication history related to dose were recorded. Adherence was measured using structured questionnaire which included question related to missing dose, discontinuation of dose, with its duration and

various reasons. For determining various affecting factors to adherence pattern, questions based on patients' factor, socio-economic factor, health system related factor, treatment-related factor and condition related factor were asked to participating patients. Adherence was recorded in such a way that patients missing more than 2 doses were considered as non-adherent and patients missing less than 2 doses or not missing single dose were referred as adherent. Similarly, patients who missed medication dose for more than 7 days were considered as the discontinuing patients. Ethical approval was taken from Institutional Review Committee, Kathmandu University School of Medical Sciences.

The laboratory investigation of the patients was based on their thyroid function tests which were performed by analyzing patients' serum and plasma on Chemiluminescence Immuno Assay. It was performed on the LIAISON Analyzer family and assessed using the reagents of DiaSorin S.p.A.

Collected data was entered in the Microsoft EXCEL 2013. The entered data was then analyzed using Statistical Package for Social Sciences (SPSS) version 23.0. The detail of working procedure is shown in Figure 1. The quantitative data was expressed in percentages and mean \pm standard deviation (SD). Similarly, the qualitative data was analyzed using Pearson's Chi-square test, Continuity Coefficient and Fischer's exact test. The p -value < 0.05 was considered statistically significant. Significant variables ($p \leq 0.05$) were further analyzed using logistic regression analysis to isolate factors of non-adherence in 95% confidence interval with $p < 0.05$ as statistically significant level.

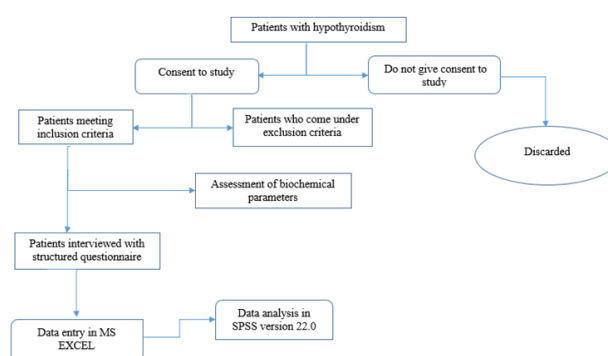


Figure 1. Flow chart showing stepwise procedure of data collection and analysis

RESULTS

Out of the 113 participating patients, 14.2% ($n=16$) were males and 85.8% ($n=97$) of them were females. The mean (\pm SD) age was 41.35(\pm 11.903) years and majority (31% ($n=35$)) of the patients were between 31 and 40 years and most of them (58.4% ($n=66$)) were literate. All the patients ($n=113$) reported of use of iodized salt and only 5.3% ($n=6$) had the history of thyroidectomy.

Among 113 patients included in the study, 43.46% ($n=49$) were prescribed with the daily dose of 50 mcg, followed

by 25 mcg (25.66% (n=29)), 75 mcg (20.35% (n=23)), 100 mcg (7.07% (n=8)) and greater than 100 mcg (3.53% (n=4)) of Levothyroxine (Table 1). Regarding the duration of medication, 21.2% (n=24) of them were using Levothyroxine for 1-3 months and 12-24 months respectively while 32.7% (n=37) of patients were under Levothyroxine therapy for 3-12 months followed by 24.8% (n=28) of patients using Levothyroxine for more than 24 months (Table1).

Table 1. Details of use of Levothyroxine among 113 patients

Variables	No. of Patients (%)
Duration of medication (n=113)	
1-3 months	24(21.3)
3-12 months	37(32.7)
12-24 months	24(21.2)
>24 months	28(24.8)
Treatment History	
Levothyroxine dose (n=113)	
25 mcg	29(25.66)
50 mcg	49(43.36)
75 mcg	23(20.35)
100 mcg	8(7.07)
>100 mcg	4(3.53)

As shown in figure 2, majority of the patients (51.3% (n=58)) were adherent to medication while 48.7% of them were non-adherent to medication. 68.08% (n=32) of the patients had missed the dose due to forgetfulness. About 16% (n=19) of the patients had discontinued the medication of which 52% (n=10) of them had discontinued due to non-specific reasons (Table 2).

