The Libyan Medical Journal
المجلة الليبية الطبية
Original Article

PREVALENCE AND DETERMINANTS OF SPICES AND SEEDS USED IN PREGNANCY

ZAHEERA SAADIA
DEPARTMENT OF OBSTETRICS & GYNAECOLOGY, QASSIM UNIVERSITY, QASSIM, SAUDI ARABIA

ARTICLE INFORMATION:

Article History:
Received: 20 July, 2013
Accepted in revised form: 23 February, 2014
Published: 4 October 2015

Corresponding author:
Zaheera Saadia,
E-mail: zaheerasaadia@hotmail.com

Keyword:
Pregnancy, Prevalence, Spices, Seeds

معلومات المقال:

تاريخ المقال:
أستلم في: 20 يوليو، 2013
قبل بعد المراجعة في: 23 فبراير، 2014
نشر في: 4 أكتوبر، 2015

المؤلف المسؤول:
البريد الالكتروني:
zaheerasaadia@hotmail.com

الكلم ات المفتاحية:
الحمل، معدل الإنتشار، التوابل، البذور

ABSTRACT

Purpose: The use of spices and seeds in pregnancy in not new however it is not subjected to any regulations like conventional medications. They are generally promoted as safe in pregnancy but concerns have been raised about their toxicity.
This study tries to determine the prevalence, and identify the commonly used seeds and spices in pregnancy. The secondary objective was to explore the factors or predictors for using these herbs in pregnancy.
Methods: This study was conducted as a cross sectional survey and comprised women attending the Qassim University clinic for a period of 6 months from July 1st 2012-31st Dec 2012. Total of 375 women were interviewed for demographic variables, type of the herbs they were using and the reason behind their use. The source of information or motivation was also asked. SPSS version 16 and Microsoft Office 2007 for windows 7 was used. Descriptive statistics was used to present the demographical variables and multinomial regression was used to explain the effects of different variables.
Results: Most of the participants were over the age of 41, attended primary school or below, were housewives and were G2-4 or above. Only 5% of participants had postgraduate education. Most of the participants (37%) were in first trimester of pregnancy. A majority of population 94.4% were using herbal products during pregnancy. Ginger (Zingiber officinale) 71 (18.93%), Black seeds (Nigella Sativa) 69 (18.4%) and hilba (Fenugreek) (15.7%), were the three most commonly used herbs.
Nausea and vomiting of pregnancy 63 (16.80%) and Gastroesophageal reflex 60 (16%) were the commonest conditions supposed to be treated by herbs. The multinomial logistic regression of herbs on age, education, occupation, parity, period of gestation, family motivation, previous experience and current diabetes was statistically significant ($\chi^2 = 87.346$, $p < .000$). The reference group for the logistic regression model was the individuals who reported no herbal use (n = 21, 5.6%). When evaluated individually education, occupation and family motivation, were significant predictors of whether a participant would be in the herbal group, compared to the group who was taking no herbs in pregnancy.
Conclusion: Herbal use is very common amongst pregnant women in the area (94.4%). Low education status and family motivation are the major determinants of using herbs in pregnancy. Ginger, hilba and black seeds are the most popular herbs. Considering the great prevalence (94.4%) of herbal use in pregnancy an urgent need exists to explore the situation all over the country. Further research is required to explore their effects on the developing offsprings and education programs are required for antenatal women to guide them regarding the safety of herbal use based on scientific evidence.

