



A SINGLE BLIND CLINICAL TRIAL TO EVALUATE THE EFFICACY OF UNANI FORMULATION IN HISATH-UL-MARARA (CHOLELITHIASIS)

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ABSTRACT

Introduction: Cholelithiasis (Hisat-e- Marara) is a crystalline concretion formed within the gall bladder by the accretion of bile components. Gallstone disease is a major health problem leading to Surgical intervention. Various biochemical and patho-physiological factors have been reported to be associated with gallstone disease such as stasis of bile, obstruction in the bile duct, infection in the bile, obesity, oestrogen level, defective function of liver and gallbladder, reduction in bile salt concentration and various precipitating factors for stone formation. In Unani literature this disease comes under the caption Hisat-e- Safravi or Hisat ul Marara which forms in biliary tract. According to unani physicians the causes of gall stone formation are dame ghaliz, Zoaf quwate dafeya, shiddate quwate jaziba, congenital narrowing of biliary system, khilte ghaliz wa lazuj etc. Gall stones are quite prevalent in most western countries (10%-15%). It is estimated that at least 25 million persons in the United States have gall stones, less frequent in India around 4%. Women are affected more often than men in theratio of 4:1. It is observed that gall stone is more common in FATTY, FORTY, FERTILE and FEMALES i.e, 4Fs.

Aim and Objectives: To assess the safety of unani compound formulation in cases of Hisath-ul-Marara. To evaluate the efficacy of unani compound formulation in the management of Hisat - ul -Marara.

Methodology: The Study was conducted as a single blind clinical trial on 40 patients in speciality Outpatient Department, Post Graduate Department Of Moalijat, Govt. Nizamia Tibbi College and General Hospital, Hyderabad. 40 patients. Patients allocated in a single group were given the test drug in form of joshanda of kulthi (7 gm) and Powder (5gm) of Khare khask, lahsun and Naushadar, twice daily up to 90 days with five follow-ups (15th ,30th ,45th, 60th,75th and 90thday). The Pre and post treatment effects were assessed based on subjective and objective parameters.

Results and conclusion: The Subjective parameters like Right Hypochondric pain, Nausea, Vomiting, Indigestion, Flatulence were reduced with statistical significance (P= <0.0001), and the USG findings were changed with (P= 0.0319). The Test drug is effective and is found safe without any adverse events during the study period.

Key Words: cholelithiasis, Hisat-e-Marara, Hisat-e-safravi, Gall stones, concretion.

INTRODUCTION

Gall stone formation is the most common disorder of the biliary tree.³

It remains one of the major causes of abdominal morbidity throughout the world. Now-a-days gallbladder disease is a frequent problem in developed countries representing a major health problem leading to surgical intervention. Women are affected more often than men in the ratio of 4:1. It is observed that gall stone is more common in FATTY, FORTY, FERTILE and FEMALES i.e, 4Fs.⁵⁰ It is rare in first two decades. Incidence gradually increases after 20 years, reaches peak in 5th and 6th decades in both sexes and all races. Some risk factors for the development of cholesterol gallstones are obesity, age, female gender, pregnancy, genetic factors, total parenteral nutrition, rapid weight loss, stasis of the gallbladder and certain medications (oral contraceptives, clofibrate, and somatostatin analogs).

EPIDEMIOLOGY:

Gall stones are quite prevalent in most western countries (10%-15%). In the United States, several series have shown gall stones in at least 20% of women and in 8% of men over the age of 40 years and in upto 40% over the age of 65 years. It is estimated that at least 25 million persons in the United States have gall stones and that one million new cases of cholelithiasis develop each year. In India gall stones are less frequent and it is estimated to be around 4% and among the people of East Africa it is 0%.

Gall stone in unani system of medicine

The Unani classical literature illustrated this disease under the caption "Safravi pathri" or "Hisat ul Mararah" which forms in the biliary tract⁶ and also there are various descriptions available which are similar to gall stone obstruction (suddah). The Unani science is fundamentally based on Hippocratic doctrine of humoral theory which hypothesises the presence of four humours i.e. dam (sanguine), balgham (phlegm), safra (yellow bile), and sawda (black bile) in the body. The equilibrium of the four humours maintains the health status of an individual. When an imbalance in the quantity or quality of anyone is found to be a diseased condition. Obstruction whether it originates in the liver or Gall Bladder, it will obstruct the flow of bile which leads to derangement of temperament of liver (su-e-mizaj kabit) results in increase production of bile.⁵

Further it is described that there are four common cellular balancing mechanisms available in the human body for maintenance of normal equilibrium of the cells. These mechanisms are 1. Absorptive power (Quwate Jazibah), 2. Retentive power (Quwate Masikah), 3. Digestive power (Quwate Hazimah) and 4. Expulsive power (Quwate Dafiah). The persistent malfunctioning of cited mechanisms may result into pathological condition and apart from it, the Shiddat Quwate Jazibah, Zoaf e Quwate Dafiah and bile sepsis (safra Ghaliz) may lead to stasis of bile (biliary sludge) and formation of Gall Stones which lead to obstructive jaundice.⁵

Unani philosophers had described various theories of cholelithiasis, choledocholithiasis and jaundice.

Avicenna (980-1037) in his canon of Medicine describes that the Obstruction either it originates in the liver or Gall Bladder, it will obstruct the flow of the bile.

He told that the causes of Gall stone formation are dam-e ghaliz, zoaf quwate dafiah, Shiddat jazibah, khilte ghaliz wa lazuj.⁵

He also mentions that in cold diseases urine turns red due to Obstruction in the duct between Gall Bladder and the intestines from the excess of phlegm diverts the bile towards the kidneys for excretion in the urine.

Galen (130-200AD) in his famous book "History of Medicine" mentioned that Jaundice is the result of Obstruction to the Bile ducts.²³

Ismail Jurjani (1040-1136AD) in his book Zakhira Khwarzami shahi mentioned that due to Obstruction (suddah) between liver and Gall Bladder, Safra (bile) does not pass to duodenum and it leads to accumulation of bile in liver and thus results in Warm -e kabit.⁴¹

Zakariya Razi (854-933 AD) in 7th volume of his book "Kitab al Hawi fi al Tibb" mentioned the types of jaundice as Obstructive and non obstructive. He also describes pain and heaviness at liver portion.⁴⁷

Allama Hakeem Kabeer uddin in his famous book Sharah-e- asbab & Tarjum-e- kabeer states that according to Nafees Ibn Awaz, Gall stone is also called as Safravi pathri or Hisath-ul-Mararah which forms in the biliary tract due to which acute pain occurs at liver site.⁶

He also describes that formation of Stone in Gall Bladder is similar to that of Kidney and bladder stones.

