Ethnic differences in drug utilization pattern during pregnancy: a cross-sectional study

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Ethnic differences in drug utilization pattern during pregnancy: a cross-sectional study

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Key words: Drug utilization, medication, pregnancy, ethnicity, Arab women.

Abstract

Objective to investigate differences in exposure to medications in a cohort of multi-ethnic pregnant women.

Methods 641 pregnant women of Western, Arab/Turkish and "other origins" participated in this cross-sectional study using a questionnaire in a university hospital in Brussels, Belgium. Assessment of the drug safety was done using the food and drug administration (FDA) risk classification system. Data analysis was performed using SPSS.

Results In overall cohort, 83.8% used at least one preparation (including multivitamins) during pregnancy and 37.0% of women used at least one drug (excluding multivitamins). Significantly more Western women (43.7%) used one or more medications compared to Arab/Turkish women (28.7%;p=0.000). This difference in exposure was most pronounced for over-the-counter drugs for occasional and pregnancy-related complaints, and was observed for potentially unsafe drugs or drugs with unknown safety. None of the women reported use of FDA X category drugs.

Conclusions The use of drugs known to be harmful was not observed but a higher prevalence of exposure to potentially harmful drugs (FDA C/D) was found among Western women who also consumed more over-the-counter drugs. This highlights the need for cautious prescribing for women in the fertile age in general and for continuous monitoring of medication use during pregnancy.

Introduction

Prescribing medications for pregnant women is a challenge for healthcare providers especially since the thalidomide disaster in the 1960s [1,2]. The use of medications during pregnancy indeed poses a potential risk to both the mother and the foetus. Despite the lack of evidence on the safety of many medications during pregnancy, many studies have reported high percentages of drug use during pregnancy [3-5]. Data on medication use during pregnancy appear to differ between countries due to differences in ethnicity, socio-cultural differences, methods of data collection and differences in study design [4,6,7]. Drug exposure during pregnancy can also be influenced by the pregnancy stage and the indication of use (chronic, occasional or pregnancy-related conditions) [7]. Assessment of medication use in multi-ethnic pregnant women in Europe, where immigration is continuously increasing, has not been given much attention so far [4]. Therefore, the aims of this study were to investigate possible differences in exposure to medications (including contraceptives and multivitamins) in a cohort of multi-ethnic pregnant women. We investigated the pattern of medication use before and during pregnancy in relation to the type of medicines, the reason for their use and their risk to the foetus. Moreover, we also focused in particular on assessing possible differences in these patterns of use between Western and immigrant Arab and Turkish women, i.e. the largest non-Western ethnicity in Belgium and a group of women that has not often been studied.

Methods

This cross-sectional study was conducted between February and September 2009 in the obstetrics outpatient clinic of the UZ Brussel, a university hospital and main medical referral centre in Brussels attracting a multi-ethnic population. After giving written informed consent, the participants completed a questionnaire that was available in four languages (Dutch, French, English and Arabic) to collect information on ethnicity and details of medication use before and during pregnancy (including multivitamins and contraceptives). Regardless of age or ethnicity, women were eligible to participate in the study if they spoke any of the four languages of the questionnaire and had enough waiting time (around 15 minutes). Among the pregnant women visiting the obstetrics clinic, a random sample of 641 women was invited for participation in the study that was approved by the local Ethical Committee. To maximize the amount of information collected, women were interviewed in the 2nd or the 3rd trimester of pregnancy.

Women were classified into three groups according to ethnical origin (Table 1): "Western" (European, Australian and North American), "Arab/Turkish" (including women originating from all Arab regions and Turkey), and women from "Other origins" (Asian, African and South American).

All medications (except contraceptives and multivitamins) were classified into three mutually exclusive categories according to the reason for their use (Table 2): (1) drugs for chronic conditions, (2) drugs for occasional and short-time use and (3) drugs for pregnancy-related symptoms. Drugs were also classified according to the Anatomical Therapeutic Chemical (ATC) coding system (WHO ATC) [8], as well as according to the FDA risk classification (A, B, C, D and X) [9]. Category A: controlled studies show no risk; category B: no evidence of risk in humans; category C: risk can not be ruled out; category D: positive evidence of risk and category X: contraindicated in pregnancy. Drugs labelled as A or B and C or D were combined together in two categories for statistical analysis purposes. Drugs for which no FDA information was available about safety were assigned as U (unknown safety).

