Characteristics of health behaviours and health status indicators among pregnant women in Slovenia

Navade, povezane z zdravjem in socialno demografske značilnosti nosečnic v Sloveniji

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Izvleček

Izhodišča: Nosečnost je obdobje, ko ženske za zdravje bodočega otroka kritično presojajo in ocenjujejo svoje zdravje ter z zdravjem povezane navade. Skupaj z zdravstvenimi delavci se srečujejo s številnimi tveganji in odločitvami, ki postanejo veliko kompleksnejše, saj je v igri vpliv na dva organizma. Namen članka je pregled ter iskanje morebitnih povezav med zdravjem, z zdravjem povezanimi navadami ter socialno demografskimi dejavniki v nosečnosti, ki so jih poročale sodelujoče ženske.

Metode: Podatke študije smo pridobili v okviru raziskovalnega projekta Analiza bioloških označevalcev presnove folatov pri ugotavljanju tveganja za nastanek napak nevralne cevi, orofacialnih shiz ter prirojenih srčnih napak, ki je potekal od maja 2013 do septembra 2015. Vprašalnik o maternalnem zdravju, z zdravjem povezanih navadah ter socialno demografskih karakteristikah je izpolnilo 450 sodelujočih žensk. Podatki zajemajo nosečnosti, ki datirajo od osemdesetih let prejšnjega stoletja pa do leta 2015.

Rezultati: Mlajše in manj izobražene ženske so pogosteje poročale o kajenju med nosečnostjo, medtem ko so starejše, bolj izobražene ter nulipare ženske v višjem odstotku jemale folatne/multivitaminske dodatke. Opazili smo U-obliko porazdelitve uporabe zdravil (brez recepta in na recept) glede na stopnjo izobrazbe. Najvišji odstotek uporabe so imele ženske z najvišjo stopnjo izobrazbe (magisterij/doktorat) in ženske z doseženo najnižjo stopnjo izobrazbe (osnovna šola). Večjo uporabo zdravil med nosečnostjo so poročale tudi starejše ženske. Opazili smo trend višanja uporabe zdravil in folatnih/multivitaminskih pripravkov kot tudi incidence nosečniške sladkorne bolezni preko preiskovanega obdobja, z najvišjo incidenco v zadnjih desetletjih. Višjo pojavnost kroničnih bolezni smo opazili v skupini multiparih žensk.

Zaključki: V navadah povezanih z zdravjem nosečnic obstajajo precejšnje socialno demografske razlike. Za izboljšanje zdravja so potrebni izboljšani javno zdravstveni ukrepi in individualno svetovanje, da lahko ustrezno naslovimo specifične potrebe socialno demografskih skupin z višjim tveganjem za neželene izide nosečnosti.

Abstract

Background: Pregnancy is a period when women reconsider their own health and health related behaviour for the sake of their future child. Along with their health providers, they are faced with a number of risk assessments and decisions, which become far more complex as their effect on two organisms rather than one is at play. This paper provides an overview of possible associations between self-reported health status, health behaviours and socio-demographics during pregnancy.

Methods: Study data were obtained from the case-control research project "Analysis of folate metabolism biomarkers in the risk assessment for neural tube defects, orofacial clefts and congenital heart defects", which recruited participants from May 2013 to September 2015. Questionnaires about maternal health, health related behaviour and socio-demographic characteristics were completed by 450 women. The data include pregnancies from the 1980s to 2015.

Results: We observed that younger and less educated women more frequently reported positive smoking status during pregnancy, while higher prevalence of folate/multivitamin supplementation was found among more educated, older and nulliparous women. There was a U-shaped distribution of medication intake (over-the-counter and prescribed) with respect to educational level, with the highest intake in mothers with a masters/PhD degree and among those that completed elementary school. Higher medication usage was also reported among older women. With increasing maternal age there was an increase in medication intake, folate/multivitamin intake, as well as incidence of gestational diabetes over the studied time period, with the highest frequencies occurring in later decades. A higher incidence of chronic diseases was observed in a group of multiparous women than among monoparous women.

Conclusions: Considerable socio-demographic disparities exist in health-related behaviour among pregnant women. Improved public health campaigns and individual health care counselling are needed to address specific requirements of socio-demographic groups at higher risks of adverse pregnancy outcomes.

1. Introduction

Pregnancy is an important time in the lives of many women. It is also the time when they may consider or reconsider their own health, as well as the health of their future child. Some women may experience a conflict between the management of the two (1).

Since the thalidomide disaster of the late 1950s and early 1960s women have been given strong messages about the importance of maintaining their health and avoiding toxins that can be transferred from mother to baby. Once pregnancy is confirmed, women are faced with a multitude of decisions and risk assessments (2). They must decide what to eat, what to drink, what test they will undergo and nearly every pregnant woman faces a decision about whether or not to take a medication during pregnancy, ranging from over-the-counter (OTC) antacids for gastroesophageal reflux to prescription medications for life-threatening chronic conditions (2,3). In the last three decades the use of medications during pregnancy has increased and it is now common during pregnancy (3,4). Estimates of the usage prevalence of at least one prescription medication during pregnancy range from less than 30 % to over 90 % of women (3). In multinational study that collected data in years 2011–2012, 71.1 % of participating women reported use of medication during pregnancy (OTC and/or prescribed medication) in Slovenia (5). The safety of medication use during pregnancy is frequently unclear because, for the majority of medications, there is a lack of sufficient data available to fully characterise the foetal risk. Thus, it is difficult to make informed clinical decisions about the best management of acute and chronic disorders during pregnancy (3,4). Since 1979, health care providers used a standard five-letter nomenclature published by the Food and Drug Administration (FDA) to assign a pregnancy risk category to medications (6). The FDA recently revised its existing system and introduced a new "Pregnancy and Lactation Labelling Rule", which became effective in June 2015.

Women also make important decisions during pregnancy in terms of other types of exposure, for example, alcohol, smoking and certain food items (1). Many women continue to consume alcohol in pregnancy despite an increasing body of evidence suggesting harm to the foetus (7,8). Maternal smoking during pregnancy also poses a significant risk to the unborn child. As there is no safe lower limit of cigarette use during pregnancy, the World Health Organization advises pregnant women to abstain from cigarettes altogether (9). Despite the extensive information about dangers that smoking poses to their foetus, some women continue smoking. It has been estimated that 10–27 % of the pregnant women in the European Union continue smoking during pregnancy (9,10). In 2014 published multi-national study, Slovenian data revealed that out of 32.9 % of women who smoked before pregnancy, 6.7 % continued smoking during pregnancy (9). According to a study, Petersen et al. (2014), on women's perception of risks of adverse foetal pregnancy outcomes that also included Slovenian data, alcohol and smoking were perceived to carry high risks in pregnancy (1). Both substances are considered deleterious to the foetus although there are still debates whether there is a safe threshold for drinking alcohol during pregnancy (1). Raymond et al. (2009) study showed that women found information and advice about safe levels of drinking in pregnancy confusing and lacking in evidence and detail (1,11).

In contrast, the importance of nutrition during pregnancy with regard to the pregnancy outcome has long been recognised (12,13). For example, pregnancy causes a two- to three-fold increase in the requirement for iron, not only for haemoglobin synthesis but also for the foetus and the production of certain enzymes. There is also a ten- to twenty-fold increase in folate requirements and a two-fold increase in the requirement for vitamin B12 (14). Over the last three decades, substantial epidemiological evidence has emerged to indicate that periconceptional folate and multivitamin supplementation reduces the risk of adverse pregnancy outcomes (15,16). Women rely not only on medical information from the expert knowledge of their health care providers but also on their own experience, education and cultural understanding (2,17). Research related to a variety of perinatal and infant health outcomes suggested that maternal socio-economic status (SES) that generally correlates with maternal level of education prominently influences perinatal and infant health (17). Although many studies have suggested that a lower SES is associated with an increased risk of neural tube defects (NTDs), many other studies found no correlation with adverse pregnancy outcomes when adjusting for race-ethnicity, multivitamin intake, cigarette smoking and binge drinking (16-18).