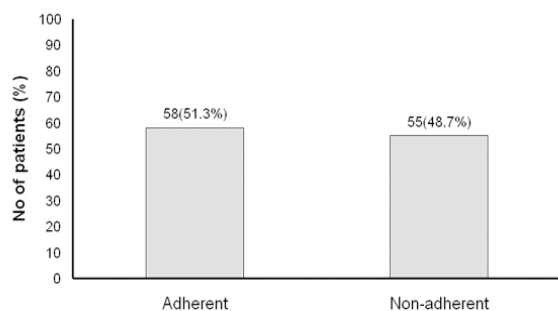


Figure 2. Bar-diagram showing adherence pattern among 113 patients

Further, our study revealed a significant association between non-adherence and educational status, missed appointment to doctors' follow-up and duration of medication. Non-adherence was common among literate people as compared to illiterate people ($p=0.003$ OR=0.305). Similarly, 58.3% (n=14) of patients exhibiting poor adherence were under Levothyroxine for over 12 months. The present study showed that patients who had missed doctors' follow-up in specified time had the odds of having non-adherence 0.346 times greater than that

Table 2. Adherence pattern among 113 patients

Characteristics	No. of Patients (%)
Patient who had missed dose (n=47)	
Missing frequency (n=47)	
Sometimes	46 (97.87)
Often	1(2.13)
Reason behind missing the dose (n=47)	
Forgetfulness	32(68.08)
Carelessness	3(6.38)
During travelling	7(14.89)
Others*	5(10.63)
Patients who had discontinued the medication (n=19)	
Reasons for discontinuation	
Duration of treatment	1(5.26)
Earthquake	3(15.78)
Doctor's advice	5(26.31)
Others [†]	10(52.63)
Duration of discontinuation	
1-30 days	9(47.36)
31-60 days	4(21.05)
61-90 days	2(10.52)
>90 days	4(21.05)
Time of discontinuing medication (months after its discontinuation)	
1-6 months	13(68.42)
7-12 months	5(26.31)
25-48 months	1(5.26)

*completion of medication, busy work schedule, earthquake, lost medicine

[†]shift to ayurvedic drugs under self-medication, busy work schedule, completion of medication, symptomatic relief, household works, gastritis problem, travelling to permanent residence

among patients without missed appointment (Table 3). However, significant association was not found between adherence and age, gender, patients' knowledge about the clinical condition and medication, adverse effects, patients' perception about the disease, medication accessibility and affordability and special attention from health care provider. (Table 3)

Statistically, clinical outcome with reference to thyroid function parameters (TSH, fT4, fT3) was not significantly associated with age group, adherence and concomitant drug use. Nevertheless, 69.1% (n=38) of the non-adherent patients had uncontrolled TSH level as compared to 30.9% (n=17) of the non-adherent patients having controlled TSH (Table 4).

DISCUSSION

Non-adherence to medication has been the problem in the management of chronic illness like hypothyroidism.¹⁴ Adherence to medication is the prior factor for the

Table 3. Demographic and other characteristics of 113 patients with regards to adherence