He also mentions that formation of gallstones in Gall Bladder occurs due to increase in concentration of Bile in Gall Bladder which is also called as Bile Stone. Some times bacteria in the gallbladder act as nucleus for stone formation.⁶

Ahmed Tabri (810-855 AD) in his book "Al Moalijat al Buqhratiya" described Obstruction as a cause of Jaundice and also mentions that the change in the physiology of the liver results in formation of stones, inflammation and ulcer.¹⁷

Ali bin Abbas Majusi (930-994 AD) in his famous book "Kamil-us-sana" mentioned that jaundice occurs due to obstruction in the bile duct by the stone. Due to which there occurs an increase production of bile in the liver and bile does not go to the gall bladder instead it gets increased its concentration in the blood leading to jaundice.¹⁶

Hakeem Mohd. Akbar Arzani in 1721 AD in his famous book "Mizan-un-Tibb" stated that thick viscid bile is the cause of gall stone.³⁵

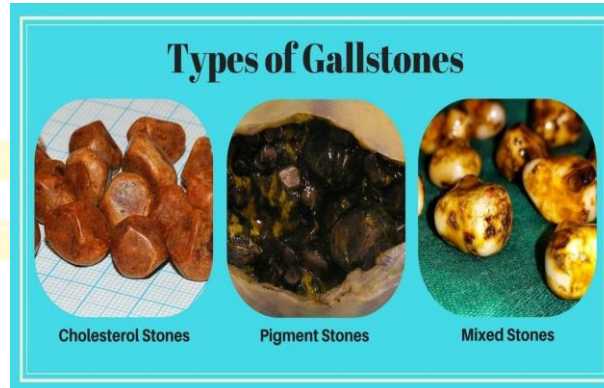
Ibn Hubal (1122-1213) in his book "Kitab al Mukhtarat fi al-tibb" mentioned the same cause of gallstone as by Ibn-e-sina with addition of two

Special diets. 1. Hareesa (the meal prepared by meat & crushed wheat) & 2. Aseeda (the meal prepared by ghee and flour).²⁴
Hakeem Mansoor Qamri in his book "Gana Mana" states that when there is obstruction between the liver and gall bladder Jaundice is developed.

TYPES OF GALLSTONES :⁵⁰

Gallstones contain cholesterol, bile pigment and calcium carbonate, either in the pure form or in various combinations. Accordingly, gallstones can be divided into three major types.

- Pure gallstones
- Mixed gallstones
- combined gallstone



-CLINICAL PRESENTATION:

Symptoms — majority of gallstones are asymptomatic and remain so. Only about 10% of those with gallstones develop clinical evidence of gallstone disease.

- Gallstones usually produce symptoms by causing inflammation (cholecystitis) or obstruction following their migration into cystic duct or CBD. The most specific and characteristic symptom is biliary colic, obstruction of the cystic duct or CBD by a stone produces increased intra-luminal pressure and distension of the viscous that cannot be relieved by repetitive biliary contractions.
- The resultant visceral pain is characteristically a severe, steady ache or fullness in the epigastrium or right upper quadrant (RUQ) of the abdomen with frequent radiation to the inter-scapular area, right scapula or shoulder.
- Biliary colic begins quite suddenly and may persist with severe intensity for thirty minutes to five hours, subsiding gradually or rapidly, Nausea and vomiting frequently accompany episodes of biliary pain. Frequently the pain starts during the night, waking the patient. Minor episodes of the same discomfort occur intermittently during the day.
- Biliary colic may be precipitated by eating a fatty meal, by consumption of large meal following a period of prolonged fasting, or by eating normal meal.
- Fever or chills with biliary pain persistent beyond 5hrs usually imply a complication that is acute cholecystitis, pancreatitis or cholangitis.
- Digestive symptoms- complaints of vague epigastric fullness, dyspepsia, eructation or flatulence may be associated.

Signs:

The abdomen moves poorly, hyperesthesia is maximal in the 8th and 9th right thoracic segments and the right upper abdominal muscles are rigid during the attacks of biliary colic, Murphy's sign is positive. The liver edge is tender and elevated level of serum bilirubin or alkaline phosphatase suggests a common duct stone.

METHODOLOGY

Before starting the project, a comprehensive protocol was checked out and put forth for ethical clearance from the Institutional Ethical Committee and registered in Clinical Trial Registry of India (CTRI). After obtaining clearance from the Ethical committee with Ref.No. NTC/M/2020/108 and registration no. 20314221013D and also **CTRI NO- CTRI/2023/02/049499**. The trial has been started by enrolling the eligible patients. This study stretched from 2022-2023.

The present study named as "**SINGLE BLIND CLINICAL TRIAL TO EVALUATE THE EFFICACY OF UNANI FORMULATION IN HISATH-UL-MARARA (CHOLELITHIASIS)**." was carried out at Govt. Nizamia General Hospital, Hyderabad during the period 2022-2023.

Total 40 patients were selected in a single group and the study was conducted for 90 days.

DURATION OF STUDY : The study was carried out during the period of 2022-2023.

STUDY DESIGN : SINGLE BLIND CLINICAL TRIAL

SAMPLE SIZE : The sample size fixed as 40 patients in a single group.

CRITERIA FOR SELECTION OF THE PATIENTS

Inclusion Criteria :

- Patient of either sex.
- Age group 20- 65 years.
- Symptomatic and asymptomatic cases of cholelithiasis.
- Patient willing to Stop on going treatment for cholelithiasis.

Exclusion Criteria :

Gall Bladder stone patient with

- Age group < 20 years and > 65years.
- Pancreatitis.
- Malignancy (Gall bladder, Hepato biliary tract).
- Common Bile Duct Calculi.

Withdrawal Criteria :

- Non -compliance
- Any adverse drug reaction.
- Drug intolerance.



SELECTION OF THE PATIENTS

Patients were selected on the basis of clinical diagnosis. Any patient of the age group 20- 65 years giving history of dyspepsia, right hypochondric pain, nausea and vomiting was selected from Speciality OPD and evaluated for the consideration as a research project. In the process of selection, USG of abdomen was done as specific investigation.

ASSESSMENT OF MIZAJ

Determination of mizaj was done on basis of different parameters mentioned in classical unani literature.

INFORMED CONSENT : Patients were kept under strict observation and advised for follow up for every fortnight in a total duration of 90 days. At every visit, patients were asked about the progression or regression in their symptoms and subjected to assess the clinical findings.

INVESTIGATION:

Routine investigations :

- Complete blood picture.
- Erythrocyte sedimentation rate (E.S.R).
- Complete Urine examination.
- Liver function test (LFT).
- Renal function test (RFT).
- Lipid profile.

Specific investigation

Ultrasonography of abdomen (USG)

Efficacy assessment: The assessment of the efficacy in the test was based on two types of parameters. a. Subjective parameters & b. Objective parameters, Subjective parameters included dyspepsia, right hypochondric region pain, nausea, vomiting, flatulence while assessment of objective parameters included laboratory investigations, radiology (Ultrasonography of abdomen) of the patients suffering from Hisat-e- Mararah (Gall stone). As these parameters differ in severity from patient to patient, an Arbitrary grading of subjective parameters was improvised for appropriate assessment and statistical evaluation of various signs and symptoms to evaluate the efficacy of the test drug.

