WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 5.045
Volume 4, Issue 1, 336-356. Research Article ISSN 2277– 7105

REVIEW ON HEALTH EFFECTS OF FOODS AVOIDED BY LITERATE BANGLADESHI WOMEN DURING PREGNANCY

***Mariz Sintaha**

Lecturer, School of Life Sciences, Independent University, Bangladesh.

Article Received on
01 Nov 2014,

Revised on 26 Nov 2014,
Accepted on 21 Dec 2014

***Correspondence for Author**
Mariz Sintaha
Lecturer, School of Life Sciences, Independent University, Bangladesh.

ABSTRACT

According to an online survey among literate women of Bangladesh, 53% of them avoided raw papaya, 46% avoided ripe papaya, 77% avoided pineapple and 40% avoided coffee consumption during pregnancy. Tea is frequently consumed and caffeinated beverage was few times consumed by most women (47% & 54% respectively). Ripe papaya blend/juice neither has any effect on pregnant rat/fetus nor affects the pregnancy any way. Crude papaya latex or latex extract induces contraction in pregnant or non-pregnant rat uterus in vitro. Unripe papaya can even induce abortion in rat in vivo. The isolated papaya proteinase I has no effect on pregnancy moreover it prevents pre-implantation loss in rat. Papaya seed extract has toxic effect on rat uterine tissue in vitro and prevents pregnancy in rat even in as low dose as 100mg/kg body weight. Neither the unripe pineapple nor extract of pineapple leaf affects pregnancy even in high dose (1000 mg/kg and 2000 mg/kg body weight respectively), though pure constituent of some chemical isolated from extract of pineapple leaf showed pre- and post-implantation abortifacient activity even in low dose (30 mg/kg) in one study. Caffeine consumption does not increase the risk of reduced fecundibility, subfecundity, failure of assisted reproductive technology, low birth weight of newborn, pre-term delivery, gestational diabetes and behavior problem of child by maternal consumption in recommended dose of 300 mg/kg body weight. Daily 2 cups of coffee is not found to be associated with neural tube defect and 4 cups of coffee (400mg/day) is associated with Sudden Infant Death Syndrome (SIDS) in human.In rat, high dose maternal caffeine consumption is associated with increased risk of seizure and impaired cognitive ability of child; moderate dose (120 mg/kg body weight) caffeine consumption is associated with increased risk of fatty liver, reduced femur length and neuroendocrine disease in child; and low dose caffeine consumption is associated with increased risk of deformation of bone shaft

(30 mg/kg body weight), impaired development of testes (20 mg/kg body weight) and impaired cardiac function (20 mg/kg body weight) of fetus. Tea consumption increases fecundibility (at a dose of 1.5 serving a day) and decreases the risk of developing gestational diabetes but might be associated with increased risk of pre-eclempsia, in human. Maternal cola consumption is not associated with pre-term delivery, low birth weight, baby being small for gestation or behavior problem of children. But cola consumption (even by 1 serving a day) decreases fecundibility.

KEYWORDS: Pregnancy, papaya, pineapple, caffeine.

INTRODUCTION

Food taboos are common among around all societies of world, which are particular apparent during the pregnancy period. Different studies showed that there are restrictions on different foods during pregnancy in different population such as in Nigeria (Odebiyi, 1989), Malaysia (Bolton, 1972) (Sharifah ZS., 2012), Papua New Guinea (Meyer-Rochow, 2009), Nigeria (Ogbeide, 1942) (Oni OA, 2012), Indonesia (Ninuk, 2005), Brazil (Trigo M, 1989), Korea (Ludman EK1, 1992), Vietnam (Manderson L, 1981), Pakistan (Ali NS, 2004) and India (Ankita Parmar, 2013) (Ferro-Luzzi, 1980) (Rajkumar Patil, 2010).

Different surveys show that, among the participants, 91.3% illiterate women and 83.9% literate women in Pondicherry (Rajkumar Patil, 2010), 82% women in Tamil Nadu (Ferro-Luzzi, 1980) and 53.5% women in Surendranagar district of Gujarat (Ankita Parmar, 2013) avoided papaya during pregnancy. Papaya is also seen as abortifacients in Indonesia, Malaysia and Myanmar (Bouquet, 1950) (Quisumbing, 1951) (Tang, 1979).

Unripe fruit juice and leave of pineapple plant, have being known to have abortifacient properties in Indian medicine for a long time (Manjunath, 1948). Some foods are classified as ‘Hot’ which are believed to have negative effect on pregnancy and some foods are classified as ‘cold’ which are believed to have no negative effect on pregnancy (Nag, 1994).Pineapple perceived as 'hot' in many regions of India such as in Karnataka community (Nichter, 1997) and in Tamil Nadu (Ferro-Luzzi, 1980). According to a survey done on 339 adults of Pondicherry, India, it was seen that 9.8% illiterate women and 6.5% literate women avoided pineapple during pregnancy (Rajkumar Patil, 2010). According to the statistics of an ayurvedic physician in Tamil Nadu, pineapple causes bleeding from uterus in 5-10% of women (Ferro-Luzzi, 1980).

Caffeine is a plant alkaloid found in highest amount in coffee, tea, caffeinated soft drinks and chocolate (Maslova E, 2010). The half life of caffeine greatly increases during pregnancy from 3 hour in non-pregnant state to 10 .5 hour in pregnant state (Knutti R, 1982). Since, caffeine crosses placenta, plasma concentration of caffeine in fetus is almost equal to maternal plasma level (Goldstein A, 1962). Moreover, the enzyme responsible for caffeine metabolism does not develop in infant up to 8 month of age (Hornung MG, 1985). It is also evident that, caffeine during pregnancy at a dose of more than 300 mg/day, equivalent to 3 or more cups of coffee, has negative effect on pregnancy (Eskenazi, 1993). American College of Obstetricians and Gynecologists, suggests to consume not more than 2 cups of coffee during pregnancy (www.acog.org, 2010).

Where, pregnancy requires some extra calorie and vitamin, abstention from certain foods may deprive the pregnant women from getting beneficial nutrients. No article was found regarding food taboo of Bangladeshi women associated with pregnancy. In this study, the food taboo of Bangladeshi women with different literacy level associated with pregnancy was attempted to reveal through an online survey and whether these fears are true or just myth was attempted to prove through literature review.

