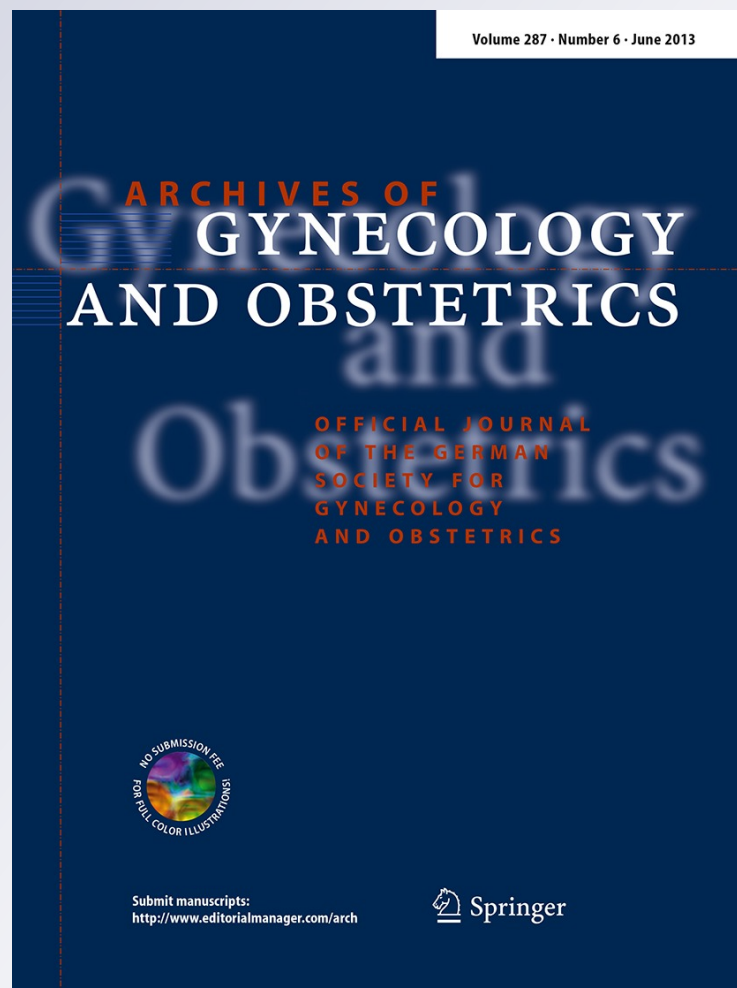*Fetal growth restriction and maternal smoking in the Macedonian Roma population: a causality dilemma*

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Fetal growth restriction and maternal smoking in the Macedonian Roma population: a causality dilemma

Asnat Walfisch · Sotir Nikolovski · Bilijana Talevska ·
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Abstract

Purpose Macedonia is one of the top five countries globally in reported smoking rates. Over 10 % of the population consists of the underprivileged Roma minority. We aimed to determine whether Roma ethnicity is an independent risk factor for adverse pregnancy outcome or merely mediating maternal smoking.

Methods Maternal data were retrieved from the perinatal computerized database for all deliveries during 2007–2011 at the only Clinical Hospital in Bitola, Macedonia. Multivariable regression models were constructed to control for confounders.

Results Of nearly 7,000 deliveries, 8.65 % were of maternal Roma ethnicity and 40 % of the Romani women admitted to regularly smoke during pregnancy. Both Roma ethnicity and maternal smoking were significantly associated with the absence of maternal education, history of abortions and intra uterine growth restriction (IUGR) in the univariate analysis. Both maternal Roma ethnicity (OR 2.46, 95 % CI 1.79–3.38) and smoking status (OR 1.37, 95 % CI 1.02–1.85) were found to be independent predictors of IUGR using the multivariate analysis. Lower birthweight and smaller head circumference were both independently associated with Roma ethnicity and smoking.

Conclusions Underprivileged ethnic background is a significant risk factor for IUGR, independent of maternal smoking status. To the best of our knowledge, this is the first publication focusing on pregnancy outcome in Romani Macedonian parturients.