Safety Assessment: The assessment of the safety of the treatment was done on the following parameters: a) Clinical assessment at every visit of follow up.

A. SUBJECTIVE PARAMETERS

1. Dyspepsia

Grade	Severity	Duration
0	Nil	0 hour
1	Mild	1-3 hrs after meal
2	Moderate	4-8hrs after meal
3	Severe	>8hrs

2. **Right Hypochondric region pain**

Grade	Severity	Symptom
0	No pain	No pain
1	Mild	Pain on deep breathing
2	Moderate	Pain on palpation
3	Severe	Pain at rest

3. **Nausea**

Grade	Severity	Duration
0	No nausea	Absent
1	Mild	Less than 30 min
2	Moderate	Half an hour to an hour
3	Severe	1-4 hrs mostly all of the day

4. **Vomiting**

Grade	Severity	Duration
0	No vomiting	0 episodes
1	Mild	1-2 episodes in 24 hrs
2	Moderate	3-4 episodes in 24 hrs
3	Severe	≥5 episodes in 24 hrs

5. **Flatulence**

Grade	Severity	No. of times
0	Absent	Absent
1	Mild	5-7 times
2	Moderate	8-15 times
3	Severe	>15 times

B. OBJECTIVE PARAMETERS

Radiological changes (USG of abdomen)

METHOD OF COLLECTION OF DATA: Data is collected from the patient through interview method and investigation records.

OUTCOME MEASURES:

Primary Outcome: Reduction in size of the Gall stone.

Secondary Outcome: To relieve abdominal pain, Nausea, vomiting, Indigestion, and Flatulence.

FOLLOW UP DURING TREATMENT : At fortnight interval the check up included the History and improvement in the sign and symptoms or any development. After 90 days second ultra sound scan of abdomen was taken and improvement was compared with the symptomatic relief, plus the Dissolution of stones, and there found Reduction of stone size in maximum cases, and complete removal of stones in few cases were observed.

WITHDRAWAL DURING TREATMENT :

Total 53 patients were included in the study. Out of which 40 patients were in proper follow up and remaining 13 were included into withdrawal section either due to unwillingness of the patient to keep on participating in the study or due to not completing treatment period.

TREATMENT GROUP CRITERIA:

The treatment group is allocated in a single group.

TEST GROUP : Have a sufoof consist of three single drugs associated with decoction of single drug.

Sufoof Or Powder : This includes the following ingredients

- Khare Khask - 3 gms
- Seer - 1 gm
- Naushadar - 1 gm

Method of preparation of powder : The above drugs are grinded into fine powder and then packets of 10gms each were prepared. Patients were advised to take one packet of 10 gms twice daily after meals.

Joshanda/Decoction : This Include The Following Ingredient.

- Habbul Qilt - 7 gms

The above drug is grinded coarsely and then packet of 14 gms were prepared. Patients were advised to take one packet of 14gms in two divided doses twice daily in 50ml decoction form before meals along with the above Powder or Sufoof.

OBSERVATION AND RESULTS

Table No.1 DISTRIBUTION OF PATIENT ACCORDING TO AGE

S. No.	Age	Frequency	Percent	Valid Percent	CumulativePercent
1	20-30	8	20.0	20.0	20.0
2	31-40	15	37.5	37.5	57.5
3	41-50	11	27.5	27.5	85.0
4	51-60	3	7.5	7.5	92.5
5	>60	3	7.5	7.5	100.0
	Total	40	100.0	100.0	

Graph No.1 Distribution Of Patient According To Age

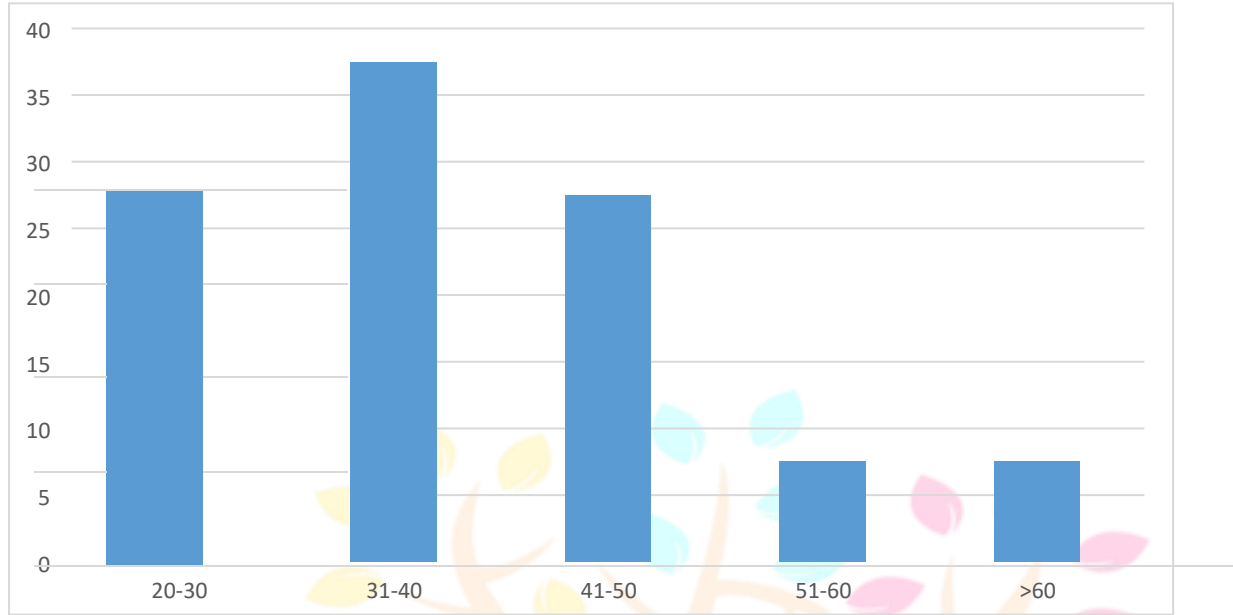


Table No.2 Incidence Of Gallstone In Either Sex

Sex	Frequency	Percentage	Valid Percent	CumulativePercent
Male	10	25.0	25.0	100.0
Female	30	75.0	75.0	75.0
Total	40	100.0	100.0	