METHOD

Foods avoided during pregnancy by Bangladeshi women with different literacy level was revealed through an online survey (http://goo.gl/XbJ8ER). The survey includes the questions about the foods, which are commonly avoided by Bangladeshi women. These foods are proved to be avoided by women of other populations in different studies.

Pubmed database (http://www.ncbi.nlm.nih.gov/pubmed) was searched to collect journal articles that examine the health effect of these foods on human fertility and fetal health when consumed during pregnancy. In total 57 journal articles published from 1942 to 2014 have been reviewed.

RESULTS

Foods Avoided by Bangladeshi Women During Pregnancy

Among the 112 participants of the survey, 48% women has completed post graduation, 38% has completed graduation, 14% has completed Higher Secondary School (12 years of education) and 4% has completed Secondary School (10 years of education). All of them either already mother or expecting the first child. 53% of them has never eaten raw papaya

during pregnancy, 29% has eaten few times and 7% has eaten papaya many times. 46% participant has never eaten ripe papaya during pregnancy, 34% has eaten few times and 12% has eaten papaya many times. Pineapple was completely avoided by 77% women where eaten few times by 13% and many times by only 3% women. Tea is frequently consumed by great percentage women (47%) during pregnancy where entirely avoided by only 11% women. Equal percentage of women (40%) never consumed and few times consumed coffee during pregnancy, where consumed many times by only 12% women. Most percentage of women (54%) consumed caffeinated beverage few times during pregnancy, where 16% consumed it frequently and 21% has never consumed caffeinated beverage during pregnancy. The result is viewable online (http://goo.gl/8p8cgY).

	Never	Few Times	Many Times
Raw Papaya	53	29	7
Ripe Papaya	46	34	12
Pineapple	77	13	3
Tea	11	34	47
Coffee	40	40	12
Caffeinated Beverage	21	54	16

Health Effect of Papaya During Pregnancy

Papaya Seed

Carica papaya seed extract has toxic effect on rat uterus. *Carica papaya* seed extracted with 80% ethanol was proved to prevent uterine contraction irreversibly in isolated pregnant or non-pregnant rat uterus by damaging endometrium and myometrium possibly by the effect of benzyl isothiocyanate (Adebiyi A, 2003). Methanol sub-fraction (MSF) of the benzene chromatographic fraction of the chloroform extract of the seeds of *Carica papaya* at a dose of 100mg/kg body weight and above prevents pregnancy while it does not inhibit pregnancy at a dose of 50mg/kg body weight. Moreover at a dose of 50mg/kg body weight it does not affect the status of the ovary, uterus and implantation, fetal body weight, soft tissues and skeletal structures of fetus (Shrivastava S, 2011). The aqueous extract of *Carica papaya* (Linn) seeds found to have abortifacient potential. in female Sprague-Dawley rats, high dose (800 mg/kg body weight) caused resorption of 30% foetus where the surviving fetus had decreased size though no external malfunction was evident. Low dose (100 mg/kg body weight) increased implantation site with decreased foetal weight (Oderinde O, 2002)

Ripe Papaya

Ripe papaya blend showed to have no effect in the number of implantation sites and viable fetuses compared to control in rat; It does not induce utrine contraction or show maternal or fetal toxicity (A. Adebiyi, 2002). Ripe papaya juice did not induce contraction in the pregnant or non-pregnant mice uterus (A. Adebiyi, 2002).

Papaya Latex

Papaya latex extract induced uterine contraction in proestrus and estrus stages (gravid uterus) and later stages of pregnancy (non-gravid uterus) in vitro possibly by the action of enzymes, alkaloids and other substances on the alpha adrenergic receptor (Cherian, 2000). Contractile effect of papaya latex (just as oxytocin and prostaglandin) on pregnant and non-pregnant rat uterus was also proved by other study at a concentration of 0·1–3·2 mg/ml (A. Adebiyi, 2002).

Unripe Papaya

Unripe fruit of Papaya induced abortion in albino rats of Wistar strain which can be prevented by administrating exogenous progesterone that leads to the birth of foetus without any abnormality (Gopalakrishnan M, 1978).

Papaya Enzyme

Standardized papain (papaya proteinase I) administered orally to Wistar rats in doses up to 800 mg/kg during blastogenesis and embryogenesis decreased preimplantation loss with no increase in postimplantation loss leading to the birth of normal foetus (Schmidt, 1995).

Health Effect of Pineapple During Pregnancy

Unripe Pineapple

Unripe pineapple juice up to the dose of 1000 mg/kg body neither affected number and weight of foetus, number of implantation site nor induces pre- or post-implantation losses, fetal death and vaginal bleeding in pregnant Wistar rats (Yakubu MT, 2011).

Pineapple Leaf

Extract of pineapple leaves in up to 2000 mg/kg body weight dose administered during the organogenesis period gestation has no affect on female fertility, maternal weight gain and fetal growth and development (Hu J, 2011).

Pure Constituent

Pure constituent and their synthetic analogues of some chemical isolated from the petroleum ether and benzene extracts of the whole leaves of pineapple were investigated for their antifertility effect. 5-Stigmastene-3ß- 7a-diol, 5-Stigmastene-3ß-7ß-diol dibenzoate and 5a-Stigmastane-3ß-5-6ß-triol 3-monobenzoate showed abortifacient effects on mice when administered orally before and after implantation at a dose of 30 mg/kg body weight where ß-Sitostero and 7-Oxo-5-stigmasten-3ß-ol benzoate showed this effect when administered before implantation only. Ergosterol peroxide showed the maximum abortifacient effect at both stages of pregnancy, but abortion occurred at a very late stage of pregnancy implantation (Basak, 1976).

