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Original Research Article

Effect of Ursodeoxycholic Acid on Clinical and Biochemical Parameters in Obstetrics Cholestasis: A Prospective Study

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Conflict of interest: Nil

Abstract:

Background: Intrahepatic cholestasis of pregnancy is a disease of unknown cause, characterized by skin pruritus and abnormal liver function tests with a predominantly cholestatic pattern. This cholestasis appears during the second half of pregnancy in previously healthy women. Aims of this study to evaluate the effect of Ursodeoxycholic acid on biochemical markers, effect of Ursodeoxycholic acid on clinical parameters, effectiveness of Ursodeoxycholic acid in treatment of intrahepatic cholestatic of pregnancy and outcome of pregnancy after treatment with Ursodeoxycholic acid.

Methods: This is a hospital based prospective study of effect of UDCA on biochemical and clinical parameters in obstetrics cholestasis was conducted on 60 patients in 2nd and 3rd trimester with diagnosis of ICP in 910 bed tertiary hospital in Bokaro Steel City under Bokaro Steel Plant.

Results: 60 women with obstetrics cholestasis were included in this study according to their inclusion and exclusion criteria and were followed from the time of diagnosis of ICP till delivery. The mean age distribution among the patients was 29.27±3.23 year which was not significant. The mean gestational age among the patient was 31.88±1.91 week which was statistically significant. Mostly the patients delivered by normal vaginal delivery which was 81.67% and was statistically significant. The rate of delivery by LSCS was 18.63% in this study.

Conclusion: Overall in my study there was significant reduction in clinical after treatment with UDCA with good perinatal outcome.

Keywords: Intrahepatic cholestatic, UDCA, Pruritis, Biochemical parameters.

Introduction

Intrahepatic cholestasis of pregnancy is liver disorder characterised by severe pruritis with elevated bile acids [1] and liver enzymes [2] in previously healthy pregnant women. It occurs typically during the second or third trimester of pregnancy and symptoms relief spontaneously within 2 to 3 weeks after delivery [3]. The condition is very common in Chile and Bolivia (6%-27%), and in Sweden (1%-1.5%). The incidence of ICP is lower elsewhere in Europe (0.1%-1.5%) and the United States (0.7%). [4,5]

The most common symptom of ICP is pruritis which typically appears in the third trimester and starts in the palms and soles. It often becomes generalized. The pathophysiology of the pruritis is still unknown. Bile salts are thought to be deposited on nerve endings of the skin causing itching. The pruritis is typically most severe at night and can cause insomnia and considerable discomfort for the patients. Other causes of itching must be excluded (atopic eczema, allergic reactions, urticarial or gestational pemphigoid and virus infections). Clinical examination of the skin is normal except for evidence of scratching.

Intrahepatic cholestasis of pregnancy is a relatively benign condition for the mother, as it typically resolves rapidly after delivery [2]. ICP resolves after delivery but it has been associated with high incidence of fetal complications. It increases the risk of preterm delivery, meconium excretion,

respiratory distress syndrome and sudden intrauterine death [6].Glantz et al. (2004) reported a 1–2% increase in the risk of spontaneous preterm labour, asphyxial events or meconium staining of the amniotic fluid and/or placenta and membranes for every additional μmol/L of maternal serum bile acids5. The risk of spontaneous preterm labour is increased in ICP pregnancies (19–60%) [7]. Patient with ICP are considered as high risk patient and timing of delivery should be decided to decrease the risk of fetomaternal complication. Routinely induction of labour is recommended for women with ICP after delivery but often recur in subsequent pregnancies or with estrogen-containing contraceptives.

There are several treatments available to correct ICP including Phenobarbital, cholestyramine, S-Adenosyl-L-methionine, dexamethasone and ursodeoxycholic acid [5,8-10]. But UDCA is recommended as the first-line treatment for ICP in European guidelines [11,12].

Its use is associated with improvement of maternal symptoms, [13-16]as well as reduction of Bile Acid and transaminase.