Keywords Maternal ethnicity · Independent risk factors · Adverse perinatal outcome · Intra-uterine growth restriction · Gypsies

Introduction

In the past several decades, smoking during pregnancy has remained one of the most consistently reported modifiable risk factors for an array of perinatal outcomes [1]. Maternal smoking during pregnancy is a well-established risk factor for a variety of complications [2] which include (but are not limited to) preterm delivery, intra-uterine growth restriction (IUGR), low birthweight, oral clefts, and increased neonatal mortality [3, 4]. In the early neonatal period, parental smoking has been shown to increase the rates of respiratory tract infections and sudden infant death syndrome [5, 6]. Prenatal tobacco exposure may also have an effect on the child's later intellectual and behavioral patterns [7].

Despite this body of evidence, cigarette smoking during pregnancy remains globally prevalent [8, 9], with rates inversely correlated with maternal age and level of education [5]. Although there is no doubt of the extremely high smoking rate in the Republic of Macedonia, estimated to be roughly 40 %, precise data is limited [10–12]. As such, Macedonia is one of the five countries reported to have the

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highest smoking rate globally (along with Russia, Greece, Bosnia, and Bulgaria) and the rate does not appear to decline [13–15].

Over 10 % of the population in Macedonia consists of the underprivileged Roma minority (Romanies, Gypsies, of northern Indian origin), which suffers from both high rates of adverse pregnancy outcome and frequent maternal smoking. This minority is a traditional ethnic minority characterized by an average low socio-economic status with all associated implications. In general, health of the Roma population is thought to lag behind other populations including aspects such as high infant mortality and shorter life expectancy, partially due to limited health awareness and low accessibility to health care services [16]. Published data on the reproductive health and habits of Macedonian Romani women do not exist (despite the large estimated share of Roma inhabitants in Macedonia), although data on Romani women from Bulgaria, Hungary, Czech Republic and Slovakia indicate higher rates of abortions, fetal growth restriction and preterm births [17–23]. Although the general association between adverse perinatal outcome and ethnic minorities is well established [24, 25], the causality issue is difficult to resolve due to clustering of multiple demographic and clinical factors (specifically high smoking rates) which may influence pregnancy outcome in any minority. We undertook this study of quantifying and characterizing maternal smoking in Macedonia, with a specific focus on the maternal Roma population. We aimed to determine whether Roma ethnicity is an independent risk factor for adverse pregnancy outcome or merely a mediator of maternal smoking.

Methods

In this retrospective population-based cohort, data were retrieved from the perinatal computerized database of the Clinical Hospital "Dr. Trifun Panovski" in Bitola, Macedonia for all deliveries occurring during the period of January 2007 to December 2011.

This clinical secondary hospital, which is located in the city of Bitola, provides medical care for all the population in the southwestern region of Macedonia. It is the leading health care facility in the region with the capacity to deliver health services to a population of approximately 300,000. This hospital also provides medical care to the Roma population concentrated in a settlement called "Bair" in the north part of Bitola with approximately 5,500 inhabitants.

The database consists of information recorded immediately after the delivery, by a neonatologist. Maternal ethnicity is ascertained using the personal ID card. Paternal ethnicity is not routinely recorded in our database although inter-racial marriages are extremely rare. Maternal smoking status is determined through maternal self report only. Coding is done after careful evaluation of the medical prenatal care records as well as the routine hospital documents in order to ensure the completeness and accuracy of the database.

The predetermined outcome measures included birthweight, head-circumference, Apgar score, and presence of IUGR. For the statistical analysis, we have included all recorded deliveries without exclusions. Statistical analysis was performed with the SPSS package (SPSS, Chicago, IL). To test the statistical significance of the categorical variables, the Fisher's exact test was used. For continuous variables Student's t test or the Mann–Whitney U test were used. In an attempt to distinguish between ethnicity and other demographic and clinical features known to have an impact on pregnancy outcome, we have conducted several multivariable regression models (logistic and linear regressions). The models were aimed at exploring possible independent predictors for fetal growth restriction (birthweight <10th percentile), birthweight, head circumference, and Apgar score. Variables included in the regression models were ethnicity, smoking status, maternal age, maternal level of education, history of abortions, parity, and mode of delivery. Odds ratios (OR) and their 95 % confidence interval (CI) were calculated from the regression coefficient. A p value <0.05 was considered statistically significant. The institutional review board of the hospital (Clinical Hospital "Dr. Trifun Panovski", Bitola, Republic of Macedonia) has provided its approval for this study. This includes collection, analysis, and publication of all relevant available data.

