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CLINICAL STUDY OF HYPOTHYROIDISM AND ITS MANAGEMENT BY A SINGLE UNANI DRUG

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ABSTRACT

Background: Hypothyroidism in the simplest terms can be defined as deficient production of thyroid hormones. Primary hypothyroidism indicates decreased secretion of thyroid hormone by factors affecting the thyroid gland itself. A decrease in serum concentrations of thyroid hormone causes an increased secretion of Thyroid Stimulating Hormone (TSH), thus resulting in elevated serum TSH concentration.[1-4] Estimates of incidence of hypothyroidism vary depending on the population studied.[5,6] In the United states,0.3% population have overt hypothyroidism and 4.3% have subclinical or mild hypothyroidism.[7] The incidence of hypothyroidism is higher among women, in the elderly, and in some ethnic and racial groups.[8,9] The incidence of Hypothyroidism in India have a female to male ratio of 6:1. The prevalence of hypothyroidism in India is 11%, compared with only 2% in the UK and 4·6% in the USA. Even though hormone replacement therapy with thyroxine has been proven effective in its management, but owing to adverse effects like myocardial infarction, adrenocortical insufficiency, congestive heart failure etc is a challenge to its long term use. So safe and effective *Unani* herbal drugs need to be researched for its management. In this context, a hypothesis was drawn that *su'- mizaj barid /su'- mizaj balghami* (impaired cold temperament/impaired phelgematic temperament) may be interpreted with the clinical features of hypothyroidism using modern scientific parameters. The principal of treatment of any disease in *Unani* medicine is based *on ilaj bi'l zid* (antogonistic therapy)…so Hypothyroidism (*Qillat-i- ifrazi darqia)* being a su'- *mizaj barid* (impaired cold temperament) disease will be treated with *harr yabis* (hot dry) drugs.[10-18] Hence, a single *Unan*i drug, *muqil* (*Commiphora mukul)* was selected which is hot & dry in temperament and has shown positive thyroid activity in experimental studies to correct the su'- *mizaj barid* (impaired cold temperament) in the body and to correct hypothyroid state.[19-22]

INTRODUCTION

Hypothyroidism in the simplest terms can be defined as deficient production of thyroid hormone. Primary hypothyroidism indicates decreased secretion of thyroid hormone by factors affecting the thyroid gland itself. A decrease in serum concentrations of thyroid hormone causes an increased secretion of Thyroid Stimulating Hormone (TSH), thus resulting in elevated serum TSH concentration.[1-4]

Estimates of incidence of hypothyroidism vary depending on the population studied.[28-29] In the United states,0.3% population have overt hypothyroidism and 4.3% have subclinical or mild hypothyroidism.[30] The incidence of hypothyroidism is higher among women, in the elderly, and in some ethnic and racial groups.[8-9]

The incidence of Hypothyroidism in India have a female to male ratio of 6:1. The prevalence of hypothyroidism in India is 11%, compared with only 2% in the UK and 4·6% in the USA. The prevalence of hypothyroidism in India varies depending upon the location. The cities like Kolkata, Delhi, Ahmedabad, Bangalore, and Hyderabad located inland have a higher prevalence of 11·7% compared with coastal cities like Mumbai, Goa, and Chennai having 9·5%. According to Ambrish Mithal, the reason behind the higher mean thyroid - stimulating hormone concentration and range in India compared with western countries is possibly linked to long-standing iodine deficiency in the country, which has only been partly corrected over the past 20 years. The highest prevalence of hypothyroidism upto 13·1% is noted in people aged 46–54 years, with people aged 18–35 years being less affected upto 7·5%.[23-25]

Classical texts *of Unani* medicine have not described *qillatt-i- ifraze darqia* (hypothyroidism) directly, but the clinical features resemble with the symptoms and signs of *Su'- Mizaj Barid/Su' Mizaj Balghami* (impaired cold temperament/impaired phelgematic temperament) which has been discussed in classical texts in detail .As per the fundamentals of *Unani* system of medicine, *Mar'd* (disease) occurs due to *Su'- Mizaj* (impaired temperament), *Su'-Tarkib* (abnormal composition/ structure) *or Tafarruq-i-Ittisal* (discontinuity). *Su'-Mizaj* (impaired temperament) has again been divided into *Su'- Mizaj Harr* (impaired hot temperament), *Su'- Mizaj Barid* (impaired cold temperament) *Su'- Mizaj Ratb* (impaired moist teerament), *Su'- Mizaj Yabis* (impaired dry temperament). The clinical features of *Su'-Mizaj Barid* (impaired cold temperament) include *tahubbuj* (puffiness), *kathra al-buzaq* (excessive salivation),*kathra al-nawm* (excessive sleep), *kusul-wa-mandgi* (somnolence), *du'f al-Ishtiha* (loss of appetite), *kund zehni* (loss of intellectual functions), *du'f al-bah* (loss of libido),*nabd layyinn-wa- bati* (pulsus mollis and pulsus tardus).[26-33]

The above discussed symptoms and signs of *su'- mizaj barid /su'- mizaj balghami* (impaired cold temperament/ impaired phelgematic temperament) somehow resemble with the clinical features of hypothyroidism described in modern medicine.

