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Maternal smoking and cannabis use during pregnancy and infant outcomes

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Sarah Sturrock[1], Emma Williams[1], Hemant Ambulkar[1], Theodore Dassios[1,2], Anne Greenough[1,3,4]

[1]Department of Women and Children's Health, School of Life Course Sciences, Faculty of Life Sciences and Medicine, King's College London, United Kingdom [2]Neonatal Intensive Care Centre, King's College Hospital NHS Foundation Trust, London, United Kingdom [3]The Asthma UK Centre for Allergic Mechanisms in Asthma, King's College London, United Kingdom, [4]NIHR Biomedical Centre at Guy's and St Thomas NHS Foundation Trust and King's College London, United Kingdom

Corresponding author: Professor Anne Greenough, Neonatal Intensive Care Centre, 4th Floor Golden Jubilee Wing, King's College Hospital NHS Foundation Trust, Denmark Hill, London, SE5 9RS, United Kingdom. Tel: 0203 299 3037; Email: anne.greenough@kcl.ac.uk

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HA collected the data and was involved in the preparation of the manuscript and approved the final version

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ABSTRACT

Background: Our aim was to determine the prevalence of tobacco smoking and e-cigarettes and cannabis use during pregnancy, whether these were influenced by ethnicity and their relationship to perinatal outcomes

Methods: A study was carried out of 4,465 infants whose mothers delivered during 2017 and 2018. Self-reported maternal smoking, e-cigarette and cannabis use at booking were recorded. Outcome measures were birthweight and head circumference z-scores and admission to neonatal intensive care unit.

Results: Two hundred and five women reported smoking cigarettes (4.7%), five were using e-cigarettes (0.11%) and 106 were using cannabis (2.43%). Women were most likely to smoke if young (15-19 years old) or from a mixed-race or white background. Cigarette smoking was associated with a lower mean z-score for birthweight (-0.587 versus -0.064) and head circumference (-0.782 versus -0.157) (both outcomes $p<0.0001$). Young, mixed-race women were most likely to be both smoking and using cannabis during pregnancy and their infants had a lower birthweight mean z score (-0.989 versus-0.587, $p=0.028$) and head circumference z score (-1.33 versus 0.782, $p=0.025$) than cigarette use alone.

Conclusion*:* Young, mixed-race women were most likely to be both smoking and using cannabis during pregnancy and should be targeted for cessation programmes.

Key words: cigarette smoking; cannabis; e-cigarettes; birth weight; head circumference

ABBREVIATIONS

THC Tetrahydrocannabinol

INTRODUCTION

Maternal smoking during pregnancy apparently remains common. Approximately one in ten (10.8%) of mothers in the UK were reported to be smoking at the time of delivery in 2017/18, this had declined from 15.8% in 2006/07 [1]. Maternal smoking has been shown to have numerous deleterious effects including an increased rate of preterm birth and fetal growth restriction, increased rate of admission to the neonatal intensive care unit and adverse effects on neurodevelopment. Maternal smoking cessation programmes have been associated with an absolute reduction in the number of smoking mothers of between three and six in 100 mothers, but have only been shown to increase birthweight with no reductions in neonatal intensive care unit admissions or perinatal or neonatal mortality [2]. Although e-cigarettes are a possible aid to smoking cessation [3], there are concerns about the safety of their use during pregnancy due to the ability of nicotine to cross the placental barrier and cause oxidative stress and inflammation in the fetus [4].

Cannabis use has been associated with lower birth weight [5, 6], more admissions to the neonatal unit [5] and a higher prevalence of preterm births [6]. A meta-analysis, however, found no significant association between cannabis use and adverse neonatal outcomes following adjustment for tobacco smoking and socioeconomic deprivation [7]. The prevalence of maternal cannabis smoking in the UK has been reported to be 2.5% [8], but the impact on neonatal morbidity is unclear with only one study in the previous meta-analysis using data from the UK [7]. The results from

that UK study suggested that maternal cannabis use was not associated with an increase in perinatal morbidity or mortality [9]. Our previous study examining positive pregnancy test urine samples in 1999, however, found that 14.5% were positive for cannabis and infants born to mothers with positive drug tests for cannabis had a significantly lower birth weight than those with negative tests [6].

