

Knowledge regarding teratogens among women of childbearing age at a large tertiary care center in Saudi Arabia

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ABSTRACT

Aim: To investigate the knowledge of Saudi women regarding the teratogenic effects of environmental agents such as fever, some chronic conditions and medications and its association with certain socio-demographic factors. **Materials and Methods:** A survey based cross-sectional study was conducted on 315 Saudi women of childbearing age visiting OB/GYN clinics at a large tertiary care centre in Riyadh, Saudi Arabia. Knowledge of subjects on teratogenic risk of common entities was measured and nonparametric Mann-Whitney and Kruskal-Wallis tests were used to associate knowledge score with various predictors. **Results:** The response rate was 75%. Most of the participants were between 28 and 37 years. Knowledge on teratogenic risk was generally poor with specifically higher knowledge regarding insulin intake and isotretinoin. Older age, higher education, being employed, and having a high monthly income were significantly associated with a higher knowledge score ($P < 0.05$). **Conclusion:** Women's knowledge regarding teratogenic risks is crucial in ensuring a safe pregnancy and a healthy fetus. Our study revealed inadequate knowledge of teratogens among the participants which implies an urgent need to increase awareness of mothers regarding the harmful effects of common teratogens.

Keywords: Childbearing age, knowledge, Saudi Arabia, teratogens

Introduction

Teratogens are environmental agents that may disturb the normal fetal development when the mother is exposed to them, resulting in prenatal mal-development or death.^[1] Previously, it was believed that congenital anomalies were only genetic until Murphy discovered that environmental agents can also cause

congenital defects.^[1] Recently, it is known that a majority of the congenital anomalies have a multifactorial pathogenesis, implicating both genetic and environmental basis.^[2] It is estimated that almost 15% of all congenital malformations are due to environmental teratogens^[3] which include metabolic conditions, physical, chemical, and infectious agents.^[4] As most of these can be considered as modifiable exposures, awareness regarding teratogenic risks among women is crucial as it can reduce the occurrence of congenital defects.^[5]

Some of the comorbidities that pose a teratogenic risk include gestational diabetes mellitus which is associated with higher risk of congenital malformation,^[6-8] thyroid related diseases and

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medications^[9,10] and epilepsy medications.^[11-13] Awareness of women showed insufficient knowledge regarding the teratogenicity of gestational diabetes mellitus,^[14] thyroid diseases and medications^[15] and epileptic medications.^[16,17] In general, medication use and safety during pregnancy is a highly debatable subject. Throughout the literature, it is evident that women's awareness on teratogenic medications is inadequate.^[18-20] A Saudi study assessing the beliefs, knowledge, and use of medications among pregnant women showed that the majority expressed awareness regarding cautious use of medications during pregnancy.^[21] Another study assessing knowledge of folic acid intake among women of child bearing age found that most of them were aware of folic acid and its preventive effect on neural tube defects.^[22]

Other teratogens include rubella, the first teratogenic virus to be described.^[23,24] A Saudi study conducted in Al-Khobar demonstrated that more than half of the women lacked information about the adverse effects of rubella infection during pregnancy.^[25] Furthermore the teratogenicity of radiation exposure during pregnancy is well established through many studies.^[26,27] Teratogenicity of radiation awareness in a Saudi study showed a high awareness regarding exposure to during pregnancy.^[28]

Most of the literature in this domain of women's awareness of teratogenic risk focuses on one type of exposure whether be it radiation, medication etc. In this study we aimed to assess women's knowledge among Saudi women of childbearing age in a tertiary care centre in Saudi Arabia on the teratogenic risks posed by several entities including fever, diabetes mellitus, thyroid, and antiepileptic medications in addition to determine its association with socio-demographic factors. Such study is highly justified since some patients are believed to make deliberate decisions regarding their medication use, based on their beliefs about the disease and its treatment.^[29,30] Effective counselling has been associated with better and positive outcomes in terms of knowledge and practice of the safe and utilization of drugs and the understanding of many medical conditions that may happen during pregnancy.