Even though hormone replacement therapy with thyroxine has been proven effective in its management, but owing to adverse effects like myocardial infarction, adrenocortical insufficiency, congestive heart failure etc is a challenge to its long term use. So safe and effective *Unani* herbal drugs need to be researched for its management.

In this context, a hypothesis was drawn that *su'- mizaj barid /su'- mizaj balghami* (impaired cold temperament/impaired phelgematic temperament) may be interpreted with the clinical features of hypothyroidism using modern scientific parameters.

The principal of treatment of any disease in *Unani* medicine is based *on ilaj bi'l zid* (antogonistic therapy)…so *qillat-i- ifrazi darqia* (hypothyroidism) being a su'- *mizaj barid* (impaired cold temperament) disease will be treated with *harr yabis* (hot dry) drugs.[10-18]

Hence, a single *Unani* drug, *muqil* (*Commiphora mukul)* was selected which is hot & dry in temperament and has shown positive thyroid activity in experimental studies to correct the su'- *mizaj barid* (impaired cold temperament) in the body and to correct hypothyroid state.[19-22.,34-44]

The present study titled 'Clinical study of Hypothyroidism (*Qillat-i- Ifraze Darqia)* and its Management by a single *Unani* drug' has been designed to evaluate the efficacy of the drug in hypothyroidism on modern scientific parameters.

The study was conducted at Regional Research institute of *Unani* Medicine (Central Council for Research in Unani Medicine, Ministry of AYUSH, Government of India) Naseem bagh Campus, University of Kashmir Srinagar Jammu and Kashmir from November 2018 – February 2019.

'A randomized single blind, standard controlled clinical study' was conducted on 60 patients distributed into two groups after randomization. Group A of 30 patients treated with test drug in the form of *safoof* (powder) in the dose of 1 gm twice a day with water orally half an hour after meals and Group B of 30 patients treated with Tab. Thyroxine 50 mcg once daily orally before breakfast for a duration of two months. Follow up of patients was done after every 15th day. Improvement of clinical features were recorded in specially designed Case Record Forms(CRF). Pre and post-treatment, investigations like CBC, LFT, KFT, ESR, BSF, Lipid Profile, ECG, Urine examination (routine) were carried out on all patients for safety and any adverse effects.

OBJECTIVES

To Evaluate the Safety of a *Unani* drug in the management of Hypothyroidism **(*Qillat-i-Ifraze-Darqia)*** against the standard controlled drug.

To Evalute the efficacy of a single *Unani* Drug in the management of **Hypothyroidism (*Qillat-i-Ifraze-Darqia)*** against the standard controlled drug.

METHODOLOGY

The study titled **"Clinical study of Hypothyroidism (*Qillatte- Ifraze- Darqia)* and its management by a Single *Unani* Drug"** was carried out at Regional Research Institute of Unani Medicine (RRIUM) Srinagar Jammu & Kashmir. Patients were enrolled from the out-patient department of RRIUM Srinagar on the basis of history, physical examination and investigations. Before starting the study, the research protocol was duly approved by Institutional Ethical Committee (IEC), RRIUM Srinagar as per the norms. Thereafter, the study was started from 01 November 2018 and the enrolment of patients was completed on 10 February 2019.Patients were randomnized into Test and control groups by Lottery method of randomization. Patients who were on any other drug(Allopathic, Ayurvedic, *Unani* etc) for this disease were stopped 15 days before enrolling into the study and were not allowed to take any other drug for hypothyroidism during the study peroid.

A. Criteria for selection of patients

1. Inclusion Criteria

- Clinically diagnosed patients of Hypothyroidism**.**
- Sex-Male, Female, Transgender.
- Patient in age group of 20 to 60 years.

- Willingness to sign the informed consent, follow the protocol and participate in clinical trial voluntarily

2. Exclusion Criteria

- Patients below 20 and above 60 years.
- Pregnancy and Lactation
- Patients on iodine containing vitamins or minerals
- Patients who have undergone thyroid surgery, taken radioactive iodine therapy
- Diabetes mellitus
- Renal dysfunction
- Patients who fail to give consent
- All complicated cases of hypothyroidism
- Liver diseases
- Gastrointestinal diseases (Peptic ulcer disease)
- IHD and hypertension
- Patients not willing to be enrolled for the study.

Selection of cases

The source for selection of cases was the Out-patient department of RRIUM Srinagar. History and clinical examination was the basis for enrolling patients for the study. Patients were asked complete history, present and past and general physical and systemic examinations were carried out. Specially designed case record forms were used for the recording of the details of the patients which included name, age, sex, address, occupation, marital status, socio economic status, dietary habits, educational background, income, chief complaints, history of present illness, past history, family history, treatment history etc. General examination include pulse, BP, temperature, respiratory rate, build, skin, hair, tongue, eyes, nails, legs and feet etc. Systemic examination was carried out to rule out any involvement of that particular system.

