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Original Research Article

# Study the changes in adiponectin in NAFLD patients and its correlation with various clinical and biochemical parameters

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**Abstract**

**Background:** *Fatty liver disease in absence of alcohol abuse is now emerging as a major health burden in the world. It represents the hepatic manifestation of the metabolic syndrome, a variably defined aggregate of disorders related to obesity, insulin resistance, diabetes mellitus type 2, hypertension, and hyperlipdemia.*

**Methods:** *This prospective observational study was conducted in 65 patients with ultrasonographic findings of fatty liver disease either from OPD or from IPD basis of department of medicine, M.Y. Hospital, Indore.*

**Results:** *Out of 65 patients, 54(83%) patients had the fibroscan score less than 7  i.e. patients had median stiffness of the liver less than the cut off value, while only 11(17%) patients i.e. patients had median stiffness of the liver more than its cut off value. We found that only 12(18%) patients had adiponectin levels less than its normal value while 53(82%) patients had adiponectin levels within the normal range. Various biochemical parameters of the patients were compared across the gender where it was found that variable like triglycerides, ALT, AST, and adiponectin levels were approximately same across the gender without any significance (P value 0.533, 0.342, 0.167, and 0.967 respectively) but cholesterol values across the gender was significant (P value=0.000).*

**Conclusions:** *In Indian population also, NAFLD has association with its risk factors like obesity, larger neck circumference, higher waist hip ratio, and triglyceride levels. Low adiponectin levels association to the NAFLD found to be less in Indian population. Further study needed in large group of subjects from India.*

**Keywords:** *Adiponectin, cholesterol, non alcoholic fatty liver disease, triglycerides.*

## Introduction

Fatty liver disease in absence of alcohol abuse is now emerging as a major health burden in the world. It represents the hepatic manifestation of the metabolic syndrome, a variably defined aggregate of disorders related to obesity, insulin resistance, diabetes mellitus type 2, hypertension, and hyperlipidemia.

Non alcoholic fatty liver disease (NAFLD) is defined by excessive fat accumulation in the form of triglycerides (steatosis) in liver (>5% of hepatocytes histologically).[1] There is no clear cut-off for how many fat vacuoles visible in the light microscope that can be regarded as normal. It has been suggested that <5% of hepatocytes involved should be considered normal.[2] However, this is based on assumption rather than hard evidence. A subgroup of the patients have liver cell injury and inflammation in addition to excessive fat (steatohepatitis), that condition is designated as Non alcoholic steatohepatitis (NASH).

The definition of the non alcoholic fatty liver disease (NAFLD) requires (a) there is evidence of hepatic steatosis, either by imaging or by histology and (b) there are no causes for secondary hepatic fat accumulation such as significant alcohol consumption, use of steatogenic drugs or hereditary disorders. NAFLD is histologically further categorized into non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH).

The true prevalence of both NAFLD and NASH are elusive but according to the American Association of the Study of the Liver Disease(AASLD) single topic conference held on 20 September 2002, estimates based on imaging and autopsy studies suggest that about 20-30% of the adults in united states and western countries have excess fat accumulation in the liver. About 10% of these, strictly speaking about 2-3% of the adult population fulfils the criteria of non alcoholic steatohepatitis (NASH).

## Methods

This prospective observational study was conducted in 65 patients from February to October, 2015, with ultrasonographic findings of fatty liver disease either from OPD or from IPD basis of department of medicine, M.Y. Hospital, Indore.

**Place of Study**: Department of Medicine, MGM Medical College & MY Hospital, Indore (MP).

**Study Design**: Prospective, non-randomized, non-interventional, observational study.

**Study Population**: This study included patients who were of non-alcoholic fatty liver disease as assessed on ultrasonography.

**Sample Size and Sampling Technique**: Total 65 patients with non-alcoholic fatty liver disease presenting to the Department of Medicine, MGM Medical College & MY Hospital, and Indore (MP) during the study period, willing to provide their voluntary written informed consent were included in the study. The convenient sampling technique was used.

**Inclusion Criteria**

1. All cases of Fatty liver disease were assessed on imaging.
2. Patients of either gender.
3. All cases of NAFLD with ongoing alcohol consumption of not taking >21 drinks/week (10 gm/drinks) in males and >14 drinks/ week in females for over two years.
4. Patients and/or his/her legally acceptable representative willing to provide written voluntary informed consent for participation in the present study.

**Exclusion Criteria**

1. Those having history of alcohol abuse more than baseline.
2. Those on steatogenic drugs for more than six month.
3. Those who cannot be followed during the study period.
4. Prisoners and orphans.
5. Patients and/or his/her legally acceptable representative not willing to provide written voluntary informed consent for participation in the present study.

**Methodology**: After identifying the suitable candidate for the study, the patient, and/or his/her legally acceptable were explained in detail about the study, its risks/benefits, costs involved, about the study procedures, etc. in detail. After getting their verbal approval for participation, a voluntary written informed consent was obtained from

patient and/or his/her legally acceptable representative.