The exposure to drugs was investigated per trimester after excluding multivitamins and contraceptives. Trimesters were defined as: 1st trimester (0-14 weeks of gestation), 2nd trimester (15-28 weeks) and 3rd trimester (29-42 weeks). Drugs used in more than one trimester were counted in each trimester separately, e.g., drug use that started in the 1st trimester and extended to the 2nd trimester was considered as exposure in the 1st as well as in the 2nd trimester.

Data analysis

The prevalence of the use of contraceptives (analysed separately), medications (with and without multivitamins; prescription and non-prescription drugs) and multivitamins was determined for the total study population. Subsequently, differences in these prevalences among the three ethnic subgroups were analyzed using χ^2 tests. ANOVA test with post hoc Bonferroni correction was used to compare the mean number of medications used among the three ethnic groups. The percentage of women exposed to certain drug categories was calculated and compared for the three ethnic groups using the significance test for comparing two proportions that is available online at: http://math.uc.edu/~brycw/classes/149/wang.htm [10]. Spearman correlation was performed to investigate the correlation between the exposures to the different drug categories. The level of statistical significance was set as *p*-value < 0.05. Data analysis was performed using SPSS (IBM-SPSS v19). The total number of patients differs according to the availability of data with regard to the different variables analyzed each time.

Results

Characteristics of the study populations

Of the 641 participants, 334 (52.1%) were Western, 209 (32.6%) Arab/Turkish and 98 (15.3%) were women from "Other origins". Women were interviewed once, either in the 2nd (244 or 38.1%) or in the 3rd trimester (397 or 61.9%), with almost the same distribution mentioned above for each ethnic group within each trimester. The age of the women ranged from 16 to 48 years with a mean of 30 years. No significant difference was observed in age categories among the three ethnic groups (p = 0.172: Table 1). A higher percentage of multiparous women was observed among Arab/Turkish women (75.9%) compared to Western women (50.6%) as shown in Table 1.

Table I to be inserted here.

Patterns of contraceptive use

As shown in Table 1, 295 out of 636 women (46.4%) reported contraceptive use before pregnancy: 181 (61.4%) used oral contraceptives, 46 (15.6%) used other contraceptive methods such as intrauterine devices (IUDs), implants or transdermal delivery systems, and 68 (23.0%) women did not report which contraceptive method they used. Contraception use was continued in 33 women after conception with 21 of them exposed to estrogen/progesterone based oral contraception. Overall, the use of contraceptives was significantly (p = 0.000) different among the three ethnic groups. The difference was, however, only significant between the Western (51.8%) and the "Other origins" group (21.6%). Among the 227 women who reported which kind of contraceptive method they used, Arab/Turkish women used contraceptive pills (89.5%) more often than Western women (75.6%; p = 0.029). Continuation of contraceptive use after conception was less prevalent in Western women than in the two other ethnic groups (p = 0.000, Table 1).

Medication use before and during pregnancy

A total of 537 (83.8%) women used at least one preparation (including multivitamins) during pregnancy, and the total number of preparations used was 1133. After exclusion of multivitamins, more than one third of women (237; 37.0%) used a total of 374 drugs, whereas 505 (78.8%) women used a total of 759 multivitamin preparations. Less than half (167; 44.6%) of these medications were prescription drugs and 205 (54.8%) over the counter (OTC) drugs.

About a quarter of the drugs were for chronic use (103; 27.5%), about half were drugs for occasional use (192; 51.3%) and the remaining drugs were for pregnancy related use (78; 20.9%). Only 104 (16.2%) women reported no use of any medication at all during pregnancy. Two drugs could not be assigned as either prescription or OTC because women did not report the medication names and, for the same reason, 1 drug could not be classified as being for chronic, occasional or pregnancy related use.

Table II to be inserted here.

Drug use according to ATC classification

Of the 374 medications used by women, 88 (23.5%) were drugs for the alimentary tract and metabolism including insulin (A), 81 (21.7%) for the nervous system (N), 68 (18.2%) for the respiratory system (R), 40 (10.7%) anti-infectives for systemic use (J), 26 (7.0%) systemic hormones excluding sex hormones and insulin (H), 19 (5.1%) drugs for blood and blood forming organs (B), 17 (4.5%) cardiovascular drugs (C), 15 (4.0%) genitourinary drugs and sex hormones (G), 12 (3.2%) dermatologicals (D), 6 (1.6%) drugs for sensory organs and 2 (0.5%) drugs for the musculo-skeletal system (M).