الهدف: استخدام التوابل والبذور في فترة الحمل ليس شيئا جديد ولكنها لا تخضع لأية رقابه مثل الأدوية التقليدية. يتم الترويج لها بصفة عامة على انها آمنة أثناء الحمل ولكن أثيرت مخاوف من سميتها
تحاول هذه الدراسة لتحديد مدى انتشار، والتعرف على البذور والتوابل التي يشيع استخدامها في فترة الحمل. كان الهدف الثاني استكشاف العوامل أو المتنبئات لاستخدام هذه الأعشاب في فترة الحمل.
الطرق: أجريت هذه الدراسة كدراسة مسح المقطعي ويشملت النساء اللواتي يحضرن عيادة جامعة القصيم لمدة 6 أشهر من 1/يوليو/2012 الى 31/ديسمبر/2012. أجريت مقابلات مع 375 امرأة حول للمتغيرات الديموغرافية و نوع الأعشاب التي كانت تستخدمها والسبب وراء استخدامها. وسئل أيضا عن مصدر المعلومات أو الدافع. تم استخدام النسخة 16 ومايكروسوفت أوفيس 2007 ويندوز 7. تم استخدام الإحصاء الوصفي لتقديم المتغيرات SPSS برنامج الديموغرافية وكان يستخدم الانحدار متعدد الحدود لشرح الآثار المترتبة على المتغيرات المختلفة.
النتائج: وكانت معظم المشاركات فوق سن ال 41،حضرن المرحلة الابتدائية أو أقل، وكن ربات البيوت وكن G أو 2-4

Copyright © 2015. LMJ. This is an open access article distributed under the Creative Commons Attribution 3.0 License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.
Citation: Libyan Medical J 1: 140 14752. 2015 - http://dx.doi.org/10.5542/LMJ.v1i0.14014752

أعلى. وكانت ٥٪ فقط من المشاركات ذوي تعليم العالي. وكانت معظم المشاركات (37%) في الأشهر الثلاثة الأولى من الحمل. وكانت غالبية السكان 94.4% يستخدمن المنتجات العشبية خلال فترة الحمل. الزنجبيل ٧١ (18.93%) والبذور السوداء (الحبة السوداء) 69 (18.4%) و الحلبة (15.7%)، كانت الأعشاب الثلاثة الأكثر شيوعا.
الغثيان والقيء من الحمل 63 (16.80%) و الجزر المعدي المريئي 60 (16%) كانت من الحالات الأكثر شيوعا من المفترض أن تعالج من قبل الأعشاب. كان الانحدار اللوجستي متعدد الحدود من الأعشاب على العمر، والتعليم، والمهنة، والمساواة، فترة الحمل، والدافع الأسرة، والخبرة السابقة والسكري الحالي ذو دلالة إحصائية (χ2 = 87.346، 0.000). وكانت المجموعة المرجعية لنموذج الانحدار اللوجستي الأفراد الذين لم يستخدمو الاعشاب (ن = 21، 5.6%). عند تقييمها بشكل فردي التعليم والمهنة والحوافز P < العائلية، متنبئات قوية عن ما إذا كان أحد المشاركين سيكون في المجموعة العشبية، مقارنة مع المجموعة التي لا تأخذ أية الأعشاب في الحمل.
الاستنتاج: استخدام الأعشاب هو شائع جدا بين النساء الحوامل في المنطقة (94.4%). حالة انخفاض التعليموالحوافز العائلية هي المحددات الرئيسية لاستخدام الأعشاب في الحمل. الزنجبيل، الحلبه والبذور السوداء هي الأعشاب الأكثر شعبية. نظرا للانتشار الكبير (94.4%) من استخدام الأعشاب في الحمل فإن ثمة حاجة عاجلة لاستكشاف الوضع في جميع أنحاء البلاد. بناء على هذا يطلب مزيد من البحوث لاستكشاف آثارها على الاطفال ويطلب برامج تعليمية تستند إلى أدلة علمية للنساء قبل الولادة لإرشادهم فيما يتعلق بسلامة استخدام الاعشاب.

INTRODUCTION

Use of herbs in the form of spices and seeds have been an old tradition.[1] Because of risk of teratogenicity to the fetus women are scare of using allopathic medications and therefore turn towards traditional spices and herbs which are promoted to be safe.[1] Peters et al researched that internet sites are promoting the use of these products without documenting any evidence of fetal risks.[2] Recently concerns have been raised on the possibility of teratogenicity of these herbal products especially if used during first trimester.[3] Traditional medications are popular in the Middle East region and a study from United Arab Emirates has reported that 60% of women are using herbal medications in pregnancy.[4] There are reports of using herbs and seeds in SaudiArabia.[5] However the data is scanty therefore in this study prevalence and predictors of using herbs in pregnancy from AlQassim region were explored. The study will serve as a pilot study to identify products on which further research can be conducted.

