

CHOLESTASIS OF PREGNANCY: A PROSPECTIVE STUDY AT SMS MEDICAL COLLEGE, JAIPUR RAJASTHAN

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Conflicts of Interest: Nil

ABSTRACT:

Background: Intrahepatic cholestasis of pregnancy (ICP) is a liver disease unique to pregnancy. It is characterised by pruritus associated with elevated serum bile acid and/or aminotransferase level with spontaneously relief of sign & symptom within 2-3 week of delivery.

Methods: Hospital based comparative analysis in pregnant women was conducted at Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur

Results: The peak value of serum bilirubin (total) ranged from 0.5-2.6 in group A and 0.40-0.80 in group B. The peak value of serum bilirubin (direct) ranged from 0.2-1.4 in group A and 0.10-0.30 in group B. The peak value of serum bilirubin (indirect) ranged from 0.2-1.2 in group A and 0.20-0.60 in group B. The peak value of SGOT ranged from 106-492 in group A and 16-28 in group B. The peak value of SGPT ranged from 112-461 in group A and 18-37 in group B. The peak value of ALP ranged from 368-1102 in group A and 68-280 in group B. The highest bilirubin level noted was 2.6 mg%. The p-value was statically significant (0.001).

Conclusion: LFT markers were significantly increased in ICP cases as compare to control group.

Key Words: Serum bilirubin, Alkaline phosphatase, Cholestasis

Introduction

During pregnancy, the human body undergoes several changes in the process of its adaptation to the growing fetus. Although these changes are physiological, there is potential for morbidity and mortality to both mother and fetus. Liver is the site of many important metabolic and synthetic functions of the body.

Intrahepatic cholestasis of pregnancy (ICP) is a liver disease unique to pregnancy. It is characterised by pruritus associated with elevated serum bile acid and/or aminotransferase level with spontaneously relief of sign & symptom with in 2-3 week of delivery.¹

The incidence of obstetric cholestasis varies and is dependent on geographic location and ethnicity. For example, the incidence is 4% in Chile; in the United Kingdom, it is 0.7%², but is higher in women of Indian and it is 1.2-1.5%.³ Obstetric cholestasis (OC) is more common in women with

pre-existing hepatitis C and gallstone disease; hence, the benefit of serum screening and liver ultrasound in all women diagnosed with the condition.⁴ Its incidence is also higher in women with multiple gestation pregnancies⁵ and in those who conceived using assisted reproduction.⁶

The hallmark symptom of obstetric cholestasis is pruritus in the absence of eruption. Most common site is on palms and soles. Itching ranges from mild to debilitating and intense and is typically worse at night. Excoriated lesions can become complicated by secondary infection. The onset of pruritus often precedes biochemical derangement. Symptoms relate to the effects of liver impairment. Bilirubin is elevated in approximately 10% of cases, and in this group, jaundice can be detected and symptoms suggestive of malabsorption of fats (e.g. steatorrhea) can occur.²

The purpose of the present study is increased the awareness and early identification of mother with obstetric cholestasis, their active management was

help reducing the fetal morbidity and mortality, as well as maternal morbidity

MATERIAL AND METHODS

Type of Study: Prospective study

Study Design: Hospital based comparative analysis in pregnant women.

Place of Study: Department of Obstetrics and Gynaecology, SMS Medical College, Jaipur

Duration of Study: April 2017 onwards for a period of one year or till desired sample size was reached for data collection and 2 month for statistical analysis.

Institutional review board and ethical committee clearance was taken.

Inclusion Criteria

For case group: (group A)

Singleton pregnancy in the age group of 20-30 year, after 28 weeks of gestation.

With history of pruritus without a rash.

Altered liver function tests (serum bilirubin:- 3-5 mg/dl, SGOT& SGPT:-Upper limit of normal value is 20% lower than that in non pregnant state, ALP:-Increase 2 to 3 fold in pregnancy).

Remissions of both following delivery.

Women giving informed & written consent.

For control group: (group B)

Singleton pregnancy in the age group of 20-30 year, after 28 weeks of gestation.

Without history of pruritus and rash.

Normal liver function tests.

Women giving informed & written consent.

Exclusion Criteria

Excluding liver diseases (hepatitis A , B , C or E , autoimmune hepatitis).

Dermatological conditions (eczema, scabies, pruritus eruption of pregnancy).

Urinary tract infection.

Sample Size : is calculated at 80% study power and alpha error of 0.05 expecting meconium stained amniotic fluid in 17.1% case of obstetric cholestasis group and 1.1% controlled group as per result of reference study (M Padmaja, Pal Bhaskar, Gupta Jayanta Kumar, Ramamurthy Seetha, Chaudhuri Mahasweta. A study of obstetric cholestasis. J Obstet Gynecol India vol.60, No. 3 : May-June 2010 pg. 225-331.)⁸

50 Patients in each group were required as sample size following above assumption which was increased to 55 patients in each group as final sample size for present study expecting 10% dropout / attrition.