Graph No.2 Incidence Of Gallstone In Either Sex

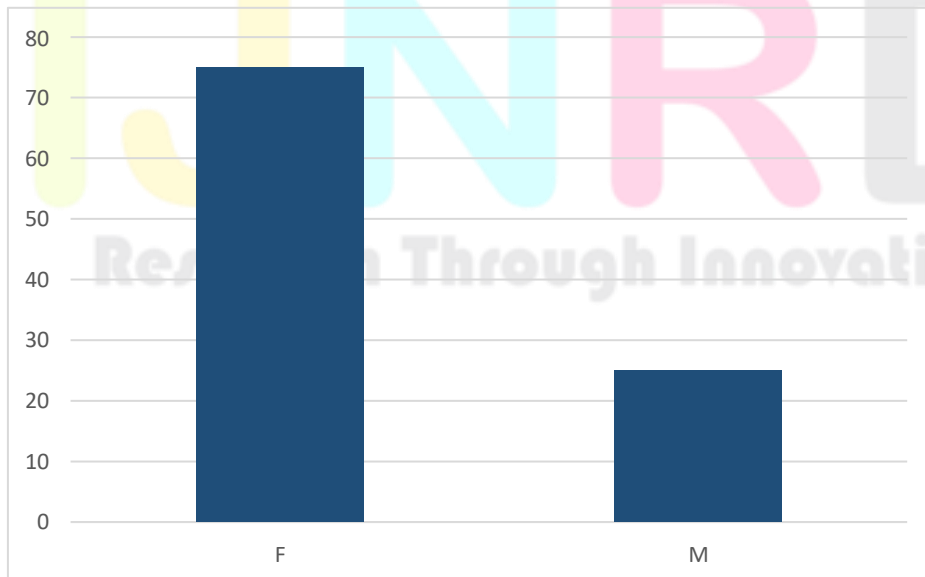
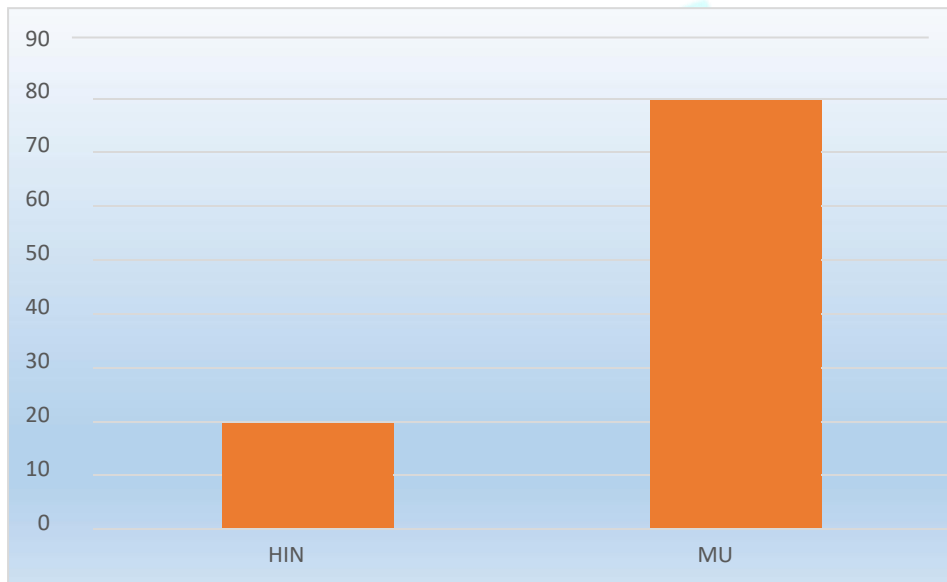


Table No.3 Distribution Of Patients According To Religion

Religion	Frequency	Percent	Valid Percent	CumulativePercent
HIN	8	20.0	20.0	20.0
MU	32	80.0	80.0	100.0
Total	40	100.0	100.0	

Graph No.3 DISTRIBUTION OF PATIENTS ACCORDING TO RELIGION**Table No.4 Distribution Of Patients According To Marital Status**

Marital status	Frequency	Percent	Valid Percent	CumulativePercent
M	35	87.5	87.5	87.5
UM	5	12.5	12.5	100.0
Total	40	100.0	100.0	

Graph No.4 Distribution Of Patients According To Marital Status

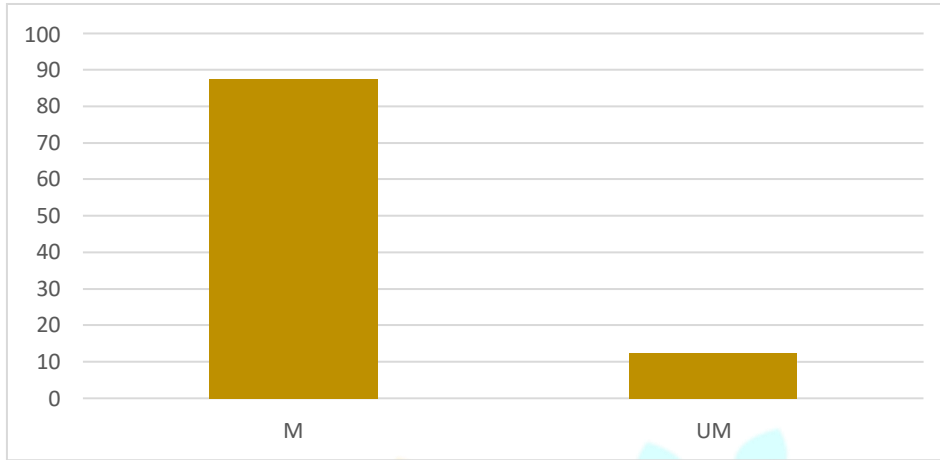


Table No.5 Distribution Of Patients According To Weight

Weight	Frequency	Percent	Valid Percent	Cumulative Percent
40-60	25	62.5	62.5	62.5
60-80	12	30.0	30.0	92.5
>80	3	7.5	7.5	100.0
Total	40	100.0	100.0	

Table No.5 Distribution Of Patients According To Weight

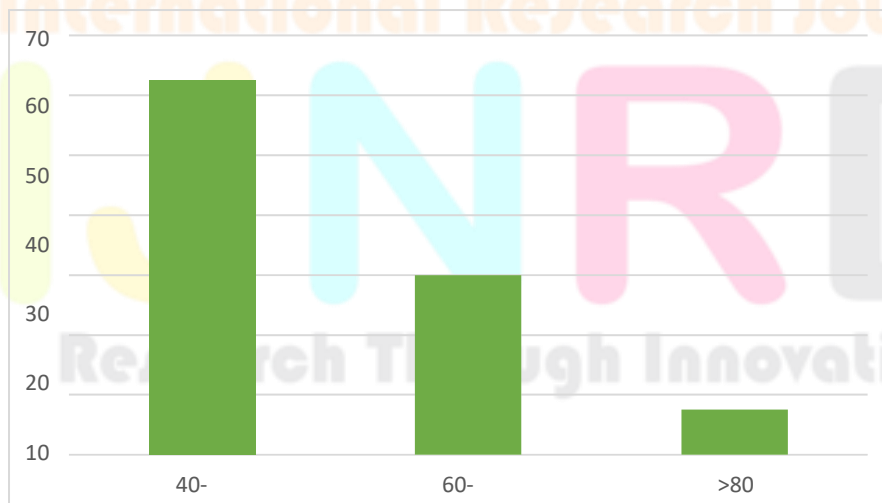


Table No.6 DISTRIBUTION OF PATIENTS ACCORDING TO MIZAJ

Mizaj	Frequency	Percent	Valid Percent	Cumulative Percent
B	23	57.5	57.5	57.5
D	6	15.0	15.0	72.5
SA	2	5.0	5.0	77.5
SF	9	22.5	22.5	100.0
Total	40	100.0	100.0	

