A COMPARATIVE CLINICAL STUDY OF QURS-E-ZARISHK AND URSODEOXYCHOLIC ACID IN NON ALCOHOLIC FATTY LIVER DISEASE

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ABSTRACT: ***Nonalcoholic fatty liver disease (NAFLD) is now considered as a hepatic feature of metabolic syndrome and is a clinical spectrum ranging from simple steatosis (Non Alcoholic Fatty Liver, NAFL) to Non Alcoholic Steatohepatitis (NASH) . The former has a benign prognosis but latter is associated with fibrosis and progression to liver cirrhosis and hepatocellular carcinoma (HCC). NAFLD is a rapidly growing disease in both developed and developing countries and is probably the most common cause of abnormal liver function tests worldwide. The prevalence of NAFLD appears to be increasing in parallel with the epidemics of obesity. Now it has become the most common cause of chronic liver disease after hepatis B, hepatitis C and alcohol. In Unani Medicine a number of herbal drugs, plants as a whole or their parts are extensively used for the cure of liver derangement, and are scientifically evaluated for their safety and efficacy. In the present study, a comparative therapeutic evaluation of Qurs-e-Zarishk and Ursodeoxycholic Acid (UDCA) in 60 patients of Nonalcoholic fatty liver was done. The study shows that the Unani Test Formulation 'Qurs-e-Zarishk' produces significant improvement in cases of Nonalcoholic fatty liver. Comparison of Qurs-e-Zarishk with the standard agent UDCA shows that in the most parameters, the later is more effective while in some parameters Qurs-e-Zarishk is more effective.***

Keywords: ***Unani Medicine, NAFLD, Ursodeoxycholic Acid (UDCA), NASH, Qurs-e-Zarishk.***

1. INTRODUCTION

NAFLD represents a spectrum of liver disease encompassing simple fatty infiltration (steatosis), fat and inflammation (non alcoholic steatohepatitis, NASH) and cirrhosis, in the absence of excessive alcohol consumption (typically a threshold of <20gm/day for women and <30gm/day for men is adopted).NAFLD may be considered to be the hepatic manifestation of the metabolic syndrome, because it is strongly associated with obesity, dyslipidaemia, insulin resistance and type 2 diabetes mellitus [1]. The association among obesity, type 2 DM, and fatty liver disease has long been recognized, cases of fatty liver disease (steatosis) with inflammation that resembles alcoholic steatosis were described thirty years ago, first in Japanese literature and then in United states. NAFLD was first described in the 1950s when fatty liver was characterized in a group of obese patients [2]. In 1980 Ludwig and Colleagues at Mayo Clinic described 20 obese, diabetic, non alcohol patient who had similar finding on liver biopsy to patients with alcoholic liver disease, and the term non alcoholic steatohepatitis (NASH) was introduced [3],[4]. The prevalence of NAFLD and NASH may be as high as 20% and 2% to 3% respectively in general population in population based studies. In obese individuals (BMI >30 kg/m2), the prevalence of steatosis is about 65-75% and the prevalence of NASH increases to 15-20% [5],[6]. NAFLD affects 10-24% of general population from different countries [7],[8], it is estimated that 20% of all adult have NAFLD and 2-3% have NASH [5],[7]. NAFLD is an important cause of liver disease in India. Epidemiological studies suggest prevalence of NAFLD in around 9% to 32% of general population in India. The prevalence is higher in those with overweight/ obesity and in those with diabetes / pre diabetes [8],[9]. NAFLD is usually asymptomatic although fatigue and discomfort in right upper quadrant may be reported [1],[10]. Clinically most patients are symptomatic with abnormal liver function test (LFT) particularly elevation of transaminases. Usually the condition presents with abdominal discomfort, flatulence, dyspepsia and complication of cirrhosis like gastrointestinal bleeding. In many cases there is accidental discovery of fatty liver when the patients are subjected to utrasonography (USG) for some other reasons. Imaging technique like utrasonography, CT and MRI scanning are reliable for detecting moderate to severe fatty changes in the liver. However the liver biopsy remains the "Gold standard" for diagnosing NAFLD especially to exclude alcoholic liver disease. Its management basically depends on weight loss and pharmacotherapy. The aim of treatment is to slow down the progression of NAFLD and to prevent liver related illness and death [11].

