Pregnancy smoking, child health and nutrition
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Chapter 8  Discussion
Discussion

This thesis evaluated birth and childhood health outcomes of smoking during pregnancy and provides some insight into possible mechanisms underlying associations identified. Maternal asthma was an independent risk factor for pre-term birth which predisposed to childhood asthma, whereas fetal growth restriction was associated with reduced risk of childhood asthma. A dose-response association was observed between pregnancy smoking exposure, short stature and obesity, implicating an important interaction with childhood nutrition. A positive dose response association of ADHD with the number of maternal cigarettes smoked during pregnancy was identified. Cigarette smoking in pregnancy was also associated with increased risk for a female birth. These cross-sectional studies have identified the role of sequential community surveys of child health in this community. Decreasing survey compliance was an increasing problem which will impact on the validity of future surveys.

Comments

Parental asthma and birth outcomes

Chapter 2 focussed on prevalence of childhood asthma in relation to intrauterine growth restriction and pre-term birth among babies born to mothers and fathers with asthma and smoking exposures. The data from three of the cross-sectional surveys (1993, 1998 and 2006) were used. For the combined surveys mothers with asthma were more likely to have a PTB than non-asthmatic mothers (OR 1.39), and in 2006 more likely to have an SGA or growth restricted baby. 40.9% of PTBs of asthmatic mothers developed doctor diagnosed asthma compared to 34.3% for term babies (adjusted OR 1.65). The corresponding estimates for the symptom triad of cough, wheeze and breathlessness were 19.4% and 17.6%. Conversely SGA babies were less likely to develop doctor diagnosed asthma (adjusted OR 0.49), or the symptom triad (adjusted OR 0.22) whether or not the mother was asthmatic. The attributable risk estimate of PTB associated with maternal asthma of 8.1% was comparable to other estimates (Kramer et al, 1995).

SGA infants of asthmatic or non-asthmatic mothers were less likely to develop doctor diagnosed asthma, or the symptom triad C+W+B+. Conversely fetal growth restriction is more frequent in babies of women who smoke in pregnancy (Dolan et al 1995), and these children would be more likely also to experience postnatal cigarette smoke exposure with associated respiratory health problems (Chinn et al 1993). The mechanism explaining the association of fetal growth restriction with reduced asthma risk in childhood is unknown, but may have a nutritional basis. There was consistency of findings across the three surveys with the combined analysis providing evidence for a protective effect of fetal growth restriction for childhood asthma, and strong evidence for the association of maternal asthma with pre-term birth

The problem of heavy smoking and adolescent smoking

The prevalence of pregnancy smoking in Liverpool is one of the highest in the United Kingdom. Delpisheh et al (2006a) reported a reduction in smoking prevalence in pregnancy in adults (≥20) in Liverpool during the 1990’s, although there was a parallel increase in smoking prevalence in adolescent pregnancies. These chronic patterns of pregnancy smoking
reflect a cycle of smoking exposures from childhood through to pregnancy and prevalence is sufficiently high enough to contribute substantially to fetal and child health. Despite a decrease in prevalence of maternal smoking during pregnancy, there was a significant increase in prevalence of heavy smokers. This suggested that heavy smokers were a core group with a more chronic problem and that these women required better targeting and prioritisation. More adverse birth and childhood health outcomes are associated with heavy smoking (Pollack et al, 2000; Floyd et al, 1993).

Some studies have shown that adolescents were more likely to smoke cigarettes during pregnancy than adult women (Smith & Pell, 2001). Dewan et al (2003) in their study in Liverpool demonstrated the significance of the association of pregnancy smoking with increased risk of low birthweight in teenage primigravidae. Delpisheh et al (2006b) in their study on pregnant women attending the Liverpool Women’s Hospital between 1998 and 2003 reported that between 46.2% of adolescents smoked during pregnancy with smoking prevalence ranging from 45.2% in 1998 to 46.3% in 2003. The progressive increase in smoking among adolescent pregnant women remains a major health problem in Liverpool despite various intervention measures to increase smoking cessation.

