Original Article

Non-Alcoholic Fatty Liver Disease in Pregnancy with Estimation of Feto-Maternal Outcome in a Tertiary Hospital in Bangladesh

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Abstract

Background: Non-alcoholic Fatty Liver Disease (NAFLD) is a growing public health concern globally. NAFLD has been linked with adverse pregnancy outcome. The prevalence of NAFLD among women in childbearing age is 10%. During pregnancy both physiologic and pathologic fluctuation in estrogen as well as rapid weight gain plays an important role in the development of NAFLD in mother and infant.

Objective: To find out clinical and laboratory profile and pregnancy outcome of patients with fatty liver disease.

Methods: We conducted this observational study between January through December 2017 in (pro-women, pro-poor) Ad-din Women Medical College Hospital in Maghbazar, Dhaka, Bangladesh. We enrolled 103 pregnant women who signed the consent (verbal) to participate in the study. Demographic and clinical information was collected using a pre-tested questionnaire.

Results: Mean age of the patients was 27 years. During first trimester 18 patients were enrolled, 32 in second and 53 in third trimesters. Of 103, 3 (2.91%) patients had known history of fatty liver disease, 11 (10.68%) had hypertension, 11 (10.68%) had Gestational Diabetes Mellitus (GDM) but none had previous history of Diabetes Mellitus (DM). Among all, 8 (7.76%) patients had previous pregnancy related complications and 32 (31%) had foetal complications including still birth, abortion, neonatal death and Intrauterine Device (IUD). Beside, 92 (89.3%) had grade 1, 10 (9.7%) had grade 2 and one (0.97%) patient had grade 3 fatty liver. 35 (32.4%) patients had high Fasting Blood Sugar level and 26 (24.1%) patients had positive Oral Glucose Tolerance Test (OGTT). And, 31% patients had a high cholesterol level, none had abnormal HDL, 5.8% had high LDL and 78.6% had high TG. USG identified 3 patients with abnormal fetal profile and only 2 patients had adverse pregnancy outcome: one IUD and one abortion.

Conclusions: Non-alcoholic fatty liver Disease increases the risk of maternal and fetal complications. Pregnant women should regularly screen for fatty liver disease for early detection and intervention.

Key Word: Pregnant women, Non-alcoholic Fatty liver, Fetal, Maternal, Tertiary Hospital

Introduction

Non-alcoholic Fatty Liver Disease (NAFLD) is a growing public health concern globally. Nonalcoholic fatty liver disease (NAFLD) is the most common liver disorder in the Western world, with an estimated prevalence of 20% to 30% in the adult population, 6.67% to 29.85% of whom progress to more advanced nonalcoholic steatohepatitis (NASH).[1,2] NAFLD is also the leading indication for liver transplantation among women.3,4 The prevalence of NAFLD varies by age, sex, ethnicity, modality of diagnosis, and prevalence of obesity in the population.5

NAFLD has been linked with adverse pregnancy outcome. The prevalence of NFALD among women in childbearing age is 10%. During pregnancy both physiologic and pathologic fluctuation in estrogen as well as rapid weight gain plays an important role in the development of NAFLD in mother and infant6. Some recent studies show insulin resistance might act as a subsequent and preceding factor in developing NFALD7-9. Although there are enough studies regarding the harmful effects of maternal hyperglycemia and

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weight gain on pregnancy and infant health10,11 data related to the effects of NFALD specifically on pregnancy are still not enough.

A study from Canada suggested that the presence of NAFLD as assessed by liver ultrasound at 11–14 weeks of gestation was significantly associated with several adverse outcomes like impaired fasting glucose, gestational impaired glucose tolerance or GDM at 24–28 weeks of gestation12. Another study conducted in Egypt revealed that women with pre-existing NAFLD were at a greater risk of GDM than the women without pre-existing NAFLD13. The prevalence of NAFLD in Bangladesh is 33.86%14 but there are not enough data about the feto-maternal outcome of NAFLD in pregnancy.

