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ORIGINAL ARTICLE

CROSS-SECTIONAL STUDY OF LIVER FUNCTION IN PREGNANT WOMEN AND MATCHED CONTROLS IN A POPULATION WITH CASSAVA AS STAPLE FOOD

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ABSTRACT: BACKGROUND: Pregnancy is a physiological state in women where the liver is highly stressed due to various changes in the body metabolism. The additional stress on the pregnant women's liver in a population with cassava or tapioca as staple food. **METHODS:** A cross-sectional study was conducted in the obstetrics outpatient department of a tertiary care hospital of central Kerala with objective to assess the liver function in pregnant women and matched controls in a population with tapioca as staple food. The liver function is tested by a panel on seven biochemical tests namely bilirubin (total, direct and indirect), total protein, serum albumin, serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT) on the same sample of blood. Collected data was entered in Microsoft excel and analyzed by SPSS version 14. 0. The descriptive of the parameters were mean and standard deviation (SD). The difference between non-pregnant and pregnant first, second and third trimesters were studied by analysis of variance (ANOVA). Non pregnant and each trimester were tested by unpaired t test. **RESULTS:** The mean values of all the parameters are comparable in non-pregnant and first trimester. The mean values were lower in second and third trimesters. There was significant difference between the mean values of all the parameters between the four groups (p less than 0.05) except for SGOT. There was no significant difference between non-pregnant and first trimester except for serum albumin. There was significant difference between non-pregnant and second trimester except for total protein. Similarly there was significant difference between non-pregnant and third trimester except for SGOT.
KEYWORDS: Cassava, liver function tests, pregnant women.

INTRODUCTION: In India, Kerala[1] accounts for 50% of cassava grown. In other states it is used to make industrial starch. It is one of the staple foods in Kerala. Liver is the master organ in pregnancy. During this period the food taken by the mother[2] is digested, absorbed and metabolized by the mother's liver. The essential nutrients in the mother's bloodstream enter the fetal blood and it is metabolized by the baby's liver.

The maternal liver alone plays an important role in detoxifying drugs, toxins and steroid hormones because the fetal liver is immature. During a normal pregnancy various physiological changes[3] occur like hemodilution, increase in basic metabolic rate (BMR) by 15% and many endocrine changes.

These changes cause great stress to the maternal liver. Features of liver failure [4] like vascular spiders, palmar erythema and oesophageal varices are commonly seen in pregnant women. These are caused by the high levels of the steroid hormone oestrogen seen in normal pregnancies and in liver failure patients. The steroid hormones from both the mother and fetus are degraded in the maternal liver by the liver enzymes cytochrome P450.[5]

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The steroid hormones degraded in the liver include aldosterone, oestrogen, progesterone and testosterone. Hormone metabolism[6] also includes inactivation of other hormones like insulin, glucagon, vasopressin and erythropoietin. In a population with cassava as a staple diet, there is more stress on the liver during a normal pregnancy. The hydrogen cyanide[7] formed from the cassava toxins by the normal gut micro flora enter the bloodstream. It is taken up by the liver. The liver enzyme rhodanese or thiosulfate: cyanide sulfur transferase, in the presence of sculpture containing amino acids convert hydrogen cyanide to thiocyanate.

The thiocyanate formed in the body is water soluble and so excreted by the kidneys within twenty four hours. Various enzymes[8] such as alkaline phosphatase, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), serum isocitrate dehydrogenase, etc. are produced mostly by the liver. During a normal pregnancy alkaline phosphatase[9] is also produced by the placenta. This causes elevated levels in alkaline phosphatase unreliable in pregnant women. Hence a cross-sectional study is planned to assess the liver function of pregnant women in the tertiary care teaching hospital of Kerala where cassava or tapioca is a staple food.

MATERIALS AND METHODS: After obtaining ethical clearance from the institutional ethics committee, the study was conducted in the out-patient department of obstetrics. Informed consent was taken from the study subjects and blood was drawn under aseptic precautions with disposable syringe and needle. It is sent to the biochemistry laboratory[10] to estimate the liver function tests.

The tests performed in this study[11] are serum total bilirubin, direct bilirubin and indirect bilirubin levels using the diazo method of Pearlman and Zee, serum total protein using Biurett reagent, serum albumin using bromo coresol green (BCG) method, serum glutamate pyruvate transaminase (SGPT) was analyzed using autozyme glutamate pyruvate transaminase and serum glutamate oxaloacetate transaminase (SGOT) was analyzed using autozyme glutamate oxaloacetate transaminase.

All readings were taken using the clinical chemistry analyzer ERBA (XL – 300). This is a fully automated computerized analyzer. Pregnant subjects were ninety in number and they were matched with ninety non-pregnant subjects. Apparently healthy women within the reproductive age group 18–45 years were included in this study. Subjects with history of drug intake[12] which affect the liver function example oral contraceptives, acetaminophen, erythromycin, tetracycline, rifampicin, barbiturates, etc. were excluded.

RESULTS: The data obtained was entered into Microsoft Excel. The data was analyzed with the help of Statistical Package for Social Sciences (SPSS) windows version 14. The results obtained were expressed as mean $\pm$ standard deviation. The mean difference between the groups was analyzed using Analysis of Variation (ANOVA) and unpaired t test.