Drug use according to FDA risk classification

Half of the drugs used (86; 49.7%) were classified as safe or reasonably safe (A + B), 95 (25.4%) were potentially harmful (C + D), and no use (0.0%) of harmful drugs (X) was reported. A quarter (90; 24.1%) of the drugs had no FDA classification (unknown safety U) and 3 drugs could not be assigned as their names were not reported.

Drug use according to active molecule

The top 10 drugs used were paracetamol (72; 19.3%), followed by the thyroid hormones (18; 4.8%), metoclopramide (14; 3.7%), salbutamol (9; 2.4%), amoxicillin (8; 2.1%), ranitidine (8; 2.1%), progesterone (8; 2.1%), antacids (8; 2.1%), domperidone (7; 1.9%) and insulin (7; 1.9%). Most of these drugs are considered to be safe but salbutamol, progesterone and domperidone are potentially harmful (FDA category C).

Out of 759 multivitamin preparations used by women, the most frequently used were folic acid preparations (499; 65.7%) followed by iron preparations (132; 17.4%) and magnesium preparations (51; 6.7%).

Correlation between exposures to different drug categories

Exposure to OTC drugs significantly correlated with the exposure to occasionally used drugs (r = 0.419; p = 0.000), pregnancy-related drugs (r = 0.200; p = 0.002) and drugs with unknown safety (r = 0.252; p = 0.000), whereas exposure to prescription drugs significantly correlated with the exposure to potentially harmful drugs (r = 0.231; p = 0.000) and drugs for chronic conditions (r = 0.464; p = 0.000).

Evolution of drug use before and during pregnancy

As shown in Table 3, the percentage of women exposed to pregnancy related drugs in the 1st trimester was five times that before conception (p = 0.000); in the 2nd trimester it was six times higher (p = 0.000) and in the 3rd trimester four times higher than before pregnancy (p = 0.013). No significant difference was detected in any of the three trimesters in exposure to chronic or occasionally used drugs compared to the preconception use. However, a significant reduction of the exposure to occasionally used drugs was observed in the 3rd trimester compared to the 2nd trimester exposure (p = 0.043). In addition, a trend to lower use of pregnancy related drugs (p = 0.056) and chronic drugs (p = 0.098) was detected in the 3rd trimester compared to the 2nd trimester without reaching statistical significance.

A significantly higher percentage of women used OTC drugs in the 2nd trimester compared to the preconception period (p = 0.026). Exposure to prescription drugs was higher in both the 1st (p = 0.026) and the 2nd trimester (p = 0.001) when compared to preconception exposure, and decreased in the 3rd trimester when compared to the 2nd trimester (p = 0.006). No significant difference was observed between the three pregnancy trimesters in OTC drug exposure.

The percentage of women exposed to safe or reasonably safe (A + B) or potentially harmful (C + D) drugs did not vary significantly in any of the pregnancy trimesters when compared to the preconception exposure. However, the difference was significant for drugs with unknown safety (U) for the 1st (p = 0.005), the 2nd (p = 0.000) and the 3rd trimester (p = 0.037) when compared with the preconception use. The exposure to these drugs increased significantly from the 1st to the 2nd trimester (p = 0.009) and then decreased again by 50% in the 3rd trimester (p = 0.008). In general, the total percentage of women exposed to drugs (excluding multivitamins) was significantly higher in both the 1st and the 2nd trimester when compared to the preconception exposure.

Table III to be inserted here.

Ethnic differences in drug exposure

As shown in Table 1, no significant difference was detected among the three ethnic groups in overall medication use including multivitamins ($p = 0.085$) or in multivitamin use alone ($p = 0.059$). However, a significant difference in the use of medications among the three groups was found when multivitamins were excluded ($p = 0.001$). Significantly more Western women used one or more medications other than multivitamins compared to Arab/Turkish women ($p = 0.000$) and "Other origins" women ($p = 0.033$).