Particular attention was given to know about past history of other diseases like, diabetes-mellitus, hypertension, Addison's-disease, Cushing's syndrome, PCOS, IHD, phaechromocytoma, liver, kidney, spleen, intestinal diseases. etc. After history taking, a complete general and systemic examination was done for any findings. The patients were allotted into the test and the control groups as per the randomization and test as well as control drugs were advised accordingly.

Investigations

A set of investigations were carried out in all the patients to include or exclude from the study and to assess the efficacy and effect of test and control drug on different parameters which included:

Complete blood counts (CBC)
Erythrocyte sedimentation rate (ESR)
Fasting Blood sugar (FBS)
Lipid profile
Liver function test (LFT)
Kidney function test (KFT)
Urine examination
E.C.G.
Thyroid function test (TSH,T_4 ,T_3)

All the above mentioned investigations were carried out in all the patients before the commencement of the study and after the completion of the study.

Consent of the patient

Before enrolling the patients for the study, every patient was provided a set of specially designed Information Consent Form (ICF) which included all the relavant information about the study, investigations, drug, method of treatment and follow-up plan with all the options to ask any query regarding the study. After that when he/she signed the Information Consent Form(ICF), the patient was enrolled for the study.

Study design

A randomized, single blind, standard controlled clinical study.

Sample size

A sample size of 60 patients with 30 in test and 30 in control group.

Allocation of group

Lottery method of randomization was used for allocation of group with Group A as Test group and Group B as control group with 30 patients in each group.

Assessment of *Mizaj* (Temperament)

Temperament of each patient was assessed as per the specially designed scale before the start of treatment.

Duration of study

The duration of study was 60 days in both the test and control groups.

Follow –up plan for patients

Follow- up was done on 15th day,30th day,45th day,60th day in both the groups. On every follow-up, patients were assessed for improvement of their symptoms or worsening of symptoms, appearance of any new symptom, adverse drug effects if any. All the clinical parameters were checked and were recorded in Case Record Form (CRF) (Annexure-II).

Test drug

The test drug was a single *Unani* drug, *Muqil (Commiphora mukul)*

Control drug

Thyroxine sodium 50mcg (Tab. Thyrox-50)

Method of Preparation, Dosage and Mode of Administration of Test Drug

The drug *Muqil* was purchased from market after inviting quotations from different suppliers by the Purchase Committee of Regional Research institute of Unani Medicine (RRIUM) Srinagar. The sample was duly identified by the experts for its originality. After proper cleaning,the drug was grinded into a granular powder from the Pharmacy Deptt. Of Unani Medical

College Institute of Asian Medical Sciences Zakura Srinagar.

The powdered form of the drug so prepared was given in the dose of 1 gm twice daily in the morning after breakfast and another dose in the evening to each patient with luke warm water.

Dose and Mode of Administration of Control Drug

The control drug Thyroxine sodium 50 mcg (Tab.Thyrox-50) was purchased from the market after inviting quotation from different suppliers by the purchasing committee of RRIUM Srinagar which was given as a single dose in the morning in control group patients.

Assessment of Efficacy/Result

The subjects in both test and control groups were assessed for subjective and objective parameters. Subjective parameters included Somnolence, Fatigue, Puffiness of face, Hoarseness of voice, dry skin, decreased libido, delayed tendon reflexes and non-pitting edema while as objective parameters included TFT, Lipid profile etc. The clinical symptoms and signs were found to be different from patient to patient and therefore, grading of subjective parameters was done arbitrary for assessment and evaluation of symptoms and efficacy of the test drug as well as control drug. Before the commencement of treatment, each subjective parameter was recorded in graded form in case record form depending upon the severity of symptoms from 0-3 with 0 for no symptoms,1-mild,2-moderate and 3-severe.

Grade-0	Absent
Grade-1	Mild
Grade-3	Moderate
Grade-4	Severe

Withdrawal criteria

a) Drug defaulter
b) Adverse drug reactions/event.
c) Non-compliance to follow the protocol.

Safety Assesment

All the patients enrolled for the study were assessed for safety pre and post treatment protocol on following parameters:

a) Clinical check-up at every follow-up.
b) Complete Blood Picture like CBC, ESR, & Urine exam on pre (Day 0) and post treatment (Day 61) after completion of the treatment protocol.
c) Blood sugar fasting, LFT, KFT, ECG were done before (Day 0) and after treatment (Day 61).

OBSERVATION AND RESULTS

Table.1: Showing Age Distribution among Test group and Control group(n=60).