As far as Unani concept is concerned the disease by this name is not found in any of the Unani classical textbook and literature as it is a newly coined term in medicine. However most of the signs and symptoms described by the ancient Unani Tabeeb (physician) in various Unani classical texts books under the topic of Amrraze Jigar (liver disorders) due to Su'Mizaj barid (impaired cold temperament) roughly correspond to the sign and symptoms of NAFLD. Almost all the ancient Unani Scholars have described Su'Mizaj barid kabid in his treatise, and all the Unani Scholars have a common consensus that cold temperament is the leading cause of this disease. According to Unani concept the deposition of fat does not take place in hot organs like liver, in comparison to cold organ. Fat deposition takes place only when hot organ's Mizaj transformed to cold [12],[13].

The present study was carried out with the following objectives - To the best of my knowledge no such comparative clinical trial has been done so far in the field of Unani Medicine. To evaluate the efficacy of our Polyherbal Unani Formulation (Qurs-e-Zarishk) and to compare its effects with control drug Ursodeoxycholic Acid (UDCA) in the management of NAFLD.

TABLE : 1
Constituents of Qurs-e-Zarishk [14]

S.No.	Contents	Botanical Name	Ratio
1	Zarishk	(Berberis aristata)	40gm

2	Rewand chini	(Rheum emodi)	10gm
3	Gul-e-surkh	(Rosa damascus)	10gm
4	Maghz Tukhm khayaren	(Cucumis sativus)	10gm
5	Sandal safed	(Santalum album)	10gm
6	Tukhm-e- Kasni	(Cychorium intybus)	10gm
7	Luk-e- maghsool	(Coccus lacca)	5gm
8	Aslussoos	(Glycyrrhiza glabra)	5gm
9	Gul-e-neelofer	(Nymphaea lotus)	5gm
10	Tabasheer	(Bambusa arundinacea)	5gm

2. MATERIAL AND METHODS

This study was a randomized single blind with comparative control clinical trial, conducted randomly on the indoor and outdoor patients of Department of Moalajat, Ajmal Khan Tibbiya College and Hospital, Aligarh Muslim University, Aligarh from may 2013 to April 2015. A written and well informed consent was taken from the patients before participation into the study.

2.1 Inclusion criteria

We include the patients who met following criteria

(i) The patients having following symptoms and signs

- Upper abdominal pain or discomfort
- Nausea and vomiting
- Anorexia
- Tenderness in hepatic region
- Obesity as a presenting features.

(ii) Patient of both the gender between 21 to 60 yrs.

2.2 Exclusion criteria

i. Pregnant and lactating mothers.
ii. Patients of intra-abdominal malignancy.
iii. Patients of portal hypertension.
iv. Patients of morbid obesity.
v. Patients of bleeding disorders.
vi. Patients using oestrogen containing contraceptive.
vii. Patients suffering from Diabetes Mellitus, Chronic Renal Failure, Nephrotic Syndrome, and Cirrhosis Of Liver.
viii. Any medical condition where physician feels that participation in the study could be detrimental to patient's well being.
ix. Non cooperative patients.
x. HB_S Ag +ve patients.
xi. Patients below 21 and above 60 yrs.
xii. Patients had taken any type of lipid lowering agents of any system of medicine for at least one year before the clinical trial were also excluded.