METHODOLOGY

It was a cross sectional survey conducted over a period of 6months starting from July 2012 to 31st December 2012. All women presenting for antenatal University clinic and willing to fill a self-structured proforma were included in the study. Total of 375 women were included after verbal consent. This sample size had a Confidence level of 95%. The proforma included details about demographic variables including age, education, period of gestation and occupation. Women were asked to name the seeds or herbs they are using and were also asked the reason behind using them. The source of information or motivation was also asked. To keep the data anonymous patients name or identification numbers were not included. SPSS version 16 and Microsoft Office 2007 for windows 7 was

Table 1: Count and Percent Statistics for Demographic Variables

Variable	Level	Frequency	Percent
Age	Below 20	82	21.9
	21-40	127	33.9
	Above 41	166	44.3
Education	Primary or below	161	42.9
	Completed school	128	34.1
	College	81	21.6
	University (Post graduation)	05	1.3
Occupation	House wife	321	85.6
	Working	54	14.4
Parity	Primiparous	57	15.2
	G2-4	155	43.7
	G5 and above	148	41.7
Period of gestation	First trimester	139	37.1
	Second trimester	75	20
	Third trimester	70	18.7
	Post-partum	91	24.3

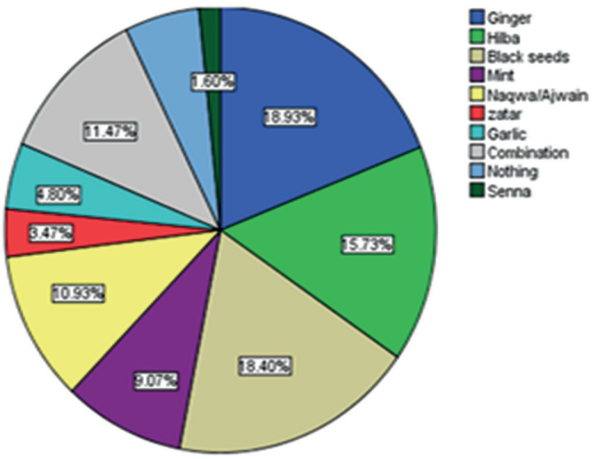

Figure 1: Percentage distribution of commonly used herbs in pregnency

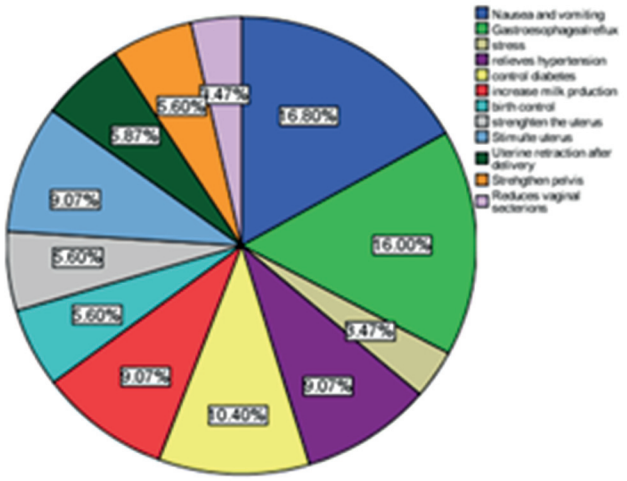

Figure 2: Conditions supposed to be treated by herbal intake

used. Descriptive statistics was used to present the demographical variables and multinomial regression was used to explain the effects of different variables.

RESULTS

Most of the participants were over the age of 41, attended primary school or below, were housewives and were G2-4 or above. Only 5% of participants had postgraduate education. Most of the participants 139 (37%) were in first trimester of pregnancy (Table 1).