Public health discourse has increasingly framed personal health choices as social and moral issues, and, as a consequence, many women feel overly responsible for producing and maintaining a healthy child (2). This increasing pressure has resulted in hyper-vigilant pregnant women going out of their way to avoid any possible toxins, while also adopting unhealthy behaviours, such as smoking and excessive eating in response to the stress of "intensive motherhood" (2,19). A recent Slovenian study reported that the same dilemmas continue during postpartum period, showing that breastfeeding mothers used less medications and nutritional supplements compared to non-breastfeeding mothers (20). Precise and accurate information on medications, possible environmental toxins, diet and other health-related behaviours during pregnancy is called for in order to help women and their health providers rationally solve their dilemmas. The action points of the European board and college of obstetrics and gynaecology (EBCOG, 2016) position statement asks the scientific public for an EU-wide assessment of current practice and future needs along with informational campaign to facilitate proactive information sharing and counselling about medication use in pregnancy (21). Considering the latter, the aim of this paper is to observe for possible associations between women's self-reported health status, health behaviours and socio-demographics during pregnancy in different time periods.

2. Methods

2.1. Study design and participants

This study was an observational, retrospective cohort study of 450 mothers that delivered live-born, healthy new-borns, with no major birth defects. It was part of the case-control research project *"Analysis of folate metabolism biomarkers in the risk assessment for neural tube defects, orofacial clefts and congenital heart defects"* (ARRS J3–5507). Women were recruited during routine post-partum 3-day hospitalization at the Division of Gynaecology and Obstetrics, University Medical Centre Ljubljana (UMCLJ) and during routine follow up examinations of their children with orofacial clefts (OFC) or congenital heart disease (CHD) at the Department of Maxillofacial and Oral Surgery at UMCLJ and the Paediatric Clinic of UMCLJ, respectively. In the latter instances pregnancy data of the healthy siblings of case children were included in the study. This is why the data do not cover just recent years but date back to 1980s because healthy siblings were born in a time interval from 1980 to 2015.

This study was an observational, retrospective cohort study of 450 mothers; 200 mothers who gave birth to healthy children without birth defects were recruited during routine 3-day post-partum hospitalisation between 2013 and 2015. They provided information about their behaviour during their just-concluded pregnancy. The most recent pregnancies included in this study were concluded in 2015.

The remainder of the study participants were recruited during doctors' appointments for their children with cleft lip/palate (OFC) or congenital heart disease (CHG). Mothers were recruited who delivered at least one live-born, healthy new-born, with no major birth defects, before delivering at least one child with cleft lip/palate (OFC) and congenital heart disease (CHG). The mothers provided questionnaire answers about their behaviour during the pregnancy of their last child born with no birth defects. The earliest pregnancies included in this study were concluded in 1980.

Every participant gave information about only one pregnancy, i.e. their last pregnancy that was concluded with a live-born child with no birth defects.

The study gathered self-reported information on the use of medication, folate and nutritional supplementation, health status, smoking status, and socio-demographic characteristics via questionnaire. Before completing the questionnaire, all mothers were required to sign informed consent forms. The study was approved by the National Medical Ethics Committee (No. 57/02/13).

2.2. Evaluation of maternal health-related and socio-demographic characteristics

All participating mothers completed a questionnaire that included questions about their age at conception, height and weight, smoking status, education, number of pregnancies, live births and miscarriages, child's gender, history of gestational diabetes and chronic diseases, drug use during pregnancy, fever during pregnancy, folate and vitamin supplementation before conception and during pregnancy.

2.3. Drug classification

Reported medications taken during pregnancy by the women in the studied cohort were classified according to the ATC (Table 2) and FDA classifications (Figure 3D). Statistical analysis was performed for drugs of all FDA classes (A,B,C,D,X) and for the three most represented (> 5 %) groups of medications in the study cohort according to ATC classification, i.e. A12C (other mineral supplements), B03A (iron preparations) and N02B (other analgesics and antipyretics) .

2.4. Statistical analysis

Variables evaluated by the questionnaire were classified as either continuous (maternal age at conception, height and weight, number of pregnancies, live births and miscarriages, year of delivery) or categorical (maternal smoking status, education, child's gender, history of gestational diabetes and chronic diseases, drug use during pregnancy, fever during pregnancy, folate and vitamin supplementation before conception and during pregnancy). The Kolmogorov-Smirnov test was used to test the distribution of continuous variables. For univariate statistical analysis the Mann-Whitney U test was used for non-Gaussian continuous and ordinal variables and Fischer's exact test for categorical variables. Logistic regression models were used to further explore characteristics of study cohort. Purposeful selection of candidate variables was done based on p value < 0.250, calculated by means of univariate statistical analysis. Only variables that met these criteria were included in the logistic regression models and adjusted for co-variables. Odds ratios (OR) were determined using logistic re-

Table 1: Main characteristics of the study cohort. N designates the number of women included in the analysis.

Characteristics	N	Number of cases (%)
Smoking in pregnancy	449	52 (12 %)
Fever in pregnancy	450	20 (4 %)
Gestational diabetes	450	43 (10 %)
Maternal chronic disease	450	54 (12 %)
Drug administration in pregnancy	450	179 (40 %)
Folate and/or multivitamin supplements in pregnancy	450	351 (78 %)
Use of folate supplements : • Containing folic acid only • Containing metafolin and folic acid	450 317 317	317 (70 %) 291 (92 %) 26 (8 %)

