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Full Title: Prevalence of smoking during pregnancy and associated social inequalities in developed countries over the 1995-2020 period: a systematic review.

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Shortened running title: Smoking during pregnancy and associated social inequalities

Abstract:

Background: Smoking during pregnancy (SDP) is a significant source of preventable morbidity and mortality for both mother and child.

Objectives: The aim of this study was to describe changes in the prevalence of SDP over the last 25 years in developed countries (Human Development Index >0.8 in 2020) and associated social inequalities.

Data sources: A systematic review was conducted based on a search in PubMed, Embase and PsycInfo databases, and government sources.

Study selection and data extraction: Published studies between January 1995 and March 2020, for which the primary outcome was to assess the national prevalence of SDP and the secondary outcome was to describe related socio-economic data were included in the analysis. The selected articles had to be written in English, Spanish, French or Italian.

Synthesis: The articles were selected after successive reading of the titles, abstracts, and full-length text. An independent double reading with intervention of a third reader in case of disagreement allowed including 35 articles from 14 countries in the analysis.

Results: The prevalence of SDP differed across the countries studied despite comparable levels of development. After 2015, the prevalence of SDP ranged between 4.2% in Sweden and 16.6% in France. It was associated with socio-economic factors. The prevalence of SDP slowly decreased over time, but this overall trend masked inequalities within populations. In Canada, France and the United States, the prevalence decreased more rapidly in women of higher socio-economic status, and inequalities in maternal smoking were more marked in

these countries. In the other countries, inequalities tended to decrease but remained significant.

Conclusions: During pregnancy, i.e., a period described as a window of opportunity, smoking and social vulnerability factors need to be detected to implement targeted prevention strategies aiming at reducing related social inequalities.

Keywords: smoking, pregnancy, socio-economic factors

Synopsis text:

Study question: The objective of this systematic review was to describe changes in the prevalence of smoking during pregnancy in developed countries over the past 25 years, as well as trends in associated socioeconomic inequalities.

What's already known: Maternal tobacco smoking during pregnancy continues to be a major cause of preventable maternal and child morbidity and mortality. Socioeconomic factors are associated with maternal smoking during pregnancy.

What this study adds: This study showed a slow decrease in smoking during pregnancy, but this overall trend masked disparities between and within countries. The decrease was observed regardless of the socio-economic level, but inequalities tended to persist or even gradually increase over time in several countries. During pregnancy, a time for health change, the early detection of smoking and of the social vulnerability of women seems essential.

BACKGROUND

Smoking is the leading cause of preventable death worldwide and one of the key determinants of health.^{1,2} Smoking during pregnancy is a major cause of morbidity and mortality for both mother and child.^{1,3} It increases the risk of ectopic pregnancy, spontaneous miscarriage, prematurity, intrauterine growth restriction, retroplacental hematoma, premature rupture of membranes and fetal death *in utero*.⁴ After birth, it is associated with an increase in sudden infant death syndrome, respiratory disorders and behavioral disturbances in children.⁴⁻⁶ In a population including 30% of women who smoke, it was estimated that 25% of fetal deaths *in utero* and 20% of neonatal mortality could be prevented if all pregnant women quit smoking before the sixteenth week of pregnancy.⁷ The timing and level of smoking during pregnancy are two aspects of smoking that could influence birth outcomes. Some studies have shown that smoking only in early pregnancy was not associated with a higher rate of suboptimal birth outcomes, while others have, but this rate appear to increase with continued smoking throughout pregnancy.⁸⁻¹⁰ Other studies have shown that the risk of neonatal and obstetric complications increases with the number of cigarettes smoked during pregnancy, the threshold of 10 cigarettes per day is used in most studies to distinguish light and heavy smoking.¹¹⁻¹³

In a recent meta-analysis, the global prevalence of smoking during pregnancy has been estimated at 1.7% (95% confidence interval (CI) 0.0, 4.5), ranging from 0.8% (95% CI 0.0, 2.2) in Africa to 8.1% (95% 4.0, 12.2) in Europe.¹⁴ High-income countries (European and the North American countries) had a much higher prevalence of smoking during pregnancy compared to middle- and low-income countries. There are also significant differences between high-income countries, that may be related to various factors such as the sampled populations, the years the measurement was made and the social groups.³ Studies have

shown that the smoking rate may be doubled or tripled in young single mothers with low educational levels and social isolation.¹⁵⁻¹⁸ To our knowledge, no recent literature review has described the socio-economic factors associated with smoking during pregnancy or their evolution over time.¹⁹ In addition, few studies have described changes in the prevalence of smoking during pregnancy in recent years and, to our knowledge, none had the primary objective of describing it internationally.²⁰⁻²²

Thus, the aim of our study was to describe changes in the prevalence of smoking during pregnancy in developed countries over the past 25 years and then to investigate trends in socio-economic and socio-demographic inequalities associated with smoking during pregnancy using individual and contextual factors.

