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A COMPARATIVE STUDY OF LIVER ENZYMES IN ANTENATAL WOMEN WITH AND WITHOUT PROGESTERONE SUPPLEMENTS

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ABSTRACT **Background:** Progesterone has a vital role in pregnancy, therefore its use in pregnancy has highly increased in an attempt to treat miscarriage or preterm labor. The aim of this study is to know the effect of various form of progesterone and its duration of therapy on liver enzymes and compare liver enzymes in antenatal women.

Methodology: Blood samples were collected from 104 cases with progesterone support and 104 pregnant women without it as control attending antenatal OPD and IPD. Liver function test was done and results were compared.

Results: In our study, 26.92% had elevated liver enzymes in the control group and 42.30% in the study group with p value 0.01 which was significant. The change in AST was found significant with mean of 46.98±24.704 U/L in cases in compare to control with mean of 41.72±15.95 U/L and p value of 0.04. Out of 4 weeks' duration group, AST(U/L) and ALT(U/L) were raised with mean AST of 39.05 ±18.31 and ALT of 37.47±22.52 with p value =0.001 in both AST and ALT. Out of 8 weeks' duration group, both AST (mean 58.08±25.36) and ALT (57.84±26.26) were raised with p value of 0.009 and 0.008 respectively. In 12 weeks' group, only AST(U/L) (mean 57.42±32.24) was significant with p value 0.04. The change in AST, ALT and ALKP were highest (13.46%) when progesterone was taken in combination form (oral and I.M) with p value 0.001. Most of them took natural micronized progesterone (56.73%). Most common route of administration was oral (67.30%). Majority of them were given progesterone with no definite indication (35.57%).

Conclusion: Taking progesterone during pregnancy has an effect on liver enzymes especially on AST more so if taken for longer duration and in combination with different forms together, therefore should be used Judiciously.

KEYWORDS : Pregnancy, Progesterone, LFT, Liver enzymes,

INTRODUCTION

After the discovery of progesterone and its vital role in pregnancy, the use of progesterone has highly increased. It is used in threatened abortion, luteal phase defect, bad obstetric history, during and post IVF. It also comes in different forms like oral, injectable, and suppositories.

With use of progesterone, there are changes in liver enzymes. Though minute, these changes are observed especially in third trimester. Therefore, a study was done to know the effect of progesterone on liver function in pregnancy in a tertiary care center in Assam with the following objectives:

- To analyze and compare LFT in antenatal women receiving progesterone support and without it.
- To compare the effect of different forms of progesterone on LFT in antenatal women.
- To compare liver enzymes in antenatal women on progesterone supplementation according to the duration of use.

METHODS

Time bound hospital based prospective study case control study was conducted in a tertiary care center in Assam from July 2019 to June 2020. A total of 104 cases with progesterone supplements in different forms and 104 controls without progesterone in between 18-35 years were taken attending ANOPD and IPD for this study.

Subjects who were willing to participate were recruited into the study with informed and valid consent after fulfilling inclusion and exclusion criteria.

INCLUSION CRITERIA

1. CONTROL GROUP: All pregnant female with single intrauterine pregnancy without progesterone support.
2. STUDY GROUP: All pregnant female with single intrauterine pregnancy with progesterone support.
3. Duration of intake of progesterone for minimum of 4 weeks.
4. Age group of 18-35years.
5. All trimesters of gestation.

EXCLUSION CRITERIA

1. Multi fetal pregnancy.
2. Recent OCP users.
3. Known case of liver disease, gall bladder disease, hepatitis, liver cancer.
4. Recent history of jaundice.
5. Patient on any hepatotoxic drugs, alcohol.
6. Non co-operative patients.
7. Pregnant women with gestational hypertension or gestational diabetes mellitus.

Five milliliter amount of blood was drawn from antecubital vein with a sterile syringe after cleaning the area with an alcohol pad. It was transferred to a red capped plain vacu container and sent to laboratory for test was done in biochemistry department. The sample was centrifuged at 3000 rpm for 10 minutes and serum was separated and stored at -20c until analyzed. Estimation was done by using a fully automated biochemical analyzer (VITROS 5600) of Ortho Clinical Diagnostics.

RESULTS

Table 1: Distribution According To Indication Of Use Of Progesterone In Cases (n=104)

INDICATION	NUMBERS	PERCENTAGE
Recurrent pregnancy loss	10	9.61%
Threatened abortion	22	21.15%
History of preterm birth	5	4.80%
Ovulation induction and luteal support	7	6.73%
Post circlage	5	4.80%
Bad obstetric history	12	11.53%
IVF	6	5.76%
No definite indication/normal	37	35.57%

The majority of indication of use of progesterone was of no definite indication in 37 cases (35.57%) which means it was prescribed empirically, 22 cases were given progesterone for threatened abortion (21.15%), 12 cases were given progesterone for bad obstetric history (11.53%), 10 cases for recurrent pregnancy loss (9.61%), 7 cases for history of ovulation induction and luteal support (6.73%), 6 cases for post IVF (5.76%), and 5 cases were given progesterone with history of preterm labor (4.80%).

Table 2: Distribution Of Cases According To Types Of Progesterone Used (n=104)

TYPES OF PROGESTERONE	NUMBERS	PERCENTAGE
NATURAL MICRONISED PROGESTERONE + HYDROXYPROGESTERONE CAPROATE	14	13.46%
NATURAL MICRONISED PROGESTERONE	59	56.73%
HYDROXYPROGESTRONE CAPROATE	18	17.30%
DYDROGESTERONE	13	12.5%

In our study, 59 cases used natural micronized progesterone (56.73%),18 cases used hydroxy progesterone caproate (17.30%), 14 cases used both hydroxy progesterone and natural micronized progesterone (13.46%) and 13 cases had dydrogesterone (12.5%).