Despite widespread uses of UDCA in treatment of ICP evidences are very less. Recently one meta-analysis found that UDCA was effective in reducing clinical symptoms and biochemical markers and also improvement in fetal outcome [15].

Contrary to that another systemic review of the effectiveness of UDCA for ICP conclude that it reduces clinical symptoms by small amount and definite improvement in perinatal outcome was absent [17]. So, my study aims to re-evaluate the effect of UDCA on clinical and biochemical parameters to avoid the adverse feto maternal outcome.

Aim and Objectives

1. To evaluate the effect of Ursodeoxycholic acid on biochemical markers.
2. To evaluate the effect of Ursodeoxycholic acid on clinical parameters.
3. To assess the effectiveness of Ursodeoxycholic acid in treatment of intrahepatic cholestatic of pregnancy.
4. To know the outcome of pregnancy after treatment with Ursodeoxycholic acid.

Material & Methods

This is a hospital based prospective study of effect of UDCA on biochemical and clinical parameters in obstetrics cholestasis was conducted on 60 patients in 2nd and 3rd trimester with diagnosis of ICP in 910 bed tertiary hospital in Bokaro Steel City under Bokaro Steel Plant.

All patients in 2nd and 3rd trimester coming with clinical suspicion of obstetrics cholestasis were evaluated. Then patient was followed up in subsequent antenatal period with treatment of UDCA till the termination of pregnancy.

The study of LB Manna et al observed that change in total BA after treatment was 1 with 95% CI of .6-1.6. Taking these values as reference, the minimum required sample size with 99% power of study and 1% level of significance was 37 patients. Taking lost to follow up and to reduce margin of error, total sample size taken was 60.

Formula used was:

Standard deviation from 95% CI of mean

SD= $\sqrt{N}$ × (Upper limit of CI – Lower limit of CI)/3.92

Where N was sample size

CI-confidence interval

For comparing mean of pre and post

$N>=(\text{standard deviation})^2/(\text{mean difference})^2 \times (Z\square + Z\square)^2$

Where $Z\square$ was value of Z at two sided alpha error of 1% and $Z\square$ was value of Z at power of 99% and mean difference was difference in mean values of pre and post.

Calculations:

Standard deviation

1. $SD_1=\sqrt{23}x\ (1.6-0.6)/3.92=1.2234$

2. $N>=(1.2234)^2 \times (2.58 + 2.33)^2$

$(1)^2>=36.08=37$(approx.)

Inclusion Criteria

- Age between 25-35 yr
- Patient in 2nd and 3rd trimester of pregnancy
- Patient with clinically suspected obstetrics cholestasis
- Patient with biochemically proven obstetrics cholestasis

Exclusion Criteria

- 1st trimester of pregnancy
- Icterus gravidarum
- Allergic condition
- Viral hepatitis
- Skin condition

Procedure

- All patients coming for routine antenatal checkup and suspicious for obstetric cholestasis was evaluated clinically and investigation like complete blood count, viral markers, uric acid, liver function test was done to rule out different causes.

- Biochemical markers including Bile Acid, SGOT, SGPT, ALP, Bilirubin level was measured in support in diagnosis of obstetrics cholestasis.

1. Bile acid should be ≥6 micromol/L[25]
2. SGPT>40 U/L[25]
3. SGOT> 35 U/L[25]
4. ALP may be elevated fourfold
5. Hyperbilirubinemia results, but total plasma concentration rarely exceeds 4 - 5 mg/dl

- Patients with increased biochemical markers and clinical symptoms of obstetrics cholestasis were treated with UDCA and dose was titrated according to severity.
- Biochemical markers and clinical evaluation was repeated after three weeks of treatment with UDCA.
- The Data was collected, and efficacy of UDCA was evaluated.
- Then biomchemical markers sensitivity and specificity was evaluated with help of tables.

Statistical Analysis

All the data was selected randomly and tabulated, and then analyzed with appropriate statistical tools "SPSS version 24".

