International Journal of Health Sciences and Research
Vol.13; Issue: 3; March 2023
Website: www.ijhsr.org
Original Research Article *ISSN: 2249-9571*

A Randomized Clinical Study on Therapeutic Evaluation of Efficacy and Safety of a Polyherbomineral Unani Formulation in Hypothyroidism

Rafiuddin Khan[1], Mohan Singh[2], Azad Hussain Lone[3], Arshad Hussain Shah[4], Amanullah Haji[5]

[1]Department of Medicine and Dermatology, Markaz Unani Medical College & Hospital Kerela, India
[2]Director Ayush, Govt of J&K Kashmir
[3]Department of Dermatology, Govt Unani Medical College & Hospital Ganderbal Kashmir
[4]Department of Surgery, Govt Unani Medical College & Hospital Ganderbal Kashmir
[5]Department of Medicine, Govt Unani Medical College & Hospital Ganderbal Kashmir

Corresponding Author: Dr Azad Hussain Lone

DOI: https://doi.org/10.52403/ijhsr.20230311

ABSTRACT

Background: Primary hypothyroidism is the most common disease of thyroid gland. It is most prevalent disease affecting up to 40/10,000 in women and 6/10,000 in men each year. It leads to various complications such as myxedema, psychosis, myocardial infarction, congestive heart failure etc. and also adversely affects quality of life. The objective of present study was to evaluate safety and efficacy of a Polyherbal Unani formulation in the management of hypothyroidism on scientific parameters.
Methods: A randomized, single-blind, standard controlled study was conducted on 60 patients of primary hypothyroidism after taking informed consents and were randomly allocated to test (A) and control (B) groups. Group A was given Ployherbomineral Unani formulation (PHMUF) in the dose of 3 gm twice a day. While Patients of Group B were treated with the control drug, Thyroxine sodium (Eltroxine) 100 µ gm tablet orally once a day. The duration of treatment in both groups was 60 days. All the patients were kept under strict observation and assessment for subjective and objective parameters was done at 30 days interval. The results were analyzed statistically by using standard tests.
Results: The PHMUF exhibited statistically significant improvement on subjective parameters such as weight gain, cold intolerance, puffiness of face and lethargy in comparison to control group. But there was no significant effect of PHUF on objective parameters such as thyroid profile, Serum cholesterol and ECG in test group. However, there was significant effect on thyroid profile and Serum cholesterol ($p<0.05$) in control group. No significant effect was found in the control group on other objective parameters.
Conclusion: The study concluded that PHMUF is effective and safe in the symptomatic treatment of Primary hypothyroidism.
Key Words: Primary hypothyroidism; Polyherbomineral Unani formulation; Thyroid Profile.

INTRODUCTION

Hypothyroidism is the clinical syndrome that results from decreased secretion of thyroid hormone from the thyroid gland. It most frequently reflects a disease of the gland itself (primary hypothyroidism) but can also be caused by pituitary disease (secondary hypothyroidism) or hypothalamic disease (tertiary hypothyroidism). [1-2] It has been reported

that hypothyroidism is prevalent to the extent of 0.5% to 2% of all patients seeking medical care. Hypothyroidism has female sex predilection in the ratio of 6:1.[3-4] In Indian scenario, there is premature occurrence by 10 to 20 years, while in North America, it is observed in the age group of 50 to 60 years, acquired impairment of thyroid dysfunction, affects 2 % of adult women and 0.1 to .27 % of adult men.[5-9] Hypothyroidism affects all the organs and systems leading to the spectrum of clinical manifestations. These symptoms are generally related to the duration and severity of hypothyroidism, the rapidity with which hypothyroidism occurs, and the psychological characteristics of the patient. The signs and symptoms of hypothyroidism includes Fatigue, Weight gain from fluid retention, Dry skin, Cold intolerance, Yellow skin, Coarseness or loss of hair, Hoarseness of voice, Goiter, Delayed reflexes, Ataxia, Constipation, Memory and mental impairment, Decreased concentration, Depression, Irregular or heavy menses, Infertility, Myalgias, Hyperlipidaemia, Bradycardia, Hypothermia, etc. [1, 3,4, 7, 10]