METHODS

Study design:

This study was a systematic review of the literature with a focus on social health inequalities reported according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) Equity 2012 guidelines (Appendix S1). This study was registered on PROSPERO under the reference CRD42016043131. No ethical procedures were required because the study was a review of previously published data.

Inclusion and exclusion criteria:

In the included articles, the primary outcome was the prevalence of smoking during pregnancy in developed countries (Human Development Index [HDI] >0.8 in 2020). The secondary outcome was to describe the associated socio-economic data. Only countries where the prevalence of smoking during pregnancy was measured using the same methodology in at least two different years, allowing for trend analysis, were included. The selected articles had to be written in English, Spanish, French or Italian, and published between January 1995 and March 2020. The prevalence of smoking during pregnancy had to be described nationally. Regional socio-economic data could be used to supplement the main data. Smoking during pregnancy was collected at different times depending on the study: at the beginning of the pregnancy, in the third trimester, throughout the pregnancy, postpartum or without specifying the time (detailed in Appendix S6). When the variable of smoking during the third trimester was available, we retained it to define smoking during pregnancy. A woman was considered a person who smoked during pregnancy if she had smoked at least one cigarette over the study period. This choice was preferred to the “daily smoking” variable for two

main reasons: smoking during pregnancy has the particularity of being fluctuating, making a daily quantification difficult²³, and there is no defined threshold below which smoking has no harmful effect.¹

Article selection:

The PubMed, Embase and PsycInfo databases were searched. The selected MeSH terms were as follows: “Smoking” OR “Tobacco Use” AND “Socioeconomic Factors” AND “Pregnancy”. The search equations were developed in collaboration with a librarian specialized in scientific information from the inter-university library of the Paris medicine pole. The equations and results of the search methodology are detailed in Appendices S2 and S3. The articles were selected after successive reading of the titles, abstracts and full-length texts. To ensure a satisfactory methodology, a double-blind reading (KB, HF) was performed using Rayyan software. In case of disagreement regarding the inclusion of an article, the opinion of a third reader was requested (GI). For the studied countries in which recent data were lacking, a search was made to find the results of national surveys on perinatal health. Publications cited by the selected articles were also reviewed. The sources and bibliographic references were managed using Zotero software. Duplicates were identified and removed.

Assessment of article quality:

The methodological quality of the articles was confirmed using Loney’s matrix that assesses articles investigating the prevalence of a health issue.²⁴ The scoring included 8 points, one for each of the following items: whole population or randomized sampling, selection explained and source of little biases, adequate sample size (>300 subjects),

quantification of smoking, prospective analysis, adequate response rate (>70%) with description of non-responders, CIs presented, estimate of the prevalence according to various socio-economic and demographic criteria.

Statistical analysis:

The characteristics of the included studies are described in Appendix S4. Data on the prevalence of smoking during pregnancy and the associated socio-economic factors, extracted from the included articles, are presented in Appendices S5 to S9. The changes in prevalence were analyzed based on data collected repeatedly over time using the same methodology. This result was summarized and presented as a graph (Figure 2). Socio-demographic data (age of the mother, marital status, parity, ethnic origin) and socio-economic data (education level, employment status, occupational category, household income level, ecological index) were then studied to highlight the variables associated with smoking during pregnancy using odds ratios (OR) and weighted prevalence (WP) (Table 1 and Table 2 respectively). We used a color gradient according to the strength of the association between maternal smoking and the factor studied (green: positive association and red: negative association) for a better visualization of the results. The confidence intervals of the OR and WP are present in the tables when they were available. Finally, the changes in prevalence of smoking during pregnancy according to the socio-economic level were presented as curves per country (Figure 3), allowing a graphical visualization of the associated social inequalities as well as their evolution. Social inequalities in maternal smoking during pregnancy were represented using absolute differences in the prevalence of smoking during pregnancy between women in the most and least advantaged socioeconomic categories. The data used to create Figure 3 are available in Appendices S8

and S9. The education level was chosen when it was available, otherwise the occupational category or the ecological index of the home neighborhood were used. Statistical analyzes were performed using R v4.0.3 software.