2.3 Methodology

Permission from the institutional ethical committee was taken before starting the clinical trial. A written and well informed consent was taken from the patients before participation into the study. Each case was studied on following manner that is history taking, physical examination, biochemical tests and USG abdomen. The liver biopsy was not done because of the lack of the facility of stand by operation theatre. Apart from personal interrogation and dietary habits including food cooking medium, detail of presenting complaints like anorexia, nausea and vomiting were recorded with specific note of the abdominal pain or discomfort in the right hypochondrium. Relevant past illness and history regarding similar attack of symptoms was also noted. The weight of the patients and BMI was also recorded. In systemic examination all the systems were examined in detail with special emphasis on gastrointestinal system. like tenderness, organomegaly, ascites, lump, hernial orifices and per rectal examination.

To assess the effect of test and control drug on subjective parameters the patients were assessed for various sign and symptoms (Abdominal pain, Nausea and Vomiting or both, Hepatic tenderness, and Anorexia). The severity was rated as severe, moderate, mild and absent and graded as 3, 2, 1 and 0, respectively, based on arbitrary grading system. The assessment was carried out on 0day, 15^{th} day, 30^{th} day,45^{th} day and 60^{th} day. While objective parameters are concerned various investigations are carried out to evaluate the effect of test and control drug. These include special biochemical tests Serum Bilirubin, AST, ALT, Alkaline Phosphotase, HBsAg, Serum cholesterol and Triglycerides. All the patients were subjected to USG abdomen before starting the treatment and at the termination of the trial. As and when require opinion of radiologist was also sought.

2.3 Grouping

A total of 60 patients were randomly allocated into two groups by simple randomization using lottery method. There were 30 patients in test group (Group A) and 30 patients in the control group (Group B).

Group A: The test group was given Qurs-e-Zarishk 3 tablets twice daily for 60 days after meal, each tablet weighing 1 gm.

Group B: The control group was given tablet Udiliv 300mg containing Ursodeoxycholic acid (UDCA) twice daily for 60 days after meal.

Follow up

Sixty (60) days study was divided into 4 visits of follow up which were made at an interval of 15 days. At every visit, patients were asked about the progression or regression in their symptoms and subjected for examination to assess clinical findings. The initial 15 days

visit was to know any side effect of drugs. The clinical examination and necessary biochemical investigations were carried out at monthly interval where as USG abdomen as already mentioned was done before and at the termination of therapy i.e. two months.

2.4 Statistical analysis:

Results are expressed as mean ± standard deviation (SD). Freidman test, Kruskal-Wallis test with Post Dunn's multiple comparison test and Student's *t* test were used to analyses the data. For inter group comparison unpaired't' test was used, and paired t test was used for intra group comparison. All P-values were two-tailed, and values <0.05 were considered statistically significant.

3. OBSERVATIONS, RESULTS AND DISCUSSION

TABLE NO. 2
Distribution of Patients according to age
Total Number of Patients (60)

Age Group	NO. of patients		Total No. of patients	Percentage (%)
	Test Group	Control Group		
<30	7	5	12	20
30-40	9	8	17	28.33
40-50	10	9	19	31.66
50-60	4	8	12	20
Total	**30**	**30**	**60**	**100**

In the study it was found that maximum number of patients i.e. 19 cases (31.66%) belong to the age group 40-50 years, followed by 17 cases (28.33%) fell in the age group of 30-40 years. This data suggested that the disease is more Prevalent in the in age group of 40-50 years. These finding corroborated with the finding of Munjal YP et al, Duseja A, who reported that highest prevalence in between 40 to 49 years of age [8]

TABLE NO. 3
Distribution Of Patients According To Gender
Total Number of Patients (60)

Gender	NO. of patients		Total No. of patients	Percentage (%)
	Test Group	Control Group		
Male	13	11	24	40
Female	17	19	36	60
Total	**30**	**30**	**60**	**100**

The highest incidence was observed in female patients 36 cases (60%), and remaining 24 cases (40%) were Male in both the group. This results shows that NAFLD prevails mostly in females. Our finding does not corroborated with the recent studies who mentioned that NAFLD is more prevalent in men than in women in any age group [8], however our finding corresponds with the finding of Bedodni G et al, who mentioned that in old studies NAFLD is more frequent in women [15]. The plausible reason behind higher numbers of female patients in our study may be the lack of physical exercise among them or it may be most probably due to the smaller sample size for incidence.