Health Effect of Caffeine During Pregnancy

Fecundability

Older studies showed contradictory relation with caffeine and fecundibility (probability of being pregnant). One study done in 1988, found that consuming more than 3150 mg/month (about 1 cup of coffee/day) was associated with a 50% reduction in fecundability (Wilcox A W. C., 1988), where another study done in 1990, shows no relation of caffeine with fecundability in coffee, tea or cola drinkers even in as higher dose as 7000 mg/month (about 2 cup of coffee/day) (Joesoef MR, 1990). Newer studies shows caffeine even in more higher dose, does not affect fecundibility. A prospective cohort study of 3628 women planning a pregnancy in Denmark (2007–2010) showed that 3 cup of coffee consumption per day (300 mg caffeine./day) has no relation with fecundability, where soda consumption (even 1 serving a day) decreases and tea consumption (2 serving a day) increases fecundability (Elizabeth E. Hatch, 2012). Positive effect of tea on fecundibility is also proved by another study that shows drinking one-half cup or more of tea daily approximately doubled the odds of conception per cycle (B Caan, 1998).

Subfecundity

A significant risk of subfecundity (defined as a waiting time of 1 year or more from cessation of contraception to achievement of pregnancy) is found in coffee drinker in various studies suggesting different safe level of drinking coffee such as 7 g/month (equivalent to 233 mg/day) (Grodstein F, 1993), 300 mg/day (Hatch EE, 1993) (Stanton CK, 1995) , 500 mg/day (Bolúmar F, 1997) and 8 cups/day (Olsen., 1991)

Success Rate of Assisted Reproductive Technology

A literature review of human studies from 2000 to 2009 reported no positive relationship between caffeine consumption and infertility, semen quality, and various end points of assisted reproductive technology (Peck JD, 2010). A 2010 study also reported no association between caffeine consumption (mean 455 mg/d) and success rate of pregnancy after in vitro fertilization (Al-Saleh I, 2010).

Male Fertility

Subcutaneous injection of caffeine at a dose of 20 mg/kg body weight in pregnant mice signifacntly lowers the serum testosterone levels of male offspring. Beside this, it reduces proliferation , of testis, follicle stimulating hormone, androgen receptors, steroidogenic acute regulatory protein and vascular endothelial growth factor where it increases apoptosis, leptin receptor, luteinizing hormone and aromatase. So, maternal caffeine consumption may alter the development of testis of the offspring in adulthood (Fernanda Silveira Cavalcante, 2014).

Low Birth Weight & Pre-Term Delivery

In an older study, interview of 1,205 mothers, from January to November 1992, in the first 24 hours after delivery, revealed no effect of caffeine on low birth weight, preterm births or intrauterine growth retardation (Santos IS, 1998). A new study done on 2012, also shows that caffeine intake by pregnant women in a dose not more than 300 mg/day does not increase the risk of premature birth, low birth weight or the Apgar score of newborns that assess the health of newborn children immediately after birth (Jarosz M, 2012). But, in one meta-analysis of 13 prospective studies showed that, each 100-mg/day increment in maternal caffeine intake (around one cup of coffee) was associated with 13% higher risk of low birth weight (Ling-Wei Chen, 2014), where another meta-analyses including 60 unique publications from 53 cohort and case-control studies it is seen that increment of 100 mg caffeine was associated with a 14 % increase in risk of spontaneous abortion, 19 % stillbirth, 2 % preterm delivery, 7 % low birth weight, and 10 % small for gestational age (SGA) infants. Since the size of the associations are generally modest within the range of usual intake, it proves the biasness of many studies. (Greenwood DC, 2014). Decrement of coffee consumption during second and third trimester by an average of 182 mg/day by coffee drinker drinking more than 3 cups of coffee per day does not affect fetal weight at birth or length of gestational period (Jahanfar S, 2013). Caffeine consumption by smokers does not

affect fetal growth but decreases the fetal weight at birth with increment 1000mg caffeine consumption per week (Cook DG1, 1996).

Inuterine Growth Restriction or Small for Gestation

Prenatal caffeine treatment intragastrically at a dose of 120 mg/kg body weight increases DNA methylation and decreases histone acetylation of the key transcription factor steroidogenic factor-1, which leads to the decrease in the gene expression of its associated steroidogenic enzymes and the production of corticosterone during fetal development. It suggests that prenatal caffeine consumption may cause intrauterine growth retardation by altering steroidogenesis which regulates intrauterine homeostasis, fetal development and maturation (Ping J, 2014). Caffeine intake from only coffee (not cola , dessert, cake etc) in a dose of 200-300 mg per day, is associated with increased length of gestation, low birth weight and baby being small for gestation where caffeine from any source is not associated with pre-term delivery (VElisabeth Elind, 2013).There is no significant relationship between caffeine intake and fetal growth restriction mediated by the symptoms of maternal nausea and vomiting (Boylan SM, 2013).

Brain Development

Caffeine is the psychostimulant most consumed worldwide. in attempt to know the effect of caffeine in brain development of embryo it was seen that, pre-natal caffeine consumption by female Wistar rat changes the concentration of synaptic protein in cortex and hippocampus of rat foetus. Moderate (0.3 g/L) and high dose (1 g/L) decreased brain-derived neurotrophic factor (BDNF), TrkB receptor and Growth Associated Protein 43 (GAP-43) in embryonic stages18, where in low (0.1 g/L) and moderate dose (0.3 g/L) increased Sonic Hedgehog (Shh) and NeuN-stained nuclei in embryonic stages 18 and embryonic stages 20. It suggests that, even in lower dose caffeine may affect brain development of fetus (Mioranzza 1, 2014). In search of the fact whether daily high consumption of caffeine affect white matter or not it was found that, high-dose caffeine (25 mg/kg caffeine base loading dose; 20 mg/kg daily maintenance dose) consumption by pregnant sheep at gestational week equivalent to human gestational week 27-34 did not affect on brain weight, oligodendrocyte density, myelination, axonal integrity, microgliosis, astrogliosis, apoptosis, or neuronal density (Atik A, 2014). Exposure of adenosine type 2A receptor antagonists including caffeine during pregnancy and lactation of mice increases neuronal network excitability and susceptibility to seizures which

leads to the loss of hippocampal GABA neurons and some cognitive ability in the adulthood of the offspring (Silva CG1, 2013).