Data collection

A detail history, physical & obstetrical examination was done.

Gestational age was determined by asking the women the date of last menstrual period, if reliable or from earliest ultrasonography.

Detail history of pruritus specifically regarding the site & severity according to prefixed score was taken.

Routine investigations– complete blood count, fasting blood sugar, ABORh, VDRL, HIV, HBsAg, urine complete microscopy, serum electrolytes, coagulation profile ,USG whole abdomen.

A liver function test was done weekly.

A liver function test was repeated after 2 week postpartum.

Statistical Analysis: Continuous variables was summarized as mean and standard deviation while nominal/ categorical variables as proportions (%).

Unpaired ‘t’ test was used for comparison of continuous variables where as chi-square test/fisher exact test for nominal/categorical variables.

P value <0.05 was taken as significant.

Medcalc 16.4 version software was used for all statistical calculations.

OBSERVATIONS

TABLE 1: DISTRIBUTION OF CASES ACCORDING TO AGE GROUP

Age group (years)	Group-A (n=50)		Group-B (n=50)		Total	
	No	%	No	%	No	%
21-25	33	66.00	33	66.00	66	66.00
26-30	17	34.00	17	34.00	34	34.00
Total	50	100.00	50	100.0	100	100.00
Mean	24.44±2.32		24.44±2.32			

p-value	0.833(NS)
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The age group of women in the present study varied between 21-30 years. The mean age of group A and group B were 24.44±2.32 and 24.44±2.32 respectively. which corresponds to the child bearing age of women.

The p-value was 0.833, which was not statically significant and both groups were comparable.

TABLE 2: DISTRIBUTION OF CASES ACCORDING TO SOCIOECONOMIC STATUS AS PER THE REVISED MODIFIED BG PRASAD SOCIOECONOMIC CLASSIFICATION SCALE 2016

Socioeconomic status	Group-A (n=50)		Group-B (n=50)		Total	
	No	%	No	%	No	%
Upper	3	6.00	2	4.00	5	5.00
Middle	30	60.00	35	70.00	65	65.00
Lower	17	34.00	13	26.00	30	30.00
Total	50	100.00	50	100.00	100	100.00

p-value	0.572
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According to socio-economic status , maximum number of women belonged to middle class followed by lower class on both group A and group B. The middle class women on group A and group B were 60% and 70% respectively. This could be due to free medical services provided by government hospital.

TABLE 3: DISTRIBUTION OF CASES ACCORDING TO GRAVIDITY

Parity	Group-A (n=50)		Group-B (n=50)		Total	
	No	%	No	No	%	No
Primigravida	28	56.00	31	62.00	59	59.00
Multigravida	22	44.00	19	38.00	41	41.00
Total	50	100.00	50	100.00	100	100.00

p-value	0.684
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In present study 56.00% women were primigravida in group A and 62.00% women were primigravida in group B. 44.00% women was multigravida in group A and 38.00% women were multigravida in group B. The parity wise difference in both groups were statically Insignificant.

TABLE 4: DISTRIBUTION OF CASES ACCORDING TO PREFIXED SCORE

Prefixed score	Group-A (n=50)		Group-B (n=50)		Total	
	No	%	No	No	%	No
0	0	0.00	50	50.00	50	50.00
1	17	34.00	0	0.00	17	17.00
2	31	62.00	0	0.00	31	31.00
3	2	4.00	0	0.00	2	2.00
Total	50	100.00	50	0.00	100	100.00

In present study 62.00% of women had prefixed score 2, where as 34.00% of women had prefixed score 1, only 4.00% of women had prefixed score 3 .

TABLE 5: DISTRIBUTION OF CASES BASED ON LIVER FUNCTION TEST

LFT	Group-A		Group-B		p-value
	Mean $\pm$ SD	Range	Mean $\pm$ SD	Range	
S.bilirubin (total) mg%	0.89 $\pm$ 0.49	0.5-2.6	0.55 $\pm$ 0.10	0.40-0.80	0.001
S.bilirubin (direct) mg%	0.34 $\pm$ 0.25	0.2-1.4	0.18 $\pm$ 0.05	0.10-0.30	0.001
S.bilirubin (indirect) mg%	0.55 $\pm$ 0.28	0.2-1.2	0.37 $\pm$ 0.11	0.20-0.60	0.001
SGOT (u/ml)	150.61 $\pm$ 69.74	106-492	22.92 $\pm$ 3.17	16.00-28.00	0.001
SGPT (u/ml)	170.72 $\pm$ 71.47	112-461	28.60 $\pm$ 5.20	18.00-37.00	0.001
ALP(u/l)	575.30 $\pm$ 194.98	368-1102	139.04 $\pm$ 55.65	68.00-280.00	0.001

In present study LFT markers were significantly increased in group A as compare to group B. The peak value of serum bilirubin (total) ranged from 0.5-2.6 in group A and 0.40-0.80 in group B. Mean $\pm$ SD was 0.89 $\pm$ 0.49 and 0.55 $\pm$ 0.10 in group A and group B respectively. The peak value of serum bilirubin (direct) ranged from 0.2-1.4 in group A and 0.10-0.30 in group B. Mean $\pm$ SD was 0.34 $\pm$ 0.25 in group A and 0.18 $\pm$ 0.05 in group B respectively. The peak value of serum bilirubin (indirect) ranged from 0.2-1.2 in group A and 0.20-0.60 in group B. Mean $\pm$ SD was 0.55 $\pm$ 0.28 in group A and 0.37 $\pm$ 0.11 in group B respectively.

The peak value of SGOT ranged from 106-492 in group A and 16-28 in group B. Mean $\pm$ SD was 150.61 $\pm$ 69.74 in group A and 22.92 $\pm$ 3.17 in group B respectively. The peak value of SGPT ranged from 112-461 in group A and 18-37 in group B.

Mean $\pm$ SD was 170.72 $\pm$ 71.47 in group A and 28.60 $\pm$ 5.20 in group B respectively. The peak value of ALP ranged from 368-1102 in group A and 68-280 in group B. Mean $\pm$ SD was 575.30 $\pm$ 194.98 in group A and 139.04 $\pm$ 55.65 in group B respectively. The highest bilirubin level noted was 2.6 mg%. The p-value was stastically significant (0.001).

DISCUSSION

Table 1- All the women admitted in both the groups was subdivided in 2 groups based on age. It was found that, in group A, 66% women were from 21-25 year age group, 34% were from 26-30 year age group, In group B ,66% and 34% respectively. Thus both the age group is similar with each other with respect to maternal age. Majority of women in each of the group fell into 21-25 year category (66% in both case and control group). In our study

maximum women were in the age of 21-25 yr and which coincides with the child bearing age. The age difference in both groups was statistically insignificant.

Similar to our study S.Kaur (2010)⁷ et al reported a mean age of 25.4 years in their study on ICP. The mean age of the women in a study by Lt Col G Singh (2007)⁸ et al was 25.8 years

In another similar study done by M.Rook (2009)⁹ et al mean age was 27.5 years. In a study done by Dang Arbinder (2010)¹⁰ et al mean age was 26.5 years. In another study by M Padmaja (2010)¹¹ et al mean age was 28.7 years.

Table 2- According to socio-economic status, maximum number of women belonged to middle class i.e. 60% and 70% in group A and group B respectively. The p value was not significant (0.572). The reason could be, this study was conducted in a government hospital which caters the middle class population and they are not much aware about this disease (ICP).

Nina Mishra (2017)¹² et al reported that in their study maximum number of cases were from lower middle class i.e. 70%

Table 3- In our study 56.00% women were primigravida in group A and 62.00% in group B. 44.00% women were multigravida in group A and 38.00% in group B. The p value was statistically not significant (0.684).

In our study, most of the cases were primigravida (56.00%) correlates well with the following studies:-

In another similarly study done by Garg Renu (2017)¹³ et al 32% were nulligravida, 44% were primigravida and 24% were multigravida. In a study conducted by Dr. Alakananda (2016)¹⁴ et al 62% were primigravida and 38% were multigravida.

Table 4- In present study 62.00% women were having prefixed score 2, 34.00% women were having prefixed score 1, 4.00% women were prefixed score 3 in cases and all women in group B were prefixed score 0.

Sita Pokhrel (2016)¹⁵ et al reported in their study that 75% women were having severe itching leading to disturbed sleep.

Table 5- In our study LFT markers were significantly increased in group A as compared to group B. The peak value of serum bilirubin (total) ranged from 0.5-2.6 in group A and 0.40-0.80 in group B. Mean $\pm$ SD was 0.89 ± 0.49 and 0.55 ± 0.10 in group A and group B respectively. The peak value of serum bilirubin (direct) ranged from 0.2-1.4 in group A and 0.10-0.30 in group B. Mean $\pm$ SD was 0.34 ± 0.25 in group A and 0.18 ± 0.05 in group B respectively. The peak value of serum bilirubin (indirect) ranged from 0.2-1.2 in group A and 0.20-0.60 in group B. Mean $\pm$ SD was 0.55 ± 0.28 in group A and 0.37 ± 0.11 in group B respectively.

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In a study done by M. Padmaja (2010)¹¹ et al Using pregnancy specific ranges for the LFTs it was found that the most frequent abnormality encountered in OC was elevated transaminases (97.8%) and GGT (42.9%). The peak value of alanine aminotransferase (ALT), aspartate aminotransferase (AST) in their study ranged from 37-631 U/L and 49-603 U/L respectively. The value of ALP in these women varied from normal to as high as 986 U/L. Mild hyperbilirubinemia was present in 18.4% of the women and the highest bilirubin level noted was 2.8 mg%

Dr. Alakananda (2016)¹⁴ et al reported in their study that Serum bile acids and Liver enzymes were raised in all cases (100%) while serum bilirubin was slightly raised in 94% of cases.

CONCLUSION

LFT markers were significantly increased in ICP cases as compared to control group.

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