Qillate Ifraze Darqia is literal meaning of hypothyroidism. There is no direct description of the hypothyroidism in the Unani classical literature. However the clinical features of this disease closely resemble with the *Alamaat Wa Awarizat* (clinical manifestations & complications) of *Sue Mizaj Barid (Altered Cold temperament). Sue Mizaj Barid* is a holistic concept and constitutes the fundamental base of pathogenesis of diseases in Greeko-Arabic Medicine commomly known as Unani Medicine in Asian subcontient. [11-12] The clinical manifestations of *Sue Mizaj Barid* amply described by eminent Greeko-Arabic scholars such as *Ibn Sina, Zakaria Razi, Rabban Tabri, Akber Arzani* in their respective treatises, include *Imtila* (congestion), dry and cold skin, *Kasrate Luabe Dahan* (excessive salivation), *Qillate Ishtiha* (decreased appetite), *kasrate naum* (excessive sleep), *Takaan* (fatigability), drowsiness, *Nabze bati* wa *mutafawit* (slow and delayed pulse), *Kund zahni* (diminished intellectual functions), puffiness of the body etc . In fact *Sue Mizaj Barid* is a descriptive phenomenon leading to other systemic manifestations such as involvement of various organs like heart, liver, brain, spleen, stomach, kidney etc. and consequently results into the spectrum of symptoms and sings.[13-15,16] In the light of above description, a hypothesis was formulated that treatment of *Sue Mizaj Barid (Balghami)* may somehow be interpretated with the management of hypothyroidism. Although thyroxine replacement therapy brought remarkable change in the management of hypothyroidism but long term duration of the treatment, drug interaction during hormone therapy and demonstration of adverse effects such as myocardial infarction, atrial fibrillation, congestive heart failure, adrenocortical insufficiency etc.[1, 3] are major drawbacks of hormone therapy which impugn its utility. Therefore, search of safe and effective drugs for the treatment of hypothyroidism through the heritage of Unani system of Medicine, is need of hour. Keeping this view into consideration, a Ployherbomineral Unani formulation was selected for the study. The ingredients of formulation are *Filfil siyah* (*Piper nigrum*), *Filfil safaid* (*Piper nigrum*), *Peepal* (*Ficus religiosa*), *Darchini* (*Cinnamomum zeylanicum), Salikha* (*Cinnamomum cassia*), *Khulanjan* (*Alpinia galanga), Naushadar* (*Ammonium chloride*), *Tukhme khayar (Cucumis sativus), Maviz munaqqa* (*Vitis vinifera*), *Podina dashti* (*Mentha longifolia*).[17] Most of the ingredients of formulation have *Haar Mizaj (Hot temperament)* and possess *Musakhkhin (Calorific)* properties, hence can be employed for the correction of *Sue Mizaj Barid* with the aim of production of *Hararat (Heat)* inside the body on the basis of principle of *Ilaj Bil Zid* (contrary therapy). [12, 18-20] Recently, in experimental studies some herbs such as *Kundur (Boswellia serrata), Muqil (Commiphora mukul),*

Asghand (Withania somnifera) etc. were proven to be effective in hypothyroidism.[21-24] Therefore, this study was envisaged to determine the efficacy and safety of a Ployherbomineral Unani Formulation in the management of hypothyroidism using standardized outcome measures.

MATERIALS AND METHODS

The present study was a randomized single blind standard controlled trial conducted at the out-patient departments of National Institute of Unani Medicine (NIUM), Bangalore and Govt Unani Medical college Hospital Ganderbal Kashmir after obtaining approval from the Institutional Ethical Committee. A total of 82 patients were enrolled in the study from the OPD of Medicine and Dermatology. Written informed consent was sought from every patient before inclusion in the study. Diagnosis was made on the basis of history, clinical examination and thyroid profile of patients. During screening, 16 patients did not fulfill inclusion criteria and excluded from the study, remaining 66 patients were allocated into test and control groups respectively through simple randomization technique by using computer generated Random Table Number. But 6 patients were lost to follow-up, leaving behind 30 patients in each group who completed the trial. Patients were enrolled in the study on the basis of inclusion & exclusion criteria.

Inclusion Criteria:

- Clinically diagnosed patients of Hypothyroidism.
- Patient of both sexes.
- Patient in age group of 20 to 60 years.