The mean number of medications, including multivitamins, used in the population as a whole was significantly different among the three groups ($p = 0.000$; Table 4). Pair wise comparisons revealed that the mean number of medications in Western women (2.02) was significantly higher than in Arab/Turkish (1.50; $p = 0.000$) and "Other origins" women (1.48; $p = 0.002$). Similarly, Western women used on average more drugs other than multivitamins (0.72) compared to both Arab/Turkish (0.42; $p = 0.000$) and "Other origins" women (0.46; $p = 0.035$). The number of multivitamins used was also significantly higher in Western women (1.29) compared to both Arab/Turkish (1.09; $p = 0.024$) and "Other origins" women (1.02; $p = 0.022$; Table 4). As for the whole group, pair wise comparisons of women who took at least one medication revealed a significantly higher mean number of medications including multivitamins in Western women (2.35) compared to Arab/Turkish (1.79; $p = 0.000$) and "Other origins" women (1.93; $p = 0.028$). However, no significant difference was detected when drug use was studied excluding multivitamins ($p = 0.200$). Multivitamin use differed significantly among the different ethnic user groups ($p = 0.034$) but statistical significance was not reached when pair wise analyses between the three groups were performed.

Table IV to be inserted here.

There were also differences between the ethnic groups when the exposure to medications was investigated in function of the medication category. As shown in table 5, the percentage of women exposed to chronic drugs was significantly higher among Western (15.0%) compared to "Other origins" women (6.0%; $p = 0.026$). The exposure to pregnancy related drugs was also significantly higher among Western (13.0%) compared to "Other origins" women (6.0%; $p = 0.047$). The exposure to occasionally used drugs was significantly higher among Western (26.0%) compared to Arab/Turkish women (14.0%; $p = 0.002$). The percentage of women exposed to OTC drugs during pregnancy was significantly higher among Western women (29.0%) compared to both Arab/Turkish (15.0%; $p =$

0.000) and "Other origins" women (18.0%; p = 0.041). No significant difference was observed among the three ethnic groups in the exposure to prescription drugs, although a trend to more frequent use was observed among Western women (22.0%) compared to both Arab/Turkish (16.0%; p = 0.058) and "Other origins" women (18.0%; p = 0.387).

With respect to the safety of the drugs that were used, the percentage of Western women exposed to safe or reasonably safe (A + B) drugs was significantly higher (28.0%) than that of "Other origins" women (17.0%; p = 0.032). At the same time, significantly more Western women (16.0%) were exposed to potentially unsafe (C + D) drugs than Arab/Turkish women (7.0%; p = 0.002). Similarly, the percentage of Western women exposed to drugs with unknown safety (U) was significantly higher (16.0%) than that of Arab/Turkish women (8.0%; p = 0.004). Potentially unsafe drugs were mainly anti-asthmatic drugs (salbutamol), corticosteroids (hydrocortisone, prednisolone, fluticasone and budesonide), codeine, tramadol, miconazole, progesterone, aspirin in low dose as an antithrombotic agent and in high dose as an analgesic (one woman), nervous system drugs (citalopram, paroxetine and lorazepam), insulin analogues, domperidone, omeprazole and sulfasalazine. Drugs with an unknown safety profile were mainly for acid related disorders (alginic acid as well as calcium, magnesium and aluminum based combinations), laxatives (macrogol, ispaghula and others), antihistaminics (ketotifen, ebastine and dimetindene), cough suppressants, nasal preparations, diosmin, zopiclone and cinchocaine.

Table V to be inserted here.

Discussion

The present study demonstrates a high prevalence of medication use throughout pregnancy when the total study population is considered. More than 80% of women used at least one medication (including multivitamins). This is similar to the results of a register-based study reported by Bakker et al (2006) and an interview-based study reported by Kebede et al (2009), who found a prevalence of medication use including multivitamins of 79% and 71.3%, respectively [7,11]. As in other studies, multivitamins, iron and folic acid preparations were the most frequently used multivitamin preparations [11,12].

Our finding that 37% of the pregnant women used medications other than multivitamins are also comparable to those of other studies conducted in Glasgow and Ethiopia who reported a drug use excluding multivitamins of 34.8% and 34.1%, respectively [11,13]. The mean number of medications including multivitamins used by our study population as a whole (1.77) was concordant with other studies reporting a mean number of 1 to 3 medications [14,15]. Our study showed that 16.2% of the women reported no use of any medication at all, which is similar to the percentage found by the European Collaborative Group on Drug Use in Pregnancy who reported that 14% of women did not take any drug [16].

The most frequently used classes of medications were analgesics followed by antibacterials, antacids, asthma medications and drugs for gastrointestinal disorders (antispasmodic and antiemetic drugs). This is in line with other studies also reporting that anti-infectives and analgesics are the most commonly used medications after multivitamins [11,17,18].

