

Blood pressure, Alkaline Phosphatase, serum Globulin, A: G ratio in pregnant women and matched controls in a population with tapioca as staple food

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Abstract

Background: Tapioca has been the staple food for the people of Kerala, India. Recent studies show that it has become more toxic due to changes in environment. There have been few studies in recent years to observe the effects of consuming more toxic tapioca.

Objective: The combination of pregnancy and tapioca diet on blood pressure (BP), serum alkaline phosphatase, serum globulin and A:G ratio are studied to assess the general health and liver function.

Materials and Methods: A descriptive cross-sectional study design was conducted in the Obstetrics out-patient department of a tertiary care hospital of central Kerala. The systolic and diastolic blood pressures were determined. The serum alkaline phosphatase, total proteins, and serum albumin levels were tested in a sample of blood collected under aseptic conditions. The serum globulin values were calculated from total protein and serum albumin values by subtraction. The A:G values were calculated by dividing the values of serum albumin and serum globulin. This study was conducted after obtaining ethical clearance from the institute.

Result: There were significant differences ($p = 0.002$) in the mean values of systolic and diastolic blood pressure in the third-trimester pregnancy. There was significant difference in the mean value of serum alkaline phosphatase levels in the first trimester ($p = 0.007$), the second trimester ($p = 0.001$) and the third trimester ($p = 0.000001$). There was significant difference in the mean value of serum globulin in the first trimester ($p = 0.03$), the second trimester ($p = 0.0003$), and the third trimester ($p = 0.000008$). The A:G ratio showed significant difference in the first trimester ($p = 0.0003$), the second trimester ($p = 0.0001$), and the third trimester ($p = 0.001$).

Conclusion: The above study shows that there is significant decrease in systolic and diastolic blood pressure towards the third trimester compared to normal controls. This is comparable to other similar studies. The alkaline phosphatase levels are also comparable with the values obtained in other studies. The serum globulin values were also comparable to other similar studies. The decreasing A:G ratio values were unique to this population.

KEY WORDS: Blood pressure, alkaline phosphatase, serum globulin, A:G ratio, pregnancy, tapioca

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Introduction

Kerala is the only state in India where tapioca is a staple food. It accounts for 50% of tapioca or cassava grown in India.^[1] In other states such as Tamil Nadu and Andhra Pradesh, it is used to make industrial starch. Tapioca starch is a cyanogenic glucoside called linamarin that when consumed is converted by the normal gut microflora to hydrogen cyanide.^[2]

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The hydrogen cyanide formed enters the bloodstream and is metabolized (detoxified) by the liver enzyme rhodanese or thiosulfate: cyanide sulfur transferase in the presence of sulfur containing amino acids methionine and cysteine, to thiocyanate. Hydrogen cyanide and thiocyanate, the by-products of tapioca metabolism, are both known to cause fall in blood pressure in acute cyanide poisoning.^[3] Tapioca is also a rich source of natural potassium.^[4] It is recommended in the diet of people with high blood pressure with normal kidney functions. Potassium salts had been used to treat hypertension in the earlier days but were stopped due to various complications.^[5] But natural potassium has the benefits of decreasing blood pressure with no associated complications. The high potassium levels in blood increases urinary filtration of potassium by renal tubules and this increases the urinary excretion of sodium chloride and water. This decreases the blood volume and cause decrease in blood pressure.

Liver is the master organ of pregnancy. The maternal liver play an important role detoxifying drugs, toxins, and steroid hormones for both mother and fetus.^[6] In a population with tapioca as staple food, there is additional stress on the liver. The normally elevated steroid hormones of pregnancy are degraded by the maternal liver enzyme cytochrome P450.^[7] The activity of this enzyme is decreased by normal pregnancy making the liver more prone to damage by toxins and infections. The liver enzyme alkaline phosphatase levels can be used to assess liver damage. During pregnancy alkaline phosphatase values will be very high because placental isoenzyme of alkaline phosphatase is elevated. Its values are especially high in pregnant women with toxic damage to liver, hypertension or with risk of pre-term delivery. Low levels are also seen in hypothyroid mothers, folic acid deficiency, malnutrition, intra uterine growth retardation or fetal death. A normal pregnancy also causes increase in blood volume by 30% due to water retention especially in the third trimester.^[8] This is due to increase steroid hormones secretions, such as, estrogen, progesterone, glucocorticoids, and aldosterone. There is also elevated levels of angiotensin II. All these contribute to water retention during a normal pregnancy. The serum globulins include alpha, beta, and gamma globulins. The alpha and beta globulins are synthesized exclusively in the liver. The small amount of gamma globulins is synthesized by B-lymphocytes. All the globulins are broken down by liver. Therefore in liver diseases, the serum globulin levels increase. Tapioca in diet interferes with protein synthesis in liver since it decreases the availability of sulfur containing amino acids methionine and cysteine. Methionine is also an essential amino acid.^[9] The important sources of this essential amino acid are eggs, fish, meat, etc. The few plant sources are plant seeds. Daily minimum protein requirement in diet for a normal person is 60–70 gm/day. This requirement increases to 150 gm/day in pregnancy. This increases the risk of dietary deficiency. The A:G ratio is an index of health. It is altered in diseases of liver, kidney, malnutrition, malabsorption, chronic inflammation, etc. Hemodilution do not alter this ratio because both serum albumin and serum globulin are diluted equally.