Age(years)	Test group		Control		P value
	No	%age	No	%age	
20-30	7	23.3	2	6.7	0.5
31-40	6	20.0	10	33.3	
41-50	10	33.3	10	33.3	
51-60	7	23.3	8	26.7	
Total	30	100.0	30	110.0	
Mean±SD	38.47±11.25		40.23±9.91		

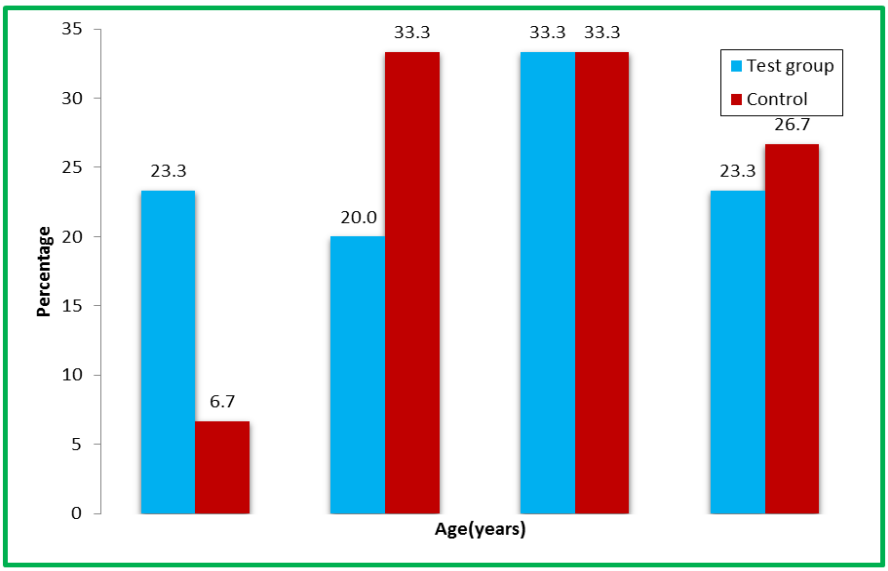

Figure.1 Showing Age Distribution among Test and Control groups (n=60).

The maximum number of patients were found in the age group 41-50 years (33.3%),followed by 20-30 years (23.3%),51-60 years(23.3%),20-30 years(6%) in test group and 31-40 years 33.3%,followed by 41-50 years (33.3%),51-60 years(26.7%),20-30 years(6.7%) in control group.

Table 2*: Showing Sex Distribution among Test group and Control group(n=60).

SEX	Test group		Conrol		P value
	No	%age	No	%age	
Male	7	23.3	6	20.0	0.75
Female	23	76.7	24	80.0	
Total	30	100	30	100	
Test applied: Fisher's exact test					

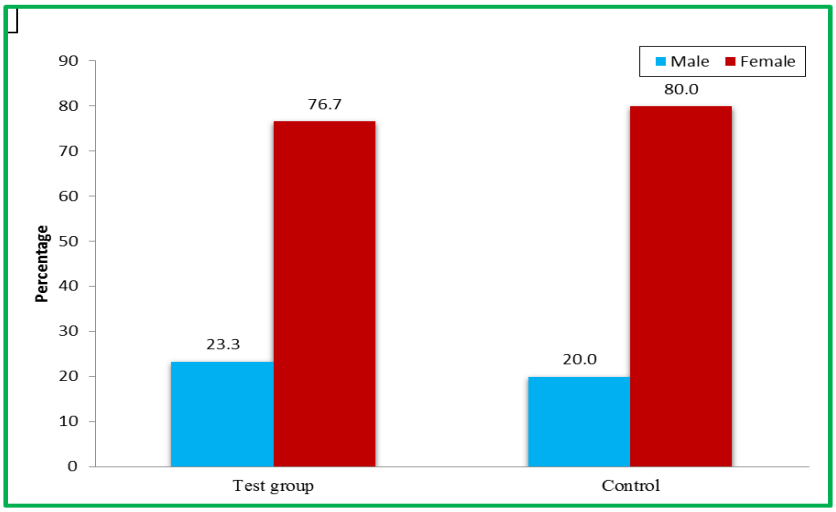

Figure.2 Showing Sex Distribution among Test and Control group (n=60).

Out of 60 patients, 76.7 % were females and 23.3% were males in Test group and 80% were females and only 20% were males in Control group.

Table.3 .*: Showing the type of Mizaj among Test group and Control group.

Mizaj type	Test group		Conrol		P value
	No	%age	No	%age	
Balghami	28	93.3	24	80.0	0.19
Damvi	0	0.0	3	10.0	
Safravi	2	6.7	3	10.0	
Sawdawi	0	0.0	0	0.0	
Total	30	100	30	100	
Test applied: Fisher's exact test					

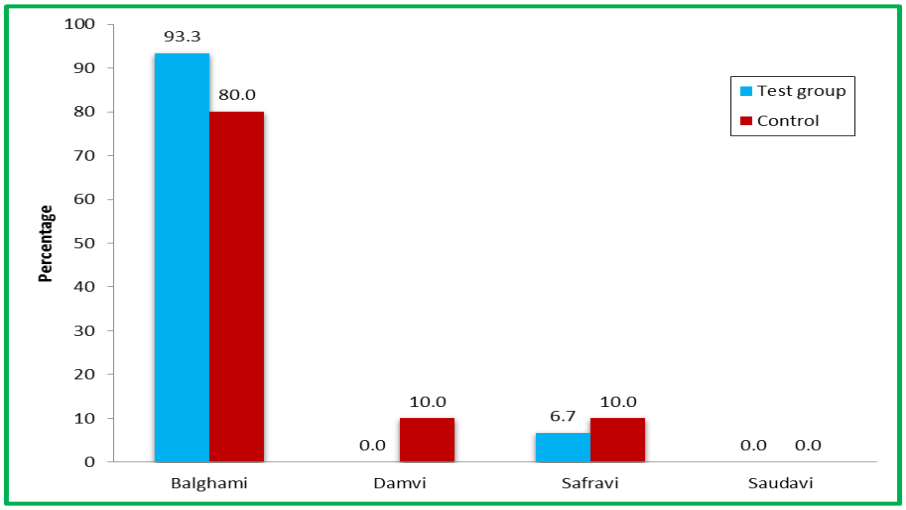

Figure.3: Showing the Pecentage of Types of *Mizaj* among Test group and Control group.