The aim of this study was to determine the current prevalence of tobacco smoking and e-cigarettes and cannabis use, whether these were influenced by ethnicity and their relationship to important perinatal outcomes, that is not only NICU admission and birth weight, but head circumference.

METHODS

The outcomes of term, live-born infants (37 to 41 weeks of gestational age) delivered at an NHS Foundation Trust between 1st August 2017 and 31st July 2018 were analysed. Patients were excluded from the analysis if their neonatal records were unavailable. Patients were identified via Badgernet, an electronic maternity and neonatal patient records system. Anonymised data were extracted from maternity booking data and the medical records for both mother and infant.

Ethical approval: The research related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration. As this project was a clinical audit, ethical approval from a

Research Ethics Committee was not required. The audit was registered with and approved by author's institutional Audit Department.

Informed consent: This was a clinical audit so informed written consent was not required.

Demographic information collected from maternal records included age, ethnicity, number of previous pregnancies and live births. Ethnicity, as recorded in maternal records, was categorised into the Office of National Statistics groups: white, mixed/multiple ethnic groups, asian/asian British, black/african/caribbean/black British and other ethnic groups [10]. Cigarette smoking and e-cigarettes and cannabis use at the time of booking were recorded. Delivery records were reviewed to obtain the birthweight and head circumference, mode of delivery and APGAR scores at one, five and ten minutes. Neonatal records were reviewed to determine whether the infant was admitted to the Neonatal Intensive Care Unit, High Dependency Unit, Special Care Baby Unit or Transitional Care.

Statistical analysis

Birthweight and head circumference z-scores were calculated on Microsoft Excel using the LMS-growth calculator add-in and UK World Health Organisation data for birthweight and head circumference [11]. The difference in birthweight and head circumference z-scores between exposed and unexposed groups were analysed for statistical significance using student T-tests. Differences in exposure rates between

age and ethnicity groups were analysed using Chi squared tests IBM SPSS Statistics for Macintosh, Version 25.0 was used.

RESULTS

Four thousand, three hundred and sixty-six women delivered live term babies during the study period. Four infants were excluded from the analysis as their neonatal notes were unavailable. The mean age of the mothers of the remaining 4,362 infants was 32.5 years and the most commonly reported ethnicity was white (n=2126). There was no record of smoking status in 46 women's records (1.05%), and no record of drug use status in 178 women's records (4.28%).

There was a significant difference in smoking rates according to ethnicity (p=0.001); women were most likely to smoke if from a mixed-race or white background compared to those from an Asian, black or other ethnic background (Table 1). Mixed-race women were more likely to be using cannabis (5.43%) when compared to Asian women (0.92%) p=0.009) or black women (2.4%) p=0.017). Younger women were significantly more likely to smoke cigarettes. The youngest age group (15-19 years, 13.46% smoking) were almost seven times more likely to smoke than the oldest age group (40+ years, 1.90% smoking, p<0.0001).

Of the 206 women who reported smoking at booking, 166 were offered a referral to smoking cessation services, 97 (58.43%) accepted the referral.

Cigarette smoking was associated with a lower mean z-score for birthweight (-0.587 versus -0.064) and head circumference (-0.782 versus -0.157) than using neither cigarettes or cannabis (both outcomes $p<0.0001$). Using cannabis alone was associated with a lower mean z score than neither cannabis nor cigarette use for birthweight (-0.255 versus 0.064) and head circumference (-0.393 versus -0.157), but neither of these differences were statistically significant ($p=0.087$ and $p=0.129$ respectively). Cannabis and cigarette use were associated with both a significantly lower birth weight z score (-0.989 versus -0.587, $p=0.028$) and head circumference z score (-1.33 versus 0.782 z scores, $p=0.025$) than cigarette use alone. Young, mixed-race women were most likely to be both smoking and using cannabis during pregnancy and their infants had a lower birthweight mean z score (-0.989 versus-0.587, $p=0.028$) and head circumference z score (-1.33 versus 0.782, $p=0.025$) than cigarette use alone.