Table 3: Comparision Of Liver Enzymes In Case And Control Group

CASES(n=104)			CONTROL(n=104)			P value
LIVER ENZYMES	NUMBERS	%	LIVER ENZYMES	NUMBERS	%	0.01
NORMAL RANGE	60	57.69 %	NORMAL RANGE	76	73.07%	
ELEVATED	44	42 .30%	ELEVATED	28	26.92%	
TOTAL	104	100 %	TOTAL	104	100%	

Out of 104 cases, 44 (42.30%) had elevation in liver enzymes and out of 104 control, only 28 (26.92%) had elevation in liver enzymes which was found to be significant with p value =0.01.

Table 4: Comparison Of Liver Enzymes In Cases (n=104) And Control (n=104)

LFT		Mean ±SD	P value
AST(U/L)	Case	46.98±24.704	0.04 (S)
	Control	41.72±15.95	
ALT(U/L)	Case	41.72±15.95	0.23
	Control	37.91±18.14	
ALKP(U/L)	Case	119.68±42.96	0.39
	Control	111.18±30.31	
GGT(U/L)	Case	28.45±7.92	0.38
	Control	26.86±8.103	
Total bilirubin(mg/dl)	Case	.71±0.29	0.88
	Control	.62±0.31	

The change in AST was found significant with mean of 46.98±24.704 U/L in cases in comparison to control with mean of 41.72±15.95 U/L and p value of 0.04. There were no significant changes in ALT, ALKP, GGT and T/bilirubin.

Table 5: Showing Variation In Liver Enzymes With Time Interval Of Use Of Progesterone In Cases (n=104)

LFT	Duration	Mean ±SD	P value
AST(U/L)	4 weeks	39.05±18.31	0.001 (S)
	8 weeks	58.08±25.36	
	12 weeks	57.42±32.24	
ALT(U/L)	4 weeks	37.47±22.52	0.004 (S)
	8 weeks	57.84±26.26	
	12 weeks	51.89±37.22	
ALKP(U/L)	4 weeks	114.52±43.28	0.36
	8 weeks	126.28±43.65	
	12 weeks	127.32±40.84	
GGT(U/L)	4 weeks	28.67±8.09	0.66
	8 weeks	29.04±8.16	
	12 weeks	27.00±7.28	
Total bilirubin(mg/dl)	4 weeks	.704±0.31	0.87
	8 weeks	.739±0.29	
	12 weeks	.703±0.23	

The changes in AST and ALT were found highly significant as p value were 0.001 and 0.004 respectively after 8 and 12 weeks of use of progesterone.

Table 6: Comparision Of Lft Among The Cases On Both Oral Micronised Progesterone And Hydroxy Progesterone Caproate (n=14) Vs Control (n=104)

LFT		Mean ±SD	P value
AST(U/L)	Case	76.86±29.91	0.001 (S)
	Control	41.72±15.95	
ALT(U/L)	Case	65.50±40.19	0.001 (S)
	Control	37.91±18.14	
ALKP(U/L)	Case	167.57±41.32	0.001 (S)
	Control	111.18±30.31	
GGT(U/L)	Case	28.71±6.85	0.41
	Control	26.86±8.103	
Total bilirubin (mg/dl)	Case	.71±0.25	0.35
	Control	.62±0.31	

The changes in the AST, ALT, and ALKP of patients on both oral micronized progesterone and hydroxy progesterone caproate when compare with the control group were significant. AST mean 76.86±29.91 (U/L) VS 41.72±15.95 (U/L) (p value=0.001), ALT mean 65.50±40.19 (U/L) VS 37.91±18.14 (U/L) (p value=0.001). There were no significant changes in GGT and T/bilirubin levels.

The mean age in case was 24.24±4.104 years and 23.38±3.473 years in control group. Majority of patients had vaginal delivery with 76.9% in cases and 82.7% in control.

DISCUSSION

In the present study, patients mean age were 24.24±4.104 years in cases and 23.38±3.473 years in control group which is comparable to the study by Y. Bacq, T. Sapey, M. Chot et al [1] where the mean age was 29±5 years both in cases and control group. The study includes 2.88% of cases taking progesterone vaginally which was nearly similar to study done by Farago, Naama, et al [2] .17.30% of cases took intramuscular progesterone where as in a study by by Tsur, Abraham, et al. [3]3.8% of cases took I.M progesterone.

Majority of the cases had raised AST and ALT with 27.88% where as Jl, Benifla et al [4] found 3.4% raised in AST and 5.6% in ALT. The minimum duration of use of progesterone is 4 weeks, similarly, Farago, Naama, et al [2] gave progesterone for 4 weeks.

Pruritus was recorded only in 1 case similar to Y. Bacq, T. Sapey, M. Chot et al [1] which also had only 1 case. The perinatal mortality was 0% where as a study by Maher, Mohammad Ahmed, et al [5] found 2.4% in the vaginal progesterone group.

CONCLUSION

From this study we came to the conclusion that AST was mostly affected than ALT or ALKP and Total bilirubin following progesterone intake. The effect on GGT was insignificant. The changes in liver enzymes were related to duration of use of progesterone. The longer it was used, the more was the value of liver enzymes. So the use may be limited to a certain duration for optimal effect and safety. The use of oral micronized progesterone, dydrogesterone and hydroxy progesterone caproate are safe as compared to control but combination of micronized progesterone with hydroxy progesterone caproate had the highest increase in liver enzymes. Mode of delivery, NICU admission and indication for LSCS was not related to use of progesterone.

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