Smoking assessment

Cross-sectional surveys commonly use questionnaires to determine prevalence of smoking habits. These are based on smoking-related questions answered by parents especially in school-based surveys. Self-reporting of smoking habits, is better quantified by means of objective tests (Gillies et al, 1982). This is because pregnant women are more reluctant to reveal their smoking habits as smoking is regarded as socially unacceptable during pregnancy (Ana et al, 2009). Various methods have been used for the quantification of pregnancy smoking such as measurement of expired carbon monoxide, carboxy-haemoglobin in blood or nicotine in urine or saliva. Salivary cotinine could be measured for monitoring maternal pregnancy smoking as an alternative to self-reported smoking exposure (Delpisheh et al, 2007; Haddow et al, 1987). Some of these methods could be used in ante-natal settings to facilitate exposure monitoring. Cotinine, being an exclusive metabolic product of tobacco smoke and the main metabolite of nicotine in saliva, blood, urine or hair is a sensitive (97%) and specific (99%) indicator of current smoking, (Couriel, 1994). A disadvantage with cotinine is that it does not measure the duration of smoking exposure or reflect other toxins present in tobacco smoke. Cotinine levels in children strongly correlate with parental smoking, (Irvine et al, 1997).

Smoking prevention and cessation program

Many women find it difficult to stop smoking during pregnancy in spite of knowing the need to stop and the harmful effects to both the mother and baby. Smoking cessation, or a significant reduction of smoking frequency during pregnancy leads to improved maternal and infant health outcomes (Susan et al, 2004). Maternal smoking is an ideal target for intervention activities as mothers who smoke during their pregnancy are more motivated to stop smoking than non-pregnant women of the same age (Haug, 1994). Greater efforts are required to promote smoking reduction in these women. The Ewles & Simnet model of health promotion planning and evaluation is a suitable model for a smoking cessation program (Ewles & Simnet, 2003). This makes use of the medical, behavioural change, educational,
empowerment and social change approaches to motivate pregnant women to stop smoking (Naidoo et al, 2004).

One of the difficulties in implementing smoking cessation programs is that although pregnant women are aware of the dangers of smoking to the fetus, some remain comfortable to continue smoking during pregnancy with the intention of having a smaller baby (Margaret et al, 2004). A further obstacle is if a pregnant woman enters the third trimester and continues to smoke, it is more difficult for her to quit smoking and there is little interest in commencing interventions (DiClemente et al, 2000). Stewart et al (2000) suggested that future smoking cessation programs should pay more attention to addressing socio-demographic and cultural factors that influence the behaviour of maternal smokers. Although pregnancy is a critical period which offers multiple windows of opportunity for smoking cessation interventions, actions for smoking cessation in pregnancy are quite difficult to design. There is a need to start with the woman’s knowledge and concerns about pregnancy smoking. Prioritisation of prevention strategies in young adolescent girls is critical.

Pharmacological interventions such as nicotine replacement therapy were initially not recommended during pregnancy, because of potential harm to the fetus. The latest guidelines suggest that this may be considered as an alternative treatment for pregnant women in the UK, who otherwise cannot stop smoking (West et al, 2000). The effectiveness of nicotine replacement therapy along with behavioural support influences the ratio of benefit to harm in the pregnancy period (Lumley et al, 1998). Nicotine replacement therapy increases the likelihood of successful smoking cessation in non-pregnant adults by 1.5 to two fold, irrespective of other smoking cessation efforts (Silagy et al, 2004). However the effects on the unborn fetus require further study (Coleman et al, 2004). Varela et al (2006) reported that using nicotine replacement therapy in the first 12 weeks of pregnancy could result in babies who were more likely to be born with birth defects. Further assessment of these possible risks is required.

Pregnancy smoking, childhood obesity and short stature.

This analysis used data from the 1998 and 2006 surveys. Childhood overweight, obesity or short stature were all associated with heavy maternal smoking during pregnancy (all p< 0.001). The adjusted odds ratio for short stature in children of heavy maternal smokers was 2.76, and 4.28, if both parents were heavy smokers. Dose-response associations of pregnancy smoking with birth and childhood health outcomes have been shown by others. Von kries (2001) and Toschke et al (2003) observed a dose-dependent association between childhood overweight or obesity and maternal smoking during pregnancy which could not be explained by a wide range of confounders suggesting that intrauterine exposure to inhaled smoke products, rather than lifestyle factors associated with maternal smoking, may have been responsible for the study findings.