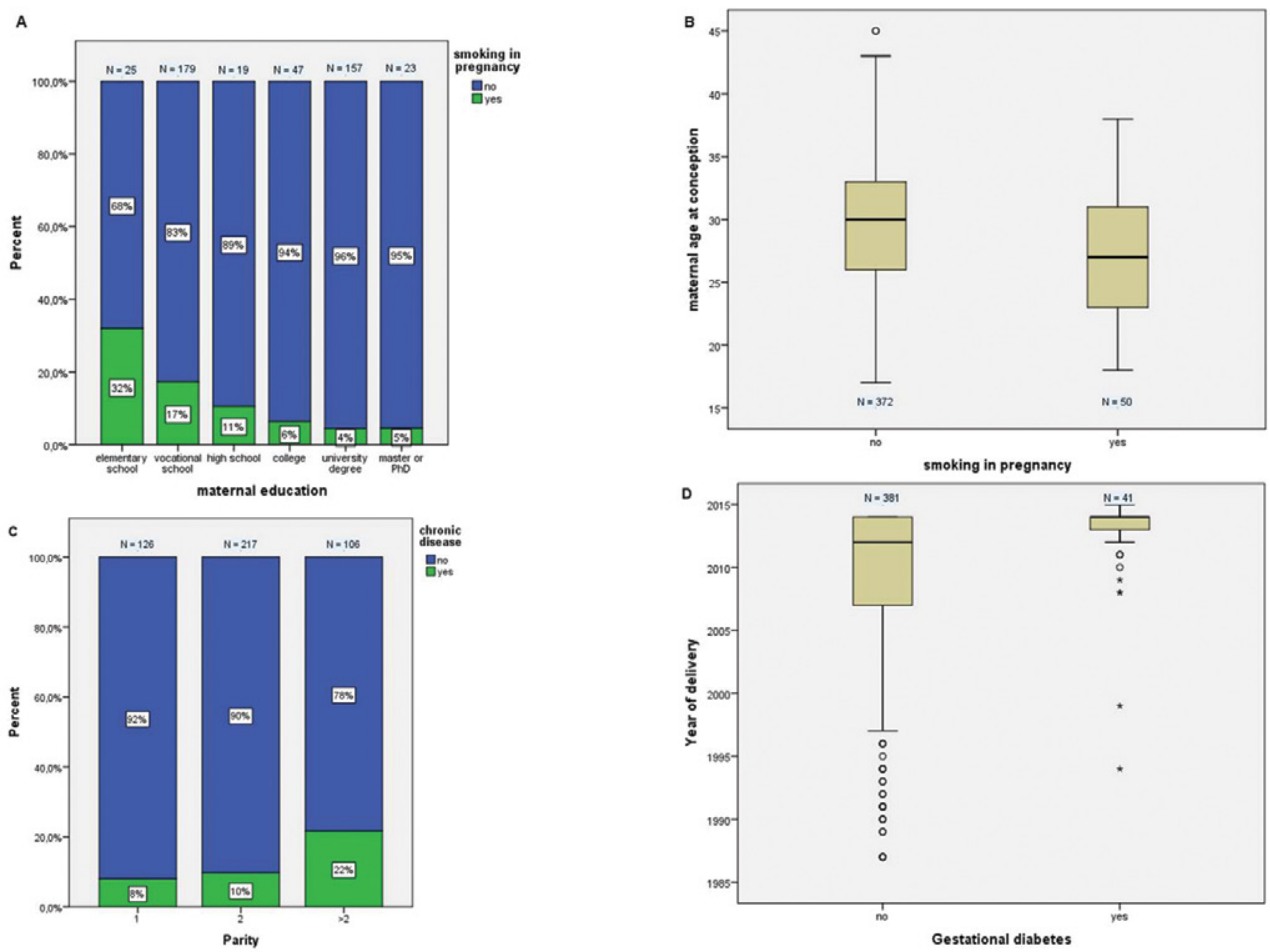

Figure 1: Association of maternal demographic characteristics with the incidence of smoking in pregnancy, maternal chronic disease and gestational diabetes.

Only characteristics exhibiting a statistically significant difference across the subgroups are shown. (A) Mothers with elementary school level of education had an increased prevalence of smoking in pregnancy compared to mothers with a college education (OR(95 %CI): 6 (1.3–26), p = 0.021) or university degree (OR(95 %CI): 10 (3–36), p < 0.001). (B) Mothers who smoked in pregnancy were younger at conception than non-smoking mothers (p = 0.019). The significance was not present after adjusting for maternal education in the logistic regression model. (C) Mothers who had more than 2 children had an increased prevalence of chronic diseases (OR(95 %CI): 3 (1.3–8), p = 0.027) compared with mono-parous mothers. (D) The data suggests a trend of increased incidence of gestational diabetes in the group of mothers who gave birth in more recent years (OR(95 %CI): 1.14 (1.04–1.26), p = 0.008).

gression models, 95 % confidence intervals for OR and p values. A p value < 0.05 was considered statistically significant. All analyses were carried out using IBM SPSS Statistics 22. To calculate the correlation between the independent variables of logistic regression models Spearmann rho test was used.

3. Results

A total of 450 women participated in the study. The main characteristics are shown in Table 1. All characteristics were investigated according to the delivery period, maternal education, parity and age.

3.1. Maternal characteristics

Of the 449 women who gave information on their smoking status, 52 (12 %) reported smoking during pregnancy (Table 1). According to the results, the percentage of smokers during pregnancy has decreased in the last 30 years, as 18 % of mothers, who delivered in 1980s, reported smoking during pregnancy compared to 10 % of woman who delivered in the period of 2011–2015. The decrease however was not statistically significant ($p = 0.372$). Difference in the percentage of smokers between study subsets with different levels of education was statistically significant ($p = 9.6 \times 10^{-5}$). A lower level of education was associated with smoking during pregnancy (32 % of women who finished elementary school smoked during pregnancy compared to just 5 % of those with masters/PhD degrees). The significant association of maternal education with smoking during pregnancy was still present after adjusting for maternal age at conception in a logistic regression model (Figure 1A). There was no correlation between parity and smoking status ($p = 0.259$), with 11 %, 14 % and 8 % of smokers among women who had 1, 2 and > 2 children, respectively. A statistically significant correlation between smoking in pregnancy and maternal age at conception was observed ($p = 0.019$): smoking mothers conceived at a younger age. Adjusting for maternal education in a logistic regression model (Figure 1B) statistical significance did not persist, possibly because of the correlation between maternal education and maternal age at conception (Spearman rho = 0.420, $p = 1.6 \times 10^{-19}$).

Out of 450 participating mothers, 20 (4 %) reported fever during pregnancy. There was no statistically significant association between reported fever during pregnancy and year of delivery ($p = 0.785$), level of maternal education ($p = 0.654$), parity ($p = 0.170$) and maternal age at conception ($p = 0.621$)). Due to the small number of subjects that experienced fever during pregnancy, logistic regression was not performed.

Chronic disease was reported by 54 (12 %) participants and 396 (88 %) denied having a chronic health condition. There was a statistically significant association between parity and reported chronic disease. Mothers with 2 (10 %) and especially more than 2 children (22 %) reported higher prevalence of chronic disease than monoparous women (8 %) ($p = 0.004$). The significance (for mothers with more than 2 children) was still present after adjusting for maternal age at conception and date of delivery in a logistic regression model (Figure 1C). There was no significant association of chronic disease with any other maternal characteristic, i.e date of delivery ($p = 0.192$), maternal level of education ($p = 0.560$) and age at conception ($p = 0.157$).

Among the 450 participants, 43 (10 %) reported occurrence of gestational diabetes (GD). There was suggested trend of higher GD incidence among women that delivered in more recent years, $p = 0.008$) (Figure 1D) and among older mothers (borderline statistical significance; $p = 0.085$). There was no significant association of GD with maternal education ($p = 0.501$) and parity ($p = 0.490$). Because of the small number of GD cases, it was not possible to construct a suitable logistic regression model.

The majority of participating mothers reported supplementation with folic acid and multivitamins (N = 351, 78 %) during pregnancy (Table 1). Women who gave birth more recently were much more likely to take folate and multivitamin supplements than those who delivered in the earlier years ($p < 0.001$). The signi-