A majority of population 354 (94.4%) were using herbal products during pregnancy Ginger Zingiber officinale) 71 (18.93%), (Nigella Sativa) 69 (18.4%) and hilba (Fenugreek) (15.7%), were the three most commonly used herbs (Figure-1).

Nausea and vomiting of pregnancy 63 (16.80%), Gastroesophageal reflex 60 (16%) were the commonest conditions supposed to be treated by herbs (Figure-2).

The multinomial logistic regression of herbs on age, education, occupation, parity, period of gestation, family motivation, previous experience and current diabetes was statistically significant ($\chi^2 = 87.346$, $p < .000$). The reference group for the logistic regression model was the individuals who reported no herbal use (n = 21, 5.6%). When evaluated individually education, occupation, family motivation, and current diabetes were significant predictors of whether a participant would be in the herbal group, compared to the group who was taking no herbs in pregnancy (Table-2).

Women with Education below primary were 6.8 times more likely to use herbs as compared to no use group (Table 2). Being house wife was a significant predictor of whether a participant was categorized in the herbal group compared to no intake of herbs. They were 7.6 times more likely to take herbs as compared to working women (Table 2). Women who had family motivation were 38.8 times more likely to say yes to herbal intake verses no intake group compared to individuals who had no family motivation. Similarly women with current diabetes were 0.014 times less likely to take herbs as compared to those who were not diabetic (Table-2). Gestational age, Parity, previous experience, current hypertension, previous history of preterm labour or IUGR was not significant predictors for herbal intake.

DISCUSSION

The increase in use of herbal products has been noticed all over the world.[6] In United States the use of traditional products increased from 14.2% in 1998-1999 to 18.8% in 2002.[7] A wide range of prevalence reported in literature ranging from 7-56% depends upon cultural and regional differences.[1,8] In this study a large number of different herbal products were noticed to be used by pregnant women including the use of Ginger (Zingiber officinale), Hilba (Fenugreek), Mint (menthe/lemiacia), Blackseeds (nigella sative/Black cumin), Naqwa/Ajwain (Carom Seeds), zatar (oreganum), garlic (Allium sativum) and senna (Cathartocarpus) (Fig-1). Most of them were used in the form of tea or seeds were mixed and crushed to make a paste. A wide variety of pregnancy associated conditions were supposed to be treated by these herbs. The most common conditions were nausea and vomiting, gastric reflux, milk let down, control diabetes, relieve stress, stimulation and strengthening of uterus and contraceptive efficacy (Fig-2). Ginger has been the most commonly used product in pregnancy which was believed to be antiemetic. Literature review reports its efficacy in relieving nausea and vomiting of pregnancy as compared to placebo.[9,10,11] However ginger has been found to inhibit testosterone binding in the fetus due to its thrombaxane synthatase activity and thus possible some mutagenic activity.[12] Thus there is no consensus yet on the safety of ginger use in pregnancy and there is a need to confirm the results of preliminary data. Second common herb popular in the region was Hilba or Fenugreek (Trigonella foenum graecum) which was being used by 15.73%

Table 2: Model Summary for Multinomial Logistic Regression of Herbs on Demographic Variables