Exclusion Criteria:

- Pregnant and lactating mothers.
- Cardiovascular diseases,
- Severe renal diseases,
- Severe hepatic diseases.
- Patients below 18 and above 62 years.
- All complicated cases of hypothyroidism including secondary hypothyroidism.
- Diabetes Mellitus.
- Hyperthyroidism.
- Patients who fail to give consent and who fail to follow up

During the selection procedure, complete history, general physical and systemic examination was carried out and recorded on a prescribed case report proforma (CRF) which was designed according to the objectives of the study. Routine investigations like complete haemogram, urine and stool examination, Liver function tests (LFT), Renal function tests (RFT), Random Blood Sugar (RBS), Electrocardiography (ECG), Lipid Profile and thyroid Function tests (TFT) were done before treatment and after completion of treatment in both the groups in order to make the proper diagnosis, to exclude other systemic ailments and to assess the efficacy /safety of various treatment groups. Patients of test Group were advised to take Polyherbomineral Unani formulation.

Method of preparation & dosage of Polyherbomineral al formulation: All the ingredients were procured from department of pharmacy. The ingredients were properly identified by an expert to ascertain their originality. The drugs were cleaned by weeding out unwanted material. Equal quantity of ingredients were grinded to form powder and mixed with half weight of sugar. *Vitis vinifera* was grinded separately and mixed with powder to form a tablet. Each patient in test group was given test drug in the dose of 3gm twice a day in the form of tablet.

In control group, one tablet of standard drug Thyroxine sodium (Eltroxin) in the dose of 100 µ gm was administered orally once a day. Duration of treatment in both test and control groups was 60 days and follow up was done monthly. At every visit, the patients were asked about the improvement or worsening in their symptoms and subjected to examination to assess clinical findings. Concomitant treatment was not allowed during the protocol period. The

patients, who were taking any other medicine as a treatment of hypothyroidism, were advised to observe abstinence for two weeks from consuming any other drug before commencing treatment with the test or control drug. All the patients were kept under strict observation and assessment of the efficacy of treatment in test and control groups was carried out on the basis of subjective and objective parameters on 0 day, 30th day, and 60th day.

Subjective parameters included lethargy, weight gain, cold intolerance, hoarseness of voice, dry and coarse skin and puffiness of the face. While assessment of objective parameters was done by biochemical markers i.e. TFT, Serum cholesterol and ECG changes of the patients. As these subjective parameters differ in severity from patient to patient, therefore an arbitrary grading of subjective parameters was advocated for appropriate assessment and statistical evaluation of various signs and symptoms to evaluate the efficacy of the Test drugs. All the subjective parameters were graded on the basis of severity of symptoms by using 4-point scale, where 0 corresponded to no symptoms, 1 to mild symptoms, 2 to moderate symptoms and 3 to severe symptoms at the maiden visit and any worsening or improvement in any of the parameters was noted down at every visit of follow up till the end of the treatment. The GCP (Good Clinical Practice) was adhered to and regular monitoring was made as stated above.

Analysis of Data

After the completion of study, the data in both groups was tabulated and analyzed statistically using Graph Pad InStat Version 3.00 for Windows (Graph Pad Software San Diego Calif. USA) The difference in the treatment groups was considered significant at $P<0.05$ and highly significant at $p<0.01$. Subjective parameters were analyzed by Friedman test, Kruskal-Wallis with Dunn's multiple comparison tests and objective parameters were analyzed by Paired and unpaired 't' tests. The overall efficacy of both herbal formulation and control drugs was assessed by Chi Square test.

OBSERVATIONS & RESULTS

Demographic data of patients is shown in Table-1. The present study was conducted on 66 patients of hypothyroidism aged between 20-60 years but 6 patients were lost to follow-up, leaving behind 30 patients in each group who completed the trial. The mean age of patients in test and control groups was 35.2 and 34.7 respectively. Out of total patients, 26.6% patients were observed in age group 20-30 years, 50% in age group 31--41 years, 16.6% in age group 41-50 years and 6.6% in age groups 51-60 years. Out of total 60 patients, 10% patients were males and 90% were females. Using the standard parameters, Mizaj of patients was evaluated as described in Unani doctrine. 83% patients were observed in *Balghami Mizaj* (Phlegmatic) , 17% patients in *Damavi Mizaj* (Sanguine) and 0% in *Safrai Mizaj* (Bilious) and *Saudavi Mizaj* (Melancholic).

Table-1. Baseline Demographic Profile of patients.

