CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES
http://doi.org/10.5281/zenodo.3518851

Available online at: http://www.iajps.com *Research Article*

# NAFLD: PREVALANCE AND ASSOCIATED COMPLICATIONS AMONG PREGNANT FEMALES

**[1]FAWAD IQBAL JANJUA, [2]JAMSHID SIDDIQUE, [3]SADIA KHAN**

[1]FCPS Gastroenterology, Head of Department Gastroenterology, DHQ/UTH, Gujranwala, Contact No.+923324455939, Email Address: fawad.iqbal001@gmail.com., [2]FCPS(T)-Gastroenterology, DHQ/UTH, Gujranwala, Contact No. +923337529175, Email Address: jamshid@hotmail.co.uk., [3]MSc Biostatistics, MPhil Public Health, Senior Lecturer, The University of Lahore, Contact No. +92333014428, Email Address: sadiakhan0607@gmail.com.

**Article Received:** August 2019 **Accepted:** September 2019 **Published:** October 2019

**Abstract:**

*Non-alcoholic liver disease (NAFLD) is the common form of chronic Liver disease (CLD), and its worldwide prevalence continues to extend with the growing epidemic. The aim of this study is to assess prevalence of NAFLD and risks of adverse physiological state and delivery outcomes in females diagnosed with NAFLD before delivery compared to population controls. A cross sectional analytical study was done from 1st May, 2019 to 5th September, 2019 in DHQ hospital, Gujranwala. 361 Women carrying a singleton pregnancy admitted for delivery were considered to the study. Data was collected with self-administered questionnaire. During the study period 59(16.3%) females were diagnosed with NAFLD prior to delivery. Grade I and II were same (i.e 40.7%) whereas Grade III NAFLD was among 18.6% of pregnant females. Maternal education, age and gender of the baby was insignificantly associated with NAFLD (p-value>0.05), whereas body mass index, pre-existing diabetes miletus and hypertension, pregnancy induced hypertension, pre-eclampsia, apgar score, low birth weight and gestational age was significantly associated with NAFLD (p-value<0.05). Positive and significant correlation has been observed among ALTs and ASTs with NAFLD Grades (p-value<0.05). NAFLD is the common problem during pregnancy and is significantly associated with pregnancy complications such as PIH, pre-eclampsia, LBW, gestational age and apgar score. Mean ALTs and ASTs level increased with the increase in the Grades of NAFLD from Grade I to III.*

**Corresponding author:**

**Sadia Khan,**

*MSc Biostatistics, MPhil Public Health, Senior Lecturer, The University of Lahore*
*Contact No. +92333014428, Email Address: sadiakhan0607@gmail.com.*

QR code

*Please cite this article in press Sadia Khan et al.,* ***Nafld: Prevalance And Associated Complications Among Pregnant Females,*** *Indo Am. J. P. Sci, 2019; 06(10).*

## INTRODUCTION:

Non-alcoholic liver disease disease (NAFLD) is the common form of chronic Liver disease (CLD), and is abundantly increasing worldwide. [1] Alcohol consumption is the common factor associated with fatty liver disease (FLD), although it is recently reported that FLD is not direct associated with alcohol consumption. The common risk factors associated with NAFLD are alcohol consumption, diabetes mellitus (DM) and hyperlipidemia. [1] NAFLD is the manifestation of metabolic syndrome, coexisting with dyslipidemia and endocrine resistance. [2] The non-alcoholic liver disease (NALD), non-alcoholic steatohepatitis (NASH), are eventually related to liver cirrhosis (LC). [3,4] The incidence and grade of NAFLD grading and its incidence differs widely with the population screening. The incidence of histologically defined NAFLD was 20 per cent and 51 per cent in two separate research involving prospective liver donors. [5]

Based on the population survey the incidence of NAFLD in south America is 31%, 32% in the Middle East, 23% reported in USA and 24% in Europe.[6] A community based incidence is 2008 reported 37.5% NAFLD in Sri Lankan female and recent research in 2017 reported 8.7% prevalence in adolescent of NAFLD in Sri Lankan population. [7]