After obtaining the consent, patients having fatty liver disease, but no history of alcohol consumption were asked to undergo following blood investigations viz. RBS, serum cholesterol, serum triglycerides, fasting insulin level, AST, ALT, and then their anthropometric measurements like neck circumference, arm circumference, height, weight, and waist to hip ratio were measured and recorded. After that he was asked to come for follow up. At follow-up, the patient was asked to undergo a sample for adiponectin levels and at the same time we also performed FIBROSCAN test on those patients.

After collection of blood sample it was centrifuged and serum was separated and kept in freezer at the temperature 2-8$^0$C. After, that with HUMAN ADIPONECTIN ELISA Assay Max kit assay was performed as per protocol, and we obtained OD value for that. The OD value we obtained was plotted against the graph and finally we got the result in terms of adiponectin concentration.

**Outcome Measures**

Following outcome were measured- RBS, serum cholesterol, serum triglycerides, fasting insulin level, AST, ALT, adiponectin levels and then their anthropometric measurements like neck circumference, arm circumference, height, weight, waist to hip ratio and Fibroscan was also performed to look for the median stiffness of the liver.

**Data Collection Method**: The data has been collected on a customized proforma designed specifically for the study purpose.

**Statistical Analysis**: For the present study, statistical analysis required was done by the statistician accordingly the appropriate tests like Mann Whitney 'U' test and Spearman's rho coefficient correlation test were applied. For analysis, statistical software SPSS latest Version 20.0 was used. A P value of <0.05 will be considered as statistically significant.

**Results**

This prospective observational study was conducted in 65 patients from February to October, 2015, with ultrasonographic findings of fatty liver disease either from OPD or from IPD basis of department of medicine, MY Hospital, Indore. Results are from this study was as follows: As shown in table 1, only 12 patients i.e. 18% of the patients had adiponectin levels less than its normal value while 53 patients i.e. 82% had adiponectin levels within the normal range.

**Table 1:** Distribution of subject according to adiponectin levels

| S.No. | Adiponectin | No. of Cases | Percentage |
|-------|-------------|--------------|------------|
| 1 | <2µG/DL | 12 | 18% |
| 2 | 2-15µG/DL | 53 | 82% |
| 3 | >15 µG/DL | 0 | 0% |

As per data shown in table 2, various biochemical parameters of the patients were compared across the gender where it was found that variable like triglycerides, ALT, AST, and adiponectin were approximately same across the gender without any significance (P value 0.533, 0.342, 0.167, and 0.967 respectively) but cholesterol values across the gender was significant (P=0.000).

**Table 2:** Distribution of the biochemical parameters across the categories of gender

| Biochemical parameters | Male | Female | P value |
|------------------------|------|--------|---------|
| Cholesterol | 154.27 ± 46.011 | 185.07 ±45.38 | 0.014 |
| Triglyceride | 159.41±49.15 | 170±57.78 | 0.533 |
| ALT | 39.14±16.49 | 54±15.495 | 0.342 |
| AST | 42.95±27.870 | 33.77±2.486 | 0.167 |
| Adiponectin | 7.20±4.66 | 7.25±4.19 | 0.967 |

As per data shown in table 3, the median stiffness of the liver evaluated through FIBROSCAN was compared across the gender and its association was seen with the various parameters. It was found that all parameters like age, BMI, neck circumference, and waist hip ratio are similar across the gender with no significance (P=0.688, 0.386, 0.584, and 0.540 respectively).

**Table 3:** Distribution of the Fibroscan across the gender and its association with various parameters

| Parameters | Male (Fibrosis < 7) | Female (Fibrosis >7) | P value |
|---|---|---|---|
| Age | 47±14.457 | 47.15 ±11.84 | 0.688 |
| BMI | 28.715±4.874 | 28.281±5.065 | 0.386 |
| Neck circumference | 34.361±3.44 | 35.06±2.729 | 0.584 |
| Waist Hip Ratio | 92.913±3.908 | 95.491±6.522 | 0.540 |

As per data shown in table 4, BMI has a positive correlation with neck circumference which is statistically significant (P value=0.000).

**Table 4:** Correlation of BMI to the various parameters

| S.No. | Pair | 'r' value | P value |
|---|---|---|---|
| 1 | BMI – Neck circumference | 0.597 | 0.000 |
| 2 | BMI-Waist hip ratio | -0.166 | 0.187 |
| 3 | BMI-Cholesterol | 0.228 | 0.067 |
| 4 | BMI triglyceride | 0.700 | 0.580 |
| 5 | BMI – ALT | 0.047 | 0.710 |
| 6 | BMI-AST | 0.067 | 0.595 |
| 7 | BMI- Fibrosis | -0.061 | 0.632 |
| 8 | BMI – Adiponectin | 0.085 | 0.500 |

As per data shown in table 5, neck circumference has a positive correlation with BMI which is statistically significant (p=0.000) and has negative correlation with fibroscan which is statistically significant (p=0.032).