This study was planned to determine the changes in blood pressure, serum alkaline phosphatase, serum globulin, and A:G ratio in pregnant women and matched controls in the tertiary care teaching hospital of central Kerala, where tapioca is a staple food, since recent studies have reported more toxic and smaller yields of tapioca due to changes in environment.

Materials and Methods

After obtaining ethical clearance from the institutional ethics committee of Government Medical College, Kottayam, this study was conducted in the out-patient department of Obstetrics and Gynaecology during a period of 6 months from January 2008 to June 2008. Informed written consent was taken from the study subjects and blood was drawn under aseptic precaution with disposable syringe and needle. It was sent to the Biochemistry laboratory of the same Institute to estimate the serum alkaline phosphatase, serum globulins, and A:G ratio values. The serum alkaline phosphatase levels were analyzed using an autozyme alkaline phosphatase as a reagent based on kinetic method using *p*-nitrophenyl phosphate.^[10] The total protein was analyzed using the Biuret reagent. The serum albumin was analyzed using bromocresol green method. The readings were taken using the clinical chemical analyzer ERBA (XL-300). This is a fully automated computerized analyzer. The serum globulin was calculated by subtract in the value of serum albumin from total protein value. The A:G ratio was calculated by dividing serum albumin and serum globulin values. The blood pressure was measured by palpatory and auscultatory methods in the sitting posture, with the help of a manual mercury sphygmomanometer and stethoscope.^[11]

Inclusion criteria

The pregnant subjects were 90 in number and they were matched with 90 non-pregnant women of reproductive age group without a history of any drugs, infection or toxins that may affect the liver function or blood pressure. The subjects gave history of eating tapioca three to four times a week as the major carbohydrate for at least one meal a day. The pregnant women were divided into three groups based on the duration of pregnancy. Pregnant women of less than 12 weeks pregnancy were first trimester, less than 24 weeks were second trimester and up to term or delivery of fetus is considered third trimester. Each group was compared to the 90 matched controls for each parameter.

The data obtained were entered into Microsoft Excel. The data were analyzed with the help of Statistical Package for Social Sciences (SPSS) windows, version 14.0. The results obtained were expressed as mean with standard deviation (SD). The mean differences between the groups were analyzed using analysis of variance (ANOVA) and unpaired “*t*” test. In ANNOVA and unpaired “*t*” test a “*p*” value of less than or equal to 0.05 were considered significant.

Table 1: Descriptive statistics of variables

Variables	Non-pregnant <i>n</i> = 90		First trimester <i>n</i> = 30		Second trimester <i>n</i> = 30		Third trimester <i>n</i> = 30	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Systolic BP	111.31	6.45	113.60	10.54	110.20	9.94	115.93	8.48
Diastolic BP	72.13	6.50	73.67	7.84	72.60	7.52	76.47	7.33
Alkaline phosphatase	172.21	43.12	146.93	46.55	142.03	42.06	280.97	125.52
Serum globulin	3.136	0.264	2.987	0.461	2.877	0.485	2.777	0.326
A:G ratio	1.444	0.178	1.394	0.24	1.406	0.242	1.368	0.190

SD, standard deviation.

Table 2: One-way ANOVA between groups

Variables	F-value	P-value
Systolic BP	2.29	0.022
Diastolic BP	2.952	0.034
Alkaline Phosphatase	30.838	0.0001
Serum Globulin	9.487	0.0001
A:G ratio	7.921	0.0001

ANOVA, analysis of variance.

Table 3: Unpaired 't' Test between the groups

Variables	Controls and first trimester	Controls and second trimester	Controls and third trimester
Systolic BP	0.15	0.48	0.002
Diastolic BP	0.39	0.74	0.002
Alkaline Phosphatase	0.007	0.001	0.000001
Serum globulin	0.03	0.0003	0.000008
A:G ratio	0.0003	0.0001	0.001

Results

After compilations of the data, appropriate statistics were applied. The following descriptive statistical analysis was done in this study. The mean and SD for each variable for the different groups were calculated. The different groups were the matched controls (*n* = 90), the first-trimester pregnant women (*n* = 30), the second-trimester pregnant women (*n* = 30), and the third-trimester pregnant women (*n* = 30). Then the one-way ANOVA for each variable between the groups were calculated. ANOVA is a general method to study the sampled-data relationships between the different groups. ANOVA signifies whether difference in values between the groups is significant or not. In ANOVA a 'p' value of less than or equal to 0.05 is considered significant. The unpaired 't' test was carried out to compare each variable in each trimester with the matched controls. In unpaired 't' tests a 'p' value of less than or equal to 0.05 is considered significant [Tables 1–3].