Apparently, due to different genetic makeup and environmental associated factors the Asian population having NAFLD had lower Basic Metabolic Index (BMI) than those in western countries. [8] This proof suggests that Asian populations have totally different genetic and environmental condition to NAFLD. In the women of childbearing age (20–40 years), the prevalence has been 10%. [9] Moreover, NAFLD is associated to polycystic ovary syndrome (PCOS). Maternal obesity is joined to adverse physiological outcomes, like physiological polygenic disorder, pre-eclampsia and Caesarean delivery. [10] Women with the history of PGD are at high risk of NAFLD. [11,12] The risks of adverse physiological state and babe outcomes severally of body mass index (BMI) are unknown. The aim of this study was to find out the prevalence of NAFLD and to assess risks of adverse physiological state and delivery outcomes in females diagnosed with NAFLD before delivery compared to population controls.

## METHODOLOGY:

A cross sectional analytical study was conducted at DHQ hospital Gujranwala, from 1st May, 2019 to 5thSeptember, 2019. This hospital served the patients acquiring tertiary care.

Pregnant females admitted in the hospital for delivery were included in this study. Data was collected from patients who were admitted in the hospital, administered questionnaire, with previous medical history. Pre-birth records were observed and data regarding females health status was reserve, weight, and outcomes of blood sugar screening were gathered. The BMI and blood pressure of the patient were checked and record was observed for difficulties in pregnancy. All patients had blood sent for Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST) and underwent an abdominal ultrasound scan (USS) during admission. Once the baby was delivered, additional data about delivery were collected from the patients record.

All female participants after taking the informed consent all female participants were confirmed that they never consumed alcohol nor smoked and have previous history of hepatitis were excluded in the study. The exclusion criteria comprising of Women diagnosed with CLD including viral hepatitis, metabolic disorder usage of alcohol and were exposed to medications resulting in hepatic steaeosis. Pregnant females with the history of fatty liver were excluded. Ultrasonography was completed by a professional radiologist and a senior professor of obstetrics and gynaecology, who was expert to perform liver USS. Similarity was defined as number of previous births after 24 weeks. If the present pregnancy is the first time a pregnancy has continued beyond 24 weeks she was considered as para1.

We do not have any pre-pregnancy, body weight, record that's why we use the body weight during pregnancy and calculate the BMI using WHO Asian calculator.

Ultrasonography was performed for diagnosis of NAFLD, The presence of NFLD, was identified by the detection of bright echogenic patterns within the liver.

During USS liver echo pattern was categorized into four grades. [13,14]

A. Grade – 0 (normal)
   Liver parenchyma has a homogeneous echo texture with fine low level echos, liver echogenic-city equal to or slightly greater than that of the normal renal cortex and spleen.
B. Grade – 1 (Mild steatosis)
   Liver echogenicity is slightly increased, and clear delineation of hepatic and portal vein walls.
C. Grade II (Moderate steatosis)

Liver echogenicity is moderately increased, obscuring the echogenic walls of hepatic and portal vein branches, Echogenic line of diaphragm is well visualized.

D. Grade III (Severe steatosis)
Marked increase in hepatic echogenicity, poor visualization echogenic walls of hepatic vessels, poor visualization diaphragm or obscure the clear delineation of diaphragm and liver, poor visualization of posterior portion of the right lobe.

Every woman whose liver echo pattern falling into grade I, II, and III were diagnosed to have NAFLD (cases). Women who were in grade 0 were identified as Non-NAFLD or Normal.

Baseline characteristics of women in the NAFLD groups were described using descriptive statistics. Variable were tested for normality using the Kolmogorov Smirnov test. Frequency and percentages were used to summarize categorical variables and mean (SD) were used to summarize continues variables. Group mean were compared between NAFLD GRADE using ANOVA. Categorical variables between NAFLD and non NAFLD were compared using chi square test, Fisher's exact test.