Behavior

Caffeine intake (coffee, caffeinated tea, and cola) during pregnancy is not associated with behavior problem, emotional problems, conduct problems, hyperactivity/inattention problems, peer relationship problems, and pro-social behavior in child at the age of 5-6 (Eva M. Loomans, 2012). Other study also denies association of caffeine with behavioral problem such as attention-deficit hyperactivity disorder (ADHD) in child even in as high dose as 10 cup coffee/day (Linnet KM, 2009). In adult caffeine consumption is associated with sleep disturbance. But night time awaking of infant (at age of 3 month) is not associated with caffeine consumption of mother during pregnancy and lactation at a dose up to 300 mg per day (Iná S. Santos, 2012).

Cardiovascular Function

Hypoxia is known to influence cardiovascular (CV) function, in part, through adenosine receptor activation. Maternal caffeine consumption has additive negative effect to fetal cardiovascular response to acute maternal hypoxia mediated via fetal adenosine A(2A) receptor inhibition during cardiovascular development of rat fetus (Nobuo Momoi, 2012).Another in vitro study on murine embryo shows that, caffeine exposure during pregnancy alters embryonic cardiac function and disrupts the normal cardiac response to hypoxia through blockade of A1 adenosine receptors (A1ARs) action which may lead to embryonic hypoxia (Daniela L. Buscariollo G. A., 2011). Evidence indicates that disruption of normal prenatal development influences an individual's risk of developing obesity and cardiovascular disease as an adult. In utero caffeine exposure at a dose of 20 mg/kg body weight in mice, reduces DNA methylation of genes associated with cardiac hypertrophy which leads to the alteration of cardiac function in adult stage of life by decreasing cardiac output and increasing left ventricular wall thickness (Daniela L. Buscariollo X. F., 2014). Coffee and 70% chocolate consumption by pregnant woman increases maternal uterine contraction and variation in fetal heart rate where coca was found to have no effect on these factors (Buscicchio G P. M., 2012) (Buscicchio G L. S., 2013).

Metabolism

Caffeine administered (up to the dose of 180 mg/kg body weight) intragastrically in pregnant Wistar rat elevates α- and β-glucose, reduces multiple lipid contents, varied apolipoprotein

contents and increases levels of a number of amino acids. Besides this, it decreases 11β-hydroxysteroid dehydrogenase 2 (11β-HSD-2), insulin-like growth factor 1 (IGF-1), IGF-1 receptor, insulin receptor expression and increases 11β-hydroxysteroid dehydrogenase 2 (11β-HSD-1), glucocorticoid receptor (GR), adiponectin receptor 2, leptin receptors and AMP-activated protein kinase α2 expression in fetus (Yansong Liu, 2013). This result suggests that, pre-natal caffeine exposure changes the fetal metabonome, which is probably attributed to the alterations of glucose and lipid metabolic pathways. Prenatal caffeine exposure at a dose of up to 120mg per kg body weight in Wistar rat decreases the expression of fetal adrenal steroid acute regulatory protein (StAR), placental 11β-hydroxysteroid dehydrogenase-2 (11β-HSD-2) and cholesterol side-chain cleavage enzyme (P450scc), as well as the level of fetal adrenal endogenous corticosterone (CORT) where it promotes the expression of 11β-hydroxysteroid dehydrogenase 1 and glucocorticoid receptor (GR). This suggest that adult HPA (Hypothalamic–pituitary–adrenal) axis dysfunction and susceptibility to metabolic syndrome may be associated with IUGR induced by caffeine (Dan Xu, 2012). This neuroendocrine dysfunction has transgenerational effect. F2 generation rat produced by breeding first generation (F1) of intrauterine growth retardation (IUGR) rats (produced by administrating caffeine at a dose of 120 mg per kg body weight, during pregnancy) and control showed to have increased serum corticosteroid, glucose and total cholesterol level and decreased triglyceride (TG) and High-density lipoprotein (HDL) after cold water stress. It proves that, indicates that reproductive and developmental toxicities and the neuroendocrine metabolic programming mechanism by prenatal caffeine ingestion have transgenerational effects in rats (Hanwen Luo, 2014).

Liver Disease

Pre-natal caffeine exposure at a dose of 120mg per kg body weight in rat, increases the susceptibility to non-alcoholic fatty liver disease mediated by alteration of intrauterine glucose and lipid metabolic programming which continues into the postnatal phase and reappeares in adulthood with the introduction of a high-fat diet (Wang L, 2014).

Bone

Several study showed that caffeine induces intrauterine growth retardation. Growth retardation is associated with skeletal development. Caffeine administration at a dose of 120 mg per kg body weight intragastrically reduces the femur length of rat fetus possibly by the increased exposure of maternal glucocorticoids and down regulation of histone methylation

of IGF-1 in fetal liver and growth plate which leads to the lower expression of IGF-1 signaling pathway components (Tan Y, 2012). It may be associated with adult osteoporosis and osteoarthritis. Caffeine consumption of pregnant Wistar rats in a dose of 30mg/day increases percent of water, decreases inorganic phase in bone and causes higher deformation of bone shaft (especially femur) (Olchowik G, 2011).

Diabetes

Many studies show, caffeine impairs glucose tolerance which is a great concern in gestational period since it may affect fetal growth. In attempt to know whether caffeine impairs glucose tolerance during gestation it is seen that, caffeine increases glucose level and decreases insulin sensitivity only in women with gestational diabetes (Robinson LE1, 2009). Moreover, it is seen that, coffee and tea consumption is associated with a decreased type 2 diabetes risk in non-pregnant adults .Moderate coffee (less than 8 cup a day) and tea (any amount) intake in first trimester is not associated with gestational diabetes, moreover it may have protective effect (Hinkle S, 2014). Even, moderate pre-pregnancy caffeine consumption has protective effect on gestational diabetes (Adeney KL1, 2007). Caffeine consumption is associated with insulin resistance in non-pregnant condition. In pregnant women caffeine and its metabolite-paraxanthine concentration (> 266 ng/ml and > 392 ng/ml respectively) in blood shows association with insulin resistance (S. Katherine Laughon, 2011).Ca

Neural Tube Defect

Spina bifida (SB) is a serious birth defect caused by improper closing of neural tube mainly due to maternal folic acid deficiency that leads to abnormal human physiology (teratological effect). Spina bifida is not increased by up to 2 cups of coffee intake during first month of pregnancy even in the women intaking less then 400 μg/day (recommended dose) of folic acid (Corey M, 2013).