Significant differences were found in the birthweight z-scores between infants whose mothers did not smoke and those who smoked <5 cigarettes/day (mean difference =0.587, $p<0.0001$), 6-10 cigarettes/day (mean difference=0.590, $p<0.0001$), 11-20 cigarettes/day (mean difference=0.457, $p=0.049$) or 21-30 cigarettes/day (mean difference=1.13, $p=0.041$). Similarly, significant differences were identified in head circumference z-score between infants whose mothers did not smoke and those who

smoked <5 or 6-10 cigarettes (mean differences=0.693 and 0.592 respectively, $p<0.0001$).

Four hundred and eighty-seven of the infants (11.31%) required admission to enhanced neonatal care: 112 were admitted to the Neonatal Intensive Care Unit, 33 to the High Dependency Unit, 199 to the Special Care Baby Unit and 143 to Transitional Care. No significant associations were found between maternal smoking or cannabis use and admission.

DISCUSSION

We have demonstrated that both smoking cigarettes and cannabis use were associated with a significant reduction in birthweight and head circumference z-scores. We used z-scores to adjust for sex and gestational age to assess those outcomes. Cannabis use alone was not associated with a significant reduction in birthweight or head circumference z-score, but the combination of cannabis and cigarette smoking resulted in a significant decrease in both z-scores compared to cigarette smoking alone. Importantly, we believe for the first time, we have demonstrated that young, mixed-race women were most likely to be both smoking and using cannabis during pregnancy and their infants had significantly lower birthweight and head circumference z scores than cigarette use alone.

Maternal smoking is known to be associated with reduced birthweight. Prenatal smoke exposure causes chronic hypoxic stress in the fetus [12], likely due to early morphological placental changes [13] which lead to reduced maternal intervillous space and reduced volume and surface area of fetal capillaries [14]. Smoking tobacco during pregnancy, particularly continuing to smoke after the pregnancy is associated with a reduction in fetal head circumference growth of -0.56mm/week [15]. Our finding that head circumference was negatively associated with maternal smoking is consistent with previous studies [16], although our study was unique in using z-scores to adjust head circumference measurements for gestational age and sex. Our results are of concern as small head circumference at birth and poor head circumference growth, is associated with neurodevelopmental impairment [17]. We found that there were significant differences between smoking no cigarettes and smoking <5 or 6-10 cigarettes/day, although no dose-response effect of smoking was demonstrated. This may be due to the low numbers of women admitting to smoking a large number of cigarettes. Previous studies, however, have identified a similar effect, with the largest decrease in birthweight being seen at low levels of prenatal smoking [18]. This indicates that smoking cessation would benefit women admitting to smoking low numbers of cigarettes prenatally and the focus should be on complete cessation rather than reducing the number of cigarettes.

The mechanism of action by which cannabis may affect fetal growth and development is less well-defined. Tetrahydrocannabinol (THC) is able to cross the

placenta, but fetal THC concentrations have been found to be lower than maternal concentrations. Cannabis smoking produces five times as much carbon monoxide as smoking cigarettes, so it is postulated that cannabis may affect fetal oxygenation, thereby altering fetal growth and development [19]. Meta-analysis of the effect of cannabis has found that it is not an independent risk factor for low birthweight or pre-term delivery [7]. Previous studies, however, have noted that it is difficult to separate the effect of cannabis use from concomitant tobacco smoking, other recreational drug use, or socioeconomic status, particularly at high levels of cannabis use [7]. Our study found that cannabis alone did not cause a significant reduction in birthweight or head circumference z-score, but cannabis and cigarette smoking did reduce both measures further to cigarette smoking alone.