Spearman's rank correlation coefficient was used to explore the association between NAFLD Grades and values of ALT and AST.

The study was approved by ethical committee. Participants informed consent prior to undergoing study procedure, which were approved by the ethical committee. Women with NAFLD were educated about the importance of regular exercises and dietary control.

## RESULTS:

During the study period, there were 361 pregnant females, among them 59(16.3%) were diagnosed with NAFLD prior to delivery. Grade I and II were same (i.e 40.7%) whereas Grade III NAFLD was among 18.6% of pregnant females.

Descriptive data of NAFLD grades among pregnant females has been depicted in Table 1. Women with the higher age group was more common in NAFLD Grades I, II and III as compared to Grade 0 (p-value: 0.261). Women with Grade II NAFLD had high BMI 28.0±4.8 when compared to normal (p-value: 0.000). Insignificant association has been observed among the grades of NAFLD in terms of maternal education and gender of the baby (p-value: 0.155 and 0.307 respectively). Preexisting diabetes mellitus and hypertension were significantly associated between the groups (p-value: 0.028 and 0.030 respectively).

Pregnancy related complications and outcomes have been presented in Table 2. Higher PIH was observed in NAFLD Grade I (33.3%) in comparison to Grade II (8.3%) and III (9.1%), (p-value:0.000). Majority of the pre-eclamptic females were from Grade III NAFLD (90.9%); (p-vale: 0.000). Overall GDM was observed in 143(39.3%) pregnant females. Among those highest percentage of GDM was seen in Grade III (63.6%). There was significant difference between the four groups in terms of GDM, mode of delivery and parity (p-value: 0.072, 0.661 and 0.788 respectively). Apgar score, low birth weight and gestational age was highly significant among the NAFLD grades (p-value: 0.000). 36.4% from Grade III were having Apgar score between 0 to 6 whereas only 2.6 % were from Non NAFLD (p-value: 0.000). Higher percentage of low birth weight was observed in Grade III, although 21.5% were from Grade 0 (p-value: 0.000). Overall there were 24.9% preterm births, among them 22.2% were from Grade 0, 12.5% were from Grade I, 41.7% from Grade II and 90.9% from Grade III (p-value: 0.000).

Biochemical analysis has shown in Table 3. There was significant correlation among NAFLD Grades in terms of ALTs and ASTs (p-value: 0.000), furthermore positive correlation has been observed in ALT vs. NAFLD Grades (r: 0.226) and AST vs. NAFLD Grades (r: 0.301).

**Table 1. Descriptive data on pregnancies in women with NAFLD Grades and Non-NAFLD**

| Variable | Total N: 361 | Normal N: 302 | NAFLD Grade I N: 24 | NAFLD Grade II N: 24 | NAFLD Grade III N: 11 | p-value |
|---|---|---|---|---|---|---|
| | | | | | | |
| **Age** | | | | | | |
| 16-25 years | 118(32.7) | 105(34.8) | 6(25) | 4(16.7) | 3(27.3) | 0.261** |
| 26-35 years | 229(63.4) | 184(60.9) | 18(75) | 20(83.3) | 7(63.6) | |
| 36 years above | 14(3.9) | 13(4.3) | 0(0) | 0(0) | 1(9.1) | |
| | | | | | | |
| **BMI** | 23.9±4.9 | 23.3±4.7 | 26.4±5.5 | 28.0±4.8 | 26.1±4.9 | 0.000*** |
| | | | | | | |
| **Maternal Education** | | | | | | |
| Primary | 143(39.6) | 121(40.1) | 7(29.2) | 9(37.5) | 6(54.5) | 0.155** |
| Secondary | 97(26.9) | 79(26.2) | 13(54.2) | 4(16.7) | 1(9.1) | |
| Undergraduate | 29(8.0) | 26(8.6) | 0(0) | 2(8.3) | 1(9.1) | |
| Graduate | 61(16.9) | 50(16.6) | 3(12.5) | 5(20.8) | 3(27.3) | |
| Post Graduate | 31(8.6) | 26(8.6) | 1(4.2) | 4(16.7) | 0(0) | |
| | | | | | | |
| **Gender of the baby** | | | | | | |
| Male | 182(50.4) | 155(51.3) | 14(58.3) | 8(33.3) | 5(45.5) | 0.307* |
| Female | 179(49.6) | 147(48.7) | 10(41.7) | 16(66.7) | 6(54.5) | |
| | | | | | | |
| **Pre Existing DM** | | | | | | |
| Yes | 8(2.2) | 4(1.3) | 2(8.3) | 2(8.3) | 0(0) | 0.028** |
| No | 353(97.8) | 298(98.7) | 22(91.7) | 22(91.7) | 11(100) | |
| | | | | | | |
| **Pre Existing HT** | | | | | | |
| Yes | 1(0.3) | 0(0) | 0(0) | 0(0) | 1(9.1) | 0.030** |
| No | 360(99.7) | 302(100) | 24(100) | 24(100) | 10(90.9) | |
| | | | | | | |