Materials and Methods

Study design, setting, and subjects

An analytical cross-sectional study using a self-administered questionnaire was conducted at a large tertiary care centre in the capital city of Saudi Arabia from January 2018 to December 2018. Saudi women of childbearing age (18–45 years) visiting the obstetrics and gynaecology (OB/GYN) clinic and were willing to participate were included using convenience sampling technique. Women in labour were excluded. The recommended sample size as computed using the Rao soft online calculator was 297 with 95% confidence level, 5% margin of error and a response distribution of 50%.^[31]

Study instrument and data collection

Data were collected using an Arabic pre-validated self-administered questionnaire. Content validation of the tool was performed by

2 content experts and a pilot study involving 30 women who fit the inclusion criteria was conducted. Unclear items and words were modified based on the comments of the pilot study subjects. Reliability analysis of the pilot data yielded a Cronbach's alpha coefficient of 0.7 which indicated acceptable reliability.

The questionnaire consisted of 27 items, including 10 questions pertaining to socio-demographic data and 17 statements assessing the participants' knowledge of teratogenic agents (2 items on physical agents, 3 items on infectious agents, 5 on metabolic agents and 7 items on chemical agents) using a 5-point Likert scale as follows: 0 as Don't know, 1 as Strongly disagree, 2 as Disagree, 3 as Agree, and 4 as Strongly agree. For negative statements in which the disagreement was the correct answer, reverse coding was performed. The overall knowledge score ranged from 0 to 17.

The co-investigators visited the OB/GYN clinic over a period of 2 months and distributed the surveys manually to the women in the waiting area and were collected immediately after they were filled. Interviews using the same structured tool were performed for illiterate women.

Ethical considerations

The study was ethically approved by the Institutional Review Board (IRB) at King Abdullah International Medical Research Centre (KAIMRC) with approval number RYD-17-419812-92225 on June 12, 2017. Informed voluntary consent was taken from each participant and information was obtained from each participant in a private setting. The data was accessible only by the principal investigator and co-investigators and confidentiality was ensured throughout the study.

Data analysis

Data were entered on Microsoft Excel and analysed using SPSS, Version 22.0 (IBM Corporation, Armonk, NY, USA). For the descriptive analysis, frequencies, and percentages were used to describe the categorical variables. Median and interquartile range (IQR: 25th percentile–75th percentile) were used to describe the knowledge scores. The association between the sociodemographic variables and knowledge score was determined using the non-parametric Mann–Whitney U and Kruskal Wallis tests. A *P* value of less than 0.05 was considered statistically significant for all tests used.

Results

The study included 315 women of childbearing age. The majority of women (55.6%) were 28–37 years old, and 94% were married; 57.8% of the participants had university education, 34% had high school education or less, 5.4% were postgraduates, and 2.9% were illiterate. More than half of the participants (56.2%) were housewives, and 20.4% were in education-related professions. Most of them (64.8%) were pregnant, and 46.8% participants had 3 or more children, while 19.6% were nulliparous. Regarding miscarriages, 53.2% had no previous miscarriages, and 12.5%

of the participants had 3 or more miscarriages previously. Only 7.9% women had a child with congenital defects, and almost half (43.4%) had a monthly income ranging between 5,000 and 9,999 SR. The demographic characteristics of the participants are presented in Table 1.

Concerning knowledge questions on teratogenic risks as shown in Table 2, responses regarding the effect of fever showed that the majority (70%) were aware of the significance of treatment of fever; however, they were less aware of the potential of fever leading to congenital malformations (31%). On whether German measles and herpes simplex infections during pregnancy can cause congenital defects, 40% and 37% agreed, respectively. Regarding syphilis, 36% women agreed that syphilis in pregnancy may affect the fetus. When asked about gestational diabetes mellitus, 38% of the participants agreed that gestational diabetes mellitus can affect the fetus, and 35% agreed that there is a relationship

between abnormal blood sugar level and congenital anomalies. Participants showed relatively good knowledge regarding insulin use during pregnancy, and 61% of them responded negatively to the statement, "Insulin use can harm the fetus". Regarding thyroid diseases, 35% of the participants agreed that there is a relationship between thyroid abnormalities and congenital defects, and 30% disagreed that stopping thyroid medications in pregnancy is important for fetal safety.