SIDS

In newzealand, a study showed that, Heavy caffeine intake (400 mg/day equivalent to 4 cups of coffee per day) by mother throughout the pregnancy has significantly increased risk of Sudden Infant Death Syndrome (SIDS) (Ford RP, 1998).

Pre-eclampsia

One study suggested that, persistent tea drinking during pregnancy may be associated with an increased risk of pre-eclampsia (Wei SQ, 2009).

DISCUSSION

Papaya

Ripe Papaya is commonly eaten by Bangladeshi population and it has shown to have no effect on rat pregnancy. So, the 46% people avoiding ripe papaya during pregnancy is just because of unnecessary fear. Crude papaya latex or latex extract induces contraction in pregnant or non-pregnant rat uterus in vitro where unripe papaya can even induce abortion in rat in vivo. Unripe papaya is usually eaten by Bangladeshi population in cooked form. Further study should be done to know whether the cooking procedure and the metabolic reaction change the active component of latex into other harmless component or not in humant. Papaya seed extract is shown to be contraceptive and abortifacient in vivo and toxic to rat uterus in vitro. But papaya seed is not eaten by the Bangladeshi population. The most fear in peoples mind about the papaya comes from its meat tenderizing property. The fear should be eliminated since study proves that isolated papaya proteinase I has no effect on pregnancy.

Pineapple

Neither unripe pineapple juice nor the extract of pineapple leaf at high dose (1000 mg/kg & 2000 mg/kg body weight respectively) causes loss of fetus though an old study (1976) shows that some pure constituent or synthetic analogs of some chemicals isolated from leaf extract has abortifacient property in rat. Neither unripe pineapple nor pineapple leaf is eaten by Bangladeshi population.

Caffeine

Fertility: According to newer study, coffee (up to the dose of 300 mg/day) consumption does not decrease, cola consumption (even by 1 serving a day) decreases and tea consumption (1.5 serving a day) increases fecundibility in human. Caffeine consumption does not increase the risk of subfecundity or failure of assisted reproductive technology in human. Caffeine consumption may alter the development of testis of the offspring in adulthood, when injected subcutaneously (at a dose of 20mg/kg body weight) in rat. So, overall, caffeine consumption from tea or coffee does not affect human fertility.

Fetal Growth & Pre-term Delivery: Caffeine consumption is not associated with low birth weight or pre-term delivery at a dose up to 300mg/day and caffeine intake from only coffee is related to baby being small for gestation in a dose of 200-300 mg per day. Only 2 meta analysis showed little association of caffeine with low birth weight and pre-term delivery and

one study showed association of caffeine with low birth weight only in smokers. Meta analysis did not show any reference value for safe level of caffeine consumption and the percentage of association with different risk factors are moderate in the common intake level. It indicates the biasness of many studies. Decrement of coffee consumption by coffee drinker drinking more than 3 cups of coffee per day, does not affect fetal weight at birth or length of gestational. So, there is no need to reduce caffeine consumption further, within the limit of recommended consumption.

Brain Development & Personality: Low dose pre-natal caffeine consumption decreases concentration of synaptic protein and high dose caffeine consumption during pregnancy and lactation increases risk of seizure and loss of some cognitive ability in mice offspring. But, in human, caffeine consumption is not associated with behavior problem, emotional problem, pro-social behavior, night time walking of child at dose of 300 mg/kg body weight and attention-deficit hyperactivity disorder (ADHD) even in higher dose (10 cup coffee/day).

Cardiac Function: In utero caffeine exposure leads to the alteration of cardiac function in adult stage of mice (at a dose of 20 mg/kg body weight) and cardiac response to maternal hypoxia by blocking adenosine receptors. In human, caffeine from coffee and dark chocolate found to increase fetal heart rate, where cola does not. More studies should be done to know the effect of caffeine on cardiac function of human fetus.

Metabolism: Caffeine exposure to pregnant Wistar rat at a dose of 120 mg/kg body weight, increases the susceptibility to non-alcoholic fatty liver disease in adulthood by altering glucose and lipid metabolism in fetus; reduces femur length (when injected intragastrically) by increasing exposure to maternal glucocorticoids by upregulating glucocorticoids receptor and downregulating IGF-1 signaling pathway components; and leads to neuroendocrine dysfunction that may be transferred to the F2 generation. More studies should be done to know the effect of caffeine on the endocrine system and metabolism of human fetus that affects bone development and liver function.

Gestational Diabetes: Though high concentration of serum caffeine and its metabolite is associated insulin resistance, caffeine consumption is found to impair glucose tolerance only in women who already has gestational diabetes mellitus. Moreover, moderate coffee (<8cup/day) or tea (any amount) consumption in first trimester and in pre-pregnancy period decreases the risk of gestational diabetes mellitus.

Tetratological Effect: Coffee consumption within recommended level does not affect neural tube formation even in women with folic acid deficiency.

Sudden Infant Death Syndrome (SIDS): 4 cups of coffee (400mg/day) consumption during pregnancy is associated with SIDS.

Tea Consumption: 1.5 servings of tea consumption increases fecundibility and consumption in any amount protects from gestational diabetes. Persistent tea consumption throughout pregnancy may be associated with pre-eclempsia.

Cola Consumption: Cola consumption (even 1 serving a day) decreases fecundibility.

Food Avoidance by Literate Bangladeshi Women

Raw papaya, ripe papaya, pineapple and coffee are entirely avoided by most women, where tea is frequently consumed and caffeinated beverage has few times consumed by Bangladeshi women during pregnancy. Neither part/form of papaya nor pineapple commonly eaten by Bangladeshi population found to have any effect on pregnancy or fetus. Caffeine consumption is not associated with human fertility, fetal development, pre-term delivery, behavior of child and teratological effect. Coffee consmption is associated with Sudden Infant Death Syndrome, tea consumption is associated with pre-eclempsia and cola consumption decreases fecundibility. Since, caffeine consumption is associated with impaired cardiac function, neuroendocrine syndrome and bone malformation in rat, more studies should be done to find the associations with human. So, avoidance of coffee consumption may save Bangladeshi women from harmful side effects. Since, tea is widely consumed by Bangladeshi women during pregnancy, more studies should be done to know the association of tea with pre-eclampsia.

