

Pregnant Women Risk Perception of Medications and Natural Products Use During Pregnancy in Alahsa, Saudi Arabia

Abdulrhman Mohammed Aljoher^{a*}, Mohammed Abdullah Alsaeed^a,
Mohammed Abdulltife AlKhlfan^a, Aishah Wassil Almethen^a,
Monirah Abdullah Almukhaitah^a, Humaira Zareen^a, Sayed Ibrahim Ali^a

^a College of Medicine, King Faisal University, Alahsa, Saudi Arabia

*Corresponding author: Abdulrhman Mohammed Aljoher, Saudi Arabia,
Telephone +966549897688, aaljoher93@gmail.com

ABSTRACT

Introduction: The use of medications during pregnancy has increased in the recent years. Some congenital anomalies, birth defects, and miscarriages have been found to be preceded by some medications use during pregnancy. The use of herbal medicines is not yet proved to be safe during pregnancy, since some herbs showed increased risk of certain congenital malformations.

Aim: This study assesses the pregnant women perception, beliefs, and attitude toward medication and natural products use and their influencers during pregnancy.

Methodology: This is a cross-sectional study targeting women in Alahsa, Saudi Arabia. More than 300 women have responded to a pretested questionnaire collecting their sociodemographic, perception and attitude toward medication and natural product. The data were analyzed using SPSS Statistics under the supervision of a statistician.

Results: This study involved 184 participants, 29.2% of pregnant women avoided using prescribed medications, 40.7% non-prescribed, and 33.3% natural products during pregnancy. Paracetamol was on the top of the avoided medications, and herbals were on the top of the avoided natural products. The most common reason for avoidance was fearing of its effect on fetus. More than half of the participants always looked for the product safeness. Pain killers, antibiotics, cinnamon, and pineapple are the most commonly believed products to be harmful during pregnancy. 1st trimester is believed to be the critical period in which medications and herbals should be avoided.

Conclusion: Pregnant women should be educated more about unsafe products during pregnancy. Women's beliefs about natural products need further exploration because of lack of evidence.

Keywords: Pregnancy, teratogenic, medication, herbals, congenital anomaly, birth defect.

INTRODUCTION

In the last 30 years, the number of pregnant women who take medications has increased more than the double to reach a ratio of 9 out of 10 women use at least one medication during pregnancy [1]. It is well known that the use of medications in pregnancy is required in some women especially for those who have certain medical conditions which require continuous treatment, such as hypertension, diabetes mellitus and asthma, otherwise their life would be in danger. Medications during pregnancy may also be used for certain medical conditions that occurs because of the pregnancy [2]. The increase in the occurrence of chronic diseases in reproductive age along with the advancement of maternal age during pregnancy are 2 factors influencing the increase in the consumption of prescribed medications in pregnancy [3,4]. Medication use during pregnancy should be controlled under the supervision of physicians, as some of these substances may cross the placenta and affect the growth of the fetus [5]. It has been reported that

mothers of infants with congenital anomalies were using aspirin, antacids, dextroamphetamine, phenobarbitone, sodium amytal, other barbiturates, cough medicines, iron, sulphonamides, and nicotinamide [6]. NSAIDs were found to be associated with the increased risk of miscarriage especially when they are used early in pregnancy or for long time [7]. Some medications have also high risk for some birth defect such as hypospadias [8-11].

On the other hand, we have a huge number of pregnant women in the developing countries who use herbal medicine because they believe that these medicines are natural and safe [12,13]. In USA, the use of herbal medicine was estimated to be 17.9% [14]. According to the complementary and alternative drugs (CAD'S), the use of herbal medicines (preparations) is not always proved and there is little data concerning the safety and the adverse consequences of their use during pregnancy as well as the purities of these preparations [15]. It is very important to know that

some herbal remedies have been found to be dangerous for pregnant women because of their adverse effects^[16]. It has been found that there is a possible risk of certain congenital malformations in the nervous system, musculoskeletal and connective tissues or the eye when pregnant women use herbal remedies especially during their first trimester^[17]. Many researches were conducted all over the world to review the use of medications in pregnancy. For example, a study was conducted in Europe (Western, Northern and Eastern), North and South America, and Australia showed that 66.9% of women reported the use of OTC medications during their pregnancies^[18].