Parameter	No. of patients	Percentage
Age in years	n	%
20-30	16	27
31-40	30	50
41-50	10	17
51-60	04	06
Total	60	100
Gender		
Male	06	10
Female	54	90
Family History		
Present	18	30
Absent	42	70
Socioeconomic status		
Upper	0	0
Upper middle	10	17
Lower middle	24	40
Upper lower	26	43
Lower	0	0
Marital Status		
Married	58	97
Unmarried	02	03
Duration of Illness		
Lessan than 1 year	16	27
01-05 years	30	50
06-15 years	14	23
16-20 years	0	0
Mizaj		
Damvi	10	17
Balghami	50	83
Safravi	0	0
Saudavi	0	0

Effect on Subjective Parameters

Effect on lethargy, weight gain, cold intolerance, puffiness of face & Hoarseness of voice: Statistically significant ($p<0.05$) results were observed in both groups. The results indicated that both PHMUF and control drugs are effective in alleviating these symptoms of hypothroid patients but PHMUF showed comparatively quick response and is more effective than the control drug. Table-2

Effect on dry and coarse skin: When the median scores of dry and coarse skin in both Groups, were compared statistically by using Friedman test for intragroup comparisons and Kruskal-Wallis test for intergroup comparison. it was found that the difference between the median scores of Test group at 60th day compared with baseline was not significant ($p>0.05$). Intergroup comparison was also not significant at 60th day ($p>0.05$). Table-2

Table No. 2 Effect of PHMUF & Control drug on Subjective Parameters (Median scores with Ranges in bracket)

Group	Parameter	Assessment days			p value
		0 day	30th day	60th day	
Test n=30	Lethargy	3 {2,3}	2 {0,3}	1{0.3}	p<0.001
	Weight gain	74.2±9.833		72.9±9.947	p<0.05.
	Cold intolerance	2{1,3}	2{1,3}	1{0,1}	p<0.001
	Puffiness of face	2{0,3}	2{0,3}	1{0,2}	p<0.001
	Hoarseness of voice	0{0,3}	0{0,2}	0{0,1}	p<0.05.
	Dry and coarse skin	0.5{0,3}	0{0,2}	0{0,2}	p>0.05.
Control n=30	Lethargy	3 {2,3 }	2 {1,3}	1 {0,2}	p<0.001
	Weight gain	70.9±13.739		69.8±13.456	p<0.05.
	Cold intolerance,	3{2,3}	2{1,3}	1{0,1}	p<0.001
	Puffiness of face	3{2,3)	2{1,3}	1{1,2}	p<0.001
	Hoarseness of voice	0{0,3}	0{0,3}	0{0,2}	p>0.05.
	Dry and coarse skin	1.5{0,2}	1{0,2}	0{0,2}	p>0.05.

Tests used = Friedman test with post Dunn's multiple compressions test for intragroup and Kruskal-Wallis test with Dunn's multiple comparisons test for intergroup

Effect on Objective Parameters

Effect on Goitre: When the median scores of goitre in both Groups, were compared statistically, it was found that the difference between the median scores of Test group at 60th day compared with baseline was not significant ($p>0.05$). Intergroup comparison was also not significant at 60th day ($p>0.05$). Table-3

Effect on Thyroid Profile (T3, T4, TSH): When Mean ± SEM score of T3, T4 and TSH in both Groups, were compared statistically by using paired and unpaired 't' tests, it was found that the difference between the Mean ± SEM score of Test group at 60th day compared with baseline was not significant ($p>0.05$) . But in case of Control group the difference between the Mean ± SEM score at 60th day compared with baseline was significant ($p<0.05$). Table-3

Table No. 3 Effect of PHMUF & Control drug on Objective Parameters (Mean ± SEM)

Group	Parameter	Assessment days		p value
		0 day	60th day	
Test n=30	Goiter	0{0,0}	0{0,0}	p>0.05
	T3	88.616±30.438	103.02±25.11	p>0.05.
	T4	9.445±13.603	6.707±1783	p>0.05.
	TSH	26.119±44.220	25.46±34.025	p>0.05.
	Serum cholesterol	180.55±39.096	123.4±24.592	P<0.05.
Control n=30	Goiter	0{0,2}	0{0,1}	p>0.05
	T3	87.863±48.727	118.9±24.219	p>0.05.
	T4	7.211±3.137	9.394±3.357	p>0.05
	TSH	26.926±45.377	7.454±11.293	p<0.05
	Serum cholesterol	184.4±13.426	196.5±23.282	p>0.05

Tests used: Paired and unpaired 't' tests.

Effect on Serum Cholesterol: When Mean ± SEM score of Serum cholesterol in both Groups were compared statistically, it was found that the difference between the Mean ± SEM score of Test and Control groups at 60th day compared with baseline was significant ($p<0.05$). Table-3

Effect on ECG: There was no significant effect of test and control drugs on ECG.