CONCLUSION

Bangladeshi women avoid raw papaya, ripe papaya and pineapple due to unnecessary fear where avoidance of coffee consumption may save them from harmful side effects. Since, tea is widely consumed during pregnancy, more studies should be done to know the association of tea with pre-eclampsia.

REFERENCE

1. A. Adebiyi, P. G. Papaya (Carica papaya) consumption is unsafe in pregnancy: fact o rfable? Scientific evaluation of a common belief in some parts of Asia using a rat model. *British Journal of Nutrition,* 2002; *88*: 199–203.
2. Adebiyi A, G. A. Tocolytic and toxic activity of papaya seed extract on isolated rat uterus. *Life Sci.,* 2003; *74*(5): 581-92.
3. Adeney KL1, W. M. Coffee consumption and the risk of gestational diabetes mellitus. *Acta Obstet Gynecol Scand.,* 2007; *86*(2): 161-6.
4. Ali NS, A. S. Womens' beliefs and practices regarding food restrictions during pregnancy and lactation: a hospital based study. *J Ayub Med Coll Abbottabad.,* 2004; *16*(3): 29-31.
5. Al-Saleh I, E.-D. I. The effect of caffeine consumption on the success rate of pregnancy as well various performance parameters of in-vitro fertilization treatment. *Med Sci Monit.,* 2010; *16*(12): CR598–605.
6. Ankita Parmar, H. K. A study on taboos and misconceptions associated with pregnancy among rural women of Surendranagar district. *Healthline,* 2013; *4*(2).
7. Appel CC, M. T. Caffeine-induced hypokalemic paralysis in pregnancy. *Obstet Gynecol.,* 2001; *97*(5): 805-7.
8. Atik A, C. J. Impact of daily high-dose caffeine exposure on developing white matter of the immature ovine brain. *Pediatr Res.,* 2014; *76*(1): 54-63.
9. B Caan, C. P. Differences in fertility associated with caffeinated beverage consumption. *Am J Public Health,* 1998; *88*(2): 270–274.
10. Basak, A. P. Abortifacient effect ofsteroids from Ananas comosus and their analogues on mice. *Journal of Reproductive Fertility,* 1976; *46*: 461-462.
11. Bolton, J. Food taboos among the Orang Asli in West Malaysia: a potential nutritional hazard. *Am J Clin Nutrit.,* 1972; *25*: 789–799.
12. Bolúmar F, O. J. Caffeine and delayed conception: a European multicentre study on infertility and subfecundity. European Study Group on Infertility Subfecundity. *Am J Epidemiol.,* 1997; *145*(4): 324–34.
13. Bouquet, A. K. Plantes Medicinales et Toxiques de la Cote d'Ivoire Haute Volta (Medicinal and Poisonous Plants in the Ivory Coast Upper Volta), 1950.
14. Boylan SM, G. D. Does nausea and vomiting of pregnancy play a role in the association found between maternal caffeine intake and fetal growth restriction? *Matern Child Health J.,* 2013; *17*(4): 601-8.

15. Buscicchio G, L. S. The effects of different concentrations of cocoa in the chocolate intaken by the mother on fetal heart rate. *J Matern Fetal Neonatal Med.*, 2013; *26*(15): 1465-8.
16. Buscicchio G, P. M. The effects of maternal caffeine and chocolate intake on fetal heart rate. *J Matern Fetal Neonatal Med.*, 2012; *25*(5): 528-30.
17. Cherian, T. Effect of papaya latex extract on gravid and non-gravid rat uterine preparations in vitro. *J Ethnopharmacol*, 2000; *70*(3): 205-12.
18. Christiansen RE, O. F. Caffeinated beverages and decreased fertility. *Lancet*, 1989; *1*: 378.
19. Cook DG1, P. J. Relation of caffeine intake and blood caffeine concentrations during pregnancy to fetal growth: prospective population based study. *BMJ*, 1996; *313*(7069): 1358-62.
20. Corey M, B. M. Risk of Spina Bifida and Maternal Cigarette, Alcohol, and Coffee Use during the First Month of Pregnancy. *Int J Environ Res Public Health.*, 2013; *10*(8): 3263–3281.
21. Corey M. Benedum, M. M. (August). Risk of Spina Bifida and Maternal Cigarette, Alcohol, and Coffee Use during the First Month of Pregnancy. . *Int J Environ Res Public Health.*, *10*(8): 3263–3281. .
22. Crozier TW, S. A. Espresso coffees, caffeine and chlorogenic acid intake: potential health implications. *Food Funct.*, 2012; *3*(1): 30-33.
23. Dan Xu, B. Z. (). Caffeine-Induced Activated Glucocorticoid Metabolism in the Hippocampus Causes Hypothalamic-Pituitary-Adrenal Axis Inhibition in Fetal Rats. *PLoS One.*, 2012; *7*(9): e44497.
24. Daniela L. Buscariollo, G. A. Caffeine Acts via A1 Adenosine Receptors to Disrupt Embryonic Cardiac Function. *PLoS One.*, 2011; *6*(12): e28296.
25. Daniela L. Buscariollo, X. F. Embryonic Caffeine Exposure Acts via A1 Adenosine Receptors to Alter Adult Cardiac Function and DNA Methylation in Mice. *PLoS One.*, 2014; *9*(1): e87547.
26. Elisabeth Elind, J. B.-L. Maternal caffeine intake during pregnancy is associated with birth weight but not with gestational length: results from a large prospective observational cohort study. *BMC Med.*, 2013; *11*: 42.
27. Elizabeth E. Hatch, L. A. Caffeinated Beverage and Soda Consumption and Time to pregnancy. *Epidemiology*, 2012; *23*(3): 393–401.