As for medication use, when asked about anti-epileptics, 42% agreed that using these medications can harm the fetus, and only 24% disagreed that pregnant women should not take anti-epileptics even if they were needed. Concerning vitamin A intake, 59% of the women agreed that vitamin A is important during pregnancy. However, only 28% agreed with the statement that high intake of vitamin A can cause congenital anomalies. Most of the women (72%) agreed that pregnant women should not take isotretinoin as it might cause congenital defects. Regarding psychiatric medications, 46% of participants agreed that medications for mental illnesses can harm the fetus, but only 13% disagreed that medications for mental illnesses should be stopped during pregnancy.

The overall median knowledge score was 7. The relationship between the median scores and the independent variables, which included age, educational level, profession, and monthly income were statistically significant with *P* values of 0.04, 0.01, 0.01, and 0.001, respectively. Older age, a higher education level and monthly income, and being employed were associated with better knowledge on teratogens. Other variables, namely marital status, current/previous pregnancy, miscarriages, and having a child with congenital malformation, were not statistically significant. The associations between the median knowledge score and the predictors are presented in Table 3.

Discussion

Women's awareness of teratogens is of high importance as it can decrease preventable congenital anomalies.^[5] This study explored women's awareness regarding the teratogenic risk posed by various entities. Regarding fever's potential to create congenital anomalies, poor knowledge was demonstrated which may be due to the fact that fever rarely cause congenital anomalies.^[32] However, due to it being more common knowledge, most of them agreed that fever must be treated in pregnancy. As there are no studies addressing women's awareness in terms of fever, the results could not be compared. On the other hand, nearly half of the study's participants were aware that German measles has harmful effects on the fetus. Similarly, another local study carried out in Al-Khobar showed that 43% of participants were aware of the teratogenic effects of German measles.^[25]

Despite the participants' poor awareness of the probable teratogenicity of rubella, herpes simplex, and syphilis, more correct responses were observed for teratogenicity of infectious agents than for fever. In this category, the effect of rubella on

Table 1: Characteristics of study subjects (n=315)

Variable	Frequency (%)
Age	
18-27 years old	85 (27.0)
28-37 years old	175 (55.6)
38-45 years old	55 (17.5)
Marital status	
Single	14 (4.4)
Married	296 (94.0)
Divorced	4 (1.3)
Widowed	1 (0.3)
Educational level	
Illiterate	9 (2.9)
High school or lower	107 (34.0)
University	182 (57.8)
Higher studies	17 (5.4)
Profession	
Homemaker	176 (56.2)
Teacher	64 (20.4)
Health professional	25 (8.0)
Student	27 (8.6)
Others	21 (6.7)
Current pregnancy	204 (64.8)
Previous pregnancies	
None	61 (19.6)
One pregnancy	52 (16.7)
Two pregnancies	53 (17.0)
Three or more pregnancies	146 (46.8)
Number of Miscarriages	
None	166 (53.2)
One	73 (23.4)
Two	34 (10.9)
Three or more	39 (12.5)
Child with congenital malformation	25 (7.9)
Monthly income	
<5,000 SR	49 (16.6)
5,000-9,999 SR	128 (43.4)
10,000- 15,000 SR	66 (22.4)
>15, 000 SR	51 (17.3)