Characteristics	No. of patients (%)	Adherence [#] (n=58)N(%)	Non-adherent ⁺ (n=55)N(%)	p-value
Age, years				
18-30	20(17.7)	6(30.0)	14(70.0)	0.225
31-40	35(31.0)	18(51.4)	17(48.6)	
41-50	33(29.2)	20(60.6)	13(39.4)	
51-60	18(15.9)	11(61.1)	7(38.9)	
>60	7(6.2)	3(42.9)	4(57.1)	
Gender				
Male	16(14.2)	5(31.2)	11(68.6)	0.143
Female	97(85.8)	31(54.6)	29(45.4)	
Literacy				
Literate	66(58.4)	26(39.4)	40(60.6)	0.003 (OR=0.305)
Illiterate	47(41.6)	32(68.1)	15(31.9)	
Medication with food				
Yes	7(6.2)	2(28.6)	5(71.4)	0.263
No	106(93.8)	56(52.8)	50(47.2)	
Hassled taking medication				
Yes	49(43.4)	23(46.9)	26(53.1)	0.531
No	64(56.6)	35(54.7)	29(45.3)	
Knowledge about their diagnosed clinical condition				
Yes	11(9.7)	5(45.5)	6(54.5)	0.926
No	102(90.3)	53(52.0)	49(48.0)	
Knowledge about the medication				
Yes	7(6.2)	3(40.0)	4(60.0)	0.712
No	106(93.8)	55(51.9)	51(48.1)	
Assistance while taking medication				
Yes	18(15.9)	7(38.9)	11(61.1)	0.371
No	95(84.1)	51(53.7)	44(46.3)	
Medication affordability				
Yes	109(96.5)	55(50.5)	54(49.5)	0.619
No	4(3.5)	3(75.0)	1(25.0)	
Medication accessibility				
Yes	89(78.8)	48(53.9)	41(46.1)	0.403
No	24(21.2)	10(41.7)	14(58.3)	
Busy work schedule				
Yes	14(10.0)	0(0.0)	14(100.0)	0
No	99(90.0)	58(58.6)	41(41.4)	
Missed appointment				
Yes	47(34.3)	17(36.2)	30(63.8)	0.007 (OR=0.346)
No	66(65.7)	41(62.1)	25(37.9)	
Avoidance of medication due symptomatic relief				
Yes	5(4.4)	0(0.0)	5(100.0)	0.025
No	108(95.6)	58(53.7)	50(46.3)	
Adverse Effects				
Yes	38(47.1)	15(39.5)	23(60.5)	0.078
No	75(52.9)	43(57.3)	32(42.7)	

Duration of medication				
1-3 months	24(21.2)	19(79.2)	5(20.8)	0.019 (OR=4.385)
3-12 months	37(32.7)	16(43.2)	21(56.8)	Ref: >24 months
12-24 months	24(21.2)	10(41.7)	14(58.3)	
>24 months	28(24.8)	13(46.4)	15(53.6)	
Concomitant drugs use				
<2	42(37.2)	19(45.2)	23(54.8)	0.506
2	18(15.9)	11(61.1)	7(38.9)	
>2	53(46.9)	28(52.8)	25(47.2)	

[#]Patients who had never missed or discontinued the medication

⁺Patients who had missed or discontinued the medication

management of hypothyroidism.¹¹ A good clinical outcome is possible only with an eradication of barriers to adherence instead of knowing the barriers to adherence in order to obtain good clinical outcomes with medication.^{11,12,15}

Majority of the patients in this study were female. In several prevalence studies of thyroid dysfunction, hypothyroidism was common in female patients.³⁻⁵ It has been reported that in women, with increasing age and during pregnancy, the postpartum period, and menopause, there is the high risk of developing hypothyroidism requiring thyroid hormone replacement therapy.^{16,17} Our study constitutes female population in their postpartum period, menopause and pregnancy.

In this study, majority of the hypothyroid patients belonged to the age group of 30-50 years. It might be because patients of this age group are more prone to stressful life. Consistent to this finding, previous study have shown stress and thyroid autoimmunity as one of the cause of hypothyroidism.¹⁸

It has been demonstrated that iodine deficiency is the common reason for inducing hypothyroidism in developing countries like Nepal.¹⁹ However, all of the patients included in this study have claimed of consuming iodized salt on daily basis. The cause of hypothyroidism in the patients might have been due to autoimmunity or due to defect in the pituitary gland so that Thyroid Stimulating Hormone (TSH) secretion was altered.²⁰ Similarly, some of the patients in this study had undergone thyroidectomy which might be one of the contributing factors for hypothyroidism as shown by another study.²¹ In the given study, there was an increment in the TSH level after the patients had encountered thyroidectomy requiring hormone replacement therapy.²¹

The present study showed that more than half of the patients had adhered to Levothyroxine therapy. This finding is consistent to the findings of previous studies in which 68.4% of the patients were adherent to Levothyroxine therapy and 67.7% of the patients had followed treatment recommendations.^{22,23}

Among the non-adherent patients, the major reason for missing the dose was forgetfulness. Our finding

Table 4. Demographic and other characteristics of patients with regards to different thyroid function parameters