We found that mothers who were young were more likely to be smoking cigarettes, which is consistent with other UK data [20]. In our study, young women were also more likely to be using cannabis and mixed-race women were more likely to be using cannabis and/or cigarettes. Previous studies have highlighted that maternal smoking in the UK is associated with socioeconomic deprivation and unplanned pregnancy [20]. A study of an Aboriginal birth cohort found that maternal smoking and cannabis use during pregnancy was more common amongst women with a lower level of education, unemployment during pregnancy and those who had begun childbearing at a young age [21]. It would be important to target smoking cessation programmes at those particularly at-risk groups. It is important to note that there is no evidence

that nicotine replacement therapy used for smoking cessation in pregnancy has negative or positive impacts on birth outcomes [22].

A weakness of the present study is that we relied on self-report measures of maternal cigarette, e-cigarette and cannabis use. It has been highlighted that self-report measures have been found to underestimate cannabis exposure by as much as half in pregnant women [23]. Our 1999 study in the same London area found the rates of tobacco and cannabis use (34.3% and 14.5% respectively) were based on urinalysis [6]. In a later study in 2008, however, we demonstrated that 34% of Caucasian women admitted to smoking by self -report [24]. The lower rates of smoking by self-report identified in the present study may, therefore, reflect the national trend of reduction in maternal smoking in recent years; less than 11% of women smoked at the time of delivery in 2017/18, compared to 16% in 2006/07 [1].

We intended to examine the association between e-cigarette use and neonatal outcomes, but only six women within our study admitted to using e-cigarettes and four were concurrently smoking conventional cigarettes. E-cigarettes may be perceived as less harmful than tobacco smoking [25]. Nevertheless, due to the perceived social stigma, some women feel uncomfortable using e-cigarettes in public especially during pregnancy [26]. It has been noted that healthcare providers less frequently assessed electronic nicotine delivery systems during prenatal visits compared to tobacco cigarette use [27]. Use of electronic cigarettes to quit smoking,

however, may be common in women of reproductive age [28]. Hence, more research is required to determine the risks and benefits of electronic cigarette use during pregnancy.

A strength of the study is the use of z-scores to adjust for the expected variation in these outcomes with gestational age and sex of the infant. We also only analysed term births, eliminating the possibility that the associations with reduced birthweight were confounded by prematurity, a known consequence of maternal smoking during pregnancy [29]. A further strength was the large sample size. The retrospective approach enabled us to quantify how many women were asked about smoking and substance misuse and how many are offered referrals without the knowledge of an ongoing study affecting staff behaviour.

In conclusion, uniquely, we found a significant reduction in head circumference z-score as well as birthweight z-score, in those exposed to tobacco smoke and cannabis. Young, mixed-race women were most likely to be smoking and using cannabis during pregnancy. That group should be a key target for maternal smoking cessation programmes.

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Table 1 Smoking and cannabis use related to ethnicity and maternal age

Data are represented as the mean (SD)

	Total	Number smoking cigarettes (%)	Number using cannabis (%)
Ethnicity			
White	2126	121 (5.7)	46 (2.20
Mixed/Multiple ethnic groups	221	17 (7.7)	12 (5.4)
Asian/Asian British	218	3 (1.4)	2 (0.9)
Black/African/Caribbean/Black British	1250	46 (3.7)	30 (2.4)
Other ethnic group	233	6 (2.6)	6 (2.6)
Not stated	*318*		
Maternal age (years)	4366		
15-19	52	7 (13.5)	8 (15.4)
20-24	344	47 (13.7)	21 (6.1)
25-29	783	43 (5.5)	14 (1.8)
30-34	1562	67 (4.3)	42 (2.7)
35-39	1256	34 (2.7)	20 (1.6)
40+	369	7 (1.9)	1 (0.3)