The close relationship between GDM and Type 2 DM raises the possibility that a relationship could also exist between NAFLD and GDM. Indeed, prior studies have explored this association, particularly on the postpartum development of NAFLD in women with a prior history of GDM.8, 9, 10, 11 The prevalence of ultrasound-detected hepatic steatosis signifying NAFLD in European women with a prior history of GDM was 38% compared to a prevalence of 17% in women without GDM.8 In Caucasian and Black American women with a previous history of GDM, a higher rate of NAFLD was detected via ultrasound or computerized tomography15

The primary aim of this systematic review and meta-analysis is to determine the prevalence of GDM in women found to have imaging evidence of NAFLD during their pregnancy. A secondary objective is to assess whether a higher occurrence of GDM develops in women with NAFLD compared to those without.

Objectives:

Aim(s) of this study was to find out clinical and laboratory profile and pregnancy outcome of patients with fatty liver disease.

Methodology:

Study design: Observational study.

Study period: Twelve months (January through December 2017)

Study area: Ad-din Women's Medical College and Hospital.

Inclusion criteria were as follows:

i. Pregnant women: Non-alcoholic Fatty Liver

Exclusion criteria were as follows:

i. Non pregnant women
ii. Pregnant women: Alcoholic Fatty Liver

Total Sample sizes: 103 pregnant women.

Maintaining the Quality Control of Data

- To assure the quality of data, each collected data will first be checked visually and rechecked by other investigator and only then it would be entered into an IMP/PC to check for logical checking.
- Data form each patient would be coded before analysis and reporting.

Data Processing and Analysis

- The data will be cleaned, checked for completeness, and then would be entered into SPSS, V. 22 The data will be analyzed using appropriate descriptive statistics, and will be tabulated using frequency, percentage, and mean.
- Both binary & multivariable logistic regression analyses will be performed. Variables in bi-variable analysis with $p< 0.2$ will be entered into a model of multivariable logistic regression.
- The strength of association of risk factors with knowledge and practice will be demonstrated by computing crude odds ratio (COR) and the adjusted odds ratio (AOR) with a 95% confidence interval (CI).
- All through the data analysis, a P-value <0.05 will be considered as statistically significant.

Results & Findings:

Table-1: Three stages during Pregnancy of enrolled pregnant women (n=103)

Three stages during Pregnancy	Frequency	Percentage
First Trimester	18	17
Second Trimester	32	31
Third Trimester	53	52

Table 1 shows that among 103 patients 18 (17%) patients were enrolled during first trimester, 32 (31%) in second and 53 (52%) in third trimesters.

Table-2: Previous history of various diseases among pregnant women (n=103)

Diseases	Frequency	Percentage
Fatty Liver	3	3
Hypertension	11	10
Gestational Diabetes Mellitus	11	10
No disease	78	77

Table 2 shows that Of 103, 3 (2.91%) patients had known history of fatty liver disease, 11 (10.68%) had hypertension, 11 (10.68%) had Gestational Diabetes Mellitus but none had previous history of Diabetes Mellitus. And, 78 (77%) had no previous history of disease.

Table-3: Previous pregnancy and fetal related complication among pregnant women (n=103)

Previous Complication	Frequency	Percentage
Previous pregnancy related complication	8	8
Previous fetal complications	32	31
None	63	64

Table 3 shows that of 103 patients, 8 (7.76%) patients had previous pregnancy related complications and 32 (31%) had fetal complications including still birth, abortion, neonatal death and intrauterine death (IUD).

Table-4: Fatty liver grade level among pregnant women (n=103)

Grade Level	Frequency	Percentage
Grade-1	92	89.3
Grade-2	10	9.7
Grade-3	1	0.9

Table 4 shows that 92 (89.3%) had grade 1, 10 (9.7%) had grade 2 and one (0.97%) patient had grade 3 fatty liver.