Potential mechanisms underlying the development of obesity related to maternal smoking during pregnancy may be grouped into two categories, as either due to hypothalamic dysfunction, or to abnormalities at the level of the fat cell (Van Der Muelen, 2002). Fetal adaptations to maintain growth, rather than the direct effects of maternal smoke on the fetus could relate to changes in body composition which occur later in life (Power & Jeffris, 2002; Barbara et al, 2002). Dose-related increases in metabolic dysregulation and neuro-endocrine dysfunction could explain this phenomenon, (Montgomery, 2002; Montgomery 2004). The
There is a need to start with the woman's knowledge and concerns about pregnancy cessation interventions, actions for smoking cessation in pregnancy are quite difficult to undertake. Pregnancy is a critical period which offers multiple windows of opportunity for smoking cessation. Although demographic and cultural factors that influence the behaviour of maternal smokers. Although smoking during pregnancy may be grouped into two categories, as either due to hypothalamic adaptations to maintain growth, rather than the direct effects of maternal smoke on the fetus (Simeoni & Zetterstrom, 2007). Catch-up growth may occur at any growth stage, but it is more often seen following severe growth restriction (Karlberg et al, 1995). Mechanisms which regulate and signal early catch-up growth in the postnatal period may influence the extent of catch-up growth (Ong et al, 2000). The cardiovascular consequences may result from systematic low grade inflammation as reported by Tzoulaki et al (2008), in a birth cohort from Finland, using C-reactive protein measurements. Fetal malnutrition resulting from maternal smoking may also influence expression or function of insulin receptors, increasing the risk of subsequent insulin resistant type 2 diabetes and obesity (Lindahl et al, 2002). This is plausible, because low birthweight, which has long been linked with maternal smoking, increases risk of insulin resistance and type 2 diabetes.

The results from this thesis show that heavy paternal smoking was associated with higher prevalence of short stature (p = 0.009), but not with overweight or obesity. When both parents were heavy smokers significant risk estimates for overweight, obesity and short stature were observed compared to either parental non-smokers or light smokers (all p<0.001). The odds of having short stature were 2.76 times more likely when the mother alone was a heavy smoker. This increased to 4.28 if both parents were heavy smokers (p = 0.012). The population attributable risk for short stature was 8.8\% for heavy maternal smokers. A study in Cleveland, UK which was conducted among 539 6-7 year old primary school children using the data from the National Study of Health and Growth collected from 28 study areas in England and Scotland indicated a similar association between childhood short stature and the number of smokers in the home, and a strong inverse association was found between child height and the number of smokers at home for both England (p<00001) and Scotland data (p<0001) (Rona et al,1981). This suggested that the child was affected by passive smoking from household members rather than maternal smoking during pregnancy.

**Genetics, metabolic polymorphisms and nicotine metabolism**

Not all mothers who smoke during pregnancy have detrimental birth or childhood health outcomes. The magnitude of the health effect of nicotine exposure from smoking during pregnancy on birth outcomes is influenced by maternal genetic polymorphisms through their influence on nicotine metabolism, (Delpisheh et al, 2006). It may operate through a mechanism in which the toxin conversion does not occur or though some influence...
genotoxic effects of smoking on pregnancy and concluded that previous heavy smoking for
ten or more years was associated with genotoxic damage to fetal epithelial cells and increased
cromosomal instability in amniocytes. Fetal well being partially depends on the genetic
ability of the mother to reduce the effects of the toxic metabolites of cigarette smoke
(Delpisheh et al, 2008). There is need for further research on gene-environmental
mechanisms and interactions during pregnancy, which may have relevance for risk profiling.

Pregnancy smoking and ADHD

The analysis of the 2006 survey data showed that ADHD prevalence was increased
five-fold in children with obesity (RR 4.80) and more than two-fold in children of mothers
who smoked during pregnancy (RR 2.44). There were significant independent associations of
ADHD with obesity (AOR, 4.66) and pregnancy smoking (AOR, 3.19), and a positive dose–
response association of ADHD with number of cigarettes smoked during pregnancy.
Measures to reduce both smoking among pregnant women and childhood obesity might
reduce prevalence of childhood ADHD. The association of maternal pregnancy smoking and
childhood ADHD has been reported by others (Milberger et al, 1996, Thapar et al, 2003). The
high population attributable risk of ADHD related to heavy maternal smoking suggests that
more than one mechanism is likely to be operating as heavy cigarette may induce multiple
effects. These associations are also governed by gene–environment interactions. It has been
established that both ADHD and smoking are highly heritable, with genetic factors
accounting for about 60% of the two phenotypes (Faraone et al, 2005; Li et al, 2003).