More than half of the drugs used by the pregnant women were OTC drugs. Correlations between exposures to different drug categories suggest that most of these OTC drugs were for occasional and pregnancy-related use. The analysis further suggests that OTC drugs are often drugs with unknown safety, whereas the exposure to prescription drugs was more often associated with potentially harmful drugs that were used for chronic conditions.

The use of contraceptive pills prior to pregnancy was extended to the 1st trimester in a considerable number of women before they recognized they were pregnant. This puts the foetus at a high risk due to the hormonal content of these pills. Most women do not realize they are pregnant until the 3rd week after conception [7].

As can be expected, pregnancy-related drug use was significantly higher in all trimesters compared to the preconception use despite a slight decline in the 3rd trimester. Such decline was also observed by Pinto Pereira et al (2010) and may be due to a decrease of the frequency of pregnancy-related complaints in the 3rd trimester and/or women becoming more tolerant to these complaints in this trimester [5]. Our results indicate that the higher use of drugs during pregnancy compared to the preconception phase is solely due to the increased use in pregnancy- related medications, which is in line with the observation of Bakker et al (2006) [7]. OTC drugs were more frequently used in the 2nd trimester compared to the preconception period but the pattern of use was not significantly different between the three trimesters.

Although it is well accepted that rational and safe drug use during pregnancy is essential for maternal health and foetal development [5], the present study indicates that a considerable number of pregnant women were exposed to potentially harmful drugs.

While the exposure to these drugs may have been unavoidable and justified in a number of cases, e.g. because being prescribed for chronic conditions, this was certainly not always the case. Aspirin for example, a drug known to be associated with potential foetal harm, was given to a woman as an analgesic/antipyretic, whereas paracetamol could have been used as a safer alternative. As reported by Wen et al (2008), asthma drugs such as salbutamol were also frequently used by our study population [19]. It is important to control asthma during pregnancy but salbutamol is known to be associated with an increased risk of congenital malformations [20]. Instead, alternative beta-agonists such as salmeterol, formoterol, or inhaled corticosteroids such as beclomethasone and budesonide are more acceptable for asthma therapy in pregnancy [21]. Domperidone was also one of the top 10 drugs used in our study and has not been classified by the FDA risk classification system. It was used occasionally by many women as an anti-emetic despite the availability of safer alternatives (FDA category B) such as metoclopramide [9]. Our observations are in line with a study conducted in the Netherlands reporting that 1.7% of chronically used and 2.3% of occasionally used drugs were harmful [7]. The zero prevalence of exposure to category X drugs in our study is a reassuring finding when compared to other studies that reported percentages ranging from 0.2 to 3.9% of exposure to proven harmful drugs during pregnancy [11,18,19,22]. However, many women were exposed to drugs without FDA safety labelling. The absence of safety information may be misleading to both the patient and the physician and creates a false perception of safety. Indeed, non-classified drugs are not necessarily safe for use during pregnancy and counselling of women concerning their use during pregnancy may be necessary [12]. In our study, these drugs

were mainly antacids, laxatives, antihistaminics, cough suppressants, nasal preparations and diosmin, which were used significantly more during pregnancy compared to preconception. Our results indicate that these drugs with uncertainty about their safety account for the higher use of OTC drugs and those used for pregnancy-related disorders. Evaluation of the safety of these commonly used drugs with unknown safety is warranted to help women and their health providers take informed decisions regarding drug use during pregnancy [2]. Educating patients about the risks of OTC drugs during pregnancy is necessary to reduce the exposure to drugs with unknown safety.

In Belgium, one study on drug use during pregnancy was conducted more than 30 years ago but the impact of ethnicity on drug use was not investigated [23]. An important finding of our study is the observation that there are ethnic differences in the use of certain medications during pregnancy. Contraceptive methods were equally utilized by Western and Arab/Turkish women, but “Other origins” women were less likely to use contraception. Arab/Turkish women used oral contraceptives more frequently compared to Western women who used relatively more often IUDs and transdermal patches. There was also a significantly higher postconception exposure to contraceptive drugs among Arab/Turkish women and among the “Other origins” women compared to Western women, possibly related to a higher unawareness of the pregnancy. This highlights the need for preconception care programs to increase the awareness of women towards the proper use of contraceptive drugs. The exposure to oral contraceptives early in pregnancy could be due to contraceptive failure resulting in an unintended pregnancy [24].