28. Englund-Ögge L1, B. A. Association between intake of artificially sweetened and sugar-sweetened beverages and preterm delivery: a large prospective cohort study. *Am J Clin Nutr*, 2012; *96*(3): 552-9.
29. Eskenazi, B. CaVeine during pregnancy: grounds for concern? *JAMA*, 1993; 2973-4.
30. Eva M. Loomans, L. H. Caffeine Intake During Pregnancy and Risk of Problem Behavior in 5- to 6-Year-Old Children. *Pediatrics*, 2012; *130*(2): e305 -e313 .
31. Fernanda Silveira Cavalcante, V. A.-P. The testis of the mice C57/BL6 offspring in adulthood have alterations due to maternal caffeine consumption. *Acta Cir. Bras.*, 2014; *29*(1).
32. Ferro-Luzzi, E. Food avoidance of pregnant women in Tamil Nadu. *Food, Ecology and Culture: Readings in the Anthropology of Dietary Practices.*, 1980; 101-108.
33. Ford RP, S. P. Heavy caffeine intake in pregnancy and sudden infant death syndrome. New Zealand Cot Death Study Group. *Arch Dis Child.*, 1998; *78*(1): 9-13.
34. Goldstein A, W. R. Passage of caffeine into human gonadal and fetal tissue. *Biochem Pharmacol.*, 1962; *11*: 166-8.
35. Gopalakrishnan M, R. M. Effect of papaya (Carica papaya linn) on pregnancy and estrous cycle in albino rats of Wistar strain. *Indian J Physiol Pharmaco*, 1978; *22*(1): 66-70.
36. Greenwood DC, T. N. Caffeine intake during pregnancy and adverse birth outcomes: a systematic review and dose-response meta-analysis. *Eur J Epidemiol.*, 2014; *29*(10): 725-34.
37. Grodstein F, G. M. Relation of female infertility to consumption of caffeinated beverages. *Am J Epidemiol.*, 1993; *137*(12): 1353-60.
38. H., S. Effect of papain on different phases of prenatal ontogenesis in rats. *Reprod Toxicol.*, 1995; *9*(1): 49-55.
39. Halldorsson TI, S. M. Intake of artificially sweetened soft drinks and risk of preterm delivery: a prospective cohort study in 59,334 Danish pregnant women. *Am J Clin Nutr.*, 2010; *92*(3): 626-33.
40. Hanwen Luo, Z. D. Prenatal caffeine ingestion induces transgenerational neuroendocrine metabolic programming alteration in second generation rats. *Toxicology and Applied Pharmacology*, 2014; *274*(3): 383-392.
41. Hatch EE, B. M. Association of delayed conception with caffeine consumption. *Am J Epidemiol.*, 1993; *138*(12): 1082-92.
42. Hinkle S, L. S. First trimester coffee and tea intake and risk of gestational diabetes mellitus: a study within a national birth cohort. *BJOG*, June 2014.

43. Hornung MG, S. C. Caffeine and human reproduction: Placental transfer of drugs. *Rev Environ Health,* 1985; *5*: 151-67.
44. *http://goo.gl/8p8cgY*. (n.d.).
45. *http://goo.gl/XbJ8ER*. (n.d.).
46. *http://www.ncbi.nlm.nih.gov/pubmed*. (n.d.).
47. Hu J, L. H. Developmental toxicity of orally administered pineapple leaf extract in rats. *Food Chem Toxicol.,* 2011; *49*(6): 1455-63.
48. Iná S. Santos, A. M. Maternal Caffeine Consumption and Infant Nighttime Waking: Prospective Cohort Study. *Pediatrics,* 2012; *129*(5): 860–868. .
49. Jahanfar S, J. S. Effects of restricted caffeine intake by mother on fetal, neonatal and pregnancy outcome. *Cochrane Database Syst Rev.,* 2013; *2*: CD006965.
50. Jarosz M, W. R. Maternal caffeine intake and its effect on pregnancy outcomes. *Eur J Obstet Gynecol Reprod Biol.,* 2012; *160*(2): 156-60.
51. Joesoef MR, B. V. Are caffeinated beverages risk factors for delayed conception? *Lancet.,* 1990; *335*(8682): 136-7.
52. Kira C. Taylor, C. M. Alcohol, Smoking, and Caffeine in Relation to Fecundability, with Effect Modification by NAT2. *Ann Epidemiol.,* 2011; *21*(11): 864–872.
53. Knutti R, R. H. The effect of pregnancy on the pharmacokinetics of caffeine. *Arch Toxicol Suppl.,* 1982; *5*: 187-92.
54. Ling-Wei Chen, Y. W.-F. Maternal caffeine intake during pregnancy is associated with risk of low birth weight: a systematic review and dose–response meta-analysis. *BMC Med,* 2014; *12*(1): 174.
55. Linnet KM, W. K. *Acta Paediatr. Coffee consumption during pregnancy and the risk of hyperkinetic disorder and ADHD: a prospective cohort study.,* 2009; *98*(1): 173–9.
56. Linnet KM, W. K. Coffee consumption during pregnancy and the risk of hyperkinetic disorder and ADHD: a prospective cohort study. *Acta Paediatr.,* 2009; *98*(1): 173–9.
57. Ludman EK1, K. K. Food beliefs and diets of pregnant Korean-American women. *J Am Diet Assoc.,* 1992; *92*(12): 519-20.
58. Manderson L, M. M. Vietnamese attitudes towards maternal and infant health. *Med J Aust.,* 1981; *1*(2): 69-72.
59. Manjunath, B. The wealth of India—raw materials. *Council of Scientific and Industrial Research,* 1948; 75-77.
60. Maslova E, B. S. Caffeine consumption during pregnancy and risk of preterm birth: a meta-analysis. *Am J Clin Nutr.,* 2010; *92*: 1120-1132.