**Table 5:** Correlation of neck circumference to the various parameters

| S. No. | Pair | 'r' value | P value |
|---|---|---|---|
| 1 | Neck circumference –BMI | 0.597 | 0.000 |
| 2 | Neck circumference Waist hip ratio | -0.137 | 0.277 |
| 3 | Neck circumference – Cholesterol | 0.188 | 0.133 |
| 4 | Neck circumference triglyceride | 0.091 | 0.472 |
| 5 | Neck circumference – ALT | 0.236 | 0.858 |
| 6 | Neck circumference -AST | 0.043 | 0.733 |
| 7 | Neck circumference Fibroscan | -0.267 | 0.032 |
| 8 | Neck circumference – Adiponectin | 0.172 | 0.170 |

As per data shown in table 6, Waist Hip Ratio has a negative correlation with cholesterol which is statistically significant (p=0.003).

**Table 6:** Correlation of Waist Hip Ratio to the various parameters

| S. No. | Pair | 'r' value | P value |
|---|---|---|---|
| 1 | Waist hip ratio – BMI | -0.166 | 0.187 |
| 2 | Waist hip ratio – Neck Circumference | -0.137 | 0.277 |
| 3 | Waist hip ratio – Cholesterol | -0.362 | 0.003 |
| 4 | Waist hip ratio – Triglyceride | -0.055 | 0.661 |
| 5 | Waist hip ratio – ALT | 0.078 | 0.536 |
| 6 | Waist hip ratio – AST | 0.015 | 0.905 |
| 7 | Waist hip ratio – Fibroscan | 0.020 | 0.872 |
| 8 | Waist hip ratio – Adiponectin | 0.068 | 0.590 |

**Discussion**

Total 65 patients with ultrasonography finding of fatty liver disease without the history of alcohol intake were selected either on OPD or on IPD basis of Department of Medicine, MY Hospital, Indore.

As per Siddharth Verma et al[3] study that there is no optimal ALT levels to predict NASH and advanced fibrosis. Metabolic risk factors should be evaluated to select patients for a liver biopsy to confirm NASH and advanced fibrosis. In our study too, out of 65 patients, 32 patients had higher ALT levels i.e. 49% patients had elevated ALT levels and remaining 33 patients i.e. 51% were having normal ALT levels. Similarly AST levels in our study also signifies that maximum patients have the normal AST levels in NAFLD i.e. out of 65 patients, only 17% patients had higher AST levels i.e. 29% patients had elevated AST level and remaining 48 patients i.e. 74% were having normal AST level.

Li et al[4] conducted a study to investigate the serum leptin and adiponectin levels in nonalcoholic fatty liver disease (NAFLD) patients, and their relationship with insulin resistance and concluded increased serum leptin levels and decreased serum adiponectin level in NAFLD patients independently associated with HOMA-IR. In our study, only 12 patients i.e. 18% of the patients had adiponectin levels less than its normal value while remaining 53 patients i.e. 82% had adiponectin levels within the normal range and with spearmans correlation test we found that adiponectin had no correlation, neither with

adiponectin ('r' =0.034, p=0.287) nor with any other parameters which is statistically significant .

In our study, we also performed fibroscan to look any advanced fibrosis but surprisingly we found that out of 65 patients, 54 patients had the fibroscan score less than 7 i.e. 83% of the patients had median stiffness of the liver less than the cut off value, while only 11 patients i.e. only 17% patients had median stiffness of the liver more than its cut off value. It suggests that although the NAFLD is emerging as major health problem in the world but if get attentive towards health and its risk factors, it can be diagnosed in earlier stage before the advanced fibrosis takes place.

In our study various parameters of the patients were compared across the gender where it was found that variable like age, BMI, and neck circumference were approximately same across the gender without any statistically significance with P values of (0.388, 0.059, and 0.155) respectively but waist hip ratio values was significant (P=0.000). Various biochemical parameters of the patients were also compared across the gender where it was found variable like triglycerides, ALT, AST, and adiponectin were approximately same across the gender without any significance with P values of (0.533, 0.342, 0.167, and 0.862) respectively but cholesterol levels across the gender was significant (P=0.000).

We also studied median stiffness of the liver that was evaluated through fibroscan, and was compared across the gender and its association was seen with the various parameters. It was found that all the parameters like age, BMI, neck circumference, and waist hip ratio are similar across the gender with no significance (P=0.688, 0.386, 0.584, 0.540) respectively, similarly biochemical parameters were compared and it was found that all the parameters like cholesterol, triglycerides, ALT, AST, and adiponectin are similar across the gender with no significance (P=0.121, 0.144, 0.540, 0.391, and 0.527) respectively.

In our study, we also studied individual parameter's correlation with other parameters and we found that BMI has a good correlation with neck circumference which is statistically significant (p=0.000), neck circumference has a good correlation with BMI which is statistically significant (p=0.000) and has weak correlation with fibroscan which is statistically significant (p=0.032), waist hip ratio has a weak correlation with cholesterol which is statistically significant (p=0.003).

## Conclusions

In Indian population also, NAFLD has association with its risk factors like obesity, larger neck circumference, higher waist hip ratio, and triglyceride levels. Adiponectin levels association to the NAFLD found to be less in Indian population. Further study needed in large group of subjects in this also.

## Disclosure

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Conflict of interest: Not declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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