Results

Of 6,968 deliveries occurring during the 5-year study period, 575 were of maternal Roma ethnicity (Table 1). Non-Roma ethnicity consisted primarily of native Macedonians (72.5 %) as well as Albanians (10.3 %), Turks (3.3 %) and others (Serbians, Vlachs, etc.). Mean maternal age in the entire study group was 27.4 ± 5.1 years, with a significantly younger mean maternal age in the Roma population (24.4 ± 5.9 years, $p < 0.001$). The share of uneducated/illiterate mothers in the Roma population was overwhelmingly high, with 63.1 % of the Romani women never receiving any form of formal education versus only 2.2 % in the rest of the study population ($p < 0.001$). Other characteristics that significantly differed in the Roma minority included higher rates of grand multiparity (defined as ≥4 births) and higher rates of abortions in these women's history (Table 1). As expected, maternal smoking was common, and admitted by 39.5 % of Romani women,

Table 1 Demographic characteristics and pregnancy outcome in the Roma and non-Roma study population

Characteristic	Roma ethnicity $n = 575$ (8.65 valid %)	Control group $n = 6{,}070$ (91.35 valid %)	Total $n = 6{,}645$ (100 %)	*p* value
Smoking (valid %)	227 (39.5)	755 (12.4)	982 (14.8)	**<0.001**[Ω]
Mean maternal age (years) ± SD	24.4 ± 5.9	27.68 ± 5.3	27.41 ± 5.1	**<0.001**°
Absence of formal education[a] (valid %)	350 (63.1)	126 (2.1)	476 (7.5)	**<0.001**[Ω]
Primiparity (valid %)	181 (31.9)	3,177 (53.1)	3,358 (51.3)	**<0.001**[Ω]
Grand multiparity[b] (valid %)	98 (17.3)	108 (1.8)	206 (3.1)	**<0.001**[Ω]
History of abortions[c] (valid %)	150 (26.1)	592 (9.8)	742 (11.2)	**<0.001**[Ω]
Pregnancy outcome				
Gestational age (weeks) ± SD	38.8 ± 1.4	39 ± 1.4	38.9 ± 1.4	0.058°
MSAF (valid %)	66 (12.8)	504 (9.1)	570 (9.5)	**0.0009**[Ω]
Apgar score 1 min <7 (valid %)	38 (6.8)	393 (6.6)	431 (6.6)	0.86[Ω]
Apgar score 5 min <7 (valid %)	7 (1.3)	120 (2.0)	127 (1.9)	0.26[Ω]
Admission to NICU (valid %)	26 (4.6)	238 (4.0)	264 (4.0)	0.43[Ω]
Cesarean section (valid %)	57 (10.2)	1,891 (31.8)	1,948 (29.9)	**<0.001**[Ω]
Birthweight (g) ± SD	3,047.7 ± 490	3,262.0 ± 507	3,243.5 ± 501	**<0.001**°
Head circumference (cm) ± SD	33.4 ± 1.7	34.2 ± 1.7	34.1 ± 1.7	**<0.001**°
PTB (valid %)	34 (5.9)	274 (4.5)	308 (4.6)	0.14[Ω]
IUGR (valid %)	62 (10.8)	259 (4.2)	321 (4.8)	**<0.001**[Ω]
Congenital anomalies[d]	8 (1.4)	55 (0.9)	63 (0.9)	0.25[Ω]
Mean post partum hospitalization length (days) ± SD	2.8 ± 2.6	3.6 ± 2.6	3.5 ± 2.5	**<0.001**[ψ]

Bold values indicate statistically significant results

SD standard deviation, *MSAF* Meconium stained amniotic fluid, *PTB* Preterm birth (<37 w), *IUGR* intrauterine growth restriction (<10th percentile)

[Ω] Fisher exact test

° Student *t* test

[ψ] Mann–Whitney *U* test

[a] Never attended school

[b] Grand multiparity defined as parity equal to or greater than four

[c] Any history of a spontaneous miscarriage

[d] Congenital anomalies—immediately recognized at birth

which was significantly higher than the rest of the study population (12.4 %, $p < 0.001$).

For pregnancy outcome, Roma ethnicity was associated with significantly higher rates of several adverse outcomes. These include MSAF (meconium stained amniotic fluid), lower birthweight, smaller head circumference, and higher rate of fetal growth restriction. Rates of preterm births and congenital anomalies were also higher in the Roma population but this did not reach statistical significance. Cesarean section rate for Romani parturients was substantially lower (10.2 vs. 31.8 %, $p < 0.001$) and mean hospitalization stay was significantly shorter (Table 1).