Different studies about the use of herbal medicine during pregnancy were done in Europe, North and South America and Australia^[19], Scotland^[20], China^[21], and Taif (KSA). The study conducted in Taif, Saudi Arabia, showed that about 40% of women have used medications and herbal remedies while they are pregnant. The conducted studies found that the commonly used drugs were paracetamol (13.2%), antibiotics (2.6%), drugs for treating nausea and vomiting (2.6%), NSAIDs, antihistaminic and heartburn medications (1.3%), and the percentage of the use of herbal remedies was (4.6%)^[22].

To the best of our knowledge, no studies were conducted in Alahsa region, Saudi Arabia that estimate pregnant women risk perception of medication and natural products use in pregnancy.

AIM OF THE STUDY

The main aims of this study are :

- 1) To assess the perception and beliefs of pregnant women about medication and natural products use risk
- 2) To assess the attitude of pregnant women toward medication and natural products
- 3) To assess the factors affecting pregnant women perceptions, beliefs, and attitudes.

METHODOLOGY

- **Study design and population**

This is a cross-sectional study targeting women in Alahsa, Saudi Arabia. To reduce the possibility of recall bias, the inclusion criteria state that participants should be either pregnant women (at any gestational age) or a mother of a child aged less than 1 year.

- **Data collection and variables**

An anonymously-filled questionnaire has been constructed in English then translated into Arabic by two native speakers and compared together for accuracy with back-translation to English. The questionnaire includes 3 sections, and they are as

follows: maternal sociodemographic and lifestyle characteristics; attitude toward use of medications and natural products; and medication and natural products risk assessment during pregnancy. The data has been reviewed thoroughly to rule out any presence of duplication using the reported maternal characteristics, date and time of questionnaire completion. Through a period of 2-3 months, the participants' responses have been collected via anonymously internet-based, self-completed, questionnaire shared through the commonly used social networks in Saudi Arabia. Furthermore, data were collected through interview using printed copies of the questionnaire at obstetrics and gynecology clinics as well as the pediatric clinics by the research team and trained volunteers. A brief pilot study preceded the main study for the purpose of testing the questionnaire for any major defect.

- **Ethics**

An informed consent has been obtained from participants. A description of the study has been given to responders, and upon this a "Yes" or "No" question have been asked for their willingness to participate. The collected data were processed and analyzed anonymously. **The study was done after approval of ethical board of King Faisal University.**

- **Data analysis**

Under the supervision of a statistician, the data were analyzed using SPSS Statistics version 21. The data were analyzed using selected appropriate statistical testes. A p value of <0.05 was considered significant in the study.

RESULTS

Biographical Data

More than 300 women have responded to the study survey. A total of 184 responders met the criteria and were involved in this study. Their average age is 27.60 ± 5.9 SD. The average number of children is 2 ± 1.9 SD. Of which, 50.5% were pregnant and 53.8% have a child less than 1 year old. 66.3% of the participants were living in the urban areas, while 33.7% were living in rural areas. The majority of participants were bachelor, representing 56% of the responders, while the remaining 26.6% are secondary school graduate and 17.4% have other educational levels. The most frequently reported occupation is house wife in 51.1% of responses followed by students 22.8%. A

summary of biographical data is reported in table 1.

Pregnant attitude

The result showed that in pregnancy 29.2% of pregnant women avoided using prescribed medications and 40.7% avoided non-prescribed. On the top of all avoided medications, paracetamol has been avoided by 33.9% women, followed by supplements (e.g. iron and calcium), antibiotic, and NSAID respectively with few other medications (Figure 1). By asking the women about the reason made them to avoid medication use, 55.3% thought that they are harmful to the fetus, 18.4% said that they may affect pregnancy (e.g. abortive), and the rest were afraid of their side effects.

In regard to natural products, 33.3% of women have avoided natural products during pregnancy. Herbal was on the top of the avoided natural product by 35.7% followed by fruits and vegetables in 28.6% of the cases and dairy products by 10.7%. Reasons given were similar to those given for medication avoidance, 70.6% for fearing of its effect on fetus and pregnancy and 17.6% for its side effect.

