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A PROSPECTIVE OBSERVATIONAL STUDY ON ASSESSMENT OF CLINICAL EFFICACY AND SAFETY OF RIFAXIMIN IN PATIENTS WITH NON- ALCOHOLIC FATTY LIVER DISEASE

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ABSTRACT:

Introduction: Non-alcoholic fatty liver disease (NAFLD) is a common liver condition characterized by macro-vesicular steatosis and absence of secondary causes like alcohol consumption or long-term medication use. NAFLD is a leading cause of liver-related morbidity and mortality, with a global prevalence of 30.05%.The prevalence of NAFLD is increasing in India due to changes in lifestyle and junk food availability, early detection and treatment are crucial to reduce NAFLD-related mortality.Treatment for NAFLD requires a multicentric approach, including drugs like GLP 1 agonists, metformin, vitamin E, and Rifaximin along with non-pharmacological strategies.

Methodology: This is a prospective observational cohort study in 90 patients for the duration of six months in a teaching hospital.

Results and Discussion: The study included 90 patients diagnosed with NAFLD, with urban residents accounting for 62.8% and rural residents at 31.1%. Urban residents are at higher risk due to their lifestyle and food habits, with most consuming ultra processed and fast food. Authorities should focus on early screening, treatment, and prevention strategies in rural areas to reduce health-related expenditure. Rifaximine and its combinational regimens had better clinical outcome in patients and prevented the hepatic encephalopathy.

Conclusion:NAFLD epidemic in India, influenced by unhealthy lifestyles, stress, smoking, diabetes, hypertension, and obesity, requires early detection, prevention, and treatment with appropriate regimens, our study concludes Rifaximin 550mg twice daily regimen for six months had significantly liver functioning and observed decreased liver enzyme values in the study population with no complications reported.

Keywords : Non-alcoholic fatty liver disease (NAFLD), Rifaximin, ALT, AST, Efficacy, Safety.

INTRODUCTION:

A wide spectrum of conditions are collectively referred to as non-alcoholic fatty liver disease (NAFLD), which is defined by the presence of macro-vesicular steatosis, or hepatic steatosis, on imaging or histology, and an absence of secondary causes of hepatic steatosis, such as significant alcohol consumption, long-term use of medications that can cause hepatic steatosis, or hereditary disorders**. (1)**

Common liver disease nonalcoholic fatty liver disease (NAFLD) is a primary contributor to associated complications such cirrhosis and hepatocellular carcinoma (HCC). Simple steatosis, nonalcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and HCC are the phases that NAFLD advances through. **(2)**

Unfortunately, NAFLD is typically not recognized in a timely manner, this is mostly because NAFLD patients typically do not exhibit any symptoms, and there is currently no reliable noninvasive screening method. While liver biopsy is considered the gold standard for NAFLD diagnosis, its high cost and invasiveness make it impractical for NAFLD screening and monitoring. In order to evaluate NAFLD, a number of noninvasive screening and diagnostic systemic measures have been developed recently like patient centric approach, liver enzymes as biomarkers to assess the severity and diseases progression during treatment.**(2)**

NAFLD is a leading cause of liver-related morbidity and mortality, so we would like to give a insight of epidemiology of NAFLD globally, an overall global prevalence of 30.05%, NAFLD prevalence highest in Latin America (44.37%), followed by Middle East and North Africa (MENA) (36.53%), South Asia (33.07%), South-East Asia (33.07%), North America (31.20%), East Asia (29.71%), Asia Pacific (28.02%), and Western Europe (25.10%).

The prevalence of NAFLD is increasing significantly in India, the rural India had witnessed the sharp surge in cases daily because of changed life styles in tier1&2 cities, availability of various junk food in rural areas had made the people to develop the NAFLD at young age even which is the dangerous sign to be think and take appropriate measures**(3)**.

The prevalence of NAFLD is different because it has been affected by various reasons like obesity, diabetes, hyperlipidemia, hypertension, metabolic syndrome. Western countries and Middle East people are more vulnerable to NAFLD because of food habits and life style**(3).**

The clinical burden of nonalcoholic fatty liver disease (NAFLD) has been demonstrated to extend beyond liver-related morbidity and mortality. A growing number of research indicates that NAFLD is a multisystem illness that impacts regulatory pathways and extra-hepatic organs. For instance, NAFLD raises the risk of heart and cardiovascular disorders, chronic kidney disease (CKD), and type 2 diabetic mellitus (T2DM). The majority of NAFLD patients' fatalities are related to cardiovascular disease (CVD), even though the primary liver pathology in the condition impacts hepatic structure and function to cause morbidity and mortality from cirrhosis, liver failure, and hepatocellular cancer. So this proves the early detection with appropriate diagnosis and treatment will hamper the NAFLD related mortality, and the prime focus must be on the rural and illiterate people who are not even aware of the disease risk factors, complications **(4)**

Because of metabolic risk factors like obesity and type-2 diabetes, the global epidemic of non-alcoholic fatty liver disease (NAFLD) is producing considerable changes in hepatology. It is anticipated that NAFLD will persist in Eastern countries as the most frequent cause of chronic liver disease in Western countries. Specialists are figuring out how to diagnose, treat, and manage conditions effectively. In order to prevent the NASH and NAFLD its related complications there is a huge scope for early screening of the vulnerable population **(5).**

As healthcare professionals, it is our duty to prevent avoidable consequences like hepatic encephalopathy. Treatment for non-alcoholic fatty liver disease (NAFLD) requires a multicentric approach to treat concurrent diseases such as diabetes, hyperlipidemia, hypertension, and polypharmacy patients. These conditions significantly worsen the disease condition and lead to furthercomplications **(6).**

Recent evidences provides a effective treatment regimens which contains the multiple drugs from various pharmacological classes like GLP 1 agonists, metformin, vitamin E, rifaximin. For better results patients are advised to follow the balanced diet with no saturated fats, alcohol, carbonated beverages, caffeinated and added sugary drinks which reduces the BMI of a obese patient a major contributor of insulin resistance, regular exercise along with appropriate food habits will provide the better results which will reflect in the liver bio markers and decreased incidence of NAFLD complications.

AIM:

To determine the clinical efficacy of Rifaximin in Non Alcoholic Fatty Liver Disease (NAFLD) patients.

OBJECTIVES:

1. To assess the clinical efficacy of rifaximin in NAFLD.
2. To determine the BMI, and other comorbodities in the study population.
3. To evaluate the liver biomarkers pre and post treatment with Rifaximin.

MATERIALS AND METHODS:

Study Site: This study has been conducted in the tertiary care hospital.

Study Duration: The study is conducted over a period of 6 months from March - August2024

Study Design: This is a prospective, observational cohort study

Sample Size: A total of 90 patients diagnosed with NAFLD

Study Criteria

Inclusion Criteria:

1. Patients aged above 18 years diagnosed with NAFLD based on laboratory parameters.
2. Willing to provide informed consent for the study and to answer the study related questions

Exclusion Criteria:

3. Pregnant women and lactating mothers.
4. Patients who diagnosed with Alcoholic liver diseases.
5. Psychiatric patients and those who are not willing to participate
6. Participation in another clinical trial during the study period.

Methodology:A total of 90 NAFLD patients, aged 18 and above, were selected through selective sampling technique based on the evidence oflaboratory data and patient case sheets.

Data collection: Data was collected in a suitable data collection form by patient interviews, and medical records.

Statistical Analysis

Microsoft excel and Graph pad prism 8

RESULTS AND DISCUSSION:

This study had a total population of 90, urban residents' accounts for a whooping number 62.8% and we were fascinated to learn that people from rural area are 31.1% which is alarming, as the part of our study we came to know most of the people are not even aware of NAFLD and its complications. Urban population are at more risk to develop NAFLD because of the life style, food habits, most of them answered they are consuming ultra processed food and fast food in our questionnaire, these predisposing factors made urban population more vulnerable to NAFLD.

As we all aware that rural India is progressing in all aspects including food and life style with comparison to urban people, fast foods and junk food had reached to the door steps of rural India, so the authorities should focus on the early screening, treatment and prevention strategies in rural areas to reduce the health related expenditure, because most of them are poor and illiterates.

Age Group	Males N (%)	Females N (%)	Total N (%)	Urban N (%)	Rural N (%)
20-30	07 (7.7)	01(1.1)	08 (8.8)	5(5.5)	3(3.3)
31-40	11(12.2)	04(4.4)	15(16.6)	9(10)	6(6.6)
41-50	17(18.8)	20(22.2)	37(41.1)	26(28.8)	11(12.2)
51-60	20(22.2)	02(2.2)	22(24.4)	17(18.8)	05(5.5)
61-70	05(5.5)	00(00)	05(5.5)	02(2.2)	03(3.3)
71-80	03(3.3)	00(00)	03(3.3)	03(3.3)	00(00)
Total	63(70)	27(30)	90(100)	62 (68)	28 (32)

Table 1: Age and gender wise distribution of study population

Social habit status of study population based on residence:

Urban population were 62 in the study which depicts the prevalence of NAFLD and its counterpart rural population accounts for 28 which is fascinating number, traditionally we assume rural people are away from the junk and fast food but the recent research provides the data that most of the metabolic disorder patients are from rural area who had sedentary life style, increased consumption of carbonated beverages which contains the added sugars these are the most common and important risk factors for NAFLD in rural regions.

In our study we identified that males are more prone to develop NAFLD and had rapid disease progression the reasons for the prevalence most of them are occupied in the tradition business, sedentary life style, lack of physical activity due to hectic schedule. These factors contributed to the insulin resistance and fat deposition in the liver. Interestingly few people who don't had any social habit, not consuming added sugars but still developed NAFLD, upon peer review of patient data and history in patient interview we came to know the reasons are using cooking oil more than 30% higher than RDA, as a part daily routine few patients had habit of eating fruits regularly irrespective of glycemic control, we assume fructose is the reason for the development of NAFLD,the data was depicted in the table 2.

Residence	Number of cases			Social Habits								
	Male (M)	Female (F)	Total	Alcoholics			Smokers			Alcohol + Smoking		
				(M)	(F)	Total	(M)	(F)	Total	(M)	(F)	Total
Rural	13	15	28	03	00	03	07	00	07	05	00	05
Urban	50	12	62	14	00	14	17	02	19	10	00	10
Total	63	27	90	17	00	17	24	02	26	15	00	15

Table 2: Residential and social habit status of the study population

A little amount of consuming alcohol, polypharmacy will increase the risk of NAFLD if the patient is pre-existing with other risk factors, in our study we had 9 alcoholics who are on poly pharmacy for various diseases which increases the liver failure chances and associated complications, and the data was presented in the table 3.

Residence	Alcoholics			Alcohol + Poly Pharmacy		
	(M)	(F)	Total	(M)	(F)	Total
Rural	03	00	03	03	00	03
Urban	14	00	14	06	00	06
Total	17	00	17	09	00	09

Table 3: Details of poly pharmacy and alcoholism as aggravating factor

We determined the BMI of the study population using standard procedure and formula and as we all aware that obesity is the leading cause of NAFLD especially android obesity in males had high risk to develop other comorbodities. Most of the patients are in obese and extreme obese upon collecting the history from these patients we came to know most of them had genetic predisposition, sedentary life style. The overweight people account for 26.6% who had insulin resistance and diabetes as etiological factors for NAFLD, we have observed that most of these patients are lately diagnosed due absence of symptoms. This show the importance of patient education on preventing life style diseases and NAFLD by following healthy life style modifications, the details were presented in the table 4.

BMI	Number	Percentage
18.5-24.9	03	3.3
25.0-29.9	24	26.6
30-34.9	47	52.2
>35.0	16	17.7
Total	90	100

Table 4: BMI details of study population

Comorbodities of study population:

Comorbidites play major in NAFLD pathology because out 90 patients 75.5% patients had comorbidites, 41.1% patients had more than 2 underlying diseases which will mitigate the patient progression and also effect the treatment. We found diabetes along with obesity is the leading conditions for NAFLD, diabetes alone had significant number with 20 cases to cause NAFLD**(7)**. Hypertension, hyperlipidemia, thyroid were also identified as risk factors because they show impact on the body mass and basal metabolic rate which had huge impact on the pathology of NAFLD, NASH, the details are presented in table 5.

Co morbidities	No: of patients
Diabetes Mellitus (DM) +Obesity	17
Hypertension (HTN)	09
DM	20
HTN+DM	07
HTN+DM+Obesity	04
Thyroid	05
Hyperlipidemia	06
Total	**68 (75.5)**

Table 5 Comorbodities of study population

Details of ADRs observed during study period:

As it is well known fact that Rifaximin had minimal systemic absorption and hence it had very less side effects during the course of treatment, so in our study patients were prescribed with Rifaximin 550mg twice daily in order to prevent the hepatic complications like hepatic encephalopathy, but this had caused very few adverse drug reaction (ADRs) in 27 study population which are mild, non-serious ADRs. We asked the patients to consult the study team if they further experience any noxious effect during the study.

Sl. No	ADR	No. of Patients
1	**Nausea**	7
2	**Diarrhea**	3
3	**Rash**	2
4	**Vomiting**	9
5	**Bloating**	6

Table 6: ADRs reported during the study

Rifaximin clinical efficacy in study population:

NAFLD patients will receive multicentric treatment modalities which include treatment for comorbodities like diabetes, hypertension, hyperlipidemia, and thyroid but our study was designed to focus on the efficacy of rifaximinbecause it controls colonic bacteria which significantly reduce and eliminate nitrogenous waste from the body, also acts as hepato protective agent with significant reduction in liver enzymes.

Rifaximin is the potent antibiotic which acts mostly on the colonic bacteria and circulating endotoxins in the body which significantly treats the inflammation of liver and prevents its associated complications like hepatic encephalopathy.

In our study Rifaximin 550mg is given twice in a day for the NAFLD patients who had 2-3 folds elevated liver enzymes on an average, which are more sensitive and specific biomarkers of liver functioning, we assessed the patient condition, LFTs, and other parameters at baseline, after 3 months, and 6 months during the study.

LFT Parameter	Baseline Mean (Std.Dev)	3rd month average values Mean (Std.Dev)	Baseline to 3 rd month comparison P Value	6th month average values Mean (Std.Dev)	Baseline to 6th month comparison P Value
AST	120 (30)	90 (20)	0.0001	45 (10)	0.0001
ALT	129 (40)	91 (10)	0.0001	35 (10)	0.0001
ALP	376 (30)	290 (10)	0.0001	120 (20)	0.0001

Table 7 Liver Parameter Values Pre and Post Treatment (Efficacy of Rifaximin)

We determined the clinical efficacy of Rifaximin by comparing baseline values with 3 months data; we observed that there is significant change in the liver enzymes and functionality. And patients are also advised to follow the healthy life style in order to get the better result along with medication.

Upon after follow up after 6 months we assessed the liver functioning parameters of the study parameters, we found excellent clinical outcomes in terms of improved liver biomarkers with a significant values which is an evident of good liver functioning, not even one fatality, hepatic encephalopathy are reported during the treatment this shows the strong clinical effect of Rifaximin therapy.

CONCLUSION:

NAFLD had become epidemic in India, even rural areas also witnessed the raised prevalence, Life style, unhealthy food habits, sedentary life style, stress, smoking, diabetes, hypertension, obesity were the leading causes of NAFLD. Early detection and prevention, treatment will help the people to minimize the complications and mortality associated with NAFLD, We would like to conclude that rifaximin 550mg twice in a day for six months had good results with the evidence of reduction in liver enzymes with very less incidence of adverse effects this proves the safety and clinical efficacy of rifaximin in NAFLD.

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CONFLICT OF INTEREST:

The authors declare that there is no conflict of interest.

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