Data was presented as mean with standard deviation or proportions as appropriate. Mean, median, standard deviation and variance was calculated and following statistical significance tests were applied.

1. Statistical analysis "Chi – square Test" was used for categorical data.
2. Gaussian single mean test was used for comparing continuous data of single mean.
3. Statistical analysis "|Z| – PROPORTION TEST" was used for comparison of proportion of categorical data.
4. Analysis of variance "ANOVA" was used for comparing more than three continuous data at a time.
5. Unpaired |t| - test also used for comparing two mean of continuous data.

Statistical methods were used to find the significance of homogeneity of study characteristics between the two groups of patients. Finally the calculated values were compared with the tabulated values at a particular degree of freedom and the level of significance was determined.

Their inference were as follows-

- $P > 0.05$ statistically insignificant
- $P < 0.05$ statistically significant
- $P < 0.01$ statistically highly significant
- $P < 0.001$ statistically very highly significant

Observation & Results

Table 1:Pruritis shown among the population

Pruritis	No. of patients (n=60)	Percentage	P Value	Results
1St visit with complain of Pruritis	44	73.33%	<0.0001	highly significant
After 1 week with UDCA	20	33.33%		
After 3rd week with UDCA	6	10%		

Pruritis among the 60 patients, at 1st visit 73.33% patients, after 1st visit 33.33% patients and 10% at 3rd week patients left. There were statistically highly significant difference shown among the patients according to their PRURITIS improvement at different point of time, with a p-value of {p<0.05} Using the "Chi- Square Test {$|\chi^2|$– Test}"

Table 2: Mean BILE ACID level shown among the population

Bile acid	Mean ± s.d	P Value	Results
At diagnosis	31.08 ± 24.43	<0.0001	highly significant
After 1 week with UDCA	17.23 ± 14.22		
After 3rd week with UDCA	12.97 ± 8.10		

Mean Bile acid decreased during treatment and the value is highly significant. There were statistically highly significant difference shown among the patients according to their mean Bile acid level improvement at different point of time, with a p-value of {p<0.0001} Using **the "Analysis of Variance (ANOVA)"**

Table 3: Mean ALT level shown among the population

Mean ALT	Mean ± s.d	P Value	Results
At diagnosis	102.58 ± 67.97	<0.0001	highly significant
After 1 week with UDCA	74.75 ± 48.07		
After 3rd week with UDCA	38.10 ± 12.63		

Mean ALT decreased during treatment and the value is highly significant. There were statistically highly significant difference shown among the patients according to their mean ALT level improvement at different point of time, with a p- value of {p<0.0001} Using the "Analysis of Variance (ANOVA)"

Table 4: Mean AST level shown among the population with UDCA

Mean AST	Mean ± s.d	P Value	Results
At diagnosis	102.25 ± 65.72	<0.0001	Highly significant
After 1 week with UDCA	68.48 ± 36.93		
After 3rd week with UDCA	38.95 ± 15.57		

Mean AST decreased during treatment and the value is highly significant. There were statistically highly significant difference shown among the patients according to their mean AST level improvement at different point of time, with a p- value of {p<0.0001} Using the "Analysis of Variance (ANOVA)"

Table 5: Mean ALP level shown among the population with UDCA

Mean ALP	Mean ± s.d	P Value	Results
At diagnosis	307.27 ± 42.98	0.1476	Not Significant
After 1 week with UDCA	295.62 ± 43.34		
After 3rd week with UDCA	296.08 ± 41.09		

Mean ALP decreased during treatment and the value is highly significant. There were statistically not significant difference shown among the patients according to their mean ALP level improvement at different point of time, with a p- value of {p>0.05}Using the "Analysis of Variance (ANOVA)"