Herbs	Predictor	B	Std. Error	Wald	Df	Sig.	Exp(B)
YES	Intercept	-21.05	2.629	64.142	1.00	0.000	
	Below 25	-0.544	0.795	0.468	1.00	0.494	0.580
	25-30	0.267	0.853	0.098	1.00	0.754	1.307
	Above 30	0b	.	.	0.00	.	.
	Primary or Below	22.645	1.541	215.837	1.00	0.000	6.833E9
	Middle School	21.497	1.124	365.797	1.00	0.00	2.168E9
	High School	23.537	0.000	.	1.00	.	1.668E10
	College or Above	0b	.	.	0.00	.	.
	Housewife	2.034	.925	4.833	1.00	0.028	7.648
	Working	0b	.	.	0.00	.	.
	Primiparous	-1.494	1.113	1.803	1.00	0.180	0.225
	G2-4	-1.442	0.814	3.138	1.00	.077	0.236
	G5 and above	0b	.	.	0.00	.	.
	First trimester	-0.659	0.815	0.655	1.00	0.418	0.517
	Second trimester	0.400	1.054	0.144	1.00	0.704	1.492
	Third trimester	1.681	1.391	1.460	0.00	0.227	5.368
	Puerperium	0b			0.00		
	Family motivation Yes	3.661	1.053	12.083	1.00	.001	38.898
	No	0b	.	.	0.00	.	.
	Previous experience						
	Yes	-1.209	1.266	0.911	1.00	0.340	0.299
	No	0b	.	.	0.00	.	.
	Internet literature						
	Yes	0.489	1.372	0.127	1.00	0.722	1.630
	No	0b	.	.	0.00	.	.
	Print media						
	Yes	1.813	1.212	2.237	1.00	0.135	6.128
	No	0b	.	.	0.00	.	.
	Previous abortion						
	Yes	-.846	0.877	0.930	1.00	0.335	0.429
	No	0b			0.00		
	Current Hypertension						
	Yes	-0.471	2.264	0.043	1.00	0.835	0.625
	No	0b			0.00		
	Current Diabetes						
	Yes	-4.288	0.995	18.588	1.00	0.000	0.014
	No	0b			0.00		
	Previous IUD/SB						
	Yes	8.461	15.619	0.293	1.00	0.588	4.728E3
	No	0b			.000		

of pregnant women. It was considered to be galactogogeous. A survey conducted in United States reported that 57% of lactation consultants were promoting the use of fenugreek.[13] Animal data has revealed that fenugreek use in pregnancy can result in intrauterine growth retardation (IUGR) and neurobehavioral problems during weaning period.[14] Similarly use of fenugreek during labour can result in maple syrup like odour in the urine of newborns.[15] This emphasizes the immediate need to consider research in its efficacy and possible side effect determination.

Mint was another commonly used herb in this study (Figure1). Women were using it to relieve gastric acidity and hypertension. When searched in the literature mint (chamomile or flax) use during the last two trimesters of pregnancy was not associated with low birth weight infants.[16] Use of menthe X villosa in rats was not associated with any type of fetal malformation however minor hemorrhages were noticed in the fetal liver, kidney and blood vessels.[17] This again raises concerns about the safety of mint use in pregnancy. Black seed (Nigella Sativa) was another commonly used herb in this study population. Women were using it both during pregnancy and in puerperium with the belief that it strengthens the uterus and promotes milk let down. Nigella Sative is found to be anti oxytocic in animal studies.[18] The hexane compound present in nigella sativa seeds has mild uterotrophic activity which has been linked to contraceptive efficacy.[19] It's also considered to be galactogogeous.[20] In this study population garlic was used by 18 (4.8%) of pregnant women (Fig-1). Women suffering from hypertension were mostly using it to prevent preeclampsia and control blood pressure. Prenatal exposure of garlic may affect behavior well into childhood. Children who were exposed during intrauterine life to garlic were more likely to eat garlic flavoured potatoes.[21] Animal studies have revealed the protective effect of garlic against the cypermethrin toxicity. It was observed that rats who were exposed to cypermethrin toxicity showed multiple malformations in their fetuses however concomitant use of garlic and ascorbic acid resulted in reduced incidence of these malformations.[22] Data from animal studies have revealed that Garlic supplementation can ameliorate the hypercholestremic related effects in pregnancy like low birthweight and reduced ossification of axial and appendicular bones.[23] Cochrane data base reveiw conducted by Meher S revealed that the data is insufficient to recommend garlic for prevention of preeclampsia.[24] Zatar (Oreganum) was used by women during puerperium to fasten the rate of involution of uterus and decrease vaginal secretions. Zatar has found to increase reproductive performance and induced increase rate of cellular deaths in embryos in animal studies.[25,26] Women were using Senna to stimulate the uterus for labour and as laxative in pregnancy There have been reports that use of senna in doses of 10-30 mg/day is not found to be associated with high risk of congenital malformations.[27] Higher doses of 4% senna occidential seeds in goats can result in post birth body development problems.[28] In this study three main predictors were noticed for herbal intake which were significant including education, occupation and family motivation (Table-2). Women with primary or below level education were 6.8 times more likely to take herbs in pregnancy as compared to women with University level education. House wives were 7.6 times more likely to take herbs as compared to working women. Family motivation was the most common drive for taking herbs and women with family motivation were 38.8 times more likely to take herbs during pregnancy. Print and electronic media has been the major source of motivation for pregnant women in the Europe as compared to this study population where family and friends were the major source of motivation.[29] The herbal products are not subjected to same regulations as the conventional drugs and their safety is not yet proven.[1] The effects of these herbs on the development of fetus are largly unknown and mostly speculated based on animal studies.[17,18,19,20] Considering the great prevalence (94.4%) use of herbs in pregnancy in the study population of AlQassim area an urgent need exists to explore the situation all over the country. Further research is required to explore their effects on the developing offsprings and education programs are required for antenatal women to guide them regarding the safety of herbal use based on scientific evidence.

