

FREQUENCY OF COMMON MATERNAL COMPLICATIONS FOLLOWING OBSTETRIC CHOLESTASIS

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ABSTRACT

Background: Pregnant women may present with obstetric cholestasis. **Objective:** To determine the frequency of common maternal complications like gestational hypertension, pre-eclampsia and gestational diabetes in obstetric cholestasis. **Methodology:** Study Design: Cross sectional study. Setting: Department of Obstetrics and Gynecology, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan. Duration: Six months from 30th September 2014 to 29th March 2015. Seventy eight women admitted in the inpatient Department of Obstetrics & Gynecology ward, meeting the inclusion criteria were included. They were enrolled for study after taking informed consent. Women with obstetric cholestasis were followed till delivery and noted for any complications like gestational hypertension, preeclampsia or gestational diabetes mellitus. The outcome variables noted were; gestational hypertension, preeclampsia or gestational diabetes mellitus on specifically designed proforma along with demographic features of the patients. Data was analyzed by using SPSS version 17. **Results:** Mean age of the patients was 26±3 years, mean gestational age was 33±2 weeks, mean AST was 103±31 U/L, Mean ALT was 110.71±35.74 U/L and mean GGT was 84.81±17.59 U/L. Gestational hypertension was the most common complication 29 (65.9%) in patients presented with intrahepatic cholestasis of pregnancy. Gestational diabetes was present in 7(15.39%) patients while pre-eclampsia was noted in 8 (18.2%) patients having intrahepatic cholestasis of pregnancy. **Conclusion:** Gestational hypertension was the most common complication in patients presented with intrahepatic cholestasis of pregnancy, followed by pre eclampsia and gestational diabetes. **Key Words:** Intrahepatic cholestasis, Gestational diabetes, Gestational hypertension, Preeclampsia, Obstetric cholestasis

INTRODUCTION

Intrahepatic cholestasis during pregnancy (ICP) is mostly a reversible liver disorder. Main features of Intrahepatic cholestasis are;^{1,2} pruritis arising in late pregnancy high serum aminotransaminases and increased bile acids. Spontaneous resolution of signs and symptoms occurs within 2 to 3 weeks postpartum.^{1,2,3} Time for occurrence of ICP is last days of second or early phase of third trimester of pregnancy. This condition is self limiting and laboratory findings also become normal later on. Serum alkaline phosphatase level rises times, but its interpretation is difficult as there are elevated placental increased many isoenzymes.^{5,6} Prothrombin time, some time is also raised mainly due to vitamin k deficiency.⁷ Recurrence is also common in subsequent pregnancies.⁸ In the diagnosis process other causes of jaundice should be ruled which may be viral hepatitis, hyperemesis gravidarum, primary biliary cirrhosis or chronic hepatitis C.⁸⁻¹¹

In numerous reports, selenium deficiency has been obstetric cholestasis.¹² ICP has many associated fetal risks, such as preterm delivery, fetal distress and intrauterine fetal death,^{4,5} which have been studied by many physicians. This study was designed to enlist frequency of common maternal complications in obstetric cholestasis.

METHODOLOGY

It was a cross sectional study conducted at the Department of Obstetrics and Gynecology Sheikh Zayed Medical College/Hospital Rahim Yar Khan for a period of six months from 30th September 2014 to 29th March 2015. Patients were selected with non-probability consecutive sampling technique. A proforma was specifically designed to record the findings of this study. Seventy eight women visiting Inpatient Department of Obstetrics & Gynecology, and meeting the inclusion criteria were enrolled for the study.

Patients were included in the study after taking informed consent and were ensured of their confidentiality. Study was conducted after approval from the Ethical Committee of the Institution.

Women with obstetric cholestasis were followed till delivery and noted for any complications like gestational hypertension, preeclampsia and gestational diabetes mellitus. Outcome variables like gestational hypertension, diabetes and preeclampsia on the proforma along with demography of the patients for each patient.

Data was analyzed by using SPSS for Windows version 17. Descriptive statistics was used to present data. Mean and standard deviation were calculated for age, gestational age of the patients, AST, ALT and GGT levels. Percentages were calculated for parity

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and complications like gestational hypertension, gestational diabetes mellitus and pre-eclampsia (yes, no).