Mizaj assessment of the patients showed that maximum number of patients were having balghami Mizaj 93.3% in test group and 80% in control group followed by safrawi 6.7% and 10% in test and control group, damvi 0% in test and 10% in control group with 0% of sawdawi mizaj patients in either group.

Table. 4.: Showing Triiodothyroxine among Test group and Control group(n=60).

Triodothyroxine (T3)	Before Treatment		After Treatment		Percent change	P-value
	Mean	SD	Mean	SD		
Test group	114.90	23.56	118.90	23.78	3.48	0.459
Control	105.51	24.60	113.10	14.84	7.19	0.055
P-value (Test group vs Control)	0.55					

n=30 in test group and n=30 in control group
p=0.55 not significant

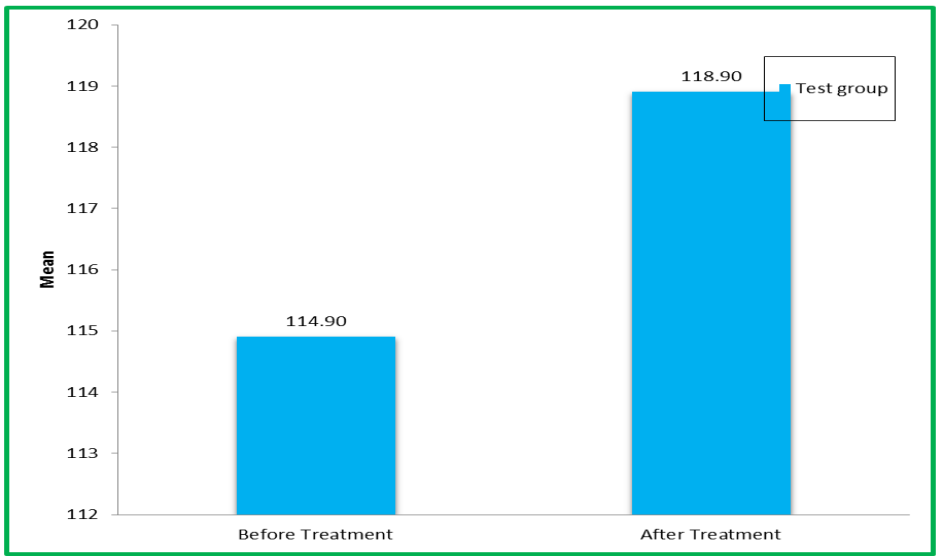

Figure.4: Showing Mean of Triiodothyroxine among Test and Control groups (n=60).

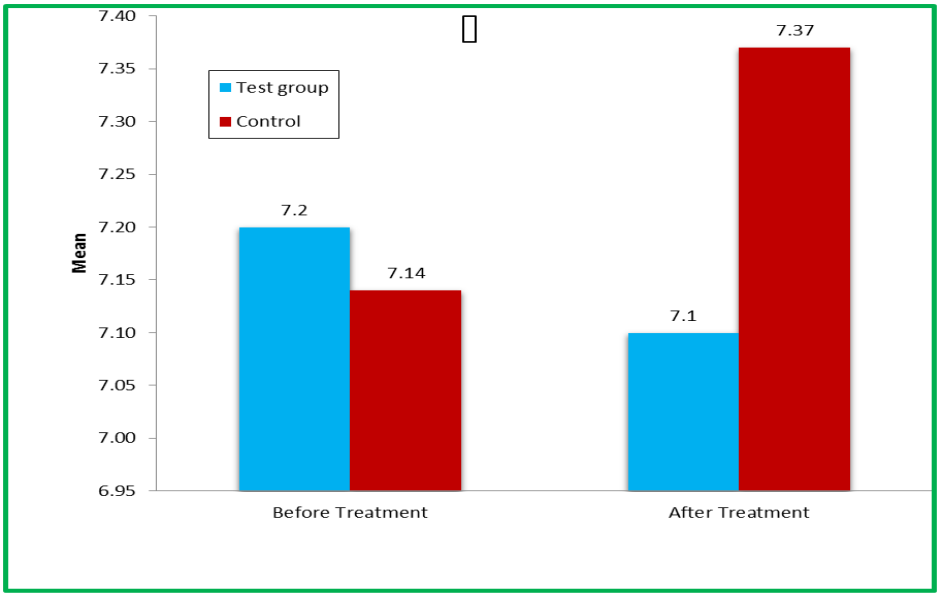

Figure.5: Showing Triiodothyroxine change in Test and control groups.