LIMITATIONS OF THE STUDY

Being a single healthcare facility study it may not ideally represent the situation all over the region. However it will still highlight the prevailing situation in the region and guides towards the need for further studies in the area.

CONFLICT OF INTEREST

Author does not have any conflict of interest.

REFERENCES

1. Nordeng H, Bayne K, Havnen GC, Paulsen BS. Use of herbal drugs during pregnancy among 600 Norwegian women in relation to concurrent use of conventional drugs and pregnancy outcome. Complement Ther Clin Pract. 2011; 17(3):147-51.
2. Peters SL, Lind JN, Humphrey JR, Friedman JM,

Honein MA, Tassinari MS, Moore CA, Mathis LL, Broussard CS. Safe lists for medications in pregnancy: inadequate evidence base and inconsistent guidance from Web-based information, 2011.Pharmacoepidemiol Drug Saf. 2013; 22(3):324-8.

3. Chuang CH, Doyle P, Wang JD, Chang PJ, Lai JN, Chen PC. Herbal medicines used during the first trimester and major congenital malformations: an analysis of data from a pregnancy cohort study. Drug Saf. 2006;29(6):537-48.
4. AlBraik FA, Rutter PM, Brown D. A cross-sectional survey of herbal remedy taking by United Arab Emirate (UAE) citizens in Abu Dhabi. Pharmacoepidemiol Drug Saf. 2008;17(7):725-32.
5. Rathi SK, Elzubier A, Srinivasan MV. Traditional healing methods prevalent in Zulfi area. Ann Saudi Med. 1993;13(1):93-4.
6. Kikura-Hanajiri R, Uchiyama N, Goda Y. Survey of current trends in the abuse of psychotropic substances and plants in Japan. Leg Med (Tokyo). 2011;13(3):109-15.
7. Kelly JP, Kaufman DW, Kelley K, Rosenberg L, Anderson TE, Mitchell AA. Recent trends in use of herbal and other natural products. Arch Intern Med. 2005;165(3):281-6.
8. Holst L, Nordeng H, Haavik S. Use of herbal drugs during early pregnancy in relation to maternal characteristics and pregnancy outcome. Pharmacoepidemiol Drug Saf. 2008;17(2):151-9.
9. Ernst E, Pittler MH. Efficacy of ginger for nausea and vomiting: a systematic review of randomized clinical trials. Br J Anaesth. 2000;84(3):367-71.
10. Borrelli F, Capasso R, Aviello G, Pittler MH, Izzo AA. Effectiveness and safety of ginger in the treatment of pregnancy-induced nausea and vomiting. Obstet Gynecol. 2005;105(4):849-56.
11. Tsui B, Dennehy CE, Tsourounis C. A survey of dietary supplement use during pregnancy at an academic medical center. Am J Obstet Gynecol. 2001;185(2):433-7.
12. Backon J. Ginger in preventing nausea and vomiting of pregnancy; a caveat due to its thromboxane synthetase activity and effect on testosterone binding. Eur J Obstet Gynecol Reprod Biol. 1991;42(2):163-4.
13. Schaffir J, Czapla C. Survey of lactation instructors on folk traditions in breastfeeding. Breastfeed Med. 2012 ;7:230-3.