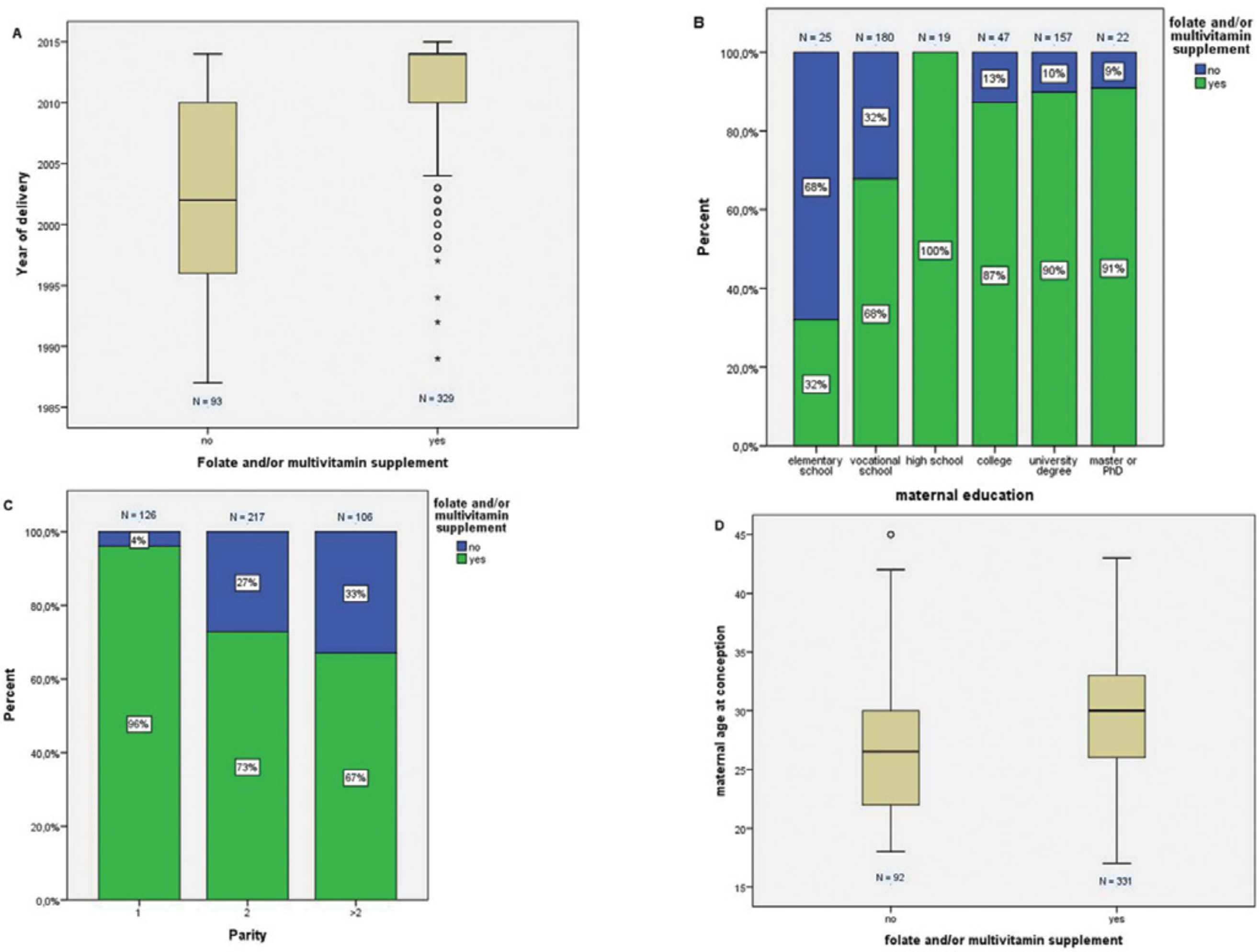

Figure 2: Association of maternal demographic characteristics with folate and multivitamin supplementation during pregnancy. *Only characteristics exhibiting statistically significant difference across the subgroups are shown. (A) Mothers who gave birth in more recent years had greater folate and multivitamin consumption in pregnancy compared to those who delivered in earlier years, OR(95 %CI): 1.17 (1.11–1.24), p < 0.001. (B) Mothers with higher levels of education (i.e. vocational school, college, university and master/PhD degree) had higher folate and multivitamin consumption in pregnancy compared to those who completed only elementary school, OR(95 %CI): 4(1.3–11), p = 0.014, 9(2–36), p = 0.003, 8(2–26), p = 0.001, 10(1.4–64), p = 0.019, respectively. (C) Mono-parous mothers had higher consumption of folates and multivitamins during pregnancy compared to mothers having two (OR(95 %CI): 4(1.1–11), p = 0.028) or more than two children (OR(95 %CI): 4(1.2–15), p = 0.021). (D) Mothers who took folate and multivitamin supplements during pregnancy were older than those who did not (p < 0.001). The significance was not present after adjusting for year of delivery, maternal education and parity in the logistic regression model.*

ficance was still present after adjusting for education, parity and maternal age at conception in the logistic regression model (Figure 2A). Furthermore, there was a significant statistical association between folate and multivitamin supplementation and the level of maternal education. Mothers with lower level of education (i.e. elementary school) had a considerably lower percentage of supplementation (32 %) in contrast to mothers with finished college (87 %), university (90 %) and master/PhD degree (91 %) ($p < 1 \times 10^{-6}$). The significance persisted after adjusting for delivery period, parity and maternal age at conception in the logistic regression model (Figure 2B). There was also a statistically significant association between supplementation and parity, with highest percentage of supplement usage among monoparous women (96 %) in comparison to women who gave birth to 2 (73 %) and more than 2 children (67 %) ($p < 1 \times 10^{-6}$). The significance persisted after adjusting for maternal education, parity and maternal age at conception in the logistic regression model, (Figure 2C). Supplement usage was more prevalent among older women, with higher age at conception, compared to younger mothers ($p < 0.001$), though significance was not present after adjusting for year of delivery, maternal education and parity in logistic regression model (Figure 2D). Since only 8 % (N = 26) of mothers who took folate supplements used 5-methylfolate preparations, further analysis in this respect was not performed.

Consumption of medications (prescribed or OTC) during pregnancy was reported by 60 % (N = 271) of participating women (Table 1). The prevalence of medication usage during pregnancy has increased in the latest decades ($p < 0.001$). None of the women who gave birth in 1980s reported medication consumption during pregnancy, while in the following decades there was a significant trend of increased consumption (in 1990s 26 %, in 2001–2010 32 % and in 2011–2015 48 %). Significant association of higher drug intake with later year of delivery was still present after adjusting for maternal education and maternal age at conception in the logistic regression model ((OR(95 %CI): 1.07(1.03–1.18), $p = 0.001$) (Figure 3A).

We observed a U distribution of reported medication usage versus the level of maternal education ($p = 0.012$). The highest prevalence of medication usage during pregnancy was noted in groups with the lowest (elementary school, 44 %) and the highest levels of education (university, 46 % and master/PhD degree, 64 %) compared to groups with middle-ranged levels of education (vocational school, 34 %, high school, 37 % and college, 26 %). In accordance with this, after adjustment in the logistic regression models, mothers with completed elementary school and masters/PhD degrees had higher prevalence of drug consumption than those with college degrees (Figure 3B). Parity showed no statistically significant correlation with medication usage during pregnancy ($p = 0.339$). There was a statistically significant trend of higher drug consumption during pregnancy among mothers that were older at conception ($p = 0.022$), however the significance did not persist after adjusting for the year of delivery and maternal education in the logistic regression model (Figure 3C).

3.2. Medication usage in pregnancy according to the ATC and FDA classifications

3.2.1. ATC classification

Intake of A12C group of drugs was reported by 27 (6 %) of participating women. The consumption of A12C medications varied across different delivery periods ($p = 8.2 \times 10^{-5}$). Ten percent of women who delivered after 2010 used A12C medications. Statistically significant increase in the incidence of A12C drug consumption was observed for mothers with higher levels of education (elementary school, 0 %, university, 8 % and master/PhD degree, 14 %; $p = 0.009$) and in monoparous mothers (15 % in contrast to mothers with 2 (4 %) or more than 2 children (0 %); $p = 1 \times 10^{-6}$). Due to the small number of women taking A12C medications a logistic regression model was inapplicable.

Iron preparation intake (ATC code B03A) was reported by 78 (17 %) par-

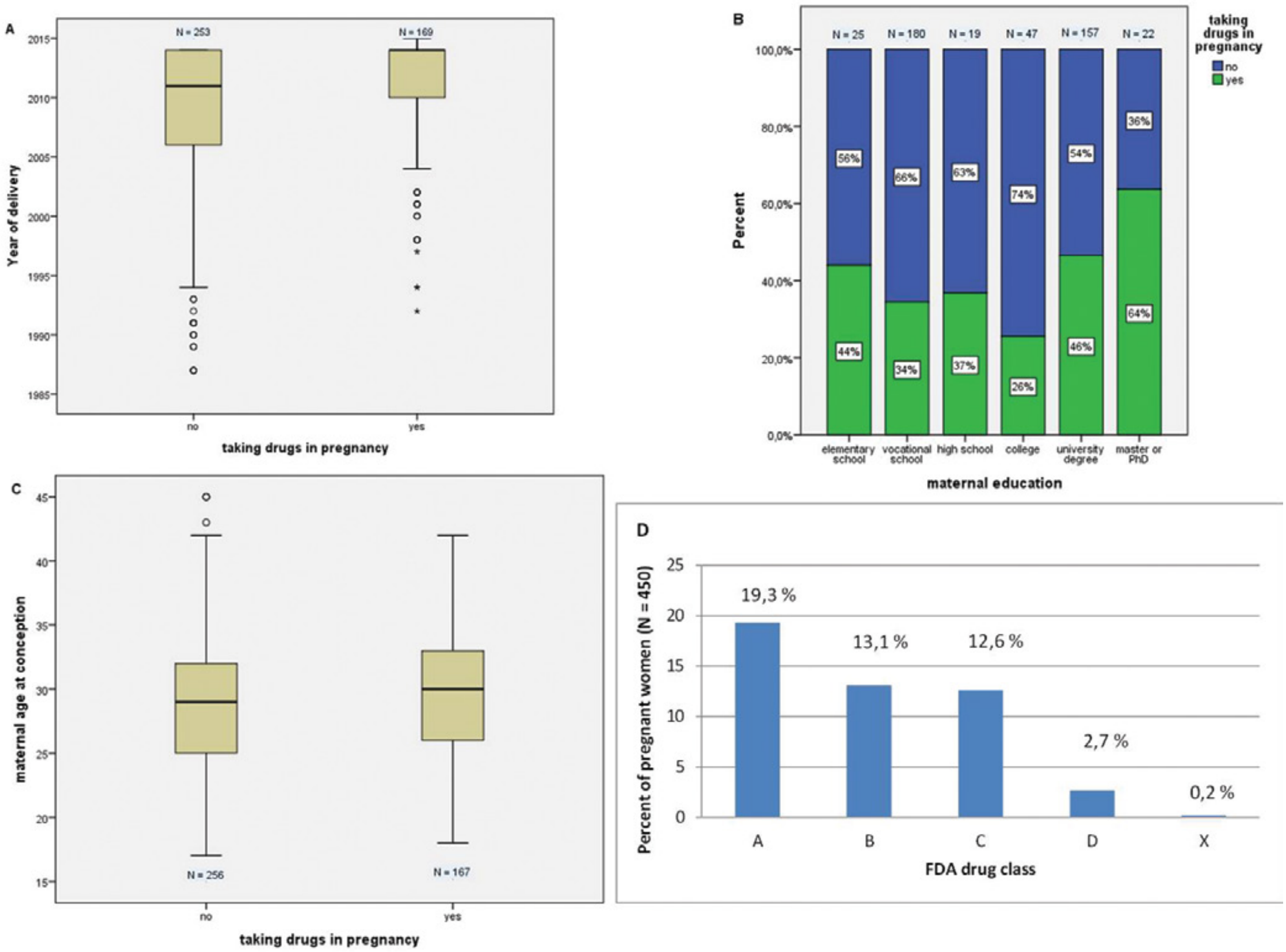

Figure 3: Association of maternal demographic characteristics with drug administration in pregnancy.
Only characteristics exhibiting statistically significant difference across the subgroups are shown. (A) Mothers who gave birth in more recent years had higher prevalence of drug consumption during pregnancy compared to those who delivered in the earlier years (OR(95 %CI): 1.07(1.03–1.18), p = 0.001). (B) The distribution of prevalence of drug consumption according to maternal education was U shaped, with higher prevalence during pregnancy in mothers with the lowest (elementary school) and highest (university and master/PhD degrees) level of education (p = 0.012). In accordance with this, after adjustment in the logistic regression models, mothers who completed elementary school (OR(95 %CI): 4(1.3–13), p = 0.018) and masters/PhD degrees (OR(95 %CI): 5(1.5–15), p = 0.007) had a higher prevalence of drug consumption than those with a college degree. (C) Mothers who took drugs during pregnancy were older than those who did not (p = 0.022). The significance was not present after adjusting for year of delivery and maternal education in the logistic regression model. (D) The distribution of incidence of drug usage during pregnancy according to FDA classification.

ticipants. All of them gave birth after 1990, the highest incidence was after 2011 (1980s: 0 %, 1990s: 13 %, 2001–2010: 13 % and 2011–2015: 22 %). This trend was borderline statistically significant with a p value of 0.058. Correlations to all other tested maternal characteristics were statistically insignificant, i.e. level of maternal education (p = 0.694), parity (p = 0.178) and maternal age at conception (p = 0.763). Due to the small number of women who took B03A medications, a logistic regression model was inapplicable.

Consumption of N02B drugs was reported by 30 (7 %) of participants. N02B intake according to maternal level of education gave U distribution, with the

Table 2: Prevalence of drug consumption during pregnancy in the study cohort according to the ATC classification.

ATC group		Cases taking drugs from the specific ATC group Count (%)
A ALIMENTARY TRACT AND METABOLISM		
A02A	Antacids	7 (1,6)
A02B	Drugs for peptic ulcer and GORD	2 (0,4)
A03B	Belladona & derivatives	10 (2,2)
A07B	Intestinal adsorbents	1 (0,2)
A07E	Intestinal antiinflammatory agents	2 (0,4)
A07F	Antidiarrheal microorganisms	1 (0,2)
A11D	Vitamin B1	1 (0,2)
A12A	Calcium	2 (0,4)
A12C	Other mineral supplements	27 (6,0)*
B BLOOD AND BLOOD FORMING ORGANS		
B01A	Antithrombotic agents	2 (0,4)
B03A	Iron preparations	78 (17,3)*
C CARDIOVASCULAR SYSTEM		
C01A	Cardiac glycosides	1 (0,2)
C01B	Antiarrhythmics, class I & III	1 (0,2)
C01D	Vasodilatators for cardiac diseases	1 (0,2)
C02A	Antiadrenergic agents, central acting	2 (0,4)
G GENITO URINARY SYSTEM AND SEX HORMONES		
G01A	Antiinfectives & antiseptics	3 (0,7)
G03C	Estrogens	1 (0,2)
G03D	Progestogens	6 (1,3)
G03F	Progesterons & estrogens in combination	1 (0,2)
G04B	Urologicals	4 (0,9)
H SYSTEMIC HORMONAL PREPARATIONS, EXCL. SEX HORMONES AND INSULINS		
H02A	Corticosteroids for systemic use	1 (0.2)
H03A	Thyroid preparations	8 (1.8)
J ANTIINFECTIVES FOR SYSTEMIC USE		
J01C	Penicillins	18 (4.0)
J01F	Macrolides, Lincosamides & Streptogramines	4 (0.9)
J01X	Other antibacterials	1 (0.2)

ATC group		Cases taking drugs from the specific ATC group Count (%)
N NERVOUS SYSTEM		
N02B	Other analgesics & antipyretics	30 (6.7)*
N02C	Antimigraine preparations	1 (0.2)
N03A	Antiepileptics	4 (0.9)
N05A	Antipsyhotics	1 (0.2)
N05B	Anxiolytics	1 (0.2)
N06A	Antidepressants	3 (0.7)
R RESPIRATORY SYSTEM		
R01A	Decongestants and other nasal preparations for topical use	1 (0.2)
R02A	Throat preparations	3 (0.7)
R03A	Adrenergics inhalants	2 (0.4)
R03B	Other drugs for obstructive airway diseases–inhalants	1 (0.2)
R03D	Other systemic drugs for obstructive airway diseases	1 (0.2)
R06A	Antihistamines for systemic use	1 (0.2)
S SENSORY ORGANS		
S01A	Antiinfectives	1 (0.2)

**Only ATC classes of drugs with prevalence of consumption above 5 % were subjected to further statistical analysis.*

highest percentage of users in groups with the lowest and highest levels of education (elementary school 12 %, master/PhD degree 23 %). Also, N02B users tended to be older. These associations had borderline statistical significance with p values of 0.063 for level of education and 0.052 for age at conception. No statistically significant association was found versus parity (p = 0.202) or date of delivery (p = 0.825). Due to the small number of women who took N02B medications, a logistic regression model was inapplicable.

3.2.2. FDA classification

Out of 450 participants, 87 (19 %) reported taking FDA class A medications. There was a trend of increasing consumption over the time period of the study. This was especially significant for mothers who gave birth after year 2011 (1990s: 13 %, 2001–2010: 16 % and 2011–2015: 23 %). The association had a borderline statistical significance with a p value of 0.087. All other tested maternal characteristics [maternal education (p = 0.584), parity (p = 0.313) and maternal age at conception (p = 0.406)] did not show statistically significant associations. Since there was only one variable that reached a threshold p value, a logistic regression model was not applicable.

Consumption of FDA class B medication was reported by 59 (13 %) of participants. The highest percentage of usage was reported by mothers with the highest levels of education (master/PhD degree, 41 %; Fisher exact test, $p = 0.010$) and among mothers who were older at conception ($p = 0.015$). There was no significant correlation with the year of delivery ($p = 0.218$) or parity ($p = 0.511$).

Intake of FDA class C medication was reported by 57 (13 %) participating mothers. Higher consumption of class C drugs was statistically significant in monoparous women ($p = 0.001$) and in women who delivered after year 2010 ($p = 0.042$). When adjusted for date of delivery, statistical significance persisted for parity (having 2 children vs. 1: OR(95 %CI): 2.2(1.1–4.6), $p = 0.028$), but significance did not persist for the year of delivery in the logistic regression model. This might be the result of the correlation between date of delivery and parity (Spearman rho = -0.456, $p < 0.001$). No significant association was found between class C usage and maternal education ($p = 0.260$) or maternal age at conception ($p = 0.431$).

Out of 450 participants 13 (3 %) reported intake of FDA class D (N = 12) or X (N = 1) drugs. None of the investigated maternal characteristics showed statistically significant correlation with class D or X consumption during pregnancy, i.e. date of birth ($p = 0.810$), maternal education ($p = 0.288$), parity ($p = 0.599$) and maternal age at conception ($p = 0.187$).

3.3. Statistically significant correlations between dependant variables

Mothers, who reported medication consumption during pregnancy, also had a higher percentage of folate and multivitamin supplementation ($p = 0.005$). As expected, mothers with chronic diseases reported higher percentage of drug usage during pregnancy ($p = 3.14 \times 10^{-4}$). A higher percentage of A12C medication usage was found in mothers who reported fever during pregnancy ($p = 0.026$) and gestational diabetes ($p = 0.034$). Mothers with gestational diabetes also reported higher folate and multivitamin supplementation ($p = 0.034$).

4. Discussion

The purpose of this study was to assess the health-related behaviours and health status of pregnant women and to discover associations among them. This study contributes a comparative descriptive data analysis of self-reported health status, medication usage, health behaviours and socio-demographics of a cohort of women from Slovenia. It provides an insights into potential determinants for suboptimal health behaviours, such as smoking, and yields several findings that may be important for clinical practice.

Mothers with a lower level of education and a lower age at conception were significantly more likely to smoke during pregnancy. After adjustment in the logistic regression model, the association remained statistically significant only for education but not for the age at conception, which is most likely because of correlation present between maternal educational level and maternal age at conception (Spearman rho = 0.420, $p = 1.6 \times 10^{-19}$). The correlation between lower maternal education and lower maternal age is expected because women increasingly delay childbirth in order to receive more education and take advantage of increased career opportunities created thereby (22). Our findings are in line with previous studies, which reported that smoking, including passive smoking, was the health behaviour most strongly associated with educational disparities, finding a higher percentage of smokers in groups of pregnant women with lower levels of education (19,23,24). Study Lu Y et al. (2001) also reported that smokers with higher levels of education were more likely to stop smoking when they discovered they were pregnant, leading to even greater disparities in smoking (19,25). According to a cross-sectional study of pregnant women and new mothers from 15 European countries, which also included data from Slovenia, prevalence of smoking during pregnancy ranged from 18.9 % in Croatia to 4.2 % in Iceland (9). Slovenia had 6.7 % of prevalence of smoking during pregnancy, which is almost two-fold less than reported in our study (12 % (95 %CI: 9–15 %)). Since our data covers pregnancy characteristics from the 1980s to 2015, while the previously cited comparative study only covers the period 2011–2012, the difference is in line with a recent decline of prevalence rates of smoking during pregnancy in western countries from 20–30 % in the 1980s to 10–20 % in the early 2000s (9,26,27). Indeed, when looking at the part of our study cohort, mothers that gave birth in the same time period as the cohort of Smedberg J et al. (9), we found that the percent of smoking pregnant women in this subgroup (9 % (95 %CI: 3–20 %)) was comparable to the one reported by the above-mentioned study (i.e. 6.7 %). A younger age at conception, in addition to being correlated with lower education, may also act as individual risk factor. The aforementioned multi-national study (9) found that pregnant women who were 20 years of age or younger were more likely to smoke before and during pregnancy. This may be explained by the menacing shift in tobacco use in women, driven by marketing directed specifically at younger women (9). Our findings are a reminder that smoking is still prevalent during pregnancy. Studies strongly suggest association of smoking during pregnancy with increased risk of spontaneous miscarriage, preterm delivery, low birth weight, premature rupture of membranes, placental abruption, placenta previa, stillbirth, higher percentage of repeated unintentional injuries in children and possible increase in pain perception levels of the newborns (9,28,29). In view of these deleterious effects of smoking during pregnancy, precautions to prevent exposure ought to be an important public health goal.

There was no statistically significant association between the maternal characteristics, which were investigated and the incidence of fever during pregnancy, except for a higher consumption of A12C medications. An increase in maternal body temperature is a well-recognized cause of birth defects (30). A12C medications are a group of mineral supplements; in the study data the majority were Mg citrate supplements. Magnesium is known antipyretic; since the work of Schutz (1916), it has been known that magnesium injected directly into the brain substance (tuberal area) may lower body temperature (31). This fact is somewhat contradicted by the higher percentage of Mg supplementation correlated to the group of women with fever during pregnancy. However, with respect to the health outcomes of these pregnancies, Mg supplementation might have a protective effect, lowering fever and diminishing the detrimental effect of fever on the foetus. This effect could be due to the role of Magnesium in protein synthesis and in the stability of the cell membrane and genome (32).

Mothers with more than two children had a higher incidence of chronic diseases; the statistical significance of this association persisted after adjustment for maternal age at conception. During pregnancy, the maternal body undergoes significant anatomical and physiological changes in order to nurture and accommodate the developing foetus (14). These changes represent a physiological challenge as they impose stress to the organism as a whole. Increase in oxygen demands, even during a normal pregnancy, is associated with an increased generation of reactive oxygen species, which have been linked to various diseases (33). Furthermore, some pre-existing chronic diseases are known to worsen during pregnancy. Studies found that the rate of hospitalizations for asthma is higher among pregnant women than non-pregnant women, after adjusting for age and exacerbation history (34,35). It is also recognised that even women with mild asthma are at increased risk of severe exacerbation during pregnancy (34). Our findings suggest that pregnancy somewhat increases pre-existing susceptibility to diseases. Additionally, higher frequency of contacts with health providers leads to the diagnosis rate of unrecognized health conditions. Up to 70 % of late-onset adult chronic diseases share their risk factors with those in pregnancy (36). For example, occurrence of gestational diabetes is linked to an increased risk of chronic diabetes mellitus type 2 in later life (37). Since over 80 % of women have at least one child, pregnancy provides a single common, widespread opportunity to profit from an increased and sustained contact with health care providers to affect behaviour change and thus benefit in terms of both pregnancy outcomes and long-term chronic disease risks for mother and child (36).

Gestational diabetes is diabetes with first onset or first recognition during pregnancy. We observed a trend of higher GD frequency among older women and women who delivered after 2010. According to Slovenian guidelines adopted in 2011 by the national health system, every pregnant woman's blood glucose must be checked at least twice during pregnancy (38). The first routine blood glucose test is at the first examination, when pregnancy is confirmed. The second test performed in a normally progressing pregnancy takes place between the 24th and 28th week in the form of a 75 g OGTT test (oral glucose tolerance test). As a result of the new guidelines, the population of pregnant women is tested far more thoroughly than in the past. Because of the time span of our study data acquisition (1980–2015) some earlier GD cases might have been undiagnosed, particularly those occurring in 1980s. Even though epidemiological studies have reported a rising trend of GD, these studies must be interpreted with caution: the rising trends of GD may be due to better diagnostics (39-42). Among women who reported having GD during pregnancy we observed higher percentage of A12C drugs (in majority these were magnesium preparations) and folate/multivitamin supplement consumption, most likely in pursuit of minimising detrimental effects of GD with health promoting behaviour.

Higher incidence of folate and multivitamin supplementation was observed in women who gave birth after 2000, mothers with higher levels of education, nulliparous women and those who were older at conception. Significance persisted after adjustment in the logistic regression model for all former instances except for age at conception, presumably because of correlation with date of birth (Spearman rho = 0.370, $p < 0.001$) and maternal education (Spearman rho = 0.420, $p < 0.001$). Since 1993 daily supplementation with 400 µg folic acid at least 3 months prior and after conception is recommended in Slovenia by the public health service (43). We observed a steady increase in the consumption of multivitamin and folate supplementation with time: in the 1980s (18 %(95 %CI: 4–47 %)), in the 1990s (26 %(95 %CI: 14–

41 %)), with highest increase after 2000 (73 %(95 %CI: 64–80 %)) that further amplified after 2010 (91 %(95 %CI: 87–94 %)). This might be explained by higher supplementation literacy among health practitioners and pregnant women that gradually increased in the decade after recommendations were formulated because of the abundance of medical and commercial attention that folic acid garnered. Our findings are in line with numerous studies that reported higher prevalence of folate and multivitamin supplementation among women with higher levels of education (5,44,45,46), nulliparous women (47) and among women who were older at conception (47). Higher maternal education is associated with higher health literacy, health control beliefs and risk adverse behaviour, which corresponds to periconceptional supplementation (9,19,48). The study by Baron et al. (2015) reported sizable disparities in unbeneficial health status and behaviours according to educational level, in that women with lower education have low health control beliefs, higher incidences of both obesity and being underweight, higher incidence of depression/anxiety, higher incidence of smoking and passive smoking exposure, lower antenatal attendance, lower folic acid supplementation, higher incidence of skipping breakfast daily and unplanned pregnancies and lower incidence of daily fruit consumption (19). Nulliparous women are perhaps more anxious about pregnancy outcome and try to minimise possible risks by following recommendations on health promoting behaviour. In contrast, women's personal experience of delivering a healthy child despite not taking folate/multivitamin supplementation might create distrust in the scientific recommendations, which results in the refusal of folate/multivitamin supplementation in succeeding pregnancies (9). Only 8 % (95 %CI: 6–12 %) of women reported the consumption of nutritional supplements with active form of folic acid – 5-methylfolate.

Interestingly, higher incidence of medicine (OTC and prescribed) consumption during pregnancy was reported by women with the highest and lowest levels of education, by women who delivered in recent years (1980s 0 % vs. 2011–2015 48 %(95 %CI:42–54 %)) and by those with higher age at conception. The latter was not significant after adjustment with date of delivery and maternal education. A 2011 study using U.S. data from 1976–2008 reported that most women (88.8 %) take at least one medication during pregnancy and 70 % take at least one prescribed medication (49). A 2014 multi-national European study on data from 2011–2012 reported that 81.2 % of women take at least one medication (OTC or prescribed) during pregnancy and 68.4 % and 17 % of women reported the use of prescribed medication for acute and chronic conditions, respectively (5). Data of our study cohort revealed a slightly lower prevalence of medication usage (40 %(95 %CI:35–44 %)) but the trend of increasing consumption is in line with an American study which observed that over the last three decades, use of prescription drugs during pregnancy has increased by over 60 % (49). There are several studies that observed an association between higher maternal education and more prevalent use of medication during pregnancy (49,50,51,52). Contrary to these, others reported more prevalent use of medications among pregnant women with lower education (5,53,54). It appears as though our study cohort with an U-shaped distribution fits with the recent findings. The aforementioned European study linked the higher prevalence of drug usage among lower educated women to a higher percentage of medications for chronic/long term conditions (5). Since we did not find such an association, higher consumption of medication observed in groups of women with the lowest and highest levels of education might reflect higher confidence in self-treatment and use of medications in general (5). Risk perceptions are lower in both groups for different reasons. Educated women have the highest health literacy while the least educated have the weakest health control beliefs (1). Furthermore, among women who took medication during pregnancy, there was a higher prevalence of folate and multivitamin supplementation. This could be explained with the correlation observed between multivitamin/folate supplementation and maternal characteristics that influence drug intake, namely the year of delivery (Spearman rho = 0.458, $p < 0.001$), level of education (Spearman rho = 0.325, $p < 0.001$) and maternal age at conception (Spearman rho = 0.247, $p < 0.001$). Unsurprisingly, there was higher medication intake reported by women with chronic health conditions.

Reported medications were classified according to ATC and FDA classes. We analysed data for possible associations with maternal characteristics and for those medication groups that were taken most frequently (> 5 % abundance).

A12C–mineral supplement medication intake (6 %(95 %CI:4–9 %)) was associated with a higher level of education and nulliparity. Women who reported A12C supplementation gave birth after 2010. In our study, A12C medications were mostly magnesium supplements (Mg citrate). Magnesium is an essential mineral required for maintaining nerve and muscle cell electrical potential, regulation of body temperature and synthesis of nucleic acids and proteins (32). Magnesium supplementation during pregnancy may be able to reduce foetal growth restriction, low birthweight and pre-eclampsia (55). Similar distribution of consumption was found for folate/multivitamin supplementation, and hence we could explain it in a similar frame; better health literacy and more vigilant health promoting behaviour among these groups. In addition, there might be some recall bias considering time distribution. Education was also associated with better recall accuracy of medications in most studies investigating this relation (57-61). The most recent Cochrane review (2014) of Mg supplementation in pregnancy concluded that there is not enough high-quality evidence to show that dietary magnesium supplementation during pregnancy is beneficial for improving maternal and neonatal/infant health outcomes. It is further stated that until additional evidence from large, well designed, randomised trials becomes available, current evidence is insufficient to make recommendations for routine clinical practice on the use of magnesium supplementation during pregnancy (55).

B03A – Iron preparations were the most prevalent group of medications (17 %(95 %CI:14–21 %)) in our study cohort. The only significant association was with increasing consumption over the studied three decades (1980s 0 %, 2011–2015 22 %(95 %CI:17–27 %)). According to WHO recommendations, daily oral iron (and folic acid supplementation) is recommended as part of the antenatal care to reduce the risk of low birth weight, maternal anaemia and iron deficiency. The latest Cochrane review (2015) on daily iron supplementation concluded that supplementation reduces risk of maternal anaemia and iron deficiency in pregnancy, but the positive effect on maternal and infant outcomes is less clear. The implementation of iron supplementation recommendations may produce heterogeneous results depending on the populations' background risk for low birthweight and anaemia, as well as the level of adherence to the intervention (56). According to the UK guidelines on management of iron deficiency during pregnancy women are encouraged to maximise iron dietary intake and absorption, though routine iron supplementation for all women in pregnancy is not recommended. There are clinical hazards of routine supplementation, such as risk of elevated Hb and oxidative stress (62,63,64). Elevated Hb was associated with higher rates of perinatal deaths, low birth weight and preterm delivery (63), and markers of oxidative stress were found to be elevated in the placenta of women with routine iron supplementation (64). In Slovenian health practice, there is an individualised approach to iron supplementation based on concentration of blood Hb, with Hb levels less than 110 g/L considered too low in pregnant women and warranting supplementation. A possible explanation for the increase in iron supplementation in the last three decades lies in wider societal dietary trends. The increase in iron supplementation runs parallel with an increase in the consumption of starchy, processed foods with low nutritional content. This might explain the greater incidence of iron supplementation in pregnancy. Nonetheless, higher recall certainty for recent pregnancies might play a role.

Intake of N02B (mostly paracetamol and acetylsalicylic acid) was reported by 7 %(95 %CI:5–9 %) of the participants. Distribution of consumption was U-shaped according to maternal education. The highest usage was reported by women with the highest and lowest levels of education and by women with a higher age at conception. The same characteristics were observed in relation to reported intake of all medications. Since we did not observe any difference in reported health status among groups of different levels of education and age at conception, the most likely explanation lies in the risk perceptions of the sub-groups. In a recent study on women's perception of risks of adverse foetal pregnancy outcomes, risk perceptions were lower with increasing age and with higher level of education, which may reflect increased access to information, personal experience and thus higher confidence in medication intake (1). In the same study individuals with lower education perceived thalidomide (a well-known teratogen) to be less risky than did women with higher education, which could indicate an increased confidence in self-drug administration among those with lower education (1).

Medications were also classified according to the FDA classes. The highest prevalence of consumption was reported for FDA class A medications (19 %(95 %CI:16–23 %)) for which adequate and well-controlled studies failed to demonstrate a risk to the foetus. In our study cohort these were mostly iron supplements (17.3 %). The only significant association was with date of delivery: the highest prevalence of intake was reported by women who delivered after 2011. This correlates with results for iron preparations.

Intake of FDA class B medications was reported by 13 %(95 %CI:10–17 %) of participants. Class B medications are those medications for which animal reproduction studies have failed to demonstrate a risk to the foetus, however there are no adequate and well-controlled studies in pregnant women available to fully define the effects of the medication. The highest consumption was found among higher educated mothers and those who were older at conception. Prevalent class B drugs in our study cohort were paracetamol and antibiotics (mostly amoxicillin). The results unsurprisingly in part correlate with characteristics of N02B consumption, since paracetamol is a major representative of both groups. The only differences are seen in the distribution according to education, in which the association between intake and education is not U-shaped as in the case of N02B. This difference may be attributed to the variability in antibiotic consumption, which would be in-line with results of a Finnish study that found higher prevalence of antibiotic consumption among women in older maternal age groups and among women belonging to a higher socio-economic group – having higher level of education (65).

FDA class C medication intake was reported by 13 %(95 %CI:10–16 %) of participating women. Class C consists of medications for which animal reproduction studies have shown an adverse effect on the foetus and there are no adequate and well-controlled studies in humans, but potential benefits may permit use of the drug in pregnant women despite potential risks. Nulliparous women and those who gave birth after 2010 had the highest percentage of class C drug intake. After adjusting in logistic regression, the association between lower parity and higher intake persisted, but we observed a correlation between date of delivery and parity (Spearman rho = -0.456, p < 0.001). Since a major representative of class C and A12C medications in our study data was magnesium citrate, groups share similar characteristics, i.e. an increasing trend of consumption and null parity.

We found no associations between the researched maternal characteristics and consumption of class D and X medications. For class D medications there is positive evidence of human foetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant the use of the drug in pregnant women despite potential risks. Class X medications have demonstrated foetal abnormalities in animal or human studies, and/or there is positive evidence of human foetal risk based on adverse reaction data from investigational or marketing experience, and the risks associated with the use of the drug in pregnant women clearly outweigh potential benefits. Most likely no associations were found due to the small number of women who reported intake of these drug classes (3 %(95 %CI:2–5 %)).

Study results must be interpreted in the view of the following limitations. The number of participants was relatively small. The study was retrospective in design and there might be some incomplete data because all researched variables are dependent on women's recall, accuracy and perception. The main limitation of the study is that the reliability of self-reports is lower in the mothers of healthy siblings of OFC/CHD cases, who were interviewed at different time-points after the corresponding pregnancy, compared to the mothers of healthy newborns who were interviewed immediately after the delivery. The comparison of the two subgroups by Fisher`s exact test revealed that they differ in almost all of the outcome characteristics, except for smoking in pregnancy and fever during pregnancy. However, it is important to note that all of the healthy newborns were born between 2011 and 2015, while only 27 % of the healthy siblings of OFC/CHD cases were born in the same period ($p < 0.001$). When comparing the healthy newborns and healthy siblings of OFC/CHD cases that were born in the same period (2011–2015), none of the outcome characteristics differed among the two groups, except for maternal chronic disease which was still more prevalent in mothers of healthy siblings of OFC/CHD cases than in the mothers of healthy newborns ($p = 0.029$). This indicates that differences in outcome characteristics between the two subgroups are due to the different delivery periods and not due to the selection bias related to the family anamnesis of OFC or CHD. The only analysis that might be biased due to the cohort heterogeneity is the chronic disease of the mother, which was indicated in some studies as one of the risk factors for OFC and CHD. Self-report bias/underreporting cannot be ruled out in the case of smoking and possible drug consumption due to the social stigma that is attached to these exposures. On the other hand, health-promoting behaviours might have been over-reported. Some selection bias cannot be excluded, as some of participating mothers had previous adverse pregnancy outcome (CHD or OFC), and thus their behaviour during subsequent pregnancies might have been more alert to adverse birth effects, which may not be representative for general population of childbearing women. However, this bias was absent in the majority of study cases, as 73 % of healthy siblings of OFC and CHD cases were born prior to their sick sibling. Study did not include possibly important factors such as exposure to passive smoking, income and employment in order to fully assess smoking and socio-economic status.

5. Conclusions

The study found considerable disparities in health conducts and socio-demographics of women during pregnancy. It revealed that level of education, parity and age have an impact on women's health behaviour, namely medications and micronutrient supplementation intake and smoking status.

Younger and less educated women more frequently reported positive smoking status during pregnancy while higher prevalence of folate/multivitamin supplementation was found among more educated, older and nulliparous women. There was a U-shaped distribution of higher prevalence of medication intake (OTC and prescribed) in the groups of women with the highest and lowest levels of education. Higher usage was also reported among older women. We observed an increasing trend of medication, folate/multivitamin intake and incidence of GD over the studied period. Higher incidence of chronic diseases was observed in a group of multiparous women.

Identification of disadvantaged women in terms of health-related risky behaviour during pregnancy provides an opportunity to assist women in reducing major health hazards and to identify the key factors of a healthy pregnancy. Public health campaigns are needed that would educate and provide healthy lifestyle choices with advice on diet, exercise, alcohol, smoking, medications and folic/multivitamin supplementation. Further qualitative research is needed to explore in-depth the dilemmas that women and their health care providers face during pregnancy (2,7).

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