61. Maslova E1, S. M. Consumption of artificially-sweetened soft drinks in pregnancy and risk of child asthma and allergic rhinitis. *PLoS One*, 2013; *8*(2): e57261.
62. Meyer-Rochow, V. B. Food taboos: their origins and purposes. *J Ethnobiol Ethnomed.*, 2009; *5*: 18.
63. Mioranzza 1, N. F. Prenatal caffeine intake differently affects synaptic proteins during fetal brain development. *Int J Dev Neurosci.*, 2014; *36*: 45-52.
64. Nag, M. Beliefs and practices about food during pregnancy. *Economic and Political Weekly* , September 1994; 2477-2438.
65. Nichter, M. a. The Ethnophysiology and Folk Dietetics of Pregnancy: A Case Study from South India. *Mark Nichter (ed) Anthropology and International Health: South Asian Case Studies. Klwer Academic, Dordrecht.*, 1997; 30-56.
66. Ninuk, T. The importance of eating rice: changing food habits among pregnant Indonesian women during economic crisis, 2005; *61*: 199-210.
67. Nobuo Momoi, J. P. Maternal hypoxia and caffeine exposure depress fetal cardiovascular function during primary organogenesis. *J Obstet Gynaecol Res.*, 2012; *38*(12): 1343–1351. .
68. Odebiyi, A. Food taboos in maternal and child health: the views of traditional healers in Ife-ife, Nigeria. *Soc Sci Med,* 1989; *28*(9): 985–996.
69. Oderinde O, N. C. Abortifacient properties of aqueous extract of Carica papaya (Linn) seeds on female Sprague-Dawley rats. *Niger Postgrad Med J.*, 2002; *9*(2): 95-8.
70. Ogbeide, O. Nutritional hazards of food taboos and preferences in Mid-West Nigeria. *Am J Clin Nutr.*, 1942; *27*: 213-216.
71. Olchowik G, C.-P. E. The influence of caffeine on the biomechanical properties of bone tissue during pregnancy in a population of rats. *Folia Histochem Cytobiol*, 2011; *49*(3): 504-11.
72. Olsen., J. Cigarette smoking, tea and coffee drinking, and subfecundity. *Am J Epidemiol.*, 1991; *133*(7): 734-9.
73. Oni OA, T. J. Identifying pregnant women who would adhere to food taboos in a rural community: a community-based study. *Afr J Reprod Health.*, 2012; *16*(3): 68-76.
74. Peck JD, L. A. A review of the epidemiologic evidence concerning the reproductive health effects of caffeine consumption: a 2000–2009 update. *Food Chem Toxicol.*, 2010; *48*(10): 2549–76.
75. Petherick ES, G. M. Relationship between artificially sweetened and sugar-sweetened cola beverage consumption during pregnancy and preterm delivery in a multi-ethnic

cohort: analysis of the Born in Bradford cohort study. *Eur J Clin Nutr.*, 2014; *68*(3): 404-7.

76. Ping J, W. J. Prenatal caffeine ingestion induces aberrant DNA methylation and histone acetylation of steroidogenic factor 1 and inhibits fetal adrenal steroidogenesis. *Toxicology.*, 2014; *321*: 53-61.
77. Quisumbing, E. Medicinal Plants of the Philippines. *Department of Agricultural and Natural Resources Technical Bulletin x,* 1951; *16.*
78. Rajkumar Patil, A. M. Taboos and misconceptions about food during pregnancy. *Calicut Medical Journal,* 2010; *8*(2): e4.
79. Robinson LE1, S. C. Acute caffeine ingestion and glucose tolerance in women with or without gestational diabetes mellitus. *J Obstet Gynaecol Can.*, 2009; *31*(4): 304-12.
80. S. Katherine Laughon, R. W. Caffeine and insulin resistance in pregnancy. *Am J Perinatol.*, 2011; *28*(7): 571–578.
81. Santos IS, V. C. Caffeine intake and low birth weight: a population-based case-control study. *Am J Epidemiol,* 1998; *147*(7): 620-7.
82. Schmidt, H. Effect of papain on different phases of prenatal ontogenesis in rats. *Reprod Toxicol.*, 1995; *9*(1): 49-55.
83. Sharifah ZS., N. P. Food restrictions during pregnancy among Indigenous Temiar women in peninsular Malaysia. *Malays J Nutr.*, 2012; *18*(2), 243-53.
84. Shrivastava S, A. A. (2011). Fertility, developmental toxicity and teratogenicity in albino rats treated with methanol sub-fraction of Carica papaya seeds. *Indian J Pharmacol, 2011; 43: 419-23, 43*(4): 419-423.
85. Silva CG1, M. C. denosine receptor antagonists including caffeine alter fetal brain development in mice. *Sci Transl Med.*, 2013; *5*(197): 97ra104.
86. Stanton CK, G. R. Effects of caffeine consumption on delayed conception. *Am J Epidemiol.*, 1995; *142*(12): 1322-9.
87. Tan Y, L. J. Caffeine-induced fetal rat over-exposure to maternal glucocorticoid and histone methylation of liver IGF-1 might cause skeletal growth retardation. *Toxicol Lett.*, 2012; *214*(3): 279-87.
88. Tang, C. Macrocyclic piperidine and piperidine alkaloid in Carica papaya. *Food Chemistry and Nutrition,* 1979; *1*: 55-68.
89. Trigo M, R. M. Food taboos in the northern region of Brazil. *Rev Saude Publica.*, 1989; *23*(6): 455-64.

90. VElisabeth Elind, J. B.-L. Maternal caffeine intake during pregnancy is associated with birth weight but not with gestational length: results from a large prospective observational cohort study. *BMC Med.*, 2013; *11*: 42.
91. Wang L, S. L. Intrauterine metabolic programming alteration increased susceptibility to non-alcoholic adult fatty liver disease in prenatal caffeine-exposed rat offspring. *Toxicol Lett.*, 2014; *224*(3): 311-8.
92. Wei SQ, X. H. Tea consumption during pregnancy and the risk of pre-eclampsia. *Int J Gynaecol Obstet*, 2009; *105*(2): 123-6.
93. Wilcox A, W. C. Caffeinated beverages and decreased fertility. *Lancet*, 1988; *2*: 1453-5.
94. Wilcox A, W. C. Caffeinated beverages and decreased fertility. *Lancet.*, 1988; *2*: 1453–1456.
95. Williams MA, M. R. *Lancet*, 1990; *335*(8705): 1603.
96. Williams MA, M. R. (199O). Coffee and delayed conception. *Lancet , 335*, 16O3.
97. *www.acog.org*. (2010, August). Retrieved from http://goo.gl/3VR7k0
98. Yakubu MT, O. O. Ananas comosus: is the unripe fruit juice an abortifacient in pregnant Wistar rats. *Eur J Contracept Reprod Health Care.*, 2011; *16*(5): 397-402.
99. Yansong Liu, D. X. Corrigendum to 'Fetal rat metabonome alteration by prenatal caffeine ingestion probably due to the increased circulatory glucocorticoid level and altered peripheral glucose and lipid metabolic pathways. *Toxicology and Applied Pharmacology* , 2013; *273*(3): 691.