Variables	Total (n)	Controlled [†] TSH (n=46) No.(%)	Uncontrolled [‡] TSH (n=67) No.(%)	p value	Total (n)	Controlled [†] fT4 (n=67) No.(%)	Uncontrolled [‡] fT4 (n=39) No.(%)	p value	Total (n)	Controlled [†] fT3 (n=28) No.(%)	Uncontrolled [‡] fT3 (n=9) No.(%)	p value
Age (years)												
18-30	20	6(30.0)	14(70.0)	0.761	20	12(60.0)	8(40.0)	0.83	3	2(66.7)	1(33.3)	0.966
31-40	35	15(42.9)	20(57.1)		33	21(63.6)	12(36.4)		14	11(78.6)	3(21.4)	
41-50	33	14(42.4)	19(57.6)		29	20(69.0)	9(31.0)		11	8(72.7)	3(27.3)	
51-60	18	7(38.9)	11(61.1)		17	9(52.9)	8(47.1)		6	5(83.3)	1(16.7)	
>60	7	4(57.1)	3(42.9)		7	5(71.4)	2(28.6)		3	2(66.7)	1(33.3)	
Adherent		29(50.0)	29(50.0)	0.061	55	37(67.3)	18(32.7)	0.484	22	16(72.7)	6(27.3)	0.908
Non-adherent		17(30.9)	38(69.1)		51	30(58.8)	21(41.2)		15	12(80.0)	3(20.0)	
Concomitant drugs												
single drug	42	20(47.6)	22(52.4)	0.211	38	27(71.1)	11(28.9)	0.33	13	10(76.9)	3(23.1)	0.853
two drugs	18	9(50.0)	9(50.0)		18	12(66.7)	6(33.3)		6	5(83.3)	1(16.7)	
> two drugs	53	17(32.1)	36(67.9)		50	28(56.0)	22(44.0)		18	13(72.2)	5(27.8)	

[†]controlled TSH level: 0.3-3.6 mIU/L

[‡]0.3 mIU/L<uncontrolled TSH level> 3.6 mIU/L

*Controlled fT4 level: 0.8- 1.7 ng/dl

[‡]0.8 ng/dl<uncontrolled fT4 level> 1.7 ng/dl

[†]Controlled fT3 level: 2.2-4.2 pg/ml

[‡]2.2 pg/ml<uncontrolled fT3 level>4.2 pg/ml

corroborates to another study in which the major cause of low adherence was forgetfulness and feeling hassled about sticking to the plan to reduce hypothyroidism.²⁴ Similarly, forgetfulness has been the major cited reason for missing the medication in different chronic diseases like chronic obstructive pulmonary disease (COPD), hypertension, diabetes etc.²⁵⁻²⁷

Treatment with Levothyroxine is less likely to exhibit adverse effects and is the standard choice as the hormone replacement therapy as compared to complicated combined treatment regimen of Levothyroxine and Liothyronine.^{28,29} However, in this study, majority of the patients reported of fatigue, severe headache, excessive sweating, trouble in breathing, chest pain as the major side effects. The adverse effects might have resulted due to over treatment or under-treatment of Levothyroxine.³⁰ It is reported that cardiovascular changes have occurred with the thyrotropin suppressive dosage of Levothyroxine.³¹ In consistent to the previous report, the chest pain reported in this study might have occurred due to the complication in cardiovascular system by the thyrotropin suppressive dose.³¹ However, there was no statistically significant association between adverse effects and adherence. Our study demonstrated a significant association between adherence and duration of medication taken by the patients. Majority of the non-adherent patients had consumed Levothyroxine for more than 3 months period. In support of our findings, it is reported that duration of treatment is considered as one of the factor that affects adherence.³² Study has shown that daily dose having longer duration of action was associated

with lower adherence.³³ Similarly, longer duration of medication might be the reason for evoking the feeling of hassled about sticking to the medication plan which was one of the main reason for low adherence in hypothyroid pregnant women.²⁴ Despite the simple monotherapy, complexity in medication, a factor, that impede medication adherence, may be ensured due to the concurrent use of comorbidity related medications in hypothyroid patients.¹⁴ In contradiction to the earlier study, our study showed that adherence was not significantly associated with concomitant drugs used for comorbid conditions. The finding of current study is in contrast to several studies which have shown pill burden, as a responsible factor for non-adherence to medication in chronic illness.³⁴⁻³⁶