Approximately, 58% of the responding women always looked at the medication leaflet before using that medication, and 50% always looked for its safeness. Regarding obtaining and understanding information about substance use or a medical condition, 32% of pregnant women never found it difficult to obtain information and 40% found it sometimes difficult to understand that information. Most frequently reported information sources were physician, internet, and friend or family members respectively. 58.3% reported that they have been asked by their doctors about their pregnancy status before prescribing medication when they were sick. The type of residency, educational level, and occupation have no significance effect on the pregnant attitude toward avoiding prescribed medication, non-prescribed, and natural products (e.g. herbal, fruits, vegetables..etc) with a p-value of more than 0.05. Table 2 shows the participants' responses.

Risk assessment:

In this section, women have reported the substances that they believe that they are harmful during pregnancy. Pain killers and antibiotics are the most common medications believed to be harmful during pregnancy, 32% and 16% respectively. 26% of the women either don't know or remember any harmful medication and

the remaining 26% represents a variety of nonspecific medications. Regarding herbals, cinnamon, ginger, and fenugreek are the most commonly believed to be harmful during pregnancy, 38%, 11%, and 10% respectively. 35% reported other random herbals, and the rest did not know any herbal to be harmful. The majority of the participants (43%) believe that pineapple must be avoided during pregnancy. Other food include spicy food (12%), caffeinated drinks (6%), and meat (5%). The remaining responses included 30% of other variable food product (like dairy and sea food) and 4% are unaware of any food to be dangerous. Table 3 shows the reported products believed to risk pregnancy. 1st trimester is believed to be the critical period in which medications and herbals should be avoided followed by the whole pregnancy period, 56% and 28% for medication use and 19% and 17% for herbals use respectively. In addition, all pregnancy is believed to be a critical period where food use should be avoided followed by the 1st trimester, 32% and 28% respectively.

Tables

Table1 : Biographical data			
		Mean	SD
Age		27.60	5.928
Number of children		2.05	1.88
		%	
Pregnancy	Non-pregnant	49.5	
	pregnant	50.5	
Child ≤ 1year	No	46.2	
	yes	53.8	
Resident	Rural	33.7%	
	Urban	66.3%	
Education	Bachelor	56.0	
	Diploma	9.8	
	Intermediate	2.7	
	Master	2.2	
	Primary	2.7	
	Secondary	26.6	
Occupation	House wife	51.1	
	Student	22.8	
	Educationalist	12.0	
	Health care provider	7.1	
	Administrative, Business, Financial, Office work	3.3	
	Other	3.8	

Before using any medication, do you look at the medication leaflet?	Always	7.8%
	Often	0.2%
	Sometimes	3.8%
	Seldom	4.6%
	Never	3.7%
Before using any medication, do you look for information about its safeness?	Always	9.5%
	Often	9.3%
	Sometimes	4.7%
	Seldom	3.3%
	Never	3.3%
Have you had a difficulty in obtaining information about substance use or your medical condition?	Always	4.6%
	Often	2.0%
	Sometimes	9.6%
	Seldom	1.3%
	Never	2.4%
Have you had a difficulty in understanding information about substance use or your medical condition?	Always	0.9%
	Often	5.5%
	Sometimes	9.8%
	Seldom	1.3%
	Never	1.5%
when you were sick, Have you been asked by the doctor about your pregnancy status before prescribing medication?	Always	8.3%
	Often	6.7%
	Sometimes	4.8%
	Seldom	5.5%
	Never	3.7%

Medication must be avoided during pregnancy	Pain Killers	32%
	Antibiotics	16%
	Nonspecific	9%
	Other	18%
	I don't know	26%
Herbal must be avoided during pregnancy	Cinamon	38%
	Ginger	11%
	Fenugreek	10%
	Garden cress	4%
	Myrrh	4%
	Other	27%
	I don't know	4%
Food must be avoided during pregnancy	Pineapple	43%
	Spicy food	12%
	Caffeinated drinks (Coffee, tea)	6%
	Meat (Processed, uncooked, red, frozen)	5%
	Other	30%
	I don't know	4%