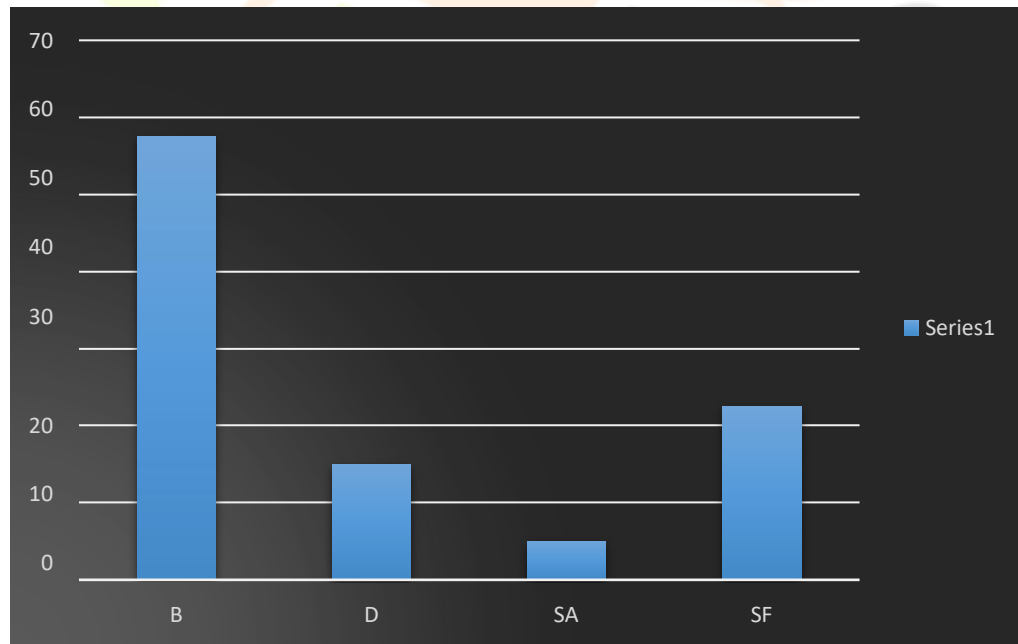
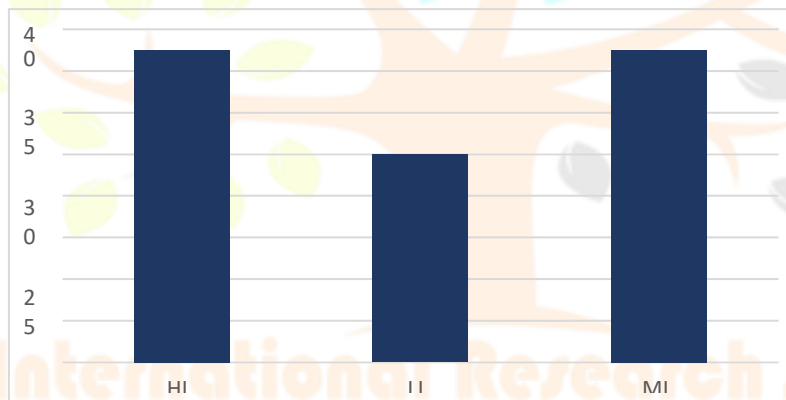
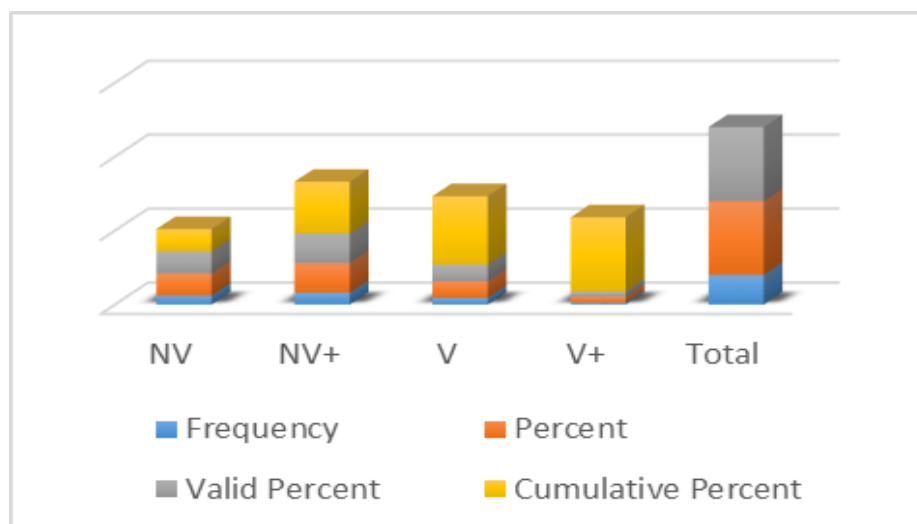
GRAPH No.6 DISTRIBUTION OF PATIENTS ACCORDING TO MIZAJ

Table No.7 DISTRIBUTION OF PATIENTS ACCORDING TO SOCIOECONOMIC STATUS

SES	Frequency	Percent	Valid Percent	Cumulative Percent
HIG	15	37.5	37.5	37.5
LIG	10	25.0	25.0	62.5
MIG	15	37.5	37.5	100.0
Total	40	100.0	100.0	