Table 2 Knowledge of females on common teratogenic risks

Statement	Strongly disagree	Disagree	Do not know	Agree	Strongly agree
Fever in pregnancy can lead to congenital malformations	14 (4.4)	70 (22.2)	134 (42.5)	85 (27.0)	12 (3.8)
A pregnant female with fever does not need treatment because fever is not associated with malformations	108 (34.6)	111 (35.6)	59 (18.9)	28 (9.0)	6 (1.9)
If pregnant female has German measles, fetus can develop malformations	14 (4.5)	22 (7.0)	150 (47.8)	102 (32.5)	26 (8.3)
Syphilis in pregnancy does not affect the fetus	52 (16.6)	61 (19.5)	147 (47.0)	43 (13.7)	10 (3.2)
Herpes infection in pregnancy can lead to congenital malformations	8 (2.6)	47 (15.1)	138 (44.4)	96 (30.9)	22 (7.1)
There is no association between gestational diabetes and congenital malformations	41 (13.1)	80 (25.6)	73 (23.3)	102 (32.6)	17 (5.4)
There is a relationship between irregular BSL and congenital malformations	19 (6.1)	77 (24.9)	104 (33.7)	87 (28.2)	22 (7.1)
Insulin use in pregnancy can harm the fetus	67 (21.3)	125 (39.8)	91 (29.0)	28 (8.9)	3 (1.0)
Thyroid problems in pregnancy have no effect on the fetus	28 (9.0)	80 (25.7)	124 (39.9)	74 (23.8)	5 (1.6)
Stopping thyroid medication in pregnancy is important for fetal safety	40 (12.8)	56 (17.9)	130 (41.5)	74 (23.6)	13 (4.2)
Using antiepileptics during pregnancy can harm the fetus	4 (1.3)	27 (8.7)	145 (46.6)	109 (35.0)	26 (8.4)
Pregnant should not use antiepileptics even if she needs it	16 (5.2)	60 (19.4)	146 (47.1)	69 (22.3)	19 (6.1)
Vitamin A is an important vitamin to take in pregnancy	16 (5.1)	32 (10.3)	76 (24.4)	163 (52.4)	24 (7.7)
There is no association between Vitamin A intake in pregnancy and congenital malformations	33 (10.6)	55 (17.7)	164 (52.7)	52 (16.7)	7 (2.3)
In pregnancy planning, Ro-Accutane tabs should be stopped	10 (3.2)	6 (1.9)	67 (21.6)	88 (28.4)	139 (44.8)
Medications for mental illnesses can cause congenital malformations	4 (1.3)	20 (6.4)	141 (45.2)	109 (34.9)	38 (12.2)
All medications for medical illnesses should be stopped in pregnancy	6 (1.9)	34 (10.9)	124 (39.7)	106 (34.0)	42 (13.5)

Table 3: Bivariate associations of various predictors and teratogen knowledge score

Variables	Knowledge score Median (Q1-Q3)	P
Age		
18-37 years old	7 (4-9)	0.04*
38-45 years old	8 (6-10)	
Marital status		
Single	8 (6-10)	0.29
Ever Married	7 (5-9)	
Educational level		
Low	7 (5-9)	0.01*
High	9 (8-11)	
Profession		
Unemployed	7 (4-9)	0.01*
Employed	8 (5-10)	
Current pregnancy		
No	8 (5-9)	0.60
Yes	7 (5-9)	
Previous pregnancies		
None	8 (4-9)	0.90
≥1	7 (5-9)	
Miscarriages		
None	7 (4-9)	0.20
≥1	7 (5-9)	
Child with congenital malformation		
No	7 (5-9)	0.90
Yes	7 (5-9)	
Monthly income		
<5,000 SR	6 (4-8)	0.001*
5,000-15,000 SR	7 (5-9)	
>15,000 SR	8 (6-11)	

*P < 0.05 for statistically significant. Q1: 25th percentile, Q3: 75th percentile

pregnancy appeared to be slightly better known than that of the other two infectious agents. The poor knowledge of these two infectious agents could be explained by the fact that some women were not familiar with the medical terminology. Regarding herpes simplex and syphilis, there are no other studies to support our findings. The awareness of the teratogenic effect of gestational diabetes mellitus was much better when compared to an Indian study.^[14] Concerning the potential teratogenic effect of diabetes mellitus, inadequate knowledge was shown on the relationship between abnormal blood sugar and congenital anomalies. This can be explained by the fact that diabetes mellitus rarely causes congenital defects.^[33] For thyroid abnormalities, only one-third of participants agreed that there is a relationship between thyroid diseases and congenital anomalies, and one-third thought that thyroid medications should not be stopped during pregnancy. This was concordant with the findings of an Indian study.^[15] As for antiepileptic medications effect on harming the fetus, another study found that 40% of participants were aware of this effect which is similar to our study findings.^[16]

Participants showed relatively good knowledge regarding the importance of vitamin A intake during pregnancy, yet poor awareness regarding the effect of increased intake of vitamin A during pregnancy. The result could not be compared as there are no other studies addressing the awareness of vitamin A intake. Women showed good knowledge regarding the importance of discontinuing isotretinoin during pregnancy, which could be due to the fact that it is widely prescribed for women of childbearing age for acne treatment.^[34] Awareness regarding the potential teratogenicity of psychiatric medications was poor, and there are no other studies to compare this result with. This could be

because psychiatric medications are not commonly discussed during medical consultations.