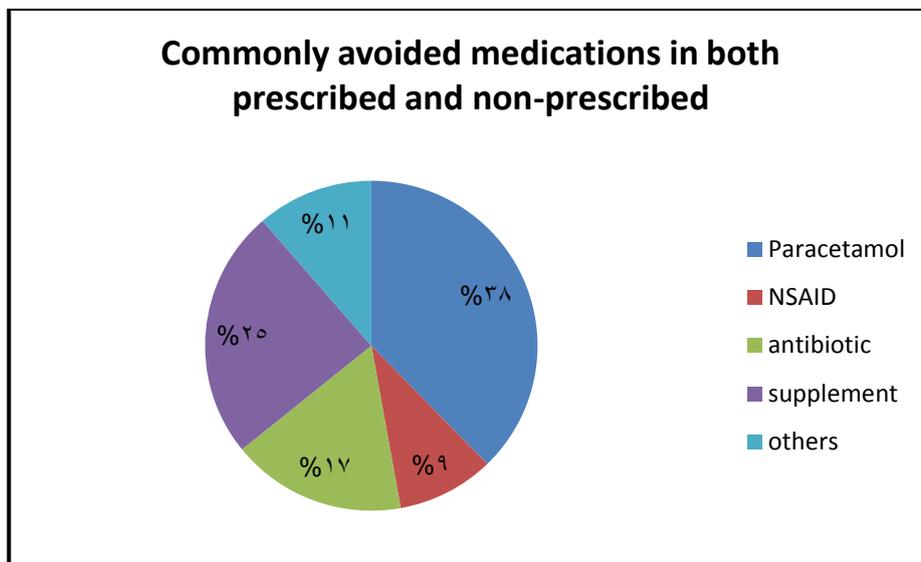


Figure 1: Commonly avoided medications in both prescribed and non-prescribed

DISCUSSION

This is the first study conducted in Alahsa region, Saudi Arabia to estimate the perception and attitude of pregnant women about medication and natural products use. The educational status of women participating in our study is in agreement with that reported for Saudi women by the World Bank in their report for the period between 2000 and 2008, which states that 95.9% of female between the age 15 and 24 and 79.4% of female aged above 15 years are educated, at least primary school. According to the World Bank report between the year 2000 and 2008, 60% of college students in Saudi Arabia are female, but only 21% of its labor force are women^[23].

The results showed that 29.2% of the pregnant women avoided using prescribed medications during pregnancy, and 40.7% avoided non-prescribed medicines. On the top of all avoided medications, paracetamol has been avoided by 33.9% of women, followed by supplements (e.g. iron and calcium), antibiotics, and NSAID respectively with few other medications. Compared to other conducted studies, it has been found that the use of medications during pregnancy was reported by most of the pregnant women, and paracetamol was the most frequent medicine used^[24].

By asking the women about the reasons that made them avoiding these medications, the majority 55.3% thought they are harmful to the fetus, 18.4% said they may affect pregnancy (i.e. abortive), and the rest were afraid of the side effects and other reasons. According to the FDA drug risk categorization, paracetamol is in the B category which is somewhat considered safe in pregnancy^[25]. The supplements like

iron and calcium are safe and important in pregnancy, but pregnant women may avoid using them because of the side effects they cause; constipation for instance^[26]. The FDA classify the common NSAIDs in the B and D groups according to the type, therefore a suitable and less risky NSAID has to be prescribed if needed^[25]. Antibiotics are variable in the risk to the fetus, some of them are safe and classified in A category, e.g. fucidic acid, and others are teratogenic and classified in the X group which should not be given to a pregnant female^[27]. In regard to natural products, 33.3% of women have avoided natural products during pregnancy. Herbal was on the top of the avoided natural products by 35.7% followed by fruits and vegetables in 28.6% of the cases and diary by 10.7%. Reasons given were similar to those given for medication avoidance, 70.6% for fearing of its effect on fetus and pregnancy and 17.6% for its side effect. Very few trials have been published regarding the potential benefits of herbal products use during pregnancy or lactation^[28]. Ginger is the only well-established herbal product as an effective treatment for nausea and vomiting as shown in a recent systematic review^[29].