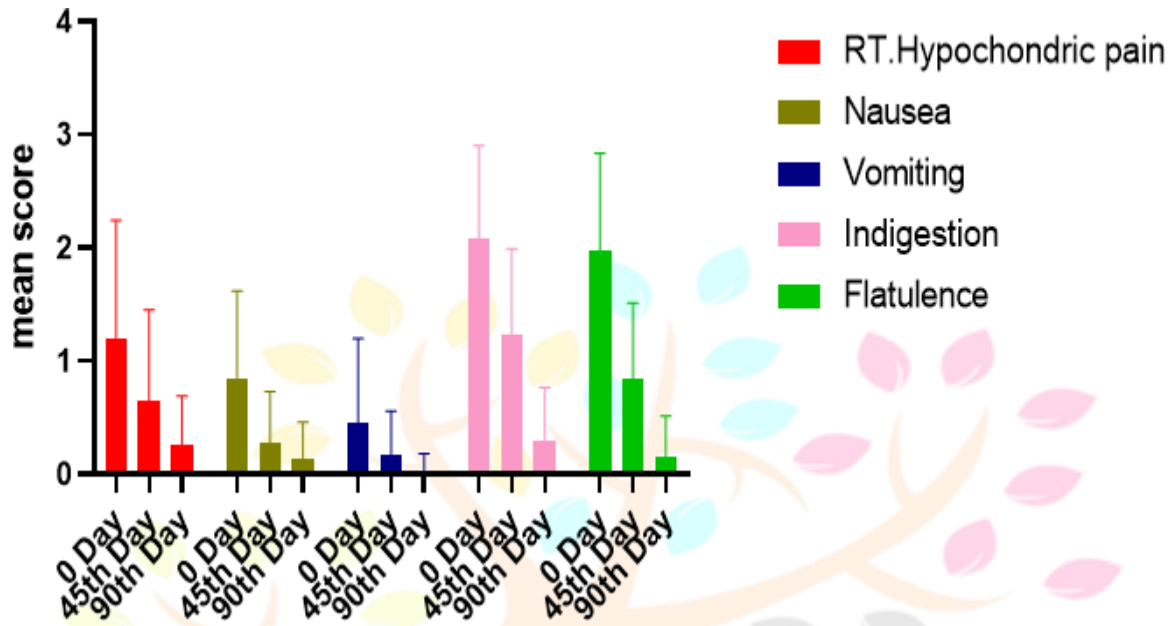
GRAPH No.7 DISTRIBUTION OF PATIENTS ACCORDING TO SOCIOECONOMIC STATUS**Table No.8 DISTRIBUTION OF PATIENTS ACCORDING TO DIET**

Diet	Frequency	Percent	Valid Percent	CumulativePercent
NV	12	30.0	30.0	30.0
NV+	16	40.0	40.0	70.0
V	9	22.5	22.5	92.5
V+	3	7.5	7.5	100.0
Total	40	100.0	100.0	

GRAPH No.8 DISTRIBUTION OF PATIENTS ACCORDING TO DIET**Table No.9 COMPARISON OF SYMPTOMS AT EACH FOLLOW-UP WITH RESPECT TO BASELINE CONDITION**

Dunnett's multiple comparisons test	MeanDiff.	95.00% CI of Below diff.threshold?	Summary Adjusted P Value
Rt. Hypochondric pain			
0 Day vs. 45th Day	0.5500	0.3183 to 0.7817	Yes **** <0.0001
0 Day vs. 90th Day	0.9500	0.6431 to 1.257	Yes **** <0.0001
Nausea			
0 Day vs. 45th Day	0.5750	0.3593 to 0.7907	Yes **** <0.0001
0 Day vs. 90th Day	0.7250	0.4405 to 1.010	Yes **** <0.0001
Vomiting			
0 Day vs. 45th Day	0.2750	0.02865 to 0.5213	Yes * 0.0269
0 Day vs. 90th Day	0.4250	0.1539 to 0.6961	Yes ** 0.0018
Indigestion			
0 Day vs. 45th Day	0.8500	0.6564 to 1.044	Yes **** <0.0001
0 Day vs. 90th Day	1.775	1.522 to 2.028	Yes **** <0.0001
Flatulence			
0 Day vs. 45th Day	1.125	0.8502 to 1.400	Yes **** <0.0001
0 Day vs. 90th Day	1.825	1.542 to 2.108	Yes **** <0.0001

Research Through Innovation

GRAPH No.9 COMPARISON OF SYMPTOMS AT EACH FOLLOW-UPWITH RESPECT TO BASELINE CONDITION**Table No.10 COMPARISION OF OBJECTIVE PARAMETERS BEFORE AND AFTER TREATMENT**

Objective Parameters		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	SGOT BT	41.0250	40	60.77765	9.60979
	SGOT AT	34.1500	40	10.39119	1.64299
Pair 2	SGPT BT	42.8750	40	58.63935	9.27170
	SGPT AT	36.9750	40	13.72157	2.16957
Pair 3	ALP BT	91.7750	40	50.82322	8.03586
	ALP AT	73.4250	40	28.59253	4.52088
Pair 4	T CHOL BT	207.8250	40	41.34898	6.53785
	T CHOL AT	165.0000	40	27.09811	4.28459
Pair 5	S.TRIG BT	151.3200	40	64.10451	10.13581
	S.TRIG AT	111.5500	40	33.54824	5.30444
Pair 6	LDL BT	130.3500	40	40.03751	6.33049
	LDL AT	95.3000	40	26.20256	4.14299
Pair 7	VLDL BT	34.2075	40	14.91615	2.35845
	VLDL AT	24.4250	40	7.10322	1.12312