Data mean (SD) or n (%).BMI: body mass index; DM: Diabetes Miletus; HT: Hypertension
*Chi-square
** Fishers Exact Test
*** ANOVA

**Table 2 Pregnancy Complications and outcomes among NAFLD Groups and Non NAFLD Group**

| Variable | Total N: 361 | Normal N: 302 | NAFLD Grade I N: 24 | NAFLD Grade II N: 24 | NAFLD Grade III N: 11 | p-value |
|---|---|---|---|---|---|---|
| | | | | | | |
| **PIH** | | | | | | |
| Yes | 20(5.5) | 0(0) | 8(33.3) | 2(8.3) | 1(9.1) | 0.000* |
| No | 341(94.5) | 302(100) | 16(66.7) | 22(91.7) | 10(90.9) | |
| | | | | | | |
| **Pre-eclampsia** | | | | | | |
| Yes | 142(39.3) | 96(31.8) | 19(79.2) | 17(70.8) | 10(90.9) | 0.000* |
| No | 219(60.7) | 206(68.2) | 5(20.8) | 7(29.2) | 1(9.1) | |
| | | | | | | |
| **GDM** | | | | | | |
| Yes | 143(39.6) | 114(37.7) | 14(58.3) | 8(33.3) | 7(63.6) | 0.072* |
| No | 218(60.4) | 188(62.3) | 10(41.7) | 16(66.7) | 4(36.4) | |
| | | | | | | |
| **Mode of delivery** | | | | | | |
| AVD | 17(4.7) | 14(4.6) | 1(4.2) | 2(8.3) | 0(0) | 0.661* |
| NVD | 223(61.8) | 189(62.6) | 16(66.7) | 13(54.2) | 5(45.5) | |
| CS | 121(33.5) | 99(32.8) | 7(29.2) | 9(37.5) | 6(54.5) | |
| | | | | | | |
| **Apgar score at 5$^{th}$ minute** | | | | | | |
| 0-6 | 25(6.9) | 8(2.6) | 7(29.2) | 6(25) | 4(36.4) | 0.000* |
| 7-10 | 336(93.1) | 294(97.4) | 17(70.8) | 18(75) | 7(63.6) | |
| | | | | | | |
| **Parity** | | | | | | |
| 1 | 298(82.5) | 249(82.5) | 20(83.3) | 19(79.2) | 10(90.9) | 0.788* |
| 2 | 52(14.4) | 44(14.6) | 4(16.7) | 3(12.5) | 1(9.1) | |
| >=3 | 11(3.0) | 9(3.0) | 0(0) | 2(8.3) | 0(0) | |
| | | | | | | |
| **LBW(<2500 g)** | | | | | | |
| Yes | 89(24.7) | 65(21.5) | 6(25) | 9(37.5) | 9(81.8) | 0.000* |
| No | 272(75.3) | 237(78.5) | 18(75) | 15(62.5) | 2(18.2) | |
| | | | | | | |
| **Gestational Age** | | | | | | |
| Preterm Birth | 90(24.9) | 67(22.2) | 3(12.5) | 10(41.7) | 10(90.9) | 0.000* |
| Term Birth | 271(75.1) | 235(77.8) | 21(87.5) | 14(58.3) | 1(9.1) | |
| | | | | | | |