Older participants had better knowledge suggesting a relation between median knowledge score and age. This might be explained by the fact that they are more experienced and might have been exposed to more sources for knowledge. Employment was also associated with better knowledge which is probably related to more exposures to medical information and terminology. In addition, high income was related to better knowledge, which could be due to easier access to healthcare facilities or being able to educate oneself on preventive measures in women's health.

Limitations of this study include being a single-centre study, which limits the generalisability of the findings. Furthermore, the study participants might not have been familiar with some of the medical terminologies used. This could have led to an over or underestimation of the participants' true awareness of these agents. Furthermore, this study included few agents that rarely cause teratogenicity, such as diabetes mellitus and fever.

Finally, this study showed that participants' awareness of the explored teratogenic agents was generally insufficient, and the median knowledge score was significantly correlated with age, employment status, and monthly income. Thus, the authors strongly recommend conducting awareness campaigns in the community and encouraging patients to seek information from their physicians regarding the harmful effects of teratogens. It should also be emphasized that women should never start or discontinue medication on their own especially if pregnant. It is also recommended that physicians highlight the most common teratogens to patients and individualise their advice based on each patient's medical condition. In conclusion, inadequate knowledge of teratogens among the participants was revealed which is alarming and might pose potential risks on a safe and healthy pregnancy.

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Conflicts of interest

There are no conflicts of interest.

References

- Kalter H. Teratology in the Twentieth Century Plus Ten. 1st ed. Dordrecht: Springer Netherlands; 2010.
- Weinhold B. Environmental factors in birth defects: What we need to know. *Environ Health Perspect* 2009;117:A440-7.
- Brent RL. The cause and prevention of human birth defects: What have we learned in the past 50 years? *Congenit Anom (Kyoto)* 2001;41:3-21.
- Gilbert-Barnes E. Teratogenic causes of malformation. *Ann Clin Lab Sci* 2010;40:99-114.
- Toralles MB, Trindade BM, Fadul LC, Peixoto Junior CF, Santana MA, Alves C. Importance of the teratogen information service in Bahia, Brazil, for prevention of congenital malformations: An initial four-review. *Cad Saude Publica* 2009;25:105-10.
- Kozma A, Radoi V, Ursu R, Bohaltea CL, Lazarescu H, Carniciu S. Gestational diabetes mellitus and the development of cleft lip/palate in newborns. *Acta Endocrinol (Buchar)* 2019;5:118-22.
- Ornoy A, Reece EA, Pavlinkova G, Kappen C, Miller RK. Effect of maternal diabetes on the embryo, fetus, and children: Congenital anomalies, genetic and epigenetic changes and developmental outcomes. *Birth Defects Res C Embryo Today* 2015;105:53-72.
- Allen VM, Armson BA; Genetics Committee; Maternal Fetal Medicine Committee. Teratogenicity associated with pre-existing and gestational diabetes. *J Obstet Gynaecol Can* 2007;29:927-34.
- Temboury Molina MC, Rivero Martín MJ, de Juan Ruiz J, Ares Segura S. Enfermedad tiroidea autoinmunitaria materna: Repercusión en el recién nacido [Maternal autoimmune thyroid disease: Relevance for the newborn]. *Med Clin (Barc)* 2015;144:297-303.
- Howley MM, Fisher SC, Van Zutphen AR, Waller DK, Carmichael SL, Browne ML, *et al.* Thyroid medication use and birth defects in the national birth defects prevention study. *Birth Defects Res* 2017;109:1471-81.
- Tomson T, Battino D, Perucca E. Teratogenicity of antiepileptic drugs. *Curr Opin Neurol* 2019;32:246-52.
- Blotiere PO, Raguideau F, Weill A, Elefant E, Perthus I, Goulet V, *et al.* Risks of 23 specific malformations associated with prenatal exposure to 10 antiepileptic drugs. *Neurology* 2019;93:e167-80.
- Alsheikh M. Prevalence of epilepsy kin Saudi pregnant women and possible effects of anti-epileptic drugs on pregnancy outcomes. *Neurosciences* 2020;25:32-7.
- Shriraam V, Rani MA, Sathiyasekaran BW, Mahadevan S. Awareness of gestational diabetes mellitus among antenatal women in a primary health centre in South India. *Indian J Endocrinol Metab* 2013;17:146-8.
- Rai S, Sirohi S, Khatri A, Dixit A, Saroshe S. Assessment of knowledge and awareness regarding thyroid disorders among women of a cosmopolitan city of central India. *Natl J Community Med* 2016;7:219-22.
- Pack AM, Davis AR, Kritzer J, Yoon A, Camus A. Antiepileptic drugs: Are women aware of interactions with oral contraceptives and potential teratogenicity? *Epilepsy Behav* 2009;14:640-4.
- Bhakta J, Bainbridge J, Borgelt L. Teratogenic medications and concurrent contraceptive use in women of childbearing ability with epilepsy. *Epilepsy Behav* 2015;52:212-7.
- Pattacini C, Tagliaferri A, Manotti C. Awareness of teratogenic effect of oral anticoagulants in fertile women. *Thromb Haemost* 2002;88:172.
- Sanz E, Gomez-Lopez T, Martinez-Quintas M. Perception of teratogenic risk of common medicines. *Eur J Obstet Gynecol Reprod Biol* 2001;95:127-31.
- Zhang N, Wang L, Ouyang Y. Survey on medication information literacy and influencing factors among pregnant Chinese Women. *J Matern Fetal Neonatal Med* 2019;1-8. doi: 10.1080/14767058.2019.1642869. [Epub ahead of print]
- Zaki N, Albarraq A. Use, attitudes and knowledge of