Graph No. 10 COMPARISON OF MEAN VALUES OF OBJECTIVE PARAMETERS

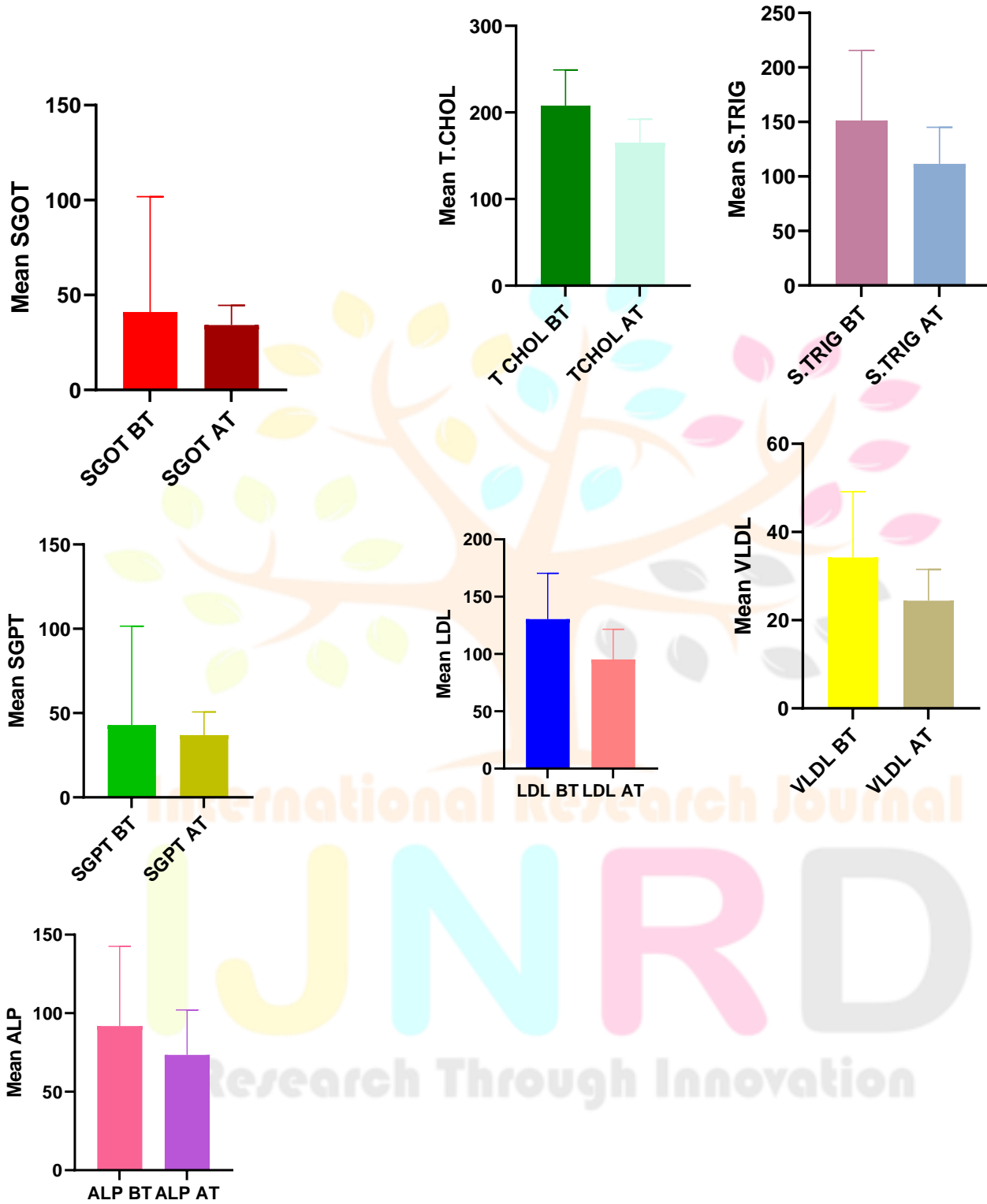


Table No.11 COMPARISION OF OBJECTIVE PARAMETERS BEFORE AND AFTER TREATMENT

Paired Samples Test									
		Paired Differences					t	df	Sig.(2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	SGOT BT - SGOT AT	6.87500	62.21929	9.83773	-	26.77370	.699	39	.489
Pair 2	SGPT BT - SGPT AT	5.90000	61.07280	9.65646	-	25.43203	.611	39	.545
Pair 3	ALP BT – ALP AT	18.35000	37.49294	5.92815	6.35918	30.34082	3.095	39	.004
Pair 4	T CHOL BT - T CHOL AT	42.82500	37.29500	5.89686	30.89748	54.75252	7.262	39	.000
Pair 5	S.TRIG BT - S.TRIG AT	39.77000	51.16993	8.09068	23.40506	56.13494	4.916	39	.000
Pair 6	LDL BT – LDL AT	35.05000	34.18573	5.40524	24.11687	45.98313	6.484	39	.000
Pair 7	VLDL BT - VLDL AT	9.78250	12.43300	1.96583	5.80623	13.75877	4.976	39	.000

Table No.12 COMPARISION OF USG IN LAST FOLLOW-UP WITH RESPECT TO THE BASE CONDITION

USG	Mean	Standard. Deviation	Ncomparision	P value
Before Treatment	9.1425	4.07323	40	-
After Treatment	7.0400	4.52343	40	Day 0 v/s Day90 0.0319

DISCUSSION

Gall stone is most common diseases of biliary tract. Gall stone formation results from many complex factors working together. The Pathologic factor related to gallstone formation is still hot debate. Bile stasis secondary to gall bladder dyskinesia is the most widely accepted theory. The present study was designed to evaluate the safety and efficacy of the Unani formulation in cases of Hisath-e-Marara (cholelithiasis). In this study, the compound Unani drugs safety and efficacy has been assessed by the improvement in the enzymatic levels. In this Study though Single Group (experimental) the symptoms disappeared in duration of 90 days.

The study conducted on 40 patients allocated in SINGLE GROUP.

The assessment is characterized with patient's Age, Sex, Religion, Marital status, Weight, Mizaj, Diet, Socio economic status, from Table 1-8 and effects of variation analysis of subjective parameters are discussed in table 9, and objective parameters in table 10-13.

Table 1 : Cholelithiasis is rare before the age of 15-20 years. The incidence gradually increased as middle age approaches. Highest incidence is observed in 4th and 5th decade.

While analyzing the age of patients during the study, they were divided into five age groups viz. 20-30 years, 31-40 yrs, 41-50 yrs, 51-60 yrs and >60 yrs, as depicted from the (Table-1). It was observed that incidence of Gall stone was found maximum in age group of 31-40 years. I.e, 15 (37.5%) patients. In the age group 41-50 years 11 (27.5%) patients were belongs, In the age group 20-30 years, 8 (20%) patients were belongs, minimum and same percentage I.e, 3 patients (7.5%) is seen in both age groups of 51-60 years and >60 years.

Table 2 : The Male to female ratio in formation of Gall stones is 1:4. Among the 40 cases, 30 were females and 10 were males.

It was observed that 25% of male and 75% of female as depicted from (Table-2). It shows Gall stone is more common in females as described in literature. The distribution of sex differ significantly between male and female.

Table 3 : In the study out of 40 (100%) patients in SINGLE GROUP, The minimum number of patients were belongs to HINDU I.e, 8 (20%), and maximum number belongs to MUSLIMS is 32 (80%).

Table 4 : In the study out of 40 (100%) patients in SINGLE GROUP. The minimum number of patients were belongs to Unmarried I.e., 5 (12.5%), and maximum number belongs to have Married is 35 (87.5%).

Table 5 : While analyzing the weight of the patients they were divided into three groups viz. 40-60 kg, 60-80 kg, and >80kg. In the study out of 40 (100%) patients in SINGLE GROUP, The maximum number of patients were belongs to 40-60 Kg I.e., 25 (62.5%), 12 (30%) patients belongs to 60-80kg and minimum number belongs to >80 I.e, 3 (7.5%).

Table 6 : The concept of Mizaj (Temperament) is an important component of Unani Medicine on which health or disease condition of human being are based. Diagnosis, treatment and prevention from diseases, is also determined by the temperament assessment. In unani system, the diseases of liver and biliary apparatus occurs due to Safravikhlith.

Out of 40 (100%) Patients in SINGLE GROUP, 23 (57.5%) Patients were of BALGAMI MIZAJ, 9 (22.5%) patients were of SAFRAVI MIZAJ, 6 (15%) patients were of DAMAVI MIZAJ, and only 2 (5%) patients were of SAUDAVI MIZAJ. From the study it shows that Balghami mizaj patients are more prone to develop Gall stones.

Table 7 : The Socio economic status has been categorized into three. I.e, High Income group, Middle Income Group, and Low Income Group. In the study out of 40 (100%) patients In SINGLE GROUP, The minimum number of patients were belongs to LOW INCOME GROUP I.e., 10 (25%)

, whereas same number belongs to HIGH INCOME GROUP i.e, 15 (37.5%) and MIDDLE INCOME GROUP i.e, 15 (37.5%). It is concluded that the two groups, High Income group and Middle Income group are more prone to develop Gall stones.

Table 8 : During study all patients were divided into four categories viz. vegetarian, vegetarian+ junk, Non-vegetarian and Non-vegetarian + junk. It was observed that 40% cases were Non-vegetarian, 30% were Non-vegetarian + junk, whereas 22.5% were vegetarian and 7.5% were vegetarian + junk. The result was according to the prevalence literature of Gall stone. i.e, it is more common in Non-vegetarians.