Table 6: Comparison between Complain of PRURITIS with BILE ACID

Complain of Pruritis		Bile Acid (Mean ± s.d)	|t|	P value	Results
At diagnosis	Yes (n=44)	34.45 ± 27.38	1.806	0.0761	Not significant
	No (n=16)	21.81 ± 8.59			
After 1 week with UDCA	Yes (n=20)	29.05 ± 19.45	5.538	<0.0001	Significant
	No (n=40)	11.48 ± 3.91			
After 3 week with UDCA	Yes (n=6)	20.67 ± 8.48	4.231	<0.0001	Significant
	No (n=54)	11.67 ± 7.00			

There were statistically highly significant difference shown among the patients according to their mean Comparison between Complain of PRURITIS with BILE ACID, with P-value of {p<0.0001}Using the "Unpaired |t|-test"

Table 7: Comparison between Complain of PRURITIS with ALT

Complain of Pruritis		ALT (Mean ± s.d)	|t|	P value	Results
At diagnosis	Yes (n=44)	108.38 ± 71.03	1.098	0.2768	Not significant
	No (n=16)	86.63 ± 57.81			
After 1 week with UDCA	Yes (n=20)	104.63 ± 46.12	6.848	<0.0001	Significant
	No (n=40)	51.73 ± 12.12			
After 3 week with UDCA	Yes (n=6)	58.67 ± 25.10	4.536	<0.0001	Significant
	No (n=54)	36.33 ± 9.16			

There were statistically highly significant difference shown among the patients according to their mean Comparison between Complain of PRURITIS with ALT, with P -value of {p<0.0001} Using the "Unpaired |t|- test"

Table 8: Comparison between Complain of PRURITIS with AST

Complain of Pruritis		AST (Mean ± s.d)	|t|	P value	Results
At diagnosis	Yes (n=44)	111.11 ± 72.37	1.763	0.0832	Not significant
	No (n=16)	77.87 ± 33.35			
After 1 week with UDCA	Yes (n=20)	102.20 ± 46.18	6.370	<0.0001	Significant
	No (n=40)	51.62 ± 14.54			
After 3 week with UDCA	Yes (n=6)	70 ± 20.98	6.879	<0.0001	Significant
	No (n=54)	35.50 ± 10.35			

There were statistically highly significant difference shown among the patients according to their mean Comparison between Complain of PRURITIS with AST, with P -value of {p<0.0001} Using the "Unpaired |t|- test"

Table 9: Comparison between Complain of Pruritis with ALP

Complain of Pruritis		ALP (Mean ± s.d)	|t|	P value	Results
At diagnosis	Yes (n=44)	314.59 ± 40.30	2.264	0.0273	Significant
	No (n=16)	287.13 ± 44.93			
After 1 week with UDCA	Yes (n=20)	315.53 ± 36.88	3.462	0.001	Significant
	No (n=40)	277.34 ± 41.13			
After 3 week with UDCA	Yes (n=6)	360 ± 12.65	4.572	<0.0001	Significant
	No (n=54)	290.09 ± 36.97			

There were statistically highly significant difference shown among the patients according to their mean Compar-

ison between Complain of PRURITIS with ALP, with P-value of {p<0.0001} Using the "Unpaired |t|- test"

Table 10: Comparison between Bilirubin with different point of time

Bilirubin	Normal		Abnormal		P Value	Results
	No.	%	No.	%		
At diagnosis	53	88.33%	7	11.67%		
After 1 week with UDCA	57	95%	3	5%		
After 3rd week with UDCA	59	98.33%	1	1.67%	0.0388	Significant

Bilirubin was significantly decreased during different period of medication. With a p-value of {p<0.05}. Using the "Chi- Square Test {$|\chi^2|$– Test}"

Table 11: Age distribution among the patients

Age (in year)	No. of patients (n=60)	Percentage	P Value	Results
25 – 27 year	15	25%	0.7051	Not Significant
27 – 29 year	14	23.33%		
29 – 31 year	10	16.67%		
31 – 33 year	9	15%		
33 – 35 year	12	20%		
Mean ± s.d	29.27 ± 3.23 year			