Discussion

In this study, a total of 180 subjects were studied. Of this, 90 were pregnant women and 90 were non-pregnant matched controls. There was significant increase in the systolic BP compared to the controls. During a normal pregnancy, the systolic BP falls during the second trimester and then it becomes normal or elevated during the third trimester due to high levels of estrogen in blood.^[12] Estrogen increases hepatic productions of angiotensinogen causing increased formation of the hormone angiotensin II, which causes elevated systolic blood pressure.^[13] This study shows significant increase in diastolic BP compared to the controls in the third trimester. The diastolic pressure is also influenced by high estrogen levels and angiotensin II levels causing increase in total peripheral resistance by causing vasoconstriction of small arterioles. There is increase in blood volume by 30% in a normal pregnancy. This contributes to increase in blood pressure especially in the third trimester. Various other hormone levels such as antidiuretic hormone (ADH) or vasopressin, and aldosterone also increases. ADH acts on kidney to increase the number of water channels (aquaporin 2) in the distal convoluted tubule (DCT) and collecting duct of nephrons.^[14] This increases water reabsorption. Aldosterone acts on kidneys to increase the number of epithelial sodium channels (ENaC) in the main cells of DCT and collecting duct of kidneys.^[15] This increases sodium reabsorption and passive water reabsorption. Both these effects cause increase in blood volume and blood pressure. This is called the hemodilution of pregnancy. A diet rich in natural potassium diet, is seen in a population with tapioca as staple food, this causes decrease in renal reabsorption of sodium and passive water reabsorption and this causes decrease in blood volume and blood pressure. In this study, the mean values for BP in each group are towards the lower limit of normal range. This may be due to the natural potassium-rich diet.

In this study, there was significant decrease in the mean serum alkaline phosphatase levels compared to the controls in the first and second trimesters. There was very significant increase in the mean values in the third trimester. The serum alkaline phosphatase normally comes from liver cells, bone cells, and placental cells (during pregnancy).^[16] Any damage to these cells or multiplication of these cells increase serum

levels. The three isoenzymes cannot be differentiated by common laboratory tests.^[17] During a normal pregnancy, the bone isoenzyme levels increase during the second trimester due to multiplication of bone cells of fetus. The placental isoenzyme levels increase as pregnancy progresses due to multiplication of placental cells.^[18] The very high values for alkaline phosphatase in the third trimester is due to increase in the placental isoenzyme. There is increased risk of liver damage in a population with tapioca as staple food due to the excess stress on liver to metabolize the hydrogen cyanide formed from cyanogenic glucosides. The microsomal monooxygenase system of liver is concerned with metabolism of xenobiotics.^[19] Liver cytochrome P450 enzymes are microsomal enzymes involved in metabolism of xenobiotics, such as, toxins and steroid hormones. The expression of this enzyme is sex dependent and it is less in females. In this study, there is decrease in serum globulin levels compared to matched controls in all three trimesters. This may be due to hemodilution or due to decreased synthesis of globulins in liver due to decreased availability of sulfur, amino acids, methionine, and cysteine, which are utilized for detoxification of tapioca toxin by the liver.^[20] Increased demand for proteins during a normal pregnancy makes the condition worse. In this study, the A:G ratio showed significant decrease as pregnancy progresses. Normally hemodilution does not alter the A:G ratio since both serum albumin and serum globulin values are diluted equally. The decreasing value in this study may be due to more decrease in serum albumin values compared to serum globulin values. Serum albumin is an indicator of nutritional status. The decrease in value may be due to nutritional deficiency of protein, increased demand for protein, liver disease, renal disease, etc. The decreased availability of the essential sulfur, amino acid methionine due to increased utilization for detoxification of tapioca toxin may alter the A:G ratio in this population. Few studies have been carried out to study the effects of more toxic tapioca on the human body. Liver is an organ with great physiological reserve. This study shows that the human body can handle the stress of normal pregnancy and also the additional stress of more toxic tapioca in the diet.

Conclusion

The above study shows that there is significant increase in systolic and diastolic blood pressure in the third trimester of pregnancy compared to matched controls. The serum alkaline phosphatase levels were significantly decreased in the first and second trimesters. But its values are significantly elevated above normal in the third trimester of a normal pregnancy compared to matched controls. These values were not conclusive of any abnormality. There is significant decrease in serum globulin in all three trimesters as seen in other similar studies. There was significant decrease in A:G ratio in all three trimesters in this study and this is not seen in other similar studies.^[21, 22]

The above study is proof of the enormous physiological reserve of the human body especially the liver in overcoming newer adversaries of modern days, like more toxic tapioca due to high carbon emission and climatic changes.^[23, 24]

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