14. Khalki L, Bennis M, Sokar Z, Ba-M'hamed S. The developmental neurobehavioral effects of fenugreek seeds on prenatally exposed mice. J Ethnopharmacol. 2012 ;139(2):672-7
15. Korman SH, Cohen E, Preminger A. Pseudo-maple syrup urine disease due to maternal prenatal ingestion of fenugreek. J Paediatr Child Health. 2001;37(4):403-4.
16. Moussally K, Berard A. Exposure to specific herbal products during pregnancy and the risk of low birth weight. Altern Ther Health Med. 2012;8(2):36-43. PubMed PMID: 22516883.
17. da Silva Bezerra Guerra KS, Silva RL, Souza Maia MB, Schwarz A. Embryo and fetal toxicity of Mentha x villosa essential oil in Wistar rats. Pharm Biol. 2012 ;50(7):871-7.
18. Aqel M, Shaheen R. Effects of the volatile oil of Nigella sativa seeds on the uterine smooth muscle of rat and guinea pig. J Ethnopharmacol. 1996;52(1):23-6.
19. Keshri G, Singh MM, Lakshmi V, Kamboj VP. Post-coital contraceptive efficacy of the seeds of Nigella sativa in rats. Indian J Physiol Pharmacol. 1995;39(1):59-62.
20. Agrawala IP, Achar MV, Tamankar BP. Galactogogue action of Nigella sativa.Indian J Med Sci. 1971 ;25(8):535-7.
21. Hepper PG, Wells DL, Dornan JC, Lynch C. Long-term flavor recognition in humans with prenatal garlic experience. Dev Psychobiol. 2012 Jul 2. doi:10.1002/dev.21059. [Epub ahead of print] PubMed PMID: 22753112.
22. Assayed ME, Khalaf AA, Salem HA. Protective effects of garlic extract and vitamin C against in vivo cypermethrin-induced teratogenic effects in rat offspring. Food Chem Toxicol. 2010;48(11):3153-8.
23. El-Sayyad HI, Abou-El-Naga AM, Gadallah AA, Bakr IH. Protective effects of Allium sativum against defects of hypercholesterolemia on pregnant rats and their offspring. Int J Clin Exp Med. 2010 10;3(2):152-63.
24. Meher S, Duley L. Garlic for preventing pre-eclampsia and its complications. Cochrane Database Syst Rev. 2006 19;(3):CD006065. Review. PubMed PMID:16856110.

25. Allan P, Bilkei G. Oregano improves reproductive performance of sows. Theriogenology. 2005;63(3):716-21.

26. Domaracký M, Rehák P, Juhás S, Koppel J. Effects of selected plant essential oils on the growth and development of mouse preimplantation embryos in vivo. Physiol Res. 2007;56(1):97-104.

27. Acs N, Bánhidy F, Puhó EH, Czeizel AE. Senna treatment in pregnant women and congenital abnormalities in their offspring--a population-based case-control study. Reprod Toxicol. 2009;28(1):100-4.

28. Barbosa-Ferreira M, Pfister JA, Gotardo AT, Maiorka PC, Górniak SL.Intoxication by Senna occidentalis seeds in pregnant goats: prenatal and postnatal evaluation. Exp Toxicol Pathol. 2011;63(3):263-8.

29. Low Dog T. The use of botanicals during pregnancy and lactation. Altern Ther Health Med. 2009;15(1):54-8. Review.