There was a significant difference in the mean number of drugs used (excluding multivitamins) by the three ethnic groups in total but this difference disappeared when investigated among users only per ethnic group. This indicates that the difference in drug use was a reflection of the percentage of women exposed rather than the number of drugs used by each woman using at least one medication. This was also confirmed by the significant differences in the percentages of women exposed to the different drug categories according to ethnicity. Western women used more often OTC drugs and medications for occasional use than Arab/Turkish women, and significantly more Western women were exposed to potentially unsafe drugs than Arab/Turkish women, as well as to drugs with unknown safety. The finding that Western women used more frequently drugs during their pregnancy than Arab/Turkish and "Other origins" women, may reflect differences in sociocultural attitudes towards medications worthwhile to further investigate in order to improve rational drug use among pregnant women.

Strengths and limitations of our study

Our study was not based on medical records but on data from interviewees. Therefore, it reflects real life drug use and exposure misclassification can be excluded. The study also provides information about OTC drugs and use of drugs dispensed to women outside our hospital. Although in such analysis recall bias cannot be excluded, we believe that interviewing our patients during the antenatal care visits helped in minimizing this bias as poorer recall is higher in the postnatal period [25]. The FDA risk classification system which we used to evaluate drug safety is a widely used risk classification system. However, it might be prone to misinterpretation and misapplication, and is now under review to provide a more reliable and clinically useful model [26,27]. We do not know if the encouraging finding of zero exposure to category X drugs in our study population is limited to our hospital or reflects a general careful attitude by pregnant women and their health care providers in Belgium. This merits further investigation.

In conclusion, the present findings demonstrate that the majority of women participating in the study take medications during their pregnancy but with a general conservative behaviour towards the use of drugs known to be harmful and with a complete absence of exposure to FDA category X drugs. However, many pregnant women use OTC drugs for occasional use or for pregnancy-related disorders of which the safety remains uncertain. A clear difference in drug utilization pattern was found between Western and Arab/Turkish women and a higher prevalence of exposure to potentially harmful drugs was observed among Western women. This highlights the need for cautious prescribing during pregnancy as well as for women in the fertile age in general, and for continuous monitoring of medication use during pregnancy. Further research is warranted to reveal the determinants of the ethnic differences in drug use during pregnancy.

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Declaration of interest

The authors report no declarations of interest.

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Table I: General characteristics and medication use according to ethnicity [n = 641]

Variables	Total n (%) 641 (100)	Western (R) n (%) 334 (52.1)	Arab/Turkish n (%) 209 (32.6)	Other origins n (%) 98 (15.3)	*p*-value
Age	[n=641]	[n=334]	[n=209]	[n=98]	
< 26 years	117 (18.3)	55 (16.5)	37 (17.7)	25 (25.5)	**0.172**
26 – 35 years	398 (62.0)	218 (65.3)	124 (59.3)	56 (57.1)	
> 35 years	126 (19.7)	61 (18.3)	48 (23.0)	17 (17.3)	
Parity	[n=618]	[n=324]	[n=199]	[n=95]	
Nulliparous	247 (40.0)	160 (49.4)	48 (24.1)*	39 (41.4)	**< 0.001**
Multiparous	371 (60.0)	164 (50.6)	151 (75.9)*	56 (58.9)	
Use of contraceptive method	[n=636]	[n=332]	[n=207]	[n=97]	
Yes	295 (46.4)	172 (51.8)	102 (49.3)	21 (21.6)*	**0.000**
No	341 (53.6)	160 (48.2)	105 (50.7)	76 (78.4)*	
Contraceptive method (users)	[n=227]	[n=135]	[n=76]	[n=16]	
Pills	181 (79.7)	102 (75.6)	68 (89.5)*	11 (68.8)	**0.029**
Others	46 (20.3)	33 (24.4)	8 (10.5)*	5 (31.3)	
Stopped contraceptive after conception	[n=262]	[n=153]	[n=90]	[n=19]	
Yes	229 (87.4)	144 (94.1)	74 (82.2)*	11 (57.9)*	**0.000**
No	33 (12.6)	9 (5.9)	16 (17.8)	8 (42.1)	
Use of medications including multivitamins	[n=641]	[n=334]	[n=209]	[n=98]	
Yes	537 (83.8)	287 (85.9)	175 (83.7)	75 (76.5)	**0.085**
No	104 (16.2)	47 (14.1)	34 (16.3)	23 (23.5)	
Use of medications excluding multivitamins	[n=641]	[n=334]	[n=209]	[n=98]	
Yes	237 (37.0)	146 (43.7)	60 (28.7)*	31 (31.6)*	**0.001**
No	404 (63.0)	188 (56.3)	149 (71.3)*	67 (68.4)*	
Use of multivitamins	[n=641]	[n=334]	[n=209]	[n=98]	
Yes	505 (78.8)	274 (82.0)	161 (77.0)	70 (71.4)	**0.059**
No	136 (21.2)	60 (18.0)	48 (23.0)	28 (28.6)	