Data n (%). PIH: Pregnancy Induced Hypertension; GDM: Gestational Diabetes Miletus; LBW: Low Birth Weight.
* Fishers Exact Test

**Table 3 Correlation between ALTs, AFTs and the grade of NAFLD**

| LABS | N | r | p-value |
|---|---|---|---|
| | | | |
| ALT | 361 | 0.226 | 0.000 |
| | | | |
| AST | 361 | 0.301 | 0.000 |

ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase

## DISCUSSION:

Globally NAFLD is the most emerging liver disease. On screened population the ratio and stage of NAFLD varies commonly and the incidence of NAFLD depends on screening of population and the diagnostic tools used for screening. The prevalence of NAFLD was intensively increasing around the world. More or less 15- 40% of general population is affected by NAFLD. [15-17] Recently a hospital based study in Pakistan reported approximately 14% prevalence. [18] In general population of India it range from 5-28%. [19]

In this study the prevalence of NAFLD in pregnant females was observed as 16.3%. The prevalence of NAFLD in pregnant females in Korea was 18.4%, Srilanka it was 18.2% whereas in Australia 15.2%. [20,21]

In current study majority of the females 229(63.4%) belong to age group 26-35 years. The mean BMI of Non-NAFLD and NAFLD females were 23±4.7 and 26.4±5.5 respectively. NAFLD females have greater BMI than Non-NAFLD. [22] It was observed in recent study that most of the children born were males, there was previous history of DM and hypertension in both groups. Complications and outcomes of pregnancy was significantly associated between both groups. It was reported that there was significant association between pregnancy induced hypertension, DM, pre-eclampsia, APGAR score, low birth weight and gestation age in both groups. These findings were also similar with the different studies conducted. [9,23]

In our study APGAR score 0-6 was more common in NAFLD group. In another study it was reported that there was no increased risk for APGAR score <7 at 5min comparing NAFLD, non-NAFLD, non-PCOS women which contradict the current study. [23]

In present study gestational diabetes was more common in Non-NAFLD group 114(37.7%). There was insignificant association was observed between both groups (p-value>0.05). These results were dissimilar with the study SeungMi Lee *at el.*, they reported that the risk of developing GDM was increased in NAFLD patients. [24]

In laboratory findings it was observed High Levels of ALT and AST while comparing these Enzymes significant correlation was observed in NAFLD. These findings were also supported by a study. The results of this study showed that ALT and AST was more raised in NAFLD (33.2±25.2 ), (34.3±47.7) respectively. [24] In another study in Srilanka also showed increased level of ALT in NAFLD population. [22]

## REFERENCES:


1. Angulo P. Nonalcoholic fatty liver disease. *New England Journal of Medicine* 2002; **346**(16): 1221-31.
2. Targher G, Bertolini L, Padovani R, et al. Prevalence of nonalcoholic fatty liver disease and its association with cardiovascular disease among type 2 diabetic patients. *Diabetes care* 2007; **30**(5): 1212-8.
3. El-Zayadi A-R. Hepatic steatosis: a benign disease or a silent killer. *World journal of gastroenterology: WJG* 2008; **14**(26): 4120.
4. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver disease: Practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. *Hepatology* 2012; **55**(6): 2005-23.
5. Lee JY, Kim KM, Lee SG, et al. Prevalence and risk factors of non-alcoholic fatty liver disease in potential living liver donors in Korea: a review of 589 consecutive liver biopsies in a single center. *Journal of hepatology* 2007; **47**(2): 239-44.
6. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease—meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology* 2016; **64**(1): 73-84.
7. Rajindrajith S, Pathmeswaran A, Jayasinghe C, et al. Non-alcoholic fatty liver disease and its associations among adolescents in an urban, Sri Lankan community. *BMC gastroenterology* 2017; **17**(1): 135.
8. Matthias AT, Seneviratne SL. Non-alcoholic Fatty Liver Disease (NAFLD) in South Asia. 2018.
9. Mousa N, Abdel-Razik A, Shams M, et al. Impact of non-alcoholic fatty liver disease on pregnancy. *British journal of biomedical science* 2018; **75**(4): 197-9.
10. Baranova A, Tran T, Birerdinc A, Younossi Z. Systematic review: association of polycystic ovary syndrome with metabolic syndrome and non-alcoholic fatty liver disease. *Alimentary pharmacology & therapeutics* 2011; **33**(7): 801-14.
11. Vernon G, Baranova A, Younossi Z. Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. *Alimentary*