Effect on Safety Parameters: Complete Haemogram, FBS, LFT, KFT and Urine analysis were done before and after the treatment to rule out toxicity in both groups. All the data were collected and analyzed by using paired and unpaired 't' tests. p value was found >0.05, which suggests that there was no significant change in all the safety parameters as they were within normal limit in both groups after the treatment. Table-4

Table No. 4 Effect of PHMUF & Control drug on safety parameters (Mean ± SEM)

Group	Parameter	Assessment days		p value
		0 day	60th day	
Test n=30	Hb (gm %)	12.24 ± 1.227	11.685±1.600	p>0.05.
	TLC (cells/cu mm)	6840±1958.9	7325±1607.2	p>0.05.
	FBS (mg/dl)	86.7±11.21	86.65±12.04	p>0.05.
	Blood Urea (mg/dl)	19.465±6.573	21.41±5.436	p>0.05.
	Serum Creatinine (mg/dl)	0.756±0.114	0.83±0.126	p>0.05.
	Serum Bilirubin (mg/dl)	0.682±0.278	0.69±0.321	p>0.05.
	SGOT (IU/L)	22.55±7.917	22.1±9.947	p>0.05.
	SGPT (IU/L)	29.49±31.22	33.2±40.36	p>0.05.
Control n=30	Hb (gm %)	12.43±1.805	12.54±0.974	p>0.05.
	TLC (cells/cu mm)	6855±2432.5	7440±1969.9	p>0.05.
	FBS (mg/dl)	85.2±9.175	84.9±6.707	p>0.05.
	Blood Urea (mg/dl)	17.1±3.755	20±4.269	p>0.05.
	Serum Creatinine (mg/dl)	0.77±0.116	0.77±0.116	p>0.05.
	Serum Bilirubin (mg/dl)	0.747 ± 0.487	0.593 ± 0.424	p>0.05.
	SGOT (IU/L)	25.4 ± 11.01	19.7 ± 5.355	p>0.05.
	SGPT (IU/L)	24.6 ± 20.38	21.6 ± 12.66	p>0.05.

Tests used: Paired and unpaired 't' tests.

DISCUSSION

Hypothyroidism is a common disorder arising more often in women than men and increasing in incidence with age, especially after the onset of middle life. Because primary hypothyroidism is much more frequent than secondary hypothyroidism (about 1000 to 1) in both sexes at all ages, TSH measurement can be used to estimate the prevalence of hypothyroidism in populations.[9, 25] The present randomized single blind standard controlled study was conducted to evaluate the efficacy of a PHMUF in the management of primary hypothyroidism. A total of 82 patients were initially registered for the study but only 60 patients completed the trial completely. Group A comprising of 30 patients was treated with PHMUF in the form of a tablet while patients of Group B were administered with control drug, Thyroxine sodium (Eltroxin). The patients of both groups were treated for a period of 60 days and assessed at interval of 30 day for any improvement or deterioration in the symptoms of disease.

The analysis of demographic data revealed that 50% patients were found in the age group 31-41 years. This data suggested that the disease is more prevalent in the age group of 31-40 years. These finding corresponds with the finding of Naik VS who mentioned that hypothyroidism is more prevalent in 4th and 5th decades of life.[5, 9, 25] The disease has a definite relation with sex because in the present study, the highest incidence of 90% was observed in female patients while 10% in male patients in both test and control groups. This study shows that hypothyroidism prevails mostly in females. These data are in conformity with the findings reported by Ashraf Aminorroaya, et al and Madhuri Devdhar, et al.[5, 26] As far as the marital status of hypothyroid patients is concerned, out of 60 patients, 97% patients were married and 3% patient was unmarried. As this disease usually occurs in the 4th and 5th decade,

therefore the majority of the patients were married.[5, 25]

As it is evident from Table-1, the disease is closely related with the socioeconomic status and the highest incidence of 43% was observed in upper lower class (IV), followed by 40% in lower middle class (III). The maximum patients belonged to the lower socioeconomic status in both groups. No convincing data is available to demonstrate the existence of this disease among different socioeconomic status in the society. The study demonstrated the corelation between *Mizaj* of the patients and the disease. A maximum of 83% patients were found having *Balghami Mizaj* followed by 17% patients having *Damvi Mizaj*. It indicated that hypothyroidism is more prevalent in *Balghami Mizaj* patients. Since the clinical features of this disease closely resemble with the clinical manifestations of *Sue Mizaj Barid Balghami*. The result of present study was obviously in consonance with the description of *Ibn Sina*, *Abu Bakr Zakaria Razi*, *Rabban Tabri*, *Akber Arzani*.[11, 13, 15, 27, 28] and thus proved the rationale of Unani Medicine that hypothroidism is more prevalent in patients having phlegmatic temperament.