RESULTS

Article selection:

The selection of the articles included in the final analysis is presented in Figure 1. Within the various databases (PubMed, PsycInfo and Embase), 3,941 articles were identified. The independent double reading of the titles, abstracts and full-length texts allowed selecting 24 articles. Five additional articles were included after further reading, from the bibliographic references of the selected articles. An additional search allowed selecting 6 national institutional sources. Thirty-five articles were included in the final analysis. The results according to the databases are detailed in Appendix S3.

Characteristics of the selected articles:

The characteristics of the 35 articles included in the final analysis are shown in Appendix S4. The analysis focused on studies conducted in the following 14 countries: Australia, Canada, Denmark, Finland, France, Germany, Italy, New Zealand, Norway, Spain, Sweden, The Netherlands, United Kingdom and the United States.^{21,22,25-59} The sample size ranged from 3,534 women in the Italian study³⁹ to 27,912,380 women in a US study.²¹ Nineteen studies were based on national birth registers (Australia, Denmark, Finland, Germany, New Zealand, Norway, Sweden, United States) and 14 studies on national cross-sectional surveys (Canada, France, Italy, Netherlands, Spain, United Kingdom). Twenty-six studies were published in the last ten years, including eleven between 2015 and 2020. The rate of available data (response rate for surveys or data completion rate for register-based studies) was greater than 70% in 27 studies. The methodological score varied according to

the studies between 5 and 8 (maximum value). The studied socio-economic characteristics were: age, education level, parity, marital status, employment status, occupational category, socio-economic status, household income, ecological index of the home neighborhood and ethnicity.

Changes in prevalence of smoking during pregnancy over time in the various studied countries:

Changes in the prevalence of smoking during pregnancy in the various countries studied between 1995 and 2018 are presented in Figure 2. All the values used to generate this figure as well as the gross prevalence per country are detailed in the appendix (Appendices S5-S6). Before 2005, Spain, Norway and France had the highest prevalence of smoking during pregnancy (28.0%, 24.9% and 20.8% respectively), while the Netherlands, Italy and Sweden had the lowest prevalence (10.1%, 9.1% and 8.8%, respectively). After 2010, France and New Zealand had the highest prevalence of smoking during pregnancy (17.0% and 13.3%, respectively), while Sweden and Italy had the lowest prevalence (6.3% and 5.3%, respectively). Figure 2 shows an overall trend towards a decreased prevalence of smoking during pregnancy over time. The countries with the strongest decrease in prevalence of smoking during pregnancy were Norway (absolute decrease by 17.3% in 15 years), Denmark (absolute decrease by 16% in 19 years), Sweden (absolute decrease by 12.9% in 23 years) and Canada (absolute decrease by 9.5% in 12 years). The countries with the smallest decrease over time were Italy (absolute decrease by 3.9% in 13 years) and New Zealand (absolute decrease by 2.8% in 5 years). No recent data were available for Spain, Germany and The Netherlands to illustrate the current trend in these countries.

Smoking during pregnancy and social health inequalities:

The analysis of associations between socio-demographic and socio-economic factors and smoking during pregnancy is presented in Table 1 and Table 2. The values are detailed in Appendix S7. The most frequently studied variables were the education level, the age of the mother, and the marital status. The education level appeared to be the variable most strongly associated with smoking during pregnancy, with ORs sometimes greater than 10. Pregnant women with lower education levels are more likely to smoke than others. The adjusted odds ratios (aOR) for this variable ranged from 1.52 (95% CI 1.44, 1.61) in Australia (25) to 14.2 (95% CI 13.7, 14.8) in Sweden (48). A young age of the mother, multiparity, being a single woman, the most disadvantaged occupational category and the most vulnerable ecological index were often associated with increased smoking during pregnancy. A foreign ethnic origin was most often associated with a lower prevalence of smoking during pregnancy. The employment status appeared to be weakly associated with the prevalence of smoking during pregnancy in these studies.