*pharmacology & therapeutics* 2011; **34**(3): 274-85.
12. Mission JF, Marshall NE, Caughey AB. Obesity in pregnancy: a big problem and getting bigger. *Obstetrical & gynecological survey* 2013; **68**(5): 389-99.
13. Hamaguchi M, Kojima T, Itoh Y, et al. The severity of ultrasonographic findings in nonalcoholic fatty liver disease reflects the metabolic syndrome and visceral fat accumulation. *The American journal of gastroenterology* 2007; **102**(12): 2708.
14. Ma X, Holalkere N-S, Mino-Kenudson M, Hahn PF, Sahani DV. Imaging-based quantification of hepatic fat: methods and clinical applications. *Radiographics* 2009; **29**(5): 1253-77.
15. Schuppan D, Gorrell MD, Klein T, Mark M, Afdhal NH. The challenge of developing novel pharmacological therapies for non-alcoholic steatohepatitis. *Liver International* 2010; **30**(6): 795-808.
16. Kistler KD, Brunt EM, Clark JM, Diehl AM, Sallis JF, Schwimmer JB. Physical activity recommendations, exercise intensity, and histological severity of nonalcoholic fatty liver disease. *The American journal of gastroenterology* 2011; **106**(3): 460.
17. Hou Xh, Zhu Yx, Lu Hj, et al. Non-alcoholic fatty liver disease's prevalence and impact on alanine aminotransferase associated with metabolic syndrome in the Chinese. *Journal of gastroenterology and hepatology* 2011; **26**(4): 722-30.
18. Niaz A, Ali Z, Nayyar S, Fatima N. Prevalence of NAFLD in healthy and young male individuals. *ISRN gastroenterology* 2011; **2011**.
19. Amarapurkar DN, Hashimoto E, Lesmana LA, et al. How common is non-alcoholic fatty liver disease in the Asia–Pacific region and are there local differences? *Journal of gastroenterology and hepatology* 2007; **22**(6): 788-93.
20. Herath RP, Siriwardana SR, Ekanayake CD, Abeysekara V, Kodithuwakku SU, Herath HP. Non-alcoholic fatty liver disease and pregnancy complications among Sri Lankan women: A cross sectional analytical study. *PloS one* 2019; **14**(4): e0215326.
21. Ayonrinde OT, Adams LA, Mori TA, et al. Sex differences between parental pregnancy characteristics and nonalcoholic fatty liver disease in adolescents. *Hepatology* 2018; **67**(1): 108-22.
22. Dassanayake AS, Kasturiratne A, Rajindrajith S, et al. Prevalence and risk factors for non-alcoholic fatty liver disease among adults in an urban Sri Lankan population. *Journal of gastroenterology and hepatology* 2009; **24**(7): 1284-8.
23. Hagström H, Höijer J, Ludvigsson JF, et al. Adverse outcomes of pregnancy in women with non-alcoholic fatty liver disease. *Liver International* 2016; **36**(2): 268-74.
24. Lee SM, Kwak SH, Koo JN, et al. Non-alcoholic fatty liver disease in the first trimester and subsequent development of gestational diabetes mellitus. *Diabetologia* 2019; **62**(2): 238-48.