Severity of symptoms, level of disability, rate of progression, severity of the disease and availability of the effective treatment are likely to have an influence on medication adherence.³⁷ In this study, it was observed that significant number of non-adherent patients had discontinued medication for some interval of time because of the reduction of symptoms due to medication. The patients have the intensity to discontinue medication when symptoms disappear as suggested by previous report.¹² Comorbidities like gastritis and diabetes often co-exist in hypothyroid patients.^{38,39} In this study, it was found that patients with gastritis had higher TSH and diabetic patients had TSH level of subclinical hypothyroidism. The reason for higher TSH level in gastritis patients might have occurred due to the defect in absorption of Levothyroxine as these patients are likely to show impaired gastric acid secretion.³⁸

This might have created alteration in thyrotropin suppressive dose of Levothyroxine in those patients so as to maintain the TSH level. Similarly, the subclinical level of TSH in diabetic patients observed in the present study might be due to polypharmacy, gastroparesis, Obesity, hypoglycemic emergencies, known to affect Levothyroxine requirements as shown by previous study.¹¹ In parallel to the finding of this study, comorbidity was associated with decrement in the adherence.²²

Patients' age, perception about the nature and severity of their illness have influence in medication adherence.^{12,40} The influences of these factors have been clarified by previous study in hypothyroid pregnant women.²⁴ Similarly, conscientiousness and perception that benefit outweighed the risk were associated with higher level of adherence.²⁴ On contrary to such finding from previous study, our study found that majority of the patients had perception of effectiveness of medication. Similarly, majority of the adherent patients reported that they did not feel hassle about sticking to hypothyroidism medication schedule. However, statistically significant association was not found between patients' adherence with their age, perception of effectiveness of medication and feeling of hassled about sticking to the hypothyroidism plan.

Patient-Provider relationship has a key role in influencing patients' perception about the disease and medication which has been shown to affect their medication adherence.^{14,23} The present study also showed that almost all of the patients visited their treating physicians for follow-up and were satisfied with the information provided by them. More than half of the adherent patients reported of satisfaction from their respective treating physicians. However, follow-up of the patients and satisfaction from the provider did not have statistical significant association with medication adherence. Another study had shown significant association between improved adherence and excellent satisfaction from the provider which highlighted the importance of patient-provider relationship in medication adherence.⁴¹ Additionally, this study showed that missed appointment to the treating physicians' follow-up in the given specified time was significantly associated with non-adherence. Missed appointment might affect adherence because people who missed the visit to treating physicians' follow-up are more likely to miss the fruitful suggestions from them regarding clinical condition, medication dosage and measures to be taken for the management of condition.⁴² This might have affected their adherence pattern. This finding corroborated with previous result from another study in hypertension which also had found that non-adherence to medication was significantly associated with irregular follow-up or missed appointment.⁴³ It is reported that physicians have a great role in the intervention of barrier to non-adherence.¹⁴ It was suggested that the likelihood of adherence is greatly increased if the physicians have an empowerment in using understandable language and in creating the friendly,

caring environment that would enlighten the doctor-patient relationship.¹⁴ It might be the potential reason due to which most of the non-adherent patients in this study had claimed of not getting special attention from their treating physicians. The finding of the present study is also consistent with the previous study which has shown that patients' involvement in the regular consultation with the healthcare professionals is the major factor for improving adherence.⁴⁴ Similarly, most of the patients reported that they did not get enough information about prescribed medication and also they did not understand every information provided by the doctor. This might have contributed in non-adherence to medication to certain extent though the association between these factors and non-adherence was not significantly established.