SL. NO	Parameters	Non-Pregnant		First Trimester		Second Trimester		Third Trimester	
		MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD
1.	Total Bilirubin	0.523	0.205	0.553	0.234	0.353	0.185	0.393	0.155
2.	Direct Bilirubin	0.294	0.115	0.305	0.123	0.202	0.109	0.213	0.02
3.	Indirect Bilirubin	0.230	0.101	0.248	0.119	0.152	0.0008	0.180	0.005
4.	Total Protein	6.956	0.665	6.960	0.388	6.813	0.441	6.537	0.361

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5.	Serum Albumin	4.864	0.360	4.073	0.328	3.937	0.175	3.760	0.292
6.	SGOT	30.12	8.20	28.17	9.78	27.03	4.82	28.67	4.36
7.	SGPT	25.06	9.48	23.5	13.89	20.30	8.32	20.60	6.58

TABLE 1: Mean Values & STANDARD DEVIATION (SD)

SL. NO	PARAMETERS	F VALUE	P VALUE
1.	Total Bilirubin	8.651	0.0001
2.	Direct Bilirubin	8.900	0.0001
3.	Indirect Bilirubin	6.988	0.0001
4.	Total Protein	4.777	0.003
5.	Serum Albumin	5.327	0.002
6.	SGOT	1.488	0.219
7.	SGPT	2.670	0.040

TABLE 2: Differences in Mean Values of Parameters (ANOVA)

A 'p' Value of ≤ 0.05 is significant in ANOVA.

SL. NO	PARAMETERS	NON PREGNANT & FIRST TRIMESTER	NON PREGNANT & SECOND TRIMESTER	NON PREGNANT & THIRD TRIMESTER
1.	Total Bilirubin	P VALUES	P VALUES	P VALUES
		0.50	0.0001	0.001
2.	Direct Bilirubin	0.67	0.0001	0.0004
3.	Indirect Bilirubin	0.41	0.0002	0.017
4.	Total Protein	0.97	0.27	0.001
5.	Serum Albumin	0.005	0.0029	0.0015
6.	SGOT	0.28	0.05	0.3
7.	SGPT	0.49	0.015	0.018

TABLE 3: Comparison Of Mean Value Between Groups

(Unpaired t test)

In unpaired t test a 'p' value of less ≤ 0.05 is significant.

DISCUSSION: Liver function tests help to assess the functional capacity of liver, diagnose insufficiency and assess progress or regress of liver diseases. The bilirubin[13] formed in the body during hemoglobin metabolism is taken up by the liver to be degraded and excreted. The mean total bilirubin, direct bilirubin and indirect bilirubin values showed significant decrease in the second and third trimester pregnant women. This may be due to water retention seen in normal pregnancies[14]

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due to the action of elevated progesterone, vasopressin and aldosterone. There is statistically significant decrease in mean total protein value in the third trimester.

Most of the plasma proteins are synthesized by the liver. In a normal pregnancy there is increased demand for proteins and dietary deficiencies can exacerbate the protein deficiency. In a developing country like India dietary protein deficiency especially among pregnant women is common. There is statistically significant decrease in mean serum albumin levels in all three trimesters of pregnancies. Albumin is synthesized exclusively by the liver. It is a good prognostic indicator of nutritional status[15] of the mother because albumin has a long half-life.

In malnutrition the body tries to maintain the serum albumin levels by increased re-distribution and decreased catabolism of protein. In most cases fetal weight gain is also normal at the expense[16] of the mother's health. The ability of humans to breakdown cyanide[7] depends largely on eating sufficient proteins along with cassava. Less protein in diet increases the risk of cyanide poisoning. Hemodilution of pregnancy and dietary protein deficiency contribute to the low values obtained. The SGPT values are not elevated.

Its values are elevated only when there is damage to hepatocytes. It is specific[16] to liver cells. This is proof of the significant physiological reserve of the liver. The SGOT mean values are also not elevated. SGOT is not specific to liver. It is also seen in RBC, skeletal muscles, GIT, brain, kidneys, etc. Normal values during pregnancy indicate no significant damage to any of organs mentioned. The microsomal mono-oxygenase system of liver is concerned with metabolism of xenobiotics like drugs, toxins and steroid hormones.

Liver cytochrome P450 is a microsomal enzyme present only in liver. The P450 enzymes are expressed in a sex dependent manner and are subject to endocrine control. It's less in females. Pregnancy has been reported to cause depression of hepatic monooxygenase activity. Low protein diet has also been associated with reduced activity of monooxygenase enzymes. The enzyme rhodanese is a mitochondrial enzyme[7] that detoxifies cyanide and many other toxins by converting it to thiocyanate. The thiocyanate formed is less toxic and can be easily excreted through urine.

CONCLUSION: The above study shows that there is significant decrease in total bilirubin, indirect bilirubin and direct bilirubin values in pregnant women in a cassava eating population especially in the second and third trimester. There is significant decrease in total protein levels in the third trimester. There is significant decrease in albumin in all three trimesters. There is no significant elevation of SGPT and SGOT values during a normal pregnancy among the cassava eating population in the state of Kerala in India. The liver function tests in this study group were subnormal[17] but not conclusive of liver diseases.

These values are comparable with the values obtained in pregnant women in a population[18] where cassava is not a staple food. Other studies conducted in pregnant also showed subnormal values in liver function tests but these are not conclusive of liver diseases but due the physiological stress of normal pregnancy. In a population with tapioca as staple food there is additional stress on the liver. A normal healthy liver is able to overcome all the normal stress of pregnancy. Any additional stress to the highly stressed liver during pregnancy can easily damage the liver. This is the cause for increased morbidity and mortality in pregnant women exposed to toxins and infections of liver. The above study is proof of the enormous physiological reserve of the liver in overcoming newer adversaries like more toxic[19] cassava due to higher carbon emission[20] and climate changes.

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