Figure 3 shows the changes in prevalence of smoking during pregnancy over time according to the socio-economic category in the various countries studied. The values are detailed in Appendix S8-S9. There was a socio-economic gradient in smoking during pregnancy in most of the countries studied. Thus, the more disadvantaged the category was, the higher the prevalence of smoking during pregnancy was. This phenomenon was identified regardless of the socio-economic variable used (education level if available, otherwise occupational category or neighborhood characteristics). In addition, in all the studied countries, the prevalence of smoking during pregnancy decreased over time regardless of the socio-economic status of women, except in the United States. In Canada, France and the United States, the decrease in smoking during pregnancy in the most

advantaged category was faster than in the disadvantaged category, showing a progressive increase in social inequalities over time. In the other studied countries, there was a trend towards a progressive reduction in inequalities over time even if they persisted. Norway was the country where inequalities were most strongly reduced with absolute differences decreased by 15.5%. However, in Norway in 2014, the prevalence of smoking in pregnant women from the least advantaged social category was still ten times higher than that in women belonging to the most advantaged category.

COMMENT

Principal findings:

Since 1995, an overall decrease in the prevalence of smoking during pregnancy was observed. The rate of decrease differed across countries. The overall decreasing trend masks disparities between and within countries. Over time, inequalities in smoking during pregnancy remained significant and persisted. Over the study period, increased inequalities were reported in Canada, the United States, and France while they remained stable or decreased in the other studied countries. In all the studied countries, demographic and socio-economic factors remained strongly associated with smoking during pregnancy.

Strengths of the study:

This study aims to estimate changes in the prevalence of smoking during pregnancy and the associated social inequalities in countries with comparable levels of development, to ensure consistency in epidemiological contexts.^{60,61} This study was reported according to the PRISMA Equity 2012 guidelines. The independent double reading with the intervention of a third reader in case of disagreement allowed limiting the selection bias of the articles. To improve the quality of this work, the search equations were validated by a librarian specialized in scientific information. The various graphs presented in this work allowed gathering existing data for better visualizing social health inequalities and their evolution, in order to develop appropriate policy measures.

3. Limitations of the data:

This study had some limitations. First, for the US study, the data available were obtained from two separate sources: the birth certificates and the Pregnancy Risk

Assessment Monitoring System (PRAMS) database. To be able to compare the studies with each other, the decision was made to limit our analysis to those based on birth certificates because they provide access to national data, and the information on maternal smoking is collected at the time of delivery which limits the recall bias.⁶² Second, due to the methodology used, the completeness of the data cannot be ascertained. Some published data might not have been included in our review, especially if they were written in a language other than those chosen. In addition, the articles included in the analysis were compared while they sometimes used different methodologies and timeframes. The primary endpoint of “smoking during pregnancy” was not measured consistently in all studies. In addition, in several studies, the primary endpoint was measured retrospectively, thus inducing a recall bias.³¹ However, Pickett et al. have described a good correlation between prospective and retrospective measurements of smoking during pregnancy.⁶³ Furthermore, self-reporting of smoking during pregnancy is the most common way to collect maternal smoking. It may induce a non-disclosure bias underlined by the phenomenon of social desirability. Self-reporting the smoking status underestimates the prevalence of smoking during pregnancy but this underreporting did not seem to follow a social gradient.^{64,65} These levels of underreporting may vary between survey-based and registry-based studies. In studies that use registry data, algorithms may have been applied to improve identification of women who smoked.⁶⁶ Finally, it would have been interesting to present a meta-analysis. We conducted a meta-analysis, but the high heterogeneity of the studies did not allow presenting pooled data.

4. Interpretation

External validity of the study:

The WHO regularly estimated the prevalence of smoking in the general population.¹ During pregnancy, two international studies have found results similar to ours: one study conducted in all countries regardless of their level of development;¹⁴ and the European PERISTAT study that has reported prevalence rates ranging between 6.1% and 33.0% in 23 countries.⁶⁷ The association between demographic and socio-economic factors and smoking during pregnancy has been investigated at national or regional scales. The results were consistent with those found in our study.^{3,15,18,19} In the published studies, a low education level was the factor most strongly associated with smoking during pregnancy.¹⁶ A foreign origin was a protective factor for smoking during pregnancy in Europe. But this protection decreased with the time spent in the host country and a high acculturation score.^{49,68,69} Other factors associated with smoking during pregnancy have also been studied in the literature. A significant link has been shown between smoking during pregnancy and the unexpected nature of the pregnancy^{19,70}, the time to get a consultation before the first prenatal visit^{25,28}, having a partner who smokes^{19,28,53}, a poor social support⁷⁰, an exposure to stressful life events²⁸, the consumption of other substances (including alcohol)⁷⁰, and with the characteristics of smoking before pregnancy (amount of cigarettes smoked, smoking duration, age of onset, degree of dependence).^{25,71}