Approximately, 58% of women always looked at the medication leaflet before using that medication, and 50% always looked for its safeness. This is reflecting a highly cautious mothers, who care about the health of their babies. The majority did not find it difficult to obtain information about substance use or medical conditions indicating a widely available access to information sources, e.g. internet, physician, pharmacist...etc. A good

level of education can be reflected by the high percentage of those who did not find it always difficult to understand information about substance use or medical conditions (Sometimes 40%, never 32%, seldom 21.3%). A very small number of less than 1% of the participants found it always difficult to understand the information. The participants were mainly referring to physicians and internet to obtain the information followed by friend and family. The majority of the participants reported that they have been asked about their pregnancy status when they have been sick and were to be prescribed with medications. This is an indicator of the physician awareness about the teratogenicity that drug may carry to the fetus. The type of residency, educational level, and occupation have no significance effect on the pregnant attitude toward medications and natural products with a p-value of more than 0.05.

32% of participant think that painkillers must be avoided during pregnancy and 16% believe that antibiotic must be avoided as well. The responses given were not specific suggesting that women should be educated more about the safer choices. However, their answers indicate cautious mothers. According to the FDA drug risk categorization, paracetamol is in the B category, which is somewhat safe in pregnancy [25]. The FDA classify the common NSAID in the B and D groups according to the type, therefore a suitable NSAID should be prescribed. Antibiotics are variable in their risk to the fetus, some of them are safe and classified in A category, e.g. fucidic acid, and others are teratogenic and classified in the X group, which should not be given to a pregnant female [27]. Cinnamon, ginger, and fenugreek were the most frequently reported herbals to be avoided during pregnancy. There is no well-established study showing the adverse effect of cinnamon during pregnancy [30]. However, some studies showed that some types of cinnamon can have emmenagogue and abortifacient effects [16]. In a large cohort study on 1020 pregnant women exposed to ginger, ginger has been found to be safe during pregnancy and did not show any congenital malformation, however, one study has reported that ginger can have abortifacient, emmenagogue and mutagenic effects [16,31,32]. It has been found that fenugreek consumption during pregnancy is associated with congenital malformation and birth defect, especially in the CNS. Furthermore, a study conducted on mice showed that fenugreek extract has impaired the

sensorimotor development and function [33]. Pineapple is the most commonly reported food product by pregnant women that must be avoided during pregnancy. Pineapple is considered as a taboo among Saudi women and women from other countries [34]. The available evidence is not enough to say that pineapple is unsafe during pregnancy. In addition, all the conducted studies did not exhibit any abortifacient or any other adverse effect of pineapple during pregnancy among rats [35], [36]. Spicy food is reported also as one of the food stuff to be avoided during pregnancy. It is in agreement with a study conducted in 1995 that showed that Saudi women have avoided spicy food during pregnancy in addition to other substance due variable reasons [37]. A study aiming to find out the triggers of spontaneous preterm delivery found that spicy food may work as a trigger for preterm labor or preterm premature rupture of membrane in susceptible women [38]. 1st trimester of pregnancy has been reported by most women as the critical trimester where congenital defect risk is increased. This shows a good knowledge of mothers about the period when the fetus is at increased risk of mutation. 1st trimester is considered as critical period, because it is the time where organogenesis occurs [39].

CONCLUSION

Most pregnant women avoid using medications and natural products during pregnancy particularly in the first trimester, but not all of them carry a risk to the pregnancy. The reasons for avoidance were variable, but it was mainly due to fear of the substance side effects on the fetus. For that reason, most of them were reading about the safety of the medications before using them, but a number of women found it difficult to understand the information about the medicines. Common beliefs about certain natural products to be harmful during pregnancy have been observed among pregnant women, however, there is no established evidence about their risk to pregnancy. There was no significant relationship between the sociodemographic characteristics of the pregnant women and their beliefs and attitude toward medications and natural products. In conclusion, pregnant women should be educated more about unsafe products during pregnancy and the time of critical period as well as that they should not use any medicines without being prescribed by their physicians. Women's beliefs about natural

products need further exploration because of the lack of evidence proving their harmfulness.

ACKNOWLEDGMENT

The authors extend their gratitude to Naqaa Mohammed Almubarak for her effort and participation in this work as a data collector.