TABLE NO.4
Distribution of Patients According to Food Habits
Total Number of Patients (60)

Food Habits	NO. of patients		Total No. of patients	Percentage (%)
	Test Group	Control Group		
Vegetarian diet	3	3	6	10
Mixed diet	27	27	54	90
Total	**30**	**30**	**60**	**100**

It was observed maximum number of cases i.e. 54 cases (90%) belongs to mixed diet group, and only 6 cases (10%) belong to vegetarian group. The higher incidence of NAFLD among mixed diet group may be due to the use of non-vegetarian diet in their diets which contains rich fat contents and of high calories that may lead to obesity, insulin resistance and its manifestation such as non alcoholic fatty liver.

TABLE NO. 5
Distribution of Patients According to their Occupation
Total Number of Patients (60)

Occupation	NO. of patients		Total No. of patients	Percentage (%)
	Test Group	Control Group		
Housewives	15	18	33	55
Student	2	2	4	6.66
Business	5	3	8	13.33
Service	7	6	13	21.66

Labor	1	1	2	3.33
Total	**30**	**30**	**60**	**100**

It was observed that maximum number of patients belong to housewife 33 followed by service 13 and business class 8. These data clearly depicted that physical exertion and low fat diet have protective effects for NAFL, as seen in the student and labour class. As the prosperity increase and physical exertion decrease, there is a marked rise in the incidence of NAFLD, hence maximum number of patients in our study belong to housewife and service class followed by business class.

TABLE NO. 6
Distribution of Patients According to Temperament
Total Number of Patients (60)

Temperament	NO. of patients		Total No. of patients	Percentage (%)
	Test Group	Control Group		
Damvi (Sanguinous)	2	5	7	11.66
Balghami (Phlegmatic)	27	23	50	83.33
Safravi (Bilious)	1	2	3	5
Saudavi (Melancholic)	0	0	0	0
Total	**30**	**30**	**60**	**100**

It was observed that maximum number of patients having Balghami Mizaj 50 (83.33%) followed by 7 (11.66%) patients having the Damvi, 3 (5%) having Safravi and not a single patient having Saudavi Mizaj in both the group. These findings indicates that Non alcoholic fatty liver is more prevalent in Balghami Mizaj patients. Since the clinical manifestations and etiology of this disease closely resemble with the Alamaat wa Asbaab of Sue Mizaj Barid Kabid. The result of present study is inconsonance with the claim made by ancient Unani physicians (Hakeem Azam Khan, Ibne Sina, Ismail Jurjani, Rabban Tabri) that excessive or incalculable dietary habits induces excessive production of Akhlat (Humour) leading to alteration in temperament of Balghami and Damvi Mizaj persons [16],[17],[18],[19].

TABLE NO. 7
Distribution of Patients According to their Body Mass Index(BMI)
Total Number of Patients (60)

Class	BMI Categories	NO. of patients		Total No. of patients	Percentage (%)
		Test Group	Control Group		
First	**BMI (<25)**	4	5	9	15
Second	**BMI (25-29)**	16	18	34	56.66
Third	**BMI (≥30)**	10	7	17	28.33
Total		**30**	**30**	**60**	**100**

As far as the relation of the disease with BMI is concerned, out of total 60 patients studied both in test and control group, majority of the patients 34 (56.66%) were overweight (BMI 25-29.9), 17 (28.33%) had grade 1 obesity (BMI >30) while only 9 (15%) patients were normal weight (BMI <25). These finding was compatible with the studies of Munjal YP et al who mentioned that highest prevalence is seen among patients with BMI >25 [9].