- medications among pregnant women: A Saudi study. *Saudi Pharm J* 2014;22:419-28.
22. Al-Holy M, Eideh A, Epuru S, Abu-Jamous D, Ashankyty I. Awareness of folic acid intake among women in the childbearing age in Hail Region—Saudi Arabia. *Food Sci Nutr* 2013;4:49-55.
 23. Greg N. Congenital cataract following German measles in the mother. *Trans Ophthalmol Soc Aust* 1941;3:35-46.
 24. Yazigi A, De Pecoulas AE, Vauloup-Fellous C, Grangeot-Keros L, Ayoubi JM, Picone O. Fetal and neonatal abnormalities due to congenital rubella syndrome: A review of literature. *J Matern Fetal Neonatal Med* 2017;30:274-8.
 25. Rasheed P, Al-Sowielem S. Health education needs for pregnancy: A study among women attending primary centers. *J Family Community Med* 2003;10:31-8.
 26. Jensch RP. Ionizing radiation and the conceptus: Neurophysiologic effects of prenatal X-radiation on offspring. *Ann Clin Lab Sci* 1985;15:185-94.
 27. Williams PM, Fletcher S. Health effects of prenatal radiation exposure. *Am Fam Physician* 2010;82:488-93.
 28. Halwani M, El-Hawary H, Alghamdi A, Alsmari B, Alghamdi N, Al Zahrani Y. Knowledge and attitude of Saudi women toward the risk of exposure to radiation during pregnancy. *Int J Curr Res* 2017;9:44784-90.
 29. Lutz BH, Miranda VIA, Silveira MPT, Dal Pizzol TDS, Mengue SS, Da Silveira MF, *et al.* Medication use among pregnant women from the 2015 Pelotas (Brazil) birth cohort study. *Int J Environ Res Public Health* 2020;17. pii: E989. doi: 10.3390/ijerph17030989.
 30. Atmadani RN, Nkoka O, Yunita SL, Chen YH. Self-medication and knowledge among pregnant women attending primary healthcare services in Malang, Indonesia: A cross-sectional study. *BMC Pregnancy Childbirth* 2020;20:42.
 31. Raosoft.com. Sample Size Calculator by Raosoft, Inc. [online] Available from: <http://www.raosoft.com/samplesize.html>.
 32. Sass L, Urhoj SK, Kjærgaard J, Dreier JW, Strandberg-Larsen K, Nybo Andersen AM. Fever in pregnancy and the risk of congenital malformations: A cohort study. *BMC Pregnancy Childbirth* 2017;17:413.
 33. Gabbay-Benziv R, Reece EA, Wang F, Yang P. Birth defects in pregestational diabetes: Defect range, glycaemic threshold and pathogenesis. *World J Diabetes* 2015;6:481-8.
 34. Layton A. The use of isotretinoin in acne. *Dermatoendocrinol* 2009;1:162-9.