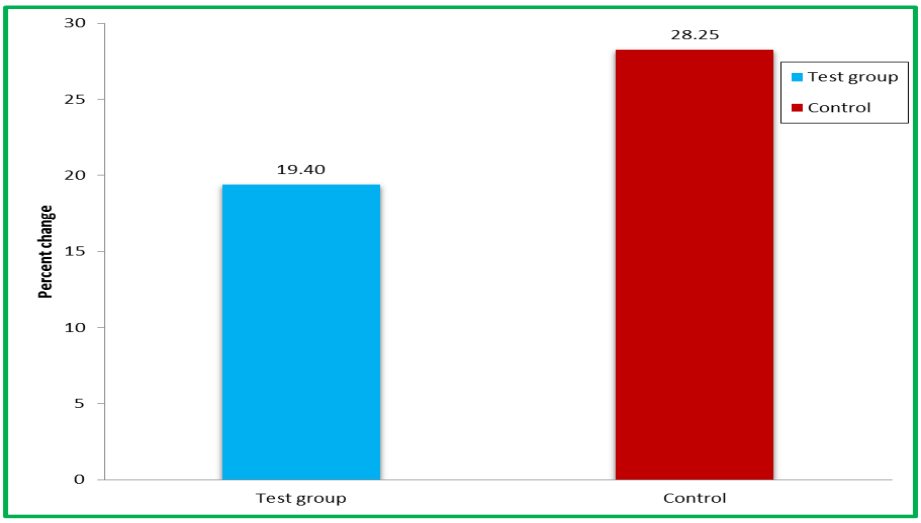

Figure.6: Showing Percent change of Thyroxine among Test and Control groups (n=60).

Table. 6: Showing Thyroid Stimulating Hormone among Test group and Control group (n=60).

									Significance of Test group vs Control group	
TSH	**Test group**				**Control**				**P- Value**	
	Before treatment		**After treatment**		**Before treatment**		**After treatment**		**Before treatment vs Before treatment**	**After treatment vs After treatment**
	No	**%age**	**No**	**%age**	**No**	**%age**	**No**	**%age**		
Normal	2.0	6.7	11.0	36.7	2.0	6.7	10.0	33.3		
Raised	28.0	93.3	19.0	63.3	28.0	93.3	20.0	66.7		
Total	30.0	100.0	30.0	100.0	30.0	100.0	30.0	100.0	1	0.786
Mean±SD=9.402±3.53			Mean±SD=7.93±4.37		Mean±SD=16.10±6.72		Mean±SD=7.55±4.705			
Test applied: Mcnemar, P- value= <0.001*					**Test applied: Mcnemar, P- value= 0.004**					

n=30 in test group and n=30 in control group
Test applied=Mcnemar's test
P<0.001 very significant in test group with respect to before and after treatment
P<0.004 significant in control group verses pre and post treatment.

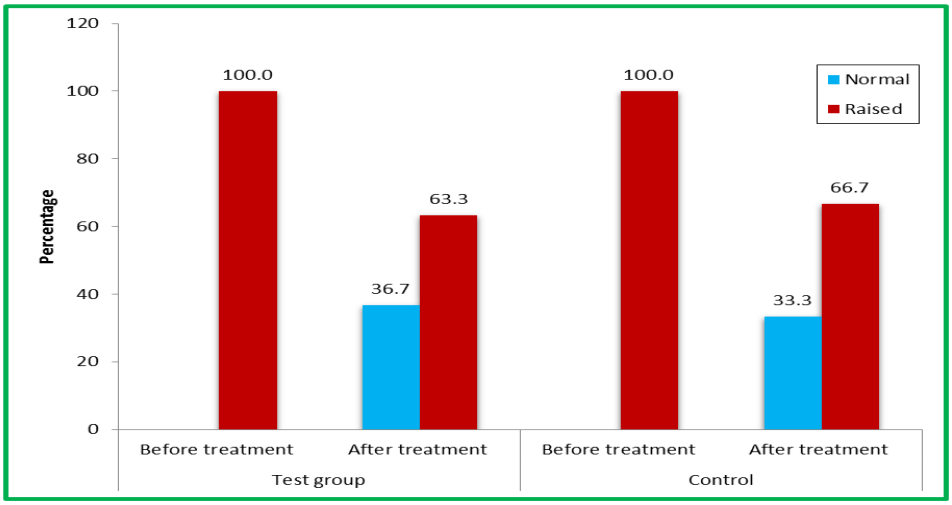

Figure 7: Showing Percent change of Thyroid Stimulating Hormone(TSH) among Test and Control groups (n=60).

DISCUSSION

The present study was conducted to evaluate the therapeutic efficacy of a single *Unani* drug *Muqil(Commiphora mukul)* in the management of Hypothyroidism (*Qillate-i-Ifraze Darqia).* A total of 72 patients were enrolled for the study ,out of those 8 didn't fulfilled the inclusion criteria and were excluded from the study.66 patients were randomly grouped and were allocated either test(Group A) or control(Group B) groups in equal distribution. During the treatment protocol,6 patients didn't completed the treatment course, and hence only 60 patients completed the treatment course with 30 in test group and 30 in control group. After the completion of treatment protocol of 60 days, stastical analysis were done.