Table 9 : The Clinical symptoms assessed in gall stones were Right hypochondric pain, Nausea, Vomiting, Indigestion, Flatulence. These Symptoms were given the grading based on the severity as (0 – Absent, 1- Mild, 2- Moderate and 3- severe) according to ARBITRARY GRADING SCALE and assessed on every 15 days as 0th day, 15th day, 30th day, 45th

day, 60th day, 75th day & 90th day and compared at each follow-up with respect to the baseline condition. After intervention clinical symptoms Right Hypochondric pain compared as 0th day v/s 45th day with mean difference of 0.5500, (P=<0.0001) and 0th day v/s 90th day with mean difference of 0.9500, (P=<0.0001). Nausea compares as 0th day v/s 45th day with mean difference of 0.5750, (P=<0.0001), and 0th day v/s 90th day with mean difference of 0.7250, (P=<0.0001). Vomiting, compares as 0th day v/s 45th day with mean difference of 0.2750, (P=0.0269) and 0th day v/s 90th day with mean difference of 0.4250, (P=0.0018). Indigestion compares as 0th day v/s 45th day with mean difference of 0.8500, (P=<0.0001) and 0th day v/s 90th day with mean difference of 1.775, (P=<0.0001). Flatulence compares as 0th day v/s 45th day with mean difference of 1.125 (P=<0.0001) and 0th day v/s 90th day with mean difference of 1.825, (P=<0.0001). The study shows that after intervention clinical symptoms improved significantly in each follow-up gradually, it proves statistically significant with mean difference and P values shown in table 9.

Table 10 : The Safety (objective) parameters are compared before and after treatment. Parameters assessed before and after treatment for 40 patients are categorized into pairs with Mean and Standard Deviation expressed as Mean ± SD.

Pair 1 (SGOT BT) – 41.025 ± 60.777, (SGOT AT) – 34.150 ± 0.3911, Pair 2 (SGPT BT) – 42.875 ± 58.639, (SGPT AT) – 36.975 ± 13.721, Pair 3 (ALP BT) – 91.775 ± 50.823, (ALP AT) – 73.425 ± 28.592, Pair 4 (T.Cholesterol BT) – 207.825 ± 41.348, (T. Cholesterol AT) – 165.00 ± 27.098, Pair 5 (Serum Triglycerides BT) – 151.32 ± 64.104, (Serum Triglycerides AT) – 111.55 ± 33.548, Pair 6 (LDL BT) – 130.35 ± 40.037, (LDL AT) – 95.300 ± 26.202, Pair 7 (VLDL BT) – 34.207 ± 14.916, (VLDL AT) – 24.425 ± 7.1032.

while analyzing the objective parameters of the 40 patients before and after treatment, It was observed that the LFT (SGOT, SGPT, Alkaline phosphatase) and Lipid profile (Total cholesterol, Serum Triglycerides, Serum LDL, VLDL) were high before treatment. Furthermore, it was concluded that the levels were low in the patients after treatment as compared to the levels before treatment.

Table 11 : The objective parameters (Liver Function Test and Lipid Profile) has been categorized into 7 pairs in accordance of before and after levels. The pair 1 (SGOT BT- SGOT AT) with Mean of 6.875 and P value 0.489, pair 2 (SGPT BT- SGPT AT) with Mean 5.900 and (P=0.0545)

Part 3 (ALP BT- ALP AT) with Mean of 18.350 and ($p=0.004$). Pair 4 (T. CHOL BT- T CHOL AT) with Mean of 42.825 and ($p=0.0000$), Pair 5 (S.TRIG BT- STRIG AT) with Mean of 39.770 and ($p=0.000$), Pair 6 (LDL BT- LDL AT) with Mean of 35.050 and ($p=0.000$), Pair 7 (LDL BT- LDL AT) with Mean of 9.765 and ($p=0.000$).

The study shows that the safety (objective) parameters levels were raised before treatment. Furthermore, it was concluded that the levels were low in the patients after treatment as compared to the levels before treatment with statistically significant P- value.

Table 12: Ultrasonography reports are compared before and after treatment. In statistical analysis of before treatment, it shows the mean as 9.142, Standard Deviation as 0.4732 and analysis of after treatment shows Mean as 7.040 and Standard Deviation as 4.523 and p value as 0.0319.

After intervention Ultrasonography shows significant dissolution of Gall stone in last follow up as compared to baseline Ultrasonography and it is statistically significant.

SUMMARY

Gallstone disease remains one of the major causes of abdominal morbidity & mortality throughout the world. Now-a-days gallstones (cholelithiasis) is a frequent problem in developed Countries representing a major health problem leading to Surgical intervention. In Unani medicine this disease comes under the caption Hisat-e- Safravi or Hisat ul Marara which forms in biliary tract.⁶ According to unani physician Avicenna the causes of gall stone formation are dame ghaliz, Zoaf quate dafeya, shiddate jaziba, congenital narrowing of biliary system, khilte ghalizwa lazuj ghaliz ashaya, mitti chuna etc. Gall stones are quite prevalent in most western countries (10%-15%). It is estimated that at least 25 million persons in the United States have gall stones, less frequent in India around 4%. Women are affected more often than men in the ratio of 4:1. It is observed that gall stone is more common in FATTY, FORTY, FERTILE and FEMALES i.e, 4Fs.⁵⁰

The present study named as "**SINGLE BLIND CLINICAL TRIAL TO EVALUATE THE EFFICACY OF UNANI FORMULATION IN HISATH-UL-MARARA (CHOLELITHIASIS).**" was carried out in speciality Outpatient Department, Govt. Nizamia General Hospital, Hyderabad during the period 2022-2023 Post Graduate Department Of Moalijat, Govt. Nizamia Tibbi College and General Hospital, Hyderabad. The Study was an experimental single blind clinical trial with sample size of 40 patients. Patients allocated in a single group were given the test drug in form of joshanda of kulthi (7 gm) and Powder (5gm) of Khare khask, lahsun and Naushadar, twice daily up to 90 days with five follow-ups (15th, 30th, 45th, 60th, 75th and 90th day). The Pre and post treatment effects were assessed based on subjective and objective parameters.

CONCLUSION :

Patients were assessed according to symptoms and changes in USG findings. After completion of study it was observed that the patients of the single group, who were given unani drugs showed improvement in the Subjective parameters such as Right Hypochondric pain, Nausea, Vomiting, Indigestion, Flatulence with in protocol duration with statistical significance ($P= <0.0001$), chemical parameters (LFT and Lipid profile) with statistical significance ($P= <0.0001$) and USG findings which shows size of Calculi reduced in maximum patients, calculi disappeared in some cases and no response is also seen with statistical significance ($P=0.0319$). The findings about the parameters suggest that the test drug was effective in cholelithiasis.



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