REFERENCES

- 1- <https://www.federalregister.gov/d/2014-28241>
- 2- **McCarter-Spaulling D (2005):** Medications in pregnancy and lactation. *American Journal of Maternal Child Nursing*, 30(1): 10–17
- 3- **Bowen ME, Ray WA, Arbogast PG, Ding H and Cooper WO (2008):** Increasing exposure to angiotensin-converting enzyme inhibitors in pregnancy. *American Journal of Obstetrics and Gynecology*, 198(3): e291–295
- 4- **Cooper WO, Hickson GB, Ray WA (2004):** Prescriptions for contraindicated category X drugs in pregnancy among women enrolled in TennCare. *Paediatric and Perinatal Epidemiology*, 18(2):106–111
- 5- **Gedeon C, Koren G (2006):** Designing Pregnancy Centered Medications: Drugs Which Do Not Cross the Human Placenta. *Placenta*, 27(8): 861-868
- 6- **Nelson MM, Forfar JO (1971):** Associations between drugs administered during pregnancy and congenital abnormalities of the fetus. *Br Med J.*, 1 (5748): 523-527
- 7- **Li DK, Liu L, Odouli R (2003):** Exposure to Non-steroidal Anti-inflammatory Drugs during Pregnancy and Risk of Miscarriage. *BMJ.*, 327 (7411): 368
- 8- **Anderka M, Mitchell AA, Louik C, Werler MM, Hernandez-Diaz S, Rasmussen SA (2012):** Medications used to treat nausea and vomiting of pregnancy and the risk of selected birth defects, *Birth Defects Res. A Clin. Mol. Teratol.*, 94(1): 22–30
- 9- **Carmichael SL, Shaw GM, Laurent C, Croughan MS, Olney RS, Lammer EJ (2005):** Maternal Progestin Intake and Risk of Hypospadias. *Arch Pediatr. Adolesc. Med.*, 159(10): 957–62.
- 10- **Czeizel AE, Kazy Z, Puho E (2003):** A Population-Based Case-Control Teratological Study of Oral Nystatin Treatment During Pregnancy. *Scand J Infect Dis.*, 35(11–12):830–835.
- 11- **Rodriguez-Pinilla E, Mejias C, Prieto-Merino D, Fernandez P, Martinez-Frias ML, Group EW (2008):** Risk of Hypospadias in Newborn Infants Exposed to Valproic Acid during the First Trimester of Pregnancy: a Case-Control Study in Spain. *Drug Saf.*, 31(6):537–43.
- 12- www.who.int/drugresistance/Manual1_HowtoInvestigate.pdf
- 13- **Khadivzadeh T, Ghabel M (2012):** Complementary and Alternative Medicine Use in Pregnancy in Mashhad, Iran. *J Nurs Midwifery Res.*, 17(4):263–269
- 14- **Wu CH, Wang CC, Kennedy J(2011):** Changes in Herb and Dietary Supplement Use in the U.S. Adult Population: a Comparison of the 2002 and 2007 National Health Interview Surveys. *Clin Ther.*, 13(11):1749–1758.
- 15- **Francesco L, Alfredo V, Martina M et al .(2010):** Use, Attitudes and Knowledge of Complementary and Alternative Drugs (CADs) among Pregnant Women: a Preliminary Survey in Tuscany. *eCAM.*, 7(4): 477.
- 16- **Ernst E (2002):** Herbal medicinal products during pregnancy: are they safe?. *BJOG.*, 109(3): 227–235
- 17- **Chuang C, Doyle P, Wang J et al .(2006):** Herbal Medicines Used During the First Trimester and Major Congenital Malformations. *Drug Safety*, 29(6): 537-548
- 18- **Lupattelli A, Spigset O, Twigg M et al (2014):** Medication Use in Pregnancy: a Cross-Sectional, Multinational Web-Based Study. *BMJ. Open*, 4 (2): e004365
- 19- **Kennedy D, Lupattelli A, Koren Get al .(2013):** Herbal medicine use in pregnancy: results of a multinational study, *BMC. Complementary and Alternative Medicine*, 13: 355
- 20- **Pallivalappila A, Stewart D, Shetty Aet al (2014):** Complementary and alternative medicine use during early pregnancy, *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 181: 251–255
- 21- **Chuang C, Changb P, Hsiehc W et al .(2009):** Chinese herbal medicine use in Taiwan during pregnancy and the postpartum period: A population-based cohort study, *International Journal of Nursing Studies*, 46 (6): 787–795
- 22- **Zaki NM, Albarraq AA (2014):** Use, attitudes and knowledge of medications among pregnant women: A Saudi study, *Saudi Pharmaceutical Journal*, 22 (5): 419-428
23. <http://documents.worldbank.org/curated/en/873011468299062424/pdf/436480WP0Box321nder1BW200701PUBLIC1.pdf>
- 24- **Headley J, Northstone K, Simmons H, Golding J (2004):** Medication use during pregnancy: data from the Avon Longitudinal Study of Parents and Children. *European Journal of Clinical Pharmacology*, 60(5): 355 - 361
- 25- **Servey J, Chang J(2014):** Over-the-Counter Medications in Pregnancy [Internet]. *American Family Physician*. Available from: <http://www.aafp.org/afp/2014/1015/p548.html#afp20141015p548-b10>
- 26- **Tolkien Z, Stecher L, Mander AP, Pereira DIA, Powell JJ (2015):** Ferrous Sulfate Supplementation Causes Significant Gastrointestinal Side-Effects in Adults: A Systematic Review and Meta-Analysis. *PLoS One*, 10(2): e0117383.
- 27- **Nahum GG, Uhl K, Kennedy DL (2006):** Antibiotic Use in Pregnancy and Lactation. *Obstetrics & Gynecology*, 107(5):1120–38.
- 28- **Westfall RE (2001):** Herbal medicine in pregnancy and childbirth. *Advances in Therapy*, 18(1):47–55.