Out of total 60 patients25% (n=15) were 25 - 27 years, 23.33% (n=14) were 27– 29 years, 16.67% (n=10) were 29 – 31 years, 15% (n=9) were33 – 35 year women respectively enrolled in study. There were statistically no significant difference in age (in year) distribution among the population, with a p-value of {p>0.05} Using the "Gaussian single mean test"

Table 12: Gestation Age distribution among the patients

GA (in week)	No. of patients (n=60)	Percentage	P Value	Results
28 – 29 week	7	11.67%	<0.0001	Highly significant
30 – 31week	14	23.33%		
32 – 33 week	30	50%		
34 – 35 week	9	15%		
Mean ± s.d	31.88 ± 1.91 week			

Gestational age of total 60 patients were 11.67% (n=7) in 28 – 29 week, 23.33% (n=14) in 30 – 31week, 50% (n=30) in 32 – 33 week and 15% (n=9) in 34 –35 week receptively. There were statistically significant differences in gestational age among the population, with a p-value of {p< 0.0001}. Majority of patients lie in gestational age group 30 to 33 weeks. Using the "Gaussian single mean test"

Table 13: Gravida among the patients

Gravida	No. of patients (n=60)	Percentage	P Value	Results
G1	28	46.67%	0.0863	Not significant
G2	15	25%		
G3	17	28.33%		

Gravida among the 60 patients were 46.67% (n=28) in G1, 25% (n=15) in G2, 28.33% (n=17) in G3 Receptively. There were statistically no significant difference in gravida among the patients, with a p-value of {p>0.05} Using the "Chi- Square Test {$|\chi^2|$– Test}"

Table 14: Mode of delivery among the population with UDCA

Mode of delivery	No. of patients (n=60)	Percentage	P Value	Results
NVD	49	81.67%	<0.0001	Significant
LSCS	11	18.33%		

Mode of delivery among the 60 patients were 81.67% (n=49) patients had NVD and 18.33% (n=11) patients had LSCS respectively. There were statistically significant difference among the patients according to their Mode of delivery among the population, with a p-value of {p<0.0001}. Using the "Chi- Square PROPORTION Test {$|\chi^2|$– Test}"

Table 15: Type of delivery among the population with UDCA

Type of delivery	No. of patients (n=60)	Percentage	P Value	Results
≥38 weeks	49	81.67%	<0.0001	Significant
< 38 weeks	11	18.33%		

Type of delivery among the 60 patients were 81.67% (n=49) patients had ≥38 weeks and 18.33% (n=11) patients had <38 weeks respectively. There were statistically significant difference among the patients according to their type of delivery among the population, with a p-value of {p<0.0001} Using the "Chi- Square PROPORTION Test {$|\chi^2|$– Test}"

Table 16: Meconium-stained amniotic fluid with UDCA

MSF	No. of patients (n=60)	Percentage	P Value	Results
Yes	16	26.67%		
No	44	73.33%	0.0003	Significant

26.67% (n=16) patients were Meconium-stained amniotic fluid among the 60 patients. There were statistically significant difference among the patients according to their MSF among the population, with a p-value of {p<0.001} Using the "Chi- Square PROPORTION Test {|χ^2|– Test}"

Table 17: Apgar score among the neonates with UDCA

APGAR Score	No. of patients (n=60)	Percentage	P Value	Results
<7	14	23.33%		
≥ 7	46	76.67%	<0.0001	Significant

APGAR Score among the 60 neonates were 23.33% (n=14) neonates had <7 and76.67% (n=46) neonates had ≥ 7 Apgar score respectively. There were statistically significant difference among the patients according to their Apgar score among the neonates, with a p-value of {p<0.0001} Using the "Chi- Square PROPORTION Test {|χ^2|– Test}"

Table 18: Birth weight among the neonates with UDCA

Birth weight	No. of patients (n=60)	Percentage	P Value	Results
≤ 2.7 kg	31	51.67%		
>2.7 kg	29	48.33%		Not Significant
Mean ± SD	2.72 ± 0.23		0.7963	

Birth weight among the 60 neonates were 51.67% (n=31) were ≤ 2.7 kg neonates and 48.33% (n=29) were >2.7 kg neonates respectively.