TABLE NO. 8
Effect of Drugs on Abdominal Pain Mean±SD (Median rating with range in brackets)
Total Number of Patients (60)

Group	Fo Follow up				
	0 day	**15 day**	**30 day**	**45 day**	**60 day**
Test	1.53±0.89 2(0,3)	1.43±0.89 2(0,3)	1.16±0.79 1(0,2)	0.9±0.66 1(0,2)*	0.53±0.68 1(0,2)**
Control	1.36±1.06 2(0,3)	1.36±1.06 2(0,3)	1.36±1.06 2(0,3)	1.23±0.95 1.5(0,3)	0.96±0.85 1(0,2)

*p<0.01 significant with respect to test group day 0. P<0.05 significant with respect to test group day 15.
**p<.001 very significant with respect to test group day 0 and day 15.
For intergroup comparison p<0.01 significant.

There was highly significant improvement in abdominal pain is seen at 60th day and significant at 45th day in test group, whereas in control group no significant improvement in abdominal pain was observed in any assessment day. In test group this improvement might be due to the various pharmacological actions of the ingredients present in test formulation such as *Mussakkin Alam* (Analgesic) properties of Rewand chini [20],[21],[22],[23],[24]. Specific effect of Luk maghssol and Rewand Chini in Hepatic pain has been mentioned by Ibne Baitar, Ibne Sina and Ibne Quf Maseehi in their treatise [20],[25].

TABLE NO. 9
Effect of Drugs on Nausea & Vomiting (Median rating with range in brackets)
Total Number of Patients 60

Group	Fo Follow up				
	0 day	**15 day**	**30 day**	**45 day**	**60 day**
Test	0.76±0.89 0(0,2)	0.66±0.88 0(0,2)	0.53±0.86 0 (0,2)	0.36±0.61 0 (0,2)	0.2±0.40* 0 (0,1)
Control	0.9±0.92 1(0,2)	0.9±0.92 1(0,2)	0.73±0.86 0(0,2)	0.6±0.72 0(0,2)	0.4±0.67 0(0,2)

*p<0.05 significant with respect to Test group day 0.
For inter group comparison p>0.05 not significant

Significant improvement in nausea and vomiting at 60thday was observed in test group, whereas in control group there was no significant improvement in nausea and vomiting in any assessment day. In test group this improvement might be due to *Muqawwi-e-Kabid* (Hepatoprotective) [20],[23],[25],[26],[27],[28],[30],[35] properties of Aslussus, Gul-e-Surkh, Tukhme Kasni, Sandal Safed, Zarishk, Luk maghsool, Rewand Chini and Tabasheer which result in the improvement in liver function thereby ameliorate the symptoms of nausea and vomiting, and this effect may be due to the use of Zarishk and Aslussus in nausea and vomiting [21],[29],[30].

TABLE NO. 10
Effect of Drugs on Hepatic Tenderness (Median rating with range in brackets)
Total Number of Patients (n=60)

Group	Fo Follow up				
	0 day	**15 day**	**30 day**	**45 day**	**60 day**
Test	0.76±0.72 1(0,2)	0.6±0.72 0(0,2)	0.33±0.54 0(0,2)	0.23±0.50* 0(0,2)	0.2±0.48* 0(0,2)
Control	0.7±0.87 0(0,2)	0.7±0.87 0(0,2)	0.6±0.81 0(0,2)	0.56±0.81 0(0,2)	0.4±0.67 0(0,2)

*p<0.05 significant with respect to Test group day 0.
For intergroup comparison p<0.05 significant.

Significant improvement in hepatic tenderness at 45thday and 60thday was seen in test group, while in control group no significant improvement in hepatic tenderness was observed in any assessment day. Mild ache over hepatic region or hepatic tenderness is a feature of *Su' mizaj barid kabid* [31]. Therefore this improvement in hepatic tenderness in test group might be due to hot temperament of Luk maghsool [22],[27],[30], RewandChini [20],[21],[22],[25] and Aslussoos [22],[30],[32] other reason same as discussed earlier.