When the study population was divided by the smoking status, we found maternal smoking to share similar demographic features and associations to adverse pregnancy outcome as maternal Roma ethnicity. These include higher rates of illiteracy, history of abortions, and IUGR as well as lower cesarean section rate, birthweight, and head circumference in the maternal smoking population (Table 2).

The multivariable regression models were aimed at exploring possible independent predictors for fetal growth restriction, lower birthweight, smaller head circumference, and lower Apgar score. Both maternal Roma ethnicity (OR 2.46, 95 % CI 1.79–3.38) and smoking status (OR 1.37, 95 % CI 1.02–1.85) were found to be independent risk factors for IUGR. Lower birthweight and smaller head circumference were both independently associated with the same predictors: Roma ethnicity, smoking, illiteracy, and low parity. As for the Apgar score, the multivariable model was constructed to identify independent predictors for a 5-min Apgar score of <7. The co-variables included in this model were maternal age, education, ethnicity, mode of delivery, preterm birth, smoking, IUGR, and congenital anomalies. Using this model, two independent predictors for a low 5-min Apgar score were found: preterm birth

Table 2 Demographic characteristics and pregnancy outcome by maternal smoking status

Characteristic	Smokers $n = 1{,}018$ (14.6 valid %)	Non-smokers $n = 5{,}947$ (85.4 valid %)	Total $n = 6{,}965$ (100 %)	p value
Mean maternal age (years) $\pm$ SD	27.16 ± 5.1	27.45 ± 5.1	27.41 ± 5.1	$0.09°$
Roma ethnicity (valid %)	227 (23.1)	348 (6.1)	575 (8.7)	**<0.001$^\Omega$**
Absence of formal education[a] (valid %)	154 (15.4)	328 (5.9)	482 (7.4)	**<0.001$^\Omega$**
History of abortions[b] (valid %)	190 (18.7)	573 (9.7)	763 (11)	**<0.001$^\Omega$**
Pregnancy outcome				
Gestational age (weeks) $\pm$ SD	39 ± 1.3	38.9 ± 1.5	38.9 ± 1.5	$0.31°$
MSAF (valid %)	100 (11)	493 (9.3)	593 (9.5)	0.09^Ω
Apgar score 1 min <7 (valid %)	48 (4.8)	473 (8.1)	521 (7.6)	**<0.001$^\Omega$**
Apgar score 5 min <7 (valid %)	15 (1.5)	185 (3.2)	200 (2.9)	**0.003$^\Omega$**
Admission to NICU	31 (3.1)	249 (4.3)	280 (4.1)	0.058^Ω
Cesarean section (valid %)	179 (18)	1,850 (32.1)	2,029 (30)	**<0.001$^\Omega$**
Birthweight (g) $\pm$ SD	$3{,}153 \pm 472$	$3{,}252 \pm 519$	$3{,}237 \pm 514$	**<0.001°**
Head circumference (cm) $\pm$ SD	33.8 ± 1.8	34.2 ± 1.8	34.1 ± 1.8	**<0.001°**
PTB^ (valid %)	40 (3.9)	286 (4.8)	326 (4.7)	0.26^Ω
IUGR (valid %)	72 (7.1)	269 (4.5)	341 (4.9)	**0.001$^\Omega$**
Congenital anomalies[c]	6 (0.6)	58 (1)	64 (0.9)	0.29^Ω
Stillbirth (valid %)	0	75 (1.3)	75 (1.1)	**<0.001$^\Omega$**
Mean post partum hospitalization length (days) $\pm$ SD	3.1 ± 2.1	3.6 ± 2.7	3.5 ± 2.6	**<0.001$^\psi$**

Bold values indicate statistically significant results

SD standard deviation, *MSAF* Meconium stained amniotic fluid, *PTB* Preterm birth (<37 w), *IUGR* intrauterine growth restriction (<10th percentile)

$^\Omega$ Fisher exact test

$°$ Student *t* test

$^\psi$ Mann–Whitney *U* test

[a] Never attended school

[b] Any history of a spontaneous miscarriage

[c] Congenital anomalies—immediately recognized at birth

(OR 6.038, 95 % CI 3.9–9.4, $p < 0.0001$) and IUGR (OR 1.95, 95 % CI 1.1–3.5, $p = 0.03$).

Discussion

We undertook this study in order to characterize two maternal populations in Macedonia which were not studied before in this part of the world: Romani women and the smoking parturient population. Our intention was to establish whether these features were independent predictors of adverse pregnancy outcomes, and specifically of IUGR. Perhaps not surprisingly, we have found considerable demographic and clinical overlap between these two groups; the smokers and the Romani parturients. Both presented features of lower socio-economic status, such as illiteracy, and higher rates of adverse pregnancy outcome, such as IUGR. Both were found to be independent predictors (in a multivariate regression model) of IUGR, although Roma ethnicity appears to be a stronger predictor with an OR of roughly 2.5.

Roma ethnicity being a strong predictor of adverse pregnancy outcome is not a surprising finding and has been shown before in the Roma population in other countries with high Roma population share [17–23]. Certainly, this finding cannot be attributed solely to the high smoking rate in this maternal population. Roma are considered the poorest and most marginalized minority group in Macedonia. As such, they exhibit multiple characteristics that may have a direct or indirect effect on pregnancy course and outcome. They usually live on the periphery of the cities in "ghetto neighborhoods", with low-quality housing and infrastructure, and suffer from the highest rate of illiteracy and the lowest employment rate. Roma women face even more challenges arising from their gender as well as ethnicity and impoverishment. In terms of reproductive health, the risks are heightened as a result of high numbers of closely spaced births, inadequate prenatal care, and inadequate nutrition [26]. High rates of maternal smoking has previously been reported in the Roma population of other countries and probably results from low level of awareness, among other reasons [27].

Our data demonstrate relatively low rates of preterm births (4.6 %) and malformations (0.9 %). We believe the reason for that to be the fact that the hospital is defined as a secondary center. As such, all high-risk pregnancies are transported to the only tertiary center in the country located in the capitol city. These high-risk pregnancies may include imminent preterm deliveries prior to 34 weeks of gestation or pregnancies with suspected fetal anomalies, which may require special care immediately following the delivery. As well, fetal malformations included in our database are only the ones that are recognizable immediately following the delivery. These two facts may explain, at least in part, the low rates stated above and may have contributed to the inability to reach statistically significant

differences between the Roma ethnicity and the rest of the study population.

Significantly lower rates of cesarean section in the Roma population, compared to the rest of the study population, are harder to explain. The younger mean maternal age, lower mean birthweight, and higher parity probably contribute to the lower cesarean rate. In addition, it has been previously shown that ethnic differences exist in different aspects of birth, the natives being generally more medicalized than the minority ethnic groups [28]. Although medical factors may contribute to this significant difference (10.2 vs. 31.8 %, $p < 0.001$), the behavior and cultural setting of the women and that of the health care providers applying different solutions to similar problems may also contribute to systematic differences in delivery care and outcomes. The significantly shorter post-partum hospitalization length is probably a direct result of this substantially lower cesarean rate in the Roma minority.

Although maternal smoking was associated with lower rates of low Apgar scores (<7) compared to non-smokers (4.8 vs. 8.1 % respectively, $p = 0.003$), the multivariate analysis showed that smoking is not an independent predictor of Apgar scores. Only IUGR and preterm birth were independently associated with low 5-min Apgar scores.

The main strength of this study is the fact that this is the first report focusing on pregnancy outcome in the Roma minority of the Republic of Macedonia, using data from a center which provides medical care to a large Roma community. We were able to show a significant independent relationship between Roma ethnicity and adverse pregnancy outcome.

Nevertheless, the study has several inherent limitations related to its retrospective design. In addition, maternal smoking status is self-reported and thus is probably an underestimation of the actual rate, although this is true for both Romani women and controls. Another limitation relates to the absence of ethnic specific growth curves for any of our study populations. The last limitation relates to the secondary nature of our center, which limits the prevalence of severe pregnancy complication due to a policy of in utero transfer to the tertiary center in the capitol city.

While taking into account these limitations, the authors of this paper believe that it provides strong and important evidence regarding the relationship between Roma ethnicity and adverse pregnancy outcome, independent of maternal smoking. Our data also agree with previous reports demonstrating the harmful impact of smoking during pregnancy. Any attempt to improve pregnancy course and outcome in the underprivileged Roma population must consider not only anti-smoking campaign but also other complex socio-demographic issues.

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