Effect modifiers like age, gestational age and parity were controlled by stratification and effect of these were seen on the outcome through chi-square test. $p\text{-value} \leq 0.05$ was taken as significant.

RESULTS

The mean age of the patients was 26.73 ± 3.34 years, mean gestational age was 33.95 ± 2.13 weeks, AST was 103.92 ± 31.43 U/L, ALT was 110.71 ± 35.74 U/L and mean GGT was 84.81 ± 17.59 U/L. Gestational hypertension was the most common complication 29 (65.9%) in patients presented with intrahepatic cholestasis of pregnancy. (Table I)

Table I: Characteristics and complications among patients with intrahepatic cholestasis of pregnancy.

| Age | |
|---------------------------|------------------|
| Age (in years) | No (Percentage) |
| 20 — 29 | 58 (74.4) |
| 30 — 39 | 20 (25.6) |
| Parity | |
| Parity | No (Percentage) |
| Primigravida | 26 (33.4) |
| Para 1– 4 | 52 (66.6) |
| Gestational Age | |
| Gestational Age (in week) | No (Percentage) |
| ≤ 37 | 68 (87.2) |
| >37 | 10 (12.8) |
| Maternal Complications | |
| Maternal Complications | No (Percentage) |
| Gestational hypertension | 29 (65.9) |
| Gestational Diabetes | 7 (15.9) |
| Pre-eclampsia | 8 (18.2) |

Gestational diabetes was present in 7 (15.39%) patients while pre-eclampsia was developed in 8 (18.2%) patients having intrahepatic cholestasis of pregnancy.

The age related distribution of the patients presented with obstetric cholestasis in relation to gestational hypertension was 21 patients with gestational hypertension between 20-29 years of age and 8 patients between 30-39 years. Similarly, 4 patients with gestational DM between 20-29 years of age and 3 patients between 30-39 years. Patients with pre-eclampsia were 5 between 20-29 years and 3 patients between 30-39 years of age. There was no statistical difference found in relation to gestational hypertension (HTN), gestational DM and pre-eclampsia.

Gestational age related distribution of patients presented with intrahepatic cholestasis of pregnancy in relation to gestational HTN was 28 patients with gestational HTN ≤ 36 weeks of gestation and only 1 patient at 37 weeks of gestation. Patients with GDM were 6 below 36 weeks of gestation and only 1 patient at >37 weeks. 8 patients were with pre-eclampsia ≤ 36 weeks of gestation and none with above this gestation. There was no statistical difference found in different patients in relation to gestational age. (Table II)

Table II: Patient age and gestational age versus complications.

| Age distribution of patients with intrahepatic cholestasis of pregnancy versus complications | | | | | | | | | |
|--|-----------------|----------|-----------|-----------|------------|-------------|----------------|-------------|-----------|
| Age (years) | Gestational HTN | | | GDM | | | Pre-Eclampsia | | |
| | Yes | No | Total | Yes | No | Total | Yes | No | Total |
| 20-29 | 21(36.2%) | 37 (64%) | 58 (100%) | 4 (7%) | 54 (93%) | 58 (100%) | 5 (8.6%) | 53(91.3 %) | 58 (100%) |
| 30-39 | 08 (40%) | 12 (60%) | 20 (100%) | 3 (15%) | 17 (85%) | 20 (100%) | 3 (15%) | 17 (85%) | 20 (100%) |
| Total | 29 (37%) | 49 (63%) | 78 (100%) | 7 (9%) | 71 (91%) | 78 (100%) | 8 (10.5%) | 70 (89.54%) | 78 (100%) |
| | P = 0.764 | | | P = 0.364 | | | P = 0.67208 | | |
| Gestational age distribution of patients with intrahepatic cholestasis of pregnancy versus complications | | | | | | | | | |
| Gestational age (weeks) | Gestational HTN | | | GDM | | | Pre- Eclampsia | | |
| | Yes | No | Total | Yes | No | Total No(%) | Yes No(%) | No No(%) | Total |
| < 36 | 28 (41%) | 40 (59%) | 68 (100%) | 06 (8.8%) | 62 (91.1%) | 68 (100%) | 8 (11.7%) | 60 (88.2%) | 68 (100%) |
| > 37 | 01 (10%) | 9 (90%) | 10 (100%) | 1 (10%) | 9 (90%) | 10 (100%) | 0 (0%) | 10 (100%) | 10 (100%) |
| Total | 29 (37%) | 49 (63%) | 78 (100%) | 7 (9%) | 71 (91%) | 78 (100%) | 8 (10.2%) | 70 (89.7%) | 78 (100%) |