TABLE NO. 11
Effect of Drugs on Anorexia (Median rating with range in brackets)
Total Number of Patients (n=60)

Group	Fo Follow up				
	0 day	**15 day**	**30 day**	**45 day**	**60 day**
Test	1.6±0.85 2(0,3)	1.46±0.86 2(0,3)	1.23±0.85 1(0,3)	0.86±0.77 1(0,2)*	0.6±0.67 .5(0,2)**
Control	1±0.90 1(0,3)	1±0.90 1(0,3)	0.86±0.81 1(0,2)	0.76±0.85 0.5(0,2)	0.53±0.73 0(0,2)

*p<0.001 very significant with respect to Test group day 0. P<0.01 significant with respect to Test group day 15.
**p<0.001 very significant with respect to Test group day 0 and day 15. P<0.05 significant with respect to Test group day 30.
For intergroup comparison p<0.001 very significant.

Highly significant improvement in anorexia at 45thday, 60thday and significant at 30thday was observed in test group, while in control group no significant improvement in anorexia was seen in any assessment day. This result indicate that test drug is highly effective than control drug in the improvement in anorexia. In test group this improvement might be due to *Mushtahi* (Appetizer) properties of Gul-e-Surkh & Rewand chini [24],[33], and *Muqawwi-e-Kabid* (Hepatoprotective) [20],[23],[25],[26],[27],[28],[30],[35] properties of Aslussus,Gul-e-Surkh,Tukhme Kasni, Sandal Safed, Zarishk, Luk maghsool, Rewand Chini and Tabasheer which result in the improvement in liver function, leads to the improvement in appetite.

TABLE NO : 12
Effects of the Drugs on Body Weight

Group	Mean Body Weight ± SD (in kg)	
	0 day	**60th day**
Test	69.46±4.79	68.86±4.61
	p<0.05	
Control	68.15±5.30	67.96±5.37
	p>0.050	

The mean body weight in test group at 0 day was 69.46 ± 4.79 (kg) , which reduced to 68.86±4.61 (kg) at the end of trial, on statistical analysis the value of p<0.05, hence the result was significant. In control group mean body weight was reduced from 68.15 ± 5.30 to 67.96 ± 5.37(kg), the result was found statistically insignificant p>0.05.

Significant effect on reducing body weight in test group may be due to the *Muhazzil* (Fat dissolvent) [22],[25],[27],[28],[30], effect of Luk maghsool, *Mulattif* (Demulcent) [22],[25],[30][34] action of Aslussoos,Gul-e-Surkh, Tukhme Kasni, Zarishk, Luk maghsool, Rewand Chini and Gul-e-Neelofer, *Mudir-e-baul* (Diuretic) [22],[23],[28],[29],[30],[32],[34] action of Aslussoos, Tukhme Kasni, Rewand Chini, Sandal Safed and Tukhm-e-Khayaren, *Mushil-e-akhlat-e-ghaliza* [21], effect of Rewand Chini, *Muarriq* (Diaphoretic) [22],[24], effect of Sandal Safed and *Mujaffif-e-ratubate badan* (Desiccant) [22],[30] effect of Luk maghsool and Rewand Chini. The above mentioned diverse pharmacological actions of drug component of the formulation might complement or synergize each other and facilitate the anti obesity effect.

TABLE NO : 13
Effect of the Drugs on Serum Cholesterol and Serum Triglyceride

Group	Mean SerumCholesterol ± SD (mg/dl)		Mean Serum Triglyceride ± SD (mg/dl)	
	0 day	60th day	0 day	60th day
Test	195.3±34.8	177.23±21.06	190.83±52.31	171.30±41
	P<0.001		P<0.001	
Control	193.63±37.53	187.50±34.43	177.57±50.28	161.83±38.29
	p<0.05		P<0.001	

The mean fasting serum cholesterol in test group 0 day was 195.3±34.8 (mg/dl) which reduced to 177.23±21.06 (mg/dl) at the end of trial, on statistical analysis the value of P<0.001, hence the result was significant. In control group mean serum cholesterol was reduced from 193.63±37.53 to 187.50±34.43 (mg/dl), the result was found statistically significant p<0.05. For intergroup comparison p<0.05, hence difference between two group was significant.