There were statistically no significant difference among the neonates according to their birth weight, with a p-value of {p>0.05}. Mean birth weight among the neonates was 2.72 ± 0.23 kg respectively. Using the "Gaussian single mean test"

Discussion

ICP is the most common liver disease during pregnancy. It is characterized by unexplained pruritus usually in the late second and third trimester of pregnancy and elevated BA and/or transaminases. It is a relatively nonthreatening condition to the mother, but it is associated with several fetal complications: higher risk for preterm delivery, MSAF, fetal distress and even IUFD (Brouwers et al 2015) [20]. It is also known to recur in subsequent pregnancies. The diagnosis of ICP is based strongly on the clinical symptom of pruritus mainly in the palms and soles and on elevated serum ALT values and/or BA concentrations. There may be several pathogenic entities behind these clinical and laboratory markers. Pruritus during pregnancy is quite common and should be distinguishable from ICP. Therefore; better specific and sensitive markers to diagnose true ICP are needed.

Currently, the best treatment for ICP is UDCA. A recent meta-analysis reported that UDCA is effective in normalizing maternal serum ALT levels compared to controls and placebo (27.8% vs 9.4% and vs 14.3%) and at reducing ALT levels (65.9% vs 25.4%, and vs 20.0%) (Bacq et al. 2012) [15]. According to the same metaanalysis, serum TBA concentrations are reduced better by UDCA (in 54.3% of patients) than by no drugs (24.4%) and placebo (18.6%) (Bacq et al. 2012) [15]. Also the severity of pruritus was reduced statistically significantly better with UDCA than with placebo or no drugs (Bacq et al. 2012) [15]. The effect of UDCA on liver function was evaluated with repeated and extended laboratory testing. Alkaline phosphatase may be elevated in ICP, but it does not have a diagnostic value since alkaline phosphatase activity is enhanced due to placental and bone production during uncomplicated pregnancies.

Treatment with UDCA reduces the levels of BA in the maternal and fetal compartments (Geenes et al. 2014) [19] and there is no significant fetal metabolism of the increased exposure of BA of maternal origin in obstetric cholestasis (Geenes et al. 2014) [19]. The dose of UDCA has varied between different randomized controlled trials. In most trials, the dose of UDCA has been between 600 and 900 mg/d (Diaferia et al. 1996 [22]; Roncaglia et al. 2004 [10]; Binder et al. 2006 [24]). In the studies of Palma et al. (1997) [13] and Glantz et al. (2005) [21] the UDCA dose was quite high, 1000 mg/d (Palma et al. 1997 [13]; Glantz et al. 2005 [21]). Floreani et al. (1996) [23] and associates used the same dosing as we did, 450 mg/d (Floreani et al. 199623).

According to our results low-dose UDCA treatment was effective in ICP patients. The perinatal outcome was good, liver enzyme levels decreased during treatment and maternal side-effects were minimal. Also Bacq et al. concluded in their meta-analysis that UDCA therapy might benefit fetal outcomes (Bacq et al. 2012) [15]. It might reduce fetal distress, and the need for NICU treatment might decrease.

Table19: Pruritis shown among the population

	Pruritis after treatment with UDCA
PresentStudy	**Decrease**
Glantz et al.(2004) [5]	Decrease
Diaferia et al. (1996) [22]	Decrease
Becq et al.(2012) [15]	Decrease
Palma et al.(1997)[13]	Decrease
Gurung et al.(2013) [17]	Decrease

My study goes parallel with the previous studies stated above. There is significant decrease in the pruritis after 3 week treatment with UDCA. The severity of pruritus was reduced statistically significantly better with UDCA than with placebo or no drugs (Bacq et al. 2012)15.