n : number of valid data available for each combination of variables may be less than 641 because of missing data in some variables or the analysis is restricted to users only as in contraceptive use details.
$p < 0.05$ (overall for the 3 groups) indicates a significant association based on Chi-square test of independence.
*: indicates a significant difference when compared to the Western reference group (R).

Table II: Categorisation of drugs according to reason for use

Category I: Drugs for chronic conditions	Category II: Drugs for occasional and short-time use	Category III: Pregnancy-related drugs
Gastrointestinal bile and liver therapy (A05)	Stomatological preparations (A01)	Antacids (A02A)
Drugs used in diabetes (A10)	Antispasmodic and anticholinergic agents and propulsives (A03, excl. A03FA01)	Antiemetics (A03FA01, R06AE)
Antithrombotic agents (B01)	Antidiarrhoeals, intestinal anti-inflammatory/anti-infective agents (A07)	Laxatives (A06)
Cardiovascular antihypertensive drugs (C02)	Antihemorrhagics (B02)	Gynaecological anti-infectives and antiseptics (G01)
Lipid modifying agents (C10)	Vasoprotectives (C05)	Sex hormones and modulators of the genital system (G03)
Corticosteroids, dermatological preparations (D07)	Antifungals for dermatological use (D01)	
Pituitary and hypothalamic hormones and analogues (H01)	Antipruritics, including antihistamines, anesthetics, etc (D04)	
Corticosteroids for systemic use (H02)	Antibiotics and chemotherapeutics for dermatological use (D06)	
Thyroid therapy (H03)	Antiseptics and disinfectants (D08)	
Anti-infective systemic antivirals (J05)	Antiacne preparations (D10)	
Anti-inflammatory and antirheumatic products (M01)	Antibacterials for systemic use (J01)	
Anti-Parkinson drugs (N04)	Immune sera and immunoglobulins (J06)	
Antipsychotics (N05A)	Analgesics and antipyretics (N02B)	
Antidepressants (N06A)	Anxiolytics (N05B)	
Antiasthmatics (R03)	Hypnotics and sedatives (N05C)	
	Antihistamines for systemic use (R06, excl. R06AD and R06AE)	
	Ear, eye, nose and throat preparations (S01, R01, R02A, R05)	

Table III: Differences in exposure to drugs before and throughout pregnancy

	Before conception Number of drugs	% women exposed (number of women)£	**First trimester** Number of drugs	% women exposed (number of women)£	***p*-value**	**Second trimester** Number of drugs	% women exposed (number of women)£	***p*-value**	**Third trimester** Number of drugs	% women exposed (number of women)$	***p*-value**
Reason of use:											
Chronic	64	7.0 (44)	84	9.0 (60)	**0.102**	78	9.0 (56)	0.697 **0.211**	33	6.0 (23)	0.098 **0.557**
Occasional	64	9.0 (58)	80	10.0 (65)	**0.507**	97	12.0 (78)	0.249 **0.070**	38	8.0 (33)	0.043 **0.623**
Pregnancy related	9	1.0 (8)	31	5.0 (29)	**0.000**	43	6.0 (40)	0.173 **0.000**	16	4.0 (14)	0.056 **0.013**
Prescription or OTC:											
OTC	62	9.0 (58)	90	12.0 (74)	**0.142**	104	13.0 (83)	0.443 **0.026**	42	9.0 (37)	0.076 **0.883**
Prescription	74	8.0 (53)	106	12.0 (77)	**0.026**	113	14.0 (90)	0.281 **0.001**	44	8.0 (33)	0.006 **0.980**
FDA risk factor:											
A/B	83	12.0 (78)	104	15.0 (93)	**0.218**	99	14.0 (88)	0.688 **0.406**	48	11.0 (42)	0.136 **0.437**
C/D	41	5.0 (34)	62	7.0 (48)	**0.110**	62	8.0 (49)	0.916 **0.089**	24	5.0 (21)	0.142 **0.992**
U	12	2.0 (12)	33	5.0 (30)	**0.005**	58	8.0 (53)	0.009 **0.000**	17	4.0 (16)	0.008 **0.037**