Table-5: Blood sugar level among pregnant women (n=103)

Blood Sugar Level	Frequency	Percentage
High Fasting Blood Sugar Level	35	32.4
OGTT	26	24.1
None	42	40.2

Table 5 shows that 35 (32.4%) patients had high Fasting Blood Sugar level and 26 (24.1%) patients had positive Oral Glucose Tolerance Test (OGTT).

Table-6: Cholesterol level status of pregnant women

Cholesterol Level	Frequency	Percentage
High	34	31
LDL	6	5.8
High TG	81	78.6

Table 6 shows that of all patients 31% (34/103) patients had a high cholesterol level, none had abnormal High-Density Lipid (HDL), 5.8% (6/103) had high Low-Density Lipid (LDL) and 78.6% (81/103) had high Triglyceride (TG) level.

Discussion:

Non-alcoholic fatty liver disease may be characterized by hepatic steatosis on imaging or biopsy, insulin resistance and increased triglyceride synthesis[16]. NFALD is itself an insulin resistance state[17]. As the pregnancy advances to third trimester, insulin sensitivity might decline to 50% of the normal expected value[18] making the situation even worse.

Study showed that 2.91% patients had known history of fatty liver disease, 10.68% had hypertension, 10.68% had GDM but none had previous history of DM. Higher BMI (>30 as opposed to <25) and the more established diabetic state DM as opposed to GDM) groups have shown a stronger association with NAFLD in pregnancy.[19] Previous studies demonstrated a strong link between both gestational diabetes and NAFLD. [8]

Ajmera et al. showed that GDM is an early risk indicator for the occurrence of NAFLD in multiparous women.[7] A meta-analysis evidenced that NAFLD is independently associated with a significant increase in maternal conditions of baseline HTN and DM, obesity, GDM, history of GDM, pre-eclampsia, and composite outcomes of hypertensive complications of pregnancy.[19] Two studies from Europe evaluated other markers of fatty liver among women with GDM. [7]

Another finding showed that 7.76% patients had previous pregnancy related complications and 31% had fetal complications including still birth, abortion, neonatal death and IUD. NAFLD in pregnancy is associated with fetal outcomes, with significantly higher odds of premature birth, a novel significant association

with a history of abortion or miscarriage and large for gestational age birth. [19]

Study showed that of all patients 31% (34/103) patients had a high cholesterol level, none had abnormal High-Density Lipid (HDL), 5.8% (6/103) had high Low-Density Lipid (LDL) and 78.6% (81/103) had high Triglyceride (TG) level. Although previous studies demonstrated that infants of pregnant NAFLD women had a higher incidence of preterm birth with low weight. [7]

The prevalence of NAFLD in pregnancy has increased almost threefold in the last decade and it is associated with various complications like hypertensive complications, postpartum hemorrhage and pre-term birth. [20]

Conclusion:

Non-alcoholic fatty liver Disease increases the risk of maternal and fetal complications. This study will help to pregnant NAFLD patients to be educated about the long-term squeal of this metabolic condition Pregnant women should regularly screen for fatty liver disease for early detection and intervention.

References:

1. Williams CD, Stengel J, Asike MI, et al. Prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: a prospective study. Gastroenterology. 2011;140(1): 124-131.
2. 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.
3. Charlton MR, Burns JM, Pedersen RA, Watt KD, Heimbach JK, Dierkhising RA. Frequency and outcomes of liver transplantation for nonalcoholic steatohepatitis in the United States. Gastroenterology. 2011;141(4):1249-1253.
4. Noureddin M, Vipani A, Bresee C, et al. NASH leading cause of liver transplant in women: updated analysis of indications for liver transplant and ethnic and gender variances. Am J Gastroenterol. 2018;113(11): 1649-1659.
5. Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of nonalcoholic fatty liver disease: practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018;67(1):328-357.
6. Hershman M, Mei R, Kushner T. Implications of Nonalcoholic Fatty Liver Disease on Pregnancy and Maternal and Child Outcomes. Gastroenterol Hepatol (N Y). 2019 Apr;15(4):221-228. PMID: 31435201; PMCID: PMC6696596.
7. Ajmera VH, Gunderson EP, VanWagner LB, Lewis CE, Carr JJ, Terrault NA. Gestational diabetes mellitus is strongly associated with non-alcoholic fatty liver disease. Am J Gastroenterol. 2016;111(5):658–664.
8. Forbes S, Taylor-Robinson SD, Patel N, Allan P, Walker BR, Johnston DG. Increased prevalence of non-alcoholic fatty liver disease in European women with a history of gestational diabetes. Diabetologia. 2011;54(3):641–647.
9. Foghsgaard S, Andreasen C, Vedtofte L et al. Nonalcoholic fatty liver disease is prevalent in women with prior gestational diabetes mellitus and independently associated with insulin resistance and waist circumference. Diabetes Care. 2017;40(1):109–116.
10. Dabelea D, Crume T. Maternal environment and the transgenerational cycle of obesity and diabetes. Diabetes. 2011;60(7):1849–1855
11. Stamnes Køpp UM, Dahl-Jørgensen K, Stigum H, Frost Andersen L, Næss Ø, Nystad W. The associations between maternal pre-pregnancy body mass index or gestational weight change during pregnancy and body mass index of the child at 3 years of age. Int J Obes (Lond). 2012;36(10): 1325–1331.
12. De Souza LR, Berger H, Retnakaran R et al (2016) Non-alcoholic fatty liver disease in early pregnancy predicts dysglycemia in mid-pregnancy: prospective study. Am J Gastroenterol 111(5):665–670.
13. Mousa N, Abdel-Razik A, Shams M et al (2018) Impact of non-alcoholic fatty liver disease on pregnancy. Br J Biomed Sci 75:197–199
14. Panel Thora Ying LihaiMarkRajaratnamc DifeiDeng bcJacobGeorgebdeDharmintraPasupathybfNgai WahCheungab) The prevalence of gestational diabetes mellitus in women diagnosed with non-alcoholic fatty liver disease during pregnancy: A systematic review and meta-analysis Author links open overlay.

15. Hossain, S. , Sultana, S. , Zaman, K. , Shafiq, S. , Rahman, A. , Hossain, S. , Islam, S. , Uddin, M. , Faroque, M. , Ferdoushi, S. , Paul, D. and Rahman, M. (2020) Triglyceride and Glucose Index (TyG) is a Reliable Biomarker to Predict Non-Alcoholic Fatty Liver Disease. Journal of Biosciences and Medicines, 8, 124-136.

16. Shulman GI. Ectopic fat in insulin resistance, dyslipidemia, and cardiometabolic disease. N Engl J Med. 2014;371:1131–1141.

17. Luo, Z. and Wu, Q. (2019) Progress in Research on Nonalcoholic Fatty Liver and Gestational Diabetes. International Journal of Clinical Medicine, 10, 251-258.

18. McLachlan K, O'Neal D, Jenkins A, Alford F. Do adiponectin, TNFα, leptin and CRP relate to IR in pregnancy? Studies in women with and without gestational diabetes, during and after pregnancy. Diabetes Metab Res Rev.

19. El Jamaly H, Eslick GD, Weltman M. Systematic review with meta-analysis: Non-alcoholic fatty liver disease and the association with pregnancy outcomes. Clinical and molecular hepatology. 2022 Jan; 28(1):52.

20. Sarkar M, Grab J, Dodge JL, Gunderson EP, Rubin J, Irani RA, Cedars M, Terrault N. Non-alcoholic fatty liver disease in pregnancy is associated with adverse maternal and perinatal. Outcomes. J Hepatol. 2020 Sep;73(3):516-522.