Group A was given *Muqil (Commiphora Mukul)* in the form of powder in the dose of 1 gm twice daily after breakfast and after evening tea with warm water for a peroid of 60 days. Group B were given Tab. Thyroxine sodium 50 mcg orally once a day for a peroid of 60 days. The patients of both groups were followed up after every 15 days for a peroid of 60 days and recording of improvement in subjective and objective parameters were done on case record forms (CRF).

For statistical analysis, recorded data was compiled and entered in a spread sheet and then exported to data editor of SPSS version 20.0, Minitab version 14, and Graph pad prism software. The continuous variables like age and duration of disease were expressed in terms of (mean ± standard deviation) and categorical variables were expressed in terms of frequency and percentage. Student's independent t-test was employed for inter-group analysis of continuous data and for intra-group analysis paired t-test was applied. Wilcoxon signed rank test was used for intra group analysis of ordinal data. Chi-square test and Fisher's exact test was employed for inter group analysis of categorical data and for intra-group (before vs after) analysis of data categorical, McNemar's test was applied. The graphical representation of data was presented by means of bar graphs. A p-value of less than 0.05 was considered statistically significant.

The Mean ± SD for age of patients in test group was 38.4 ± 11.25 and 40.23 ±9.91 in control group. The difference in age of patients in test and control group was not significant(p=0.5) using paired "t" test. The age were analysed in both the groups which showed that hypothyroidism in the age group 36-45 years(33.3%) , 15-25 years (23.3%) ,46-60 years (23.3%) and 26-35 years (20%). which shows that hypothyroidism is more prevalent in 3rd & 4th decade of life.(Table.1/Figure.1)

As far as the sex is concerned, the disease is more common in females with 76.6% females and 23.3% males in test group and 80% females with 24% males in control group which clearly indicates the highest incidence in females. (Table.2/Figure.2) Stastical analysis for the *Mizaj* (temperament) indicated that 93.3% patients having *Balghami al-Mizaj* (phlegmatic temperament) were in test group and 80% in control groups. There was no patient with *Damvi al-Mizaj* (sanguine temperament)-0% in test group but 10% in control group. The percentage of patients with *Safrawi al- Mizaj* (bilious temperament) were 6.7% in test and 10% in control group.There was no patient with *Sawdawi al-Mizaj* (melancholic temperament) either in test and or in control group.Thus it strongly supports our hypothesis that hypothyroidism is a *balghami mar'd* (phlegmic disease) as the incidence of disease is highest in *Balghami al- Mizaj* (phlegmatic temperament)people. (Table .3/Figure.3)

To evaluate the clinical efficacy of test and control drugs on various subjective and objective parameters like somnolence, fatigue, hoarseness of voice, puffiness of face, loss of libido, hypothermia, delayed tendon reflexes, arbitary grading system was used with absent, mild, moderate and severe as 0,1,2,3 depending upon the

severity of symptoms and signs. Clinical assessment were carried out on 0^{th},30^{th},60^{th} days respectively.

The Mean ± SD for T_3 in test group was 114.90 ± 23.56 at baseline and 118.90 ±23.78 on 60th day, wheras in control group the Mean ± SD score for T_3 was 105.51 ± 26.40 at baseline and 113.10 ± 14.84 at 60th day. When Mean ± SD score for T_3 in both test and control group were compared statistically ,it was found that the difference between the Mean ± SD score for T_3 at 60th day compared with baseline was not significant (P>0.05). (Table.4/Figure.4,5)

The Mean ± SD for T_4 in test group was 7.20 ± 1.506 at baseline and 7.10 ± 1.93 on 60th day, wheras in control group the Mean ± SD score for T_4 was 7.14 ± 2.08 at baseline and 7.37 ± 1.48 at 60th day. When Mean ± SD score for T_4 in both test and control group were compared statistically, itwas found that the difference between the Mean ± SD score for T_4 at 60^{th} day compared with baseline was not significant (P>0.05). (Table.5/Figure.6,)

The Mean ± SD for TSH in test group was 9.40 ±3.53 at baseline and 7.93 ± 4.37 on 60^{th} day, wheras in control group the Mean ± SD score for TSH was 16.10 ± 6.72 at baseline and 7.55 ± 4.705 at 60^{th} day. When Mean ± SD score for TSH in both test and control group were compared statistically using Mcnemar test, it was found that the difference between the Mean ± SD score for TSH at 60^{th} day compared with baseline was not significant (P>0.05). When the Mean ± SD for TSH was compared with base line verses 60^{th} day in test groups,it was highly significant (p=.001) and in control group it was also significant (p=.004). (Table.6/Figure.7)

Safety parameters like Hb%, TLC, DLC, LFT, KFT, BSF, ECG, Urine examinations were done before and after the treatment to assess any toxic effect of test or control drugs. Statistical analysis using students independant t-test were done in all the cases and it is found that there was no significant change in these parameters as p value in all these parameters was greater than .05. (Table.31-40/Figure.21-41)