The present study proved the efficacy and safety of a PHMUF in the management of primary hypothyroidism. The effectiveness of PHMUF may be due to regression of various symptoms and signs by different pharmacological actions like calorific, diuretic, resolvent, rubefacient, anti-inflammatory and diaphoric of various ingredients present in it. To assess the effects of PHMUF and Control drugs on subjective and objective parameters, the patients were assessed for various signs and symptoms on 0 day, 30th day and 60th day respectively. The severity was rated as severe, moderate, mild and absent and graded as 3, 2, I and 0, respectively, based on arbitrary grading system. The results indicated that both the test and control drugs are effective in reducing lethargy, weight gain, cold intolerance, puffiness of face & hoarseness of voice but the test formulation is more effective than the control drug. The improvement in lethargy may be due to the *Muqawwie aam* (Generalized tonic), *Muharrik asab* (Nervine stimulant) and *Muqawwie asab (Nervine tonic)* effect of Piper nigrum, Cinnamomum zeylanicum, Cinnamomum cassia, Alpinia galanga present in PHMUF .[18-20, 29, 30]

The improvement in weight gain might be due to *Mudir* (Diuretic), *Muhallil* (Anti-inflammatory), *Mushile balgham* (Phlegmatic Perogative), *Dafae fasade balgham* (Anti Phlegmatic impairment), and *Muarriq* (Diaphoretic) properties of most of the ingredients i.e. *Piper nigrum*, *Ficus religiosa*, *Cinnamomum zeylanicum*, *Cinnamomum cassia*, *Alpinia galanga*, *Ammonium chloride*. These results are in accordance with the properties of the drugs suggested by *Ibn Baitar*, *Ibn Hubal Baghdadi*, *Ibn Rushd*, *Najmul Ghani*, *Kabeeruddin*, etc.[18-20, 29-31] The response of PHMUF in alleviating cold intolerance may be attributed to the fact that most ingredients of test formulation have *Haar Mizaj* (Hot temperament) and possess *Musakhkhin* (Calorofic) properties like *Piper nigrum*, *Piper nigrum*, *Ficus religiosa*, *Cinnamomum zeylanicum*, *Cinnamomum cassia*, *Alpinia galanga*, *Ammonium chloride* etc. These results are in accordance with the properties of the drugs suggested by *Ibn Baitar*, *Ibn Hubal Baghdadi*, *Ibn Rushd*, *Najmul Ghani*, *Kabeeruddin*, etc. [18-20, 29, 30] Similarly the improvement in puffiness of face & hoarseness of voice might be due to *Mudir* (Diuretic), *Muhallil* (Anti-inflammatory), *Jazib* (Absorbent), and *Dafae fasade balgham* (Anti Phlegmatic impairment) properties of most of the ingredients of test drug i.e. *Piper nigrum*, *Ficus religiosa*, *Cinnamomum zeylanicum*, *Cinnamomum cassia*, etc. These results coincide with the actions documented by *Ibn Hubal Baghdadi*, *Ibn Rushd*, *Najmul Ghani*, *Kabeeruddin*, etc. [18-20, 29, 30]

The effects of test and control drugs on objective parameters such as goitre, thyroid

profile, serum cholesterol and ECG were assessed. Changes in thyroid profile was seen in patients of both groups. After analysing the Mean ± SEM score for T3, T4 and TSH in test group, statistically, it was found that difference between Mean ± SEM score of Test group at 60th day compared with baseline was not significant ($p>0.05$). But in case of Control group, difference between Mean ± SEM score at 60th day compared with baseline was significant ($p<0.05$).