The mean fasting serum triglyceride in test group at 0 day was 190.83±52.31 (mg/dl) which reduced to 171.30±41 (mg/dl)) at the end of trial, on statistical analysis the value of P<0.001,hence the result was significant.. In control group mean serum triglyceride was reduced from177.57±50.28 to 161.83±38.29 (mg/dl), the result was found statistically significant P<0.001. For intergroup comparison p>0.05, hence difference between two group was not significant.

Above result clearly showed that the effect of both test and control drug in reducing serum cholesterol and triglyceride level was statistically significant. For intergroup comparison it was found insignificant. However the test drug is comparatively more effective than control drug in reducing serum cholesterol level. The better result seen in test group may be due to the lipid lowering effect of the Luk maghsool which possess *Muhazzil* weight reducing property that is probably achieved by increased utilization of fat for energy production, moreover increased physical exertion is associated with increased energy consumption that might be provided by the burning of the body fat. It may be due to the *Mulayyin* (Laxative) properties of Gul-e-Surkh, Aslussus [22],[30],[33],[35],[36],[37] and *Mujaffif-e-ratubate badan* effect of Luk maghsool and Rewand Chini, which causes hindrance in the absorption of fat from the gastro intestinal tract. According to the Unani concept fat is considered as *Akhlate-e-ghaleeza*, and one of the test drug component Rewand Chini possess *Mushil-e-akhlat-e-ghaliza* property, hence this medicinal effect might reduced serum cholesterol and triglyceride. Other possibilities may be due to the lifestyle intervention adopted during the study.

Table NO: 14
Effect of drugs on Serum Bilirubin and Serum Alkaline phosphatase

Group	SerumBilirubin Mean ± SD (mg/dl)		Serum Alkaline phosphatase Mean ± SD (u/dl)	
	0 day	60th day	0 day	60th day
Test	0.92±0.09	0.89±0.076	120.37±11.83	116±9.01
	p<0.05		p<0.05	
Control	0.98±0.093	0.95±0.08	124.43±15.34	118.56±10.19
	P<0.001		p<0.05	

The mean serum bilirubin in test group at 0 day was 0.92±0.09 (mg/dl) which reduced to 0.89±0.076 (mg/dl) at the end of trial, on statistical analysis the value of p<0.05, hence the result was significant. In control group mean serum bilirubin was reduced from .98±.093 to .95±.08 (mg/dl), the result was found statistically significant P<0.001. For intergroup comparison p >0.05, hence difference between two group was not significant.

The mean Serum Alkaline phosphatase in test group at 0 day was 120.37±11.83 (u/dl) which reduced to 116±9.01 (u/dl) at the end of trial, on statistical analysis the value of p<0.05, hence the result was significant. In control group Serum Alkaline phosphatase was reduced from 124.43±15.34 to 118.56±10.19 (u/dl), the result was found statistically significant p<0.05. For intergroup comparison p >0.05, hence difference between two group was not significant.

TABLE NO : 15
Effect of drugs on Serum AST and ALT

Group	Serum AST Mean ± SD (U/L)		Serum ALT Mean ± SD (u/ml)	
	0 day	60th day	0 day	60th day
	32.70±9.25	30.13±7.70	47.90±5.70	45.5±5.19

Test	p<0.05		p<0.05	
Control	33.23±9.02	30.93±7.86	46.46±4.87	44.66±4.69
	p<0.05		p<0.05	

The mean serum AST in test group at 0 day was 32.70±9.25 (U/L) which reduced to 30.13±7.70 (U/L) at the end of trial, on statistical analysis the value of p<0.05, hence the result was significant. In control group mean serum AST was reduced from 33.23±9.02 to 30.93±7.86 (U/L), the result was found statistically significant p<0.05. For intergroup comparison p >0.05, hence difference between two group was not significant.

The mean serum ALT in test group at 0 day was 47.90±5.70 (u/L) which reduced to 45.5±5.19 (u/L) at the end of trial, on statistical analysis the value of p<0.05, hence the result was significant. In control group mean serum ALT was reduced from 46.46±4.87 to 44.66±4.69 (u/L), the result was found statistically significant p<0.05. For intergroup comparison p >0.05, hence difference between two group was not significant.

From above result it is depicted that the effect of both test and control drug in reducing the deranged liver enzyme and serum bilirubin was statistically significant. For intergroup comparison it was found insignificant. Control drug is comparatively more effective than test drug in reducing serum bilirubin level. However the baseline and final values of serum bilirubin were within normal limit. The overall improvement in LFT in control group due to its known hepatoprotective and anti-inflammatory effect. While in test group this improvement might be due to the various pharmacological action of ingredient of test drug particularly such as *Muhallil* (Anti-inflammatory) properties [12],[21],[22],[23],[30] of Zarishk, Aslussus, Gul-e-Surkh, Tukhme Kasni, Sandal Safed, Luk maghsool, Rewand Chini, Tabasheer and Gul-e-Neelofer, these drugs might have acted on Kuffer's cells of liver reducing their inflammation and thereby facilitating the flow of bile. Other possible mechanism involved may be due to the *Mudir-e-baul* (Diuretic) effect of Aslussoos, Tukhme Kasni, Rewand Chini, Sandal Safed and Tukhm-e-Khayaren, and *Muqawwi-e-Kabid* properties of Aslussus,Gul-e-Surkh,Tukhme Kasni, Sandal Safed, Zarishk, Luk maghsool, Rewand Chini and Tabasheer.

TABLE NO: 16
Effect of drugs on Brightness of Live

Group	**USG Impression- Brightness of Liver**		**Improved percentage**
	BT Number of patients	**AT Number of patients**	
Test	30	25	16.67
Control	30	28	6.34

Ultrasonography of Hepatobiliary system was carried out in all the patients subjected for the study before and after treatment in both the groups. Brightness of the liver on the gray scale was noted objectively in all the 60 patients enrolled, showing brightness of liver, indicates fatty liver before starting the treatment. There was no significant Ultrasonographical changes was noted in most of the patients after treatment. However the echogenicity (brightness of liver) was moderately decreased in 5 patients of test group and 2 patients of control group. These changes was find statistically insignificant.

Regarding the decrease in liver brightness inferred the decrease in fat concentration in liver. The better result seen in test group might be due to the various pharmacological actions of test formulation particularly *Muhazzil* effect of Luk maghsool, which cause resolving of fat from hepatocyte and *Mufatteh Sudad* (Deobstruent) [20],[21],[22],[25],[27],[28],[30] effect of Gul-e-Surkh, Tukhme Kasni, Luk maghsool, Rewand Chini, Tukhme Kheera, removes the obstruction within the hepatocytes and facilitates the export of triglyceride from the liver, thus decreasing the fat content of liver. It may also be due to the hot temperament of our drugs Luk maghsool, Rewand Chini, and Aslussoos, which might have caused redistribution and dislocation of fat from hepatocytes. In control group it is due to the known effect of Ursodeoxycholic acid such as lipid lowering properties, decreases the intestinal absorption of fat [2].

4. CONCLUSION

In the light of above results and discussion the overall conclusions which can be drawn is that in most of the clinical and laboratory parameters both test and control drug have almost parallel medicinal efficacy, however the test drug formulation have showed greater improvement in ameliorating the subjective parameters. Hence in the light of above discussion we can say that our drug combination has some potential in the management of Non alcoholic fatty liver disease and it can be safely used for the purpose. Since the study was conducted on a shorter sample size and for short duration, therefore it is suggested and proposed that a clinical trial on larger sample size either by readjusting the dose of drug or prolongation the course of trial may show more significant effect in lowering the elevated serum lipids, restoring the deranged liver function and decreasing the fat content of liver.

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