It has been estimated that 52.9% (95% CI: 45.6, 60.3) of women who smoked daily continued to smoke during their pregnancy.¹⁴ When women stopped smoking during pregnancy, cessation mainly occurred in early pregnancy.^{72,73} Pregnancy was described as a window of opportunity during which the perception of the health risks is increased. In

addition, quitting smoking during this period appeared to be associated with a long-term effect on the smoking behavior of women, with smoking cessation for several years.⁷⁴ Socio-demographic factors also appeared to be associated with postpartum resumption.^{73,75}

Maintaining postpartum smoking cessation was associated with several challenges.

Social health inequalities and perspectives:

It seems necessary to combine comprehensive prevention measures for smoking during pregnancy with more specific measures aimed at reducing social inequalities.

Epidemiological monitoring allows both identifying target groups for prevention programs but also assessing the impact of preventive measures.⁷⁶ The most popular strategies to reduce smoking during pregnancy lead to an overall decrease in prevalence, but they can also increase social health inequalities during pregnancy.⁷⁷

Social inequalities in health imply a social gradient, whereby persons who are not in the most advantaged socioeconomic positions have higher health risks than those who are the most advantaged. Thus, prevention efforts should target women who are the most disadvantaged but also those who are in intermediate positions and carry the highest burden of poor health.

According to Barker's hypothesis, the period of pregnancy and the intrauterine environment are crucial and have a direct impact on long-term health and the development of chronic diseases.⁷⁸ This is an important period where prevention and intervention issues are major for future generations. Life course epidemiology provides a useful perspective for examining preconception factors and their effects on maternal and child health. The relationship of exposures to outcomes can be considered in terms of critical periods, sensitive periods, and cumulative effects.⁷⁹ The prenatal period is considered as a critical

period when exposure to smoking can have both short-term and long-term consequences for the offspring. Although the negative effects of smoking during pregnancy on women and children are well known and multiple, there is still no consensus on optimal management. Many trials have examined strategies to improve smoking cessation during pregnancy.⁸⁰ Interventions include psychosocial interventions (counselling, health education, feedback, incentives, social support, exercise, and dissemination) and pharmacological interventions (nicotine replacement therapy, bupropion, and varenicline).^{3,81} Finally, interventions that improved smoking cessation rates in pregnancy may be achieved using a holistic approach and a multi-professional approach. Additional studies are needed to specifically assess the efficacy of smoking cessation interventions in pregnant women from disadvantaged socio-economic categories as little data are available.⁷⁷

Pregnancy is a time of opportunity when the woman has many medical check-ups and can receive prevention messages that can be a motivation for change. In France, the early prenatal interview, recommended since May 2020 for all pregnant women regardless of their socio-economic level, allows an early and systematic identification of vulnerable situations.⁸² It is an opportunity to collect data on the mental health status of the mother, psycho-social risks and addictive behaviors in particular. This early identification is a key step in supporting women and proposing personalized prevention strategies. The subsequent birth preparation and the postnatal interview allow a follow-up of women and couples. All pregnant women need to benefit from prevention strategies in order to improve their own health and their offspring's, however, women from more disadvantaged socio-economic categories need to have more resources and strategies in place to support them, according to a principle of proportionate universalism. Finally, in order to avoid prenatal smoking, it

seems important to also carry out targeted prevention actions to avoid adolescents entering smoking, in order to avoid starting a pregnancy by smoking.

CONCLUSIONS

Smoking during pregnancy is a major risk factor for morbidity and mortality for both mother and child. This study showed a slow decrease in smoking during pregnancy over the past 25 years, but this overall trend masked disparities between and within countries. The decrease in smoking was observed regardless of the socio-economic level but inequalities tended to persist or even gradually increase over time in several countries. During pregnancy, a time for health change, the early detection of smoking and of the social vulnerability of women seems essential. Health prevention strategies aimed at supporting smoking cessation should be implemented in all pregnant women as well as other strategies specifically targeting the most socio-economically disadvantaged population, according to a principle of proportionate universalism.

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Disclosure of interest:

The authors declare that they have no conflicts of interest concerning this article.

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