Fetal sex ratio

There was a significant association between maternal smoking during pregnancy
with an increased risk for a female birth as shown by the results from both the hospital study
conducted between 1998 and 2003, and from the results of the community child health
surveys in 1998 and 2006, which demonstrated a dose-response association. The hospital
study identified that maternal smoking during pregnancy was associated with an increased
likelihood of a female birth controlling for birth year, socio-economic status, alcohol
exposure, maternal haemoglobin and maternal body mass index (adjusted OR: 1.41, 95% CI
1.12–1.92, p < 0.001). The findings were similar with the community sample controlling for
socio-economic status (OR 1.13, 95% CI 1.03–1.24, p < 0.015 in 1998, and 1.31, 95% CI
1.16–1.48, p < 0.001 in 2006). Secular trends showed decreasing male : female ratios in
hospital and community samples for both smokers and non-smokers. The significant dose–
response association between maternal smoking during pregnancy and increased female
birth in the hospital sample confirmed the validity of this finding in the community sample.

A detrimental effect of cigarette smoking on sperm quality has been reported,
(Künzle et al, 2003) with a decrease in sperm density, total sperm count, motility,
morphology, citrate concentration and pH (Vine et al, 1994; Vine et al, 1996 ; Shi et al.,
2000 ; Künzle et al, 2003; Zitzmann et al., 2003). The mechanism of the effects of tobacco
on sperm health is not known, but tobacco contains more than 30 chemical agents known to
be mutagenic, or carcinogenic in model systems and direct deleterious effects on male sperm
cells or embryos are plausible, (Zenzes, 2000). HCG levels were reported to be higher in
mothers who smoked and who gave birth to a male child (Brennan et al, 2002). These
influences are considered to operate at the time of conception (Fukuda et al, 2002) and may be due to a selective effect on sperm motility which is more marked in XY spermatozoa, (Viloria et al, 2005).

**Asthma trends**

Chapter 6 focused on trends of childhood asthma defined by prevalence of doctor diagnosed asthma, the symptom triad of cough, wheeze and breathlessness, and parental asthma between 1991 and 2006. The four cross-sectional surveys (1991, 1993, 1998 and 2006 were used for this analysis. There was a substantial reduction in childhood asthma prevalence between 1998 and 2006 following the sequential rise prior to 1998. There was also a decrease in childhood admissions for respiratory illness between 1998 and 2006 which is consistent with the decreased prevalence of DDA and of the symptom triad of C+W+B+, possibly indicating a decrease in the number of severe cases. However the proportion of children reported with well controlled asthma decreased. This may reflect changing perceptions in parental understanding of well controlled asthma, or that improved control was not achieved in a residual group of cases. Reduced prevalence of childhood asthma could relate to improved patient awareness and better asthma management, with increased attention to preventive measures. Prevalence of parental asthma had increased between 1991-2006, and showed no plateau between 1998 and 2006.

**Concluding remarks**

**Limitations**

Cross-sectional studies are limited to identifying associations rather than casual factors. The analysis adopted certain definitions for which agreement is not universal. For example, there is no universally accepted definition for childhood obesity and overweight. There also has been confusion regarding the definition for heavy smoking based on the number of cigarettes smoked during pregnancy. Differences in the cut-offs used for classification of heavy and light smokers could result in dose-related biases (Diane, 2004). Different cut-off values for cigarette number such as more than or equal to 10,15,20,24,25, and 40 cigarettes, have been used (Soares et al, 2007; Jack et al, 2001). The most common cut-off values used were 10 and 20 cigarettes per day (Lloyd & Donald, 2004; Jack et al, 2001). Maternal smoking in pregnancy was not quantified using cotinine estimation and was based on self-reporting. Asthma and ADHD status were defined by questions based on reported doctor diagnosis and were not validated by family doctor, or hospital clinical data.

**Decreasing compliance with cross sectional surveys - an emerging problem**

Although, the use of schools for the distribution and collection of questionnaires has been very popular and can yield good returns compared to postal surveys, decrease in parental questionnaire compliance is an emerging major problem. Despite using the same questionnaire, methodology, age group, and same monthly period for the four health surveys in 1991, 1993, 1998 and 2006, the parental questionnaire compliance decreased sequentially from 92% in 1991 to 30.3% in 2006.
Socio-economic status was uniform for all the surveys with little change in ethnic composition. An important reason for the decrease in parental compliance could be reduced concern following the introduction of environmental control measures by the Health Authority and Borough Council aimed at reducing airborne pollution in the Bootle dock area. However, in the 2006 survey the response rate was only 30.3%, the lowest of all surveys. The explanation for this very low response rate could relate to the increased number of surveys conducted in schools and parental reluctance to complete questionnaires, when both parents are employed. The 2006 survey still represented the same primary schools, populations for the same areas and similar groups of children as those surveyed in previous years. The same efforts to enrol child absentees were used in all these surveys, but despite this considerable effort, good compliance was not attained.

Future implications and potential benefits of this research

Information from this study should help to motivate and create awareness among women who