Thus, from all these subjective, objective, safety parameters and stastical analysis, it has become evident that the test drug has significant effect on most of the subjective parameters as well as on Serum TSH levels. The test drug ***Muqil (Commiphora mukul)*** having actions like *muhallil waram* (anti-inflammatory), *mulayyin* (laxative), *mudirr-i- bawl* (diuretic), *mudirr-i-haiz* (emmenogogue), *kasir al-riyah* (carminative), *mufattit al-hasah* (lithotriptic), *muqaww-i al-bah*(aphrodisiac), *munafis al- balgham* (expectorant), *jail* (rubifacient), *musakhkhin* (calorific), *muqaww-i A'sab*(nervine tonic), *muhrik* A'sab (nerve stimulant)[19-22,34-40] significantly improved the symptoms and signs of hypothyroidism such as somnolence, fatigue, hypothermia, libido, puffiness of face while its effect on hoarseness of voice and delayed tendon reflexes were insignificant The effects of test drug on lowering the raised Serum TSH are attributed to the thyroid activities of the test drug .Scientific studies have demonstrated that ***muqil*** activates the production of thyroid hormones Thyroxine (T_4), Triiodothyronine (T_3), and improves the symptoms and signs of hypothyroidism. Its lipid lowering effect is also related to its thyroid activity. 2-guggulestrone-a ketosteroid counteracts the thyroid suppressant activity of carbimazole. Its calorific (thermogenic) effect helps in cold intolerance of hypothyroid patients.[99,100,101,102,103] There was no toxic effect of either test or control dug on safety parameters. So it became evident that the test drug has significant effect on most of the subjective and objective parameters of hypothyroidism with no toxic effects on safety parameters. Therfore, the test drug ***Muqil (Commiphora mukul)*** is safe, effective, economical and has wide pharmacological actions. The test drug ***Muqil (Commiphora mukul)*** as a single drug or *Unani* compound formulations having this drug as main constituent may be tried in such patients as an alternative.

SUMMARY AND CONCLUSION

Hypothyroidism is a common endocrine disease resulting from deficient production of thyroid hormone. The term primary hypothyroidism indicates decreased secretion of thyroid hormone by factors affecting the thyroid gland itself. A decrease in serum concentrations of thyroid hormone causes an increased secretion of TSH, thus resulting in elevated serum TSH concentration. A decrease secretion in thyroid hormone can also be caused because of insufficient stimulation of the thyroid gland by TSH, because of the factors directly interfering with pituitary TSH release (secondary hypothyroidism) or indirectly by ablating hypothalamic TRH release (tertiary hypothyroidism). Even though the classical texts of *Unani* system of *medicine* has no direct mention of *qillatte ifraze darqia*(Hypothyroidism), but the clinical features of this disease are attributed to *su' mizaj barid maddi (balghami)* (impaired cold substative temperament). Hormone replacement therapy is successfully used to treat this disease but due to certain adverse effects, the need for a safe and holistic drug from the Treaures of *Unani* system of medicine is highly soughted for the treatment of this disease.

Hence, a research study titled 'Clinical Study of Hypothyroidism and its Management by a single *Unani* drug.' was carried out at Regional Research Institute of Unani Medicine (RRIUM) Srinagar, for therapeutic evaluation of a single *Unani* drug *Muqil(Commiphora mukul)* in the management of the above said disease. A total of 72 patients were enrolled for the study, 08 patients were excluded, 66 patients were randomized into test and control groups with 33 patients in each group. The patients of test group were given the test drug (*Muqil)* in powdered form in the dose of 1gm twice daily with warm half an hour after breakfast and after evening

tea water for a peroid of 60 days .Control group patients were given Tablet Thyroxine sodium 50mcg once daily before breakfast for a peroid of 60 days. 6 patients didn't completed the treatment protocol, and were considered drop outs. All the subjective and objective parameters were recorded in specially designed case record forms (CRF). Pre and post treatment safety parameters were monitored. Statistical analysis of all the data were done using Student's independant "t" test, Fishers exact test, Wilcoxan sign rank test, Mcnemar's test etc to evaluate the efficacy of the test drug.

The test drug ***Muqil (Commiphora mukul)*** showed significant effect on most of the subject parameters like somnolence, fatigue, puffiness of face, hypothermia, loss of libido, but showed no significant effect on hoarseness of voice and delayed tendon reflexes. The test drug showed significant effect on TSH levels, which vindicated our hypothesis that the drug has effect in primary hypothyroidism.

Hence, it may be concluded that the test drug has significant effect on most of the subjective and objective parameters of primary hypothyroidism without having any toxic effect on any of the safety parameters. The sample size was small, so trials on larger sized samples needs to be carried out to furthur evaluate the efficacy of the drug on large scale. Therefore, the test drug *Muqil (Commiphora mukul)* is safe, effective, economical and has wide pharmacological actions. The drug *Muqil (Commiphora mukul)* as a single drug or *Unani* compound formulations having this drug as main constituent, may be tried in such patients as an alternative.

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