Appropriate social support may help in the improvement of adherence pattern with decrement in the risk of hospitalization, improving patients' quality of life.¹⁴ In our study, majority of the patients reported of taking their medication by themselves without support of family, friends, care-taker etc. However, most of the patients on social support for taking their medication were non-adherent though the association was not statistically significant. It might be because of the lack of knowledge regarding the clinical condition and medication among the family members which might have affected patients' medication taking behavior.⁴⁵ This concurs well with the previous studies which have suggested that family or social group members are likely to create confusion in patients regarding their medication taking pattern because of their divergent views on patients illness and treatment, as a result of which, poor medication adherence is assured.^{46,47} However, other studies have found that patients receiving social support had improved adherence to medication regimen.^{35,36} Furthermore, the present study showed that there was no significant association between medication affordability, accessibility and adherence to medication. Nevertheless, most of the non-adherent patients reported that they could not access medication easily. This finding is in consistent with study in antiretroviral therapy in which travel cost to assess the medication was found as a significant barrier to adherence.⁴¹ Similarly, according to another study, expensive price of medication and missed medicine due to cost were highlighted as the important predictors of non-adherence to antihypertensive medication.⁴¹ Illiteracy has been the major barrier to medication adherence in different chronic illness.^{40,43,48,49} In contrast to previous studies, our study found a significant association between adherence and illiteracy which is noteworthy. The possible explanation for this might be that they were more aware of the condition with the feeling that carelessness could lead to severe manifestations. This finding is in agreement with the previous study in which educational booklet did not seem to have effect in the improvement of adherence in general practice setting. Health literacy determines an individuals' health status.⁵⁰ Another study reported that health literacy

including knowledge of health and medication is positively associated with medication adherence.⁴⁵ However, health literacy was not significantly associated with the adherence in this study. Though, majority of the patients reported that they were not familiar with the clinical condition they were diagnosed of and the medication to follow which might have affected medication adherence to certain extent. Study has suggested that busy schedules that might hinder medication taking behavior have to be properly maintained for improvement of adherence in hypothyroidism.¹³ In contrary to previous study, this recent study showed that significant number of non-adherent patients reported busy schedule as a confounding factor in medication taking behavior. In support of this finding, another study has shown that medication adherence level of 100% was achieved in patients to clinical schedules for prescription refills.⁵¹ Busy working schedule might have affected medication adherence because patients being too busy are likely to miss appointment to clinical schedules such that their prescription refill is also disturbed.⁵¹

The present study showed that most of the patients exhibiting poor adherence had higher TSH. The reason for higher level of TSH in non-adherent patients might have occurred due to their missed or discontinuation of appropriate dose which is likely to have an effect on thyrotropin suppressive therapy of Levothyroxine.²⁴ This finding is in consistent with finding of previous study in which non-compliant patients had higher TSH. However, in the current study, medication adherence; age and concomitant drug use did not have significant association with clinical outcome referencing to thyroid function parameters. It might be because of other factors playing prior role in affecting clinical outcomes in patients and limited sample size of our study though it is unlikely. Similar finding was also shown by another study in diabetic patients in which medication adherence was not significantly associated with the glycemic control.²⁶ However, another study on association of protease inhibitor therapy with successful virologic outcome contradicts the current finding.⁵² This discrepancy might have occurred because of limited sample size encompassed in this study. Mono centered study might have also limited the findings too.

This study lacks the “gold standard” method of measuring adherence. The open-ended questionnaire used in our study might be another limiting factor in the interpretation of the study though it is highly unlikely. Further, recall bias of the patients regarding medication taking behavior,

presence of comorbid conditions might have had an impact in the overall outcomes of the study. Additionally, possible chances of false claims by the patients though rarely expected might have in one way or the other affected result of our study. Despite these limitations, it is believed that our study has provided an insight to address the factors that have led to suboptimal adherence to medication. Moreover, our findings might contribute in achieving higher adherence to medication by directing efforts to attenuating the factors leading to poor adherence. Nevertheless, this study may have not enrolled entire population. A need therefore arises for further research.

CONCLUSION

Non-adherence to medication in chronic clinical condition is associated with increased use of medical resources such as physician visits, laboratory tests, prolonged hospital stays etc. Improving adherence to medication is the only way to overcome barriers to adherence which is one of the major concerns in chronic diseases like hypothyroidism.

Our study reveals that nearly half of the hypothyroid patients did not stick to medication plan. Forgetfulness was the major reason for non-adherence. Similarly, non-adherence was significantly associated with literacy, missed appointment to doctors' follow-up and long duration of medication. This study is the first of its kind in Nepal to provide an insight into the problem of non-adherence in hypothyroid patients on Levothyroxine therapy.

If hypothyroid patients do not adhere to their medication plan without accompanying thyroid function tests, their quality of life is severely affected. Thus, better clinical outcome can be only achieved with good adherence. In developing country like Nepal, community based awareness and various intervention programs have to be emphasized such that they can help manage the most prevalent thyroid dysfunction in the world.

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