- 29- Ernst E, Pittler MH (2000):** Efficacy of ginger for nausea and vomiting: a systematic review of randomized clinical trials. *British Journal of Anaesthesia*, 84(3):367–71.
- 30- Zaidi SF, Aziz M, Muhammad JS, Kadowaki M (2015):** Review: Diverse pharmacological properties of *Cinnamomum cassia*: A review. *Pakistan journal of pharmaceutical sciences*, 28(4):1433–1438.
- 31- Choi JS, Han JY, Ahn HK, Lee SW, Koong MK, Velazquez-Armenta EY et al (2014):** Assessment of fetal and neonatal outcomes in the offspring of women who had been treated with dried ginger (*Zingiberis rhizoma siccus*) for a variety of illnesses during pregnancy. *Journal of Obstetrics and Gynaecology*, 35(2):125–30.
- 32- Heitmann K, Nordeng H, Holst L(2013):** Safety of ginger use in pregnancy: results from a large population-based cohort study. *European Journal of Clinical Pharmacology*, 69(2):269–277.
- 33- Khalki L, M’Hamed S, Sokar Z, Bennis M, Vinay L, Bras H et al .(2013):** Prenatal Exposure to Fenugreek Impairs Sensorimotor Development and the Operation of Spinal Cord Networks in Mice. *PLoS ONE*, 8(11):e80013
- 34- Trigo M, Roncada M, Stewien G, Pereira I (1989):** Food taboos in the northern region of Brazil. *Revista de Saúde Pública*, 23(6):455–64.
- 35- Yakubu M, Olawepo O, Fasoranti G (2011):** Ananas comosus: Is the unripe fruit juice an abortifacient in pregnant Wistar rats?. *The European Journal of Contraception & Reproductive Health Care*, 16(5):397–402.
- 36- Hu J, Lin H, Shen J, Lan J, Ma C, Zhao Y et al .(2011):** Developmental toxicity of orally administered pineapple leaf extract in rats. *Food and Chemical Toxicology*, 49(6):1455–1463.
- 37- Al-Kanhal MA, Bani IA (1995):** Food habits during pregnancy among Saudi women. *Int J Vitam Nutr Res.*, 65(3):206–210.
- 38- Hernández-Díaz S, Boeke CE, Romans AT et al. (2014):** Triggers of spontaneous preterm delivery – Why today?. *Paediatric and perinatal epidemiology*, 28(2):79-87.
- 39- Thorpe PG, Gilboa SM, Hernandez-Diaz S et al. (2013):** Medications in the First Trimester of Pregnancy: Most Common Exposures and Critical Gaps in Understanding Fetal Risk. *Pharmacoepidemiology and drug safety*, 22(9):1013-1018.