DISCUSSION

Intrahepatic cholestasis of pregnancy is reported to be associated with other hepatobiliary diseases. It is an irritating and very tiring condition adding in morbidly and resolved after child birth. There is a risk in subsequent pregnancies, a history of ICP is known to result in elevated risk of gallstones.

Present study was designed to determine common maternal complications like gestational hypertension, pre-eclampsia and gestational diabetes in obstetric cholestasis. The age of the patients was 26.73±3.34 years. Gestational hypertension was the most common complication 29 (65.9%) in patients presented with intrahepatic cholestasis of pregnancy. Gestational diabetes was present in 7 (15.39%) patients while pre-eclampsia was developed in 8 (18.2%) patients having intrahepatic cholestasis of pregnancy. These results are comparable with available literature.¹⁷⁻²⁰

Martineau et al¹³ studied the association between ICP and gestational diabetes.¹ They found that the incidence of GDM in pregnancies with ICP was 13.6% (p=0.03) as compared to the control group.

Hanns-Ulrich Marschallet al¹⁴ worked to determine the association between ICP and gestational diabetes and preeclampsia. In ICP, preeclampsia (1.1%) and gestational diabetes (1.2%), were seen more commonly as compared to non-ICP pregnancies

Kenyon et al,¹⁵ studied 70 cases of obstetric cholestasis in a series and reported 3 cases with gestational diabetes (4.3%), and 2 cases having essential hypertension (2.9%) in patients with obstetric cholestasis.

Wikström Shemer et al¹⁶ worked in a recent population-based cohort study. They assessed associations between ICP and cancer, and other diseases in women with ICP and matched women without ICP. They also found a special association of ICP with diabetes mellitus.

Li et al,¹⁷ systematically reviewed ICP cases managed in a hospital in China and generated a comprehensive clinical profile of intrahepatic cholestasis of pregnancy. They found seven patients presented with pruritus out of the total nine ICP patients. Other complications associated with ICP included gestational hypertension 33.3%, diabetes mellitus 11.1% and impaired glucose tolerance 11.1%, and pre-eclampsia 11.1%.

Melanie Bannister-Tyrrell et al¹⁸ reported in their study that patients with ICP were likely to develop gestational diabetes (OR 1.77). Also an increased incidence of pregnancy induced hypertension was noted as compared to women without ICP was noted.

Association between obstetric cholestasis and gestational diabetes has been reported in a number of studies. A recent population based cohort study¹⁹ was done to see association of diabetes mellitus with ICP. They also noted an increased incidence of gestational diabetes in women with ICP (OR 2.8). Ray Alokanda et al²⁰ showed that 1/32 (3.13%) women with ICP had gestational diabetes while postpartum hemorrhage was seen, in 8/32 (25%) women.

Association between obstetric cholestasis and preeclampsia has been reported in a number of studies as well.^{12,21,22} Mei-Ting et al have reported 13.3%,²¹ Andrea Y. Lausman et al¹² 9.09%, Lo TK et al²² 25% cases of preeclampsia in obstetric cholestasis. While other epidemiological studies could not find any association between obstetric cholestasis and pre-eclampsia.^{23,24}

Obstetric cholestasis has a relatively rare occurrence. Therefore more studies with large sample size are needed to investigate the association of obstetric cholestasis with Gestational diabetes, hypertension and preeclampsia.

CONCLUSION

This study concludes that Gestational hypertension was the most common complication in patients presented with intrahepatic cholestasis of pregnancy, followed by pre-eclampsia.

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