The Mean ± SEM score for Serum cholesterol in both the groups was compared statistically and it was found that the difference between Mean ± SEM score of Test and Control groups at 60th day compared with baseline was significant ($p<0.05$). This significant response of PHMUF is attributed to the *Mudir* (Diuretic), *Muhallil* (Anti-inflammatory), *Muarriq* (Diaphoretic) and hypolipedemic actions of *Piper nigrum*, *Piper nigrum*, *Ficus religiosa*, *Cinnamomum zeylanicum.* [29-31]

The safety evaluation was assesed by conducting Complete Haemogram, FBS, LFT, KFT and Urine analysis in all enrolled patients before and after the treatment to rule out toxicity in both groups. After statistically comparing this data, no significant change was observed in the safety parameters in both groups after the treatment as p value was found >0.05. In the light of above discussion, it was apparent that PHMUF produced significant effect on various subjective parameters without demonstrating any sign of toxicity or side effects. Individual drugs that constitute the composition of PHMUF have been reported to possess some interesting pharmacological effects that directly or indirectly supported the hypothesis regarding the efficacy of the trial formulation. Pertinently *Musakhkhin* and *Muharrik asab* properties of *Filfil siyah, Khulanjan, Darchini, Salikha, Peepal,* and *Naushader* [29-31] enhanced the metabolic activity and increased *Hararate Tabiya (innate heat)* helped to bring back normal temperament in patients. The *Muhallil* and *Mujaffif* properties of *Peepal, Darchini, Salikha,* and *Naushader* resolve the morbid matter, particularly *Rutubate Mukhatia (mucous secretions)* and helped to reduce edematous condition of the body. [18-20] Furthermore, the *Mudir* effect of the drugs viz *Tukhme khayar, Podina dashti, Maviz Munaqqa, Filfil siyah, Peepal, Darchini, Salikha* etc [18-20] helped in excretion of morbid material through diuresis and *Muarriq* action of the *Khulanjan, Salikha, Podina dashti* and *Filfil siyah* also helped to excrete the *Fuzlate fazila (morbid fluids)* through skin [29-31]. Therefore, the amelioration in the subjective parameters seems to be cumulative effect of various ingredients of the trial formulation and diverse mechanism of action of the PHMUF. Regarding objective parameters there was no significant effect of PHMUF on thyroid profile and ECG. Whereas significant effect on thyroid profile and serum cholesterol was observed in control group.

CONCLUSION

Thus it may be concluded that PHMUF is safe, economical and devoid of any obnoxious side effects. Hence may be used for the management of subjective symptoms of hypothyroidism. It is obvious that PHMUF is relatively ineffective on thyroid profile. The non significant effect of PHMUF might be due to small sample size and short duration of treatment in the present study. Therefore, authors recommend that long term study with a bigger sample size, double blind study and Phase III clinical trials can be carried out to elucidate other pharmacological actions of PHMUF.

Declaration by Authors

Ethical Approval: Approved

Acknowledgement: Authors are highly grateful to Dr.Shabeer Gaffari, Nodal Officer/DMS Govt Unani Medical college and associated Hospital Ganderbal Kashmir for providing all the necessary facilities during the study.