Table20: Mean BILEACID level shown among the population

	Bile acid after treatment with UDCA
Present Study	**Decrease**
Grand' Maison et al.(2014) [25]	Decrease
Mazzella et al. (2001) [28]	Decrease
Bacq et al.(2012) [15]	Decrease

Here present study shows decrease in bile acid after 3 week treatment with UDCA from the time of diagnosis which is similar to the studies mentioned above and the decrease is significant. According to the same meta-analysis, serum TBA concentrations are reduced better by UDCA (in 54.3% of patients) than by no drugs (24.4%) and placebo (18.6%) (Bacq et al. 2012) [15].

Table 21: Mean ALT level shown among the population

	ALT after treatment with UDCA
Present Study	**Decrease**
Bacq et al.(2012) [15]	Decrease
Glantz et al(2004) [5]	Decrease
Diaferia et al. (1996) [22]	Decrease
Palmaet.al. (1997) [13]	Decrease
Grand' Masion et al(2014) [25]	Decrease

My study shows significant decrease in ALT levels after treatment with UDCA after 3 weeks from the time of diagnosis of ICP which is similar with the studies mentioned above. A recent meta-analysis reported that UDCA is effective in normalizing maternal serum ALT levels compared to controls and placebo (27.8% vs 9.4% and vs 14.3%) and at reducing ALT levels (65.9% vs 25.4%, and vs 20.0%) (Bacq et al. 2012) [15].

Table 22: Mean AST level shown among the population with UDCA

Mean AST	**Mean ± SD**	**P Value**	**Results**
At diagnosis	102.25 ± 65.72	<0.0001	highly significant
After 1 week with UDCA	68.48 ± 36.93		
After 3rd week with UDCA	38.95 ± 15.57		

My study showed significant decrease in mean AST after 3 week treatment with UDCA from the time of diagnosis of ICP. In recent meta-analysis UDCA was also effective in reducing pruritus and improving liver test results in patients with ICP (Bacq et al 2012) [15].

Table 23: Mean ALP level shown among the population with UDCA

Mean ALP	**Mean ± SD**	**P Value**	**Results**
At diagnosis	307.27 ± 42.98	0.1476	Not Significant
After 1 week with UDCA	295.62 ± 43.34		
After 3rd week with UDCA	296.08 ± 41.09		

Alkaline phosphatase may be elevated in ICP, but it does not have a diagnostic value since alkaline phosphatase activity is enhanced due to placental and bone production during uncomplicated pregnancies.

Table 24: Age distribution among the patients

	Maternal Age in years Mean ± SD	**P value**	**Results**
Present Study	**29.27 ± 3.23year**	**0.7051**	**Not significant**
Joutsiniemi T et al(2015) [3]	29.9		Not significant
Antonin Parizek et al[27]	31.9± 4.6		Not Significant
Joutsiniemi T et al(2016)[28]	29.9		Not Significant

The present study was not significant for age distribution among patients which was consistent with the previous above mentioned studies.

Table 25: Gestation Age distribution among the patients

	Gestational Age in week (Mean ±SD)	P value	Results
Present Study	**31.88 ±1.91week**	**<0.0001**	**Highly Significant**
Antonin Parizek et al [26]		<0.0001	Highly Significant
Joutsiniemi T et al (2015) [3]	33.3	<0.05	Significant

My study showed significant correlation for the gestational age distribution among the patients which was similar with the above mentioned studies. In my study, perinatal outcome was good and there were no perinatal deaths at all.

Only 26.67 % patients had meconium stained amoniotic fluid fetus and rest 73.33% patients had clear liquor.

Most of the newborn had APGAR score >= 7 and good birth weight more than 2.7 kg. About 81.67% patients had Normal vaginal delivery and mostly delivered after 38 weeks.

Conclusion

1. Ursodeoxycholic acid reduces maternal pruritis.
2. Ursodeoxycholic acid also reduces bile acid and improves other biochemical markers.
3. The side effects of Ursodeoxycholic acid for the mother are minimal.
4. The obstetric outcome is favourable with Ursodeoxycholic acid treatment resulting in more term deliveries, more normal vaginal deliveries, neonate with good apgar score and good birth weight.

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