£: number of women for whom information was available (n = 641).
$: number of women for whom information was available (n = 397).
Third trimester drug use: information was only available for 397 women (third trimester interviewee) and proportions for the third trimester were calculated according to this number.
% women exposed: represents the percentage of women who used drugs from the respective categories; Proportions were calculated as: number of women exposed to certain kind of drugs / total number in each group.
The **bold** font *p*-values: compared to the **before conception** exposure.
The normal font *p*-values: compared to the preceding trimester.
First trimester exposure was by default compared to the preceding period.
$p < 0.05$: indicates a statistically significant difference based on the significant test for comparing two proportions (Two-sided z-test). The test is available online: http://math.uc.edu/~brycw/classes/149/wang.htm.

Table IV: Differences in mean number of preparations used according to ethnicity

	Total population	*p*-value overall test	Western (R)	Arab/Turkish	*p*-value	Other origins	*p*-value
ANOVA test (mean number for the whole group):							
Medications including multivitamins	1.77	**0.000**	2.02	1.50	**0.000**	1.48	**0.002**
Medications excluding multivitamins	0.58	**0.000**	0.72	0.42	**0.000**	0.46	**0.035**
Multivitamins	1.18	**0.004**	1.29	1.09	**0.024**	1.02	**0.022**
ANOVA test (mean number for users only in each group):							
Medications including multivitamins	2.11	**0.000**	2.35	1.79	**0.000**	1.93	**0.028**
Medications excluding multivitamins	1.58	**0.200**	1.66	1.45	**0.352**	1.45	**0.683**
Multivitamins	1.50	**0.034**	1.58	1.41	**0.059**	1.43	**0.373**

n : number of valid data available for each group
$p < 0.05$ (overall for the 3 groups or pair-wise) indicates a significant difference based on ANOVA test (with Bonferroni post hoc test) and using the Western group as the reference group (R).

Table V: Differences in exposure to drugs among the three ethnic groups

	Total drug use Number of drugs	**Western women (R) (n = 334)** Number of drugs	% women exposed (number of women)	**Arab/ Turkish women (n = 209)** Number of drugs	% women exposed (number of women)	***p*-value**	**Other origins women (n = 98)** Number of drugs	% women exposed (number of women)	***p*-value**
Reason of use:									
Chronic	103	69	15.0 (49)	26	10.0 (21)	**0.118**	8	6.0 (6)	**0.026**
Occasional	192	120	26.0 (86)	42	14.0 (30)	**0.002**	30	24.0 (24)	**0.801**
Pregnancy related	78	50	13.0 (45)	19	9.0 (18)	**0.085**	7	6.0 (6)	**0.047**
Prescription or OTC:									
OTC	205	135	29.0 (96)	47	15.0 (32)	**0.000**	23	18.0 (18)	**0.041**
Prescription	167	105	22.0 (75)	39	16.0 (33)	**0.058**	22	18.0 (18)	**0.387**
FDA risk factor:									
A/B	186	113	28.0 (94)	50	22.0 (45)	**0.086**	23	17.0 (17)	**0.032**
C/D	95	66	16.0 (52)	19	7.0 (14)	**0.002**	10	8.0 (8)	**0.062**
U	90	61	16.0 (54)	18	8.0 (16)	**0.004**	11	10.0 (10)	**0.144**

% women exposed: represents the proportion of women who used drugs from the respective categories; Proportions were calculated as: number of women exposed to certain kind of medications / total number in each group.
The Western group is the reference group (R) that was compared with the Arab/Turkish and with the "Other origins" group.
n : number of valid data available for each group.
The total number of medications is less than 374 because of missing values.
$p < 0.05$ (overall for the 3 groups) indicates a statistically significant difference based on the significant test for comparing two proportions (Two-sided z-test). The test is available online: http://math.uc.edu/~brycw/classes/149/wang.htm.