Source of Funding: None
Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Fauci AS, Braunwald E, Kasper L. Dennis. *Harrison's Principal of Internal Medicine*. Vol. II.17th ed. New York: McGraw Hill; 2008: 2229-2233.
2. Walter Siegenthaler. *Differential Diagnosis in Internal Medicine*.19th ed. Germany: Georg Thieme Verlag Rüdigerstrasse Stuttgart; 2007: 482,488.
3. Wilson, Foster, Kronenberg. *Williams Textbook of Endocrinology*. 9th ed. Philadelphia, Pennsylvania: Saunders Company; 1998: 460-465,467-72.
4. Gaurav S, Singh Savita, Singh KP., et al. Effect of yoga on pulmonary function tests of hypothyroid patients. *Indian J Physiol Pharmacol* 2009; 54: 51 -56.
5. Madhuri Devdhar, Yasser H. Ousman, Kenneth D, et al. Hypothyroidism. *Endocrinol Metab Clin N Am* 2007; 36: 595–615.
6. Thomas W. and Grahm G. Hypothyroidism, presenting as psychosis: Myxedema Madness. *Primary care companion J Clin Psychiatry* 2003; 5: 260-266.
7. Birte Nygaard. Hypothyroidism (primary). *Clinical Evidence* 2010; (1): 605-607.
8. Lloyd WH. Goldberg JL. Incidence of hypothyroidism in the elderly. *British Medical Journal* 1961; 11(9):1258-1259.
9. Caroline GP, Paul W Ladenson. Hypothyroidism. *Lancet* 2004; 363: 793–803.
10. Becker KL, Ronald C. *Principles and Practice of Endocrinology and Metabolism*. 3rd ed. New York: Lippincott Williams & Wilkins Publishers; 2002: 398,399.
11. Kabeerudin M. *Kulliyate Qanoon* (Urdu translation) Vol. I. New Delhi: Aijaz Publishing House; 2007: 240, 356.
12. Razi AMBZ. *Kitab al Mansoori* (Urdu translation by CCRUM) 1st ed. New Delhi: Ministry of H & FW, Govt. of India; 1991:63,111,112,142,141.
13. Ahmad Altaf Azmi. *Basic Concepts of Unani Me*dicine. 1st ed. New Delhi: Jamia Hamdard, Hamdard nagar; 1995: 60-66.
14. Khan MA. *Al-Akseer* (Urdu translation by Kabeeruddin M). Vol I & II. New Delhi: Aijaz publishing house; 2003: 27, 29,631,632,573,810.
15. Tabri AAM. *Al-Mualajat Al-Buqratiyah* (Urdu translation by CCRUM). Vol. III. New Delhi: Ministry of Health and Family Welfare; 1997: 21, 28, 202, 203, 338.
16. Zaidi IH, Zulkifle M, Ahmad SN, *Temperamentology- A scientific appraisal of Human temperament*. 1st ed. Aligarh 1999:18, 19, 68-98.
17. Qamari AMH. *Ghina Muna*. New Delhi: CCRUM; 2008: 453,454.
18. Ghani N. *Khazainul Advia*. New Delhi: Idara Kitabul Shifa; YNM: 495- 496,682-684, 509, 1063-1064, 1324-1325, 1102, 479, 1284.
19. Anonymous. *Standardisation of single drugs of Unani medicine*. Part I. CCRUM, Ministry of H&FW, Govt of India; 1987: 60, 65,175-179, 215,217,219,240-241.
20. Anonymous. *The Unani Pharmacopeia of India*. Vol. I & IV. New Delhi: Ministry of Health and Family Welfare, Govt. of India; 2007: 38-40, 26-27, 96-97.
21. Mishra LC, Singh BB, Dagenais S. Scientific Basis for the Therapeutic Use of *Withania somnifera* (Ashwagandha): A Review. *Alternative Medicine Review* 2000; (5): 32-38.
22. Panda S, Kar A. Gugulu (Commiphora mukul) induces triiodothyronine production: possible involvement of lipid peroxidation. *Life Sci*1999; 12:137-41.
23. Tripathi YB, Tripathi Pratibha, et.al. Thyroid Stimulatory Action of (Z)-Guggulsterone: Mechanism of Action. *Planta Medica* 1988; 9: 271-277.
24. Panda S, Kar A. Changes in thyroid hormone concentrations after administration of ashwagandha root extract to adult male mice. *J Pharm Pharmacol* 1998; 9:1065-8.
25. Naik VS. Hypothyroidism. *The journal of general Medicine*. 2008; 3: 13-17.
26. Ashraf A, Mohsen Janghorbani, et al. The Prevalence of Thyroid Dysfunction in an Iodine-Sufficient Area. *Arch Iranian Med* 2009; 12 (3): 262 – 270.
27. Majoosi A. *Kamilus Sana* (Urdu translation by Kantoori GH) Vol. I. Lucknow: Munshi Nawal Kishore; 1889:25, 28,426.
28. Jurjani SI. *Zakhira Khawarizm Shahi* (Urdu translation by khan HH) Vol. VII. Lucknow: Munshi Nawal Kishore; 1996: 35,36.
29. Momin M. *Tuhfatul Momenin*. Matba Hasni; 1272 AH: 188,113,112,189.

30. Ibnul Quf AF. *Kitab al Umda fil Jarahat* (Urdu translation by CCRUM) Vol. I New Delhi: Ministry of Health and Family Welfare; YNM: 261,270, 240,296, 265.
31. Ibn Rushd AWM. *Kitabul Kulliyat* (Urdu Translation). 2nd ed. New Delhi: CCRUM; 1987:360-363.

How to cite this article: Rafiuddin Khan, Mohan Singh, Azad Hussain Lone et.al. A randomized clinical study on therapeutic evaluation of efficacy and safety of a Polyherbomineral Unani formulation in hypothyroidism. *Int J Health Sci Res.* 2023; 13(3):116-125.
DOI: *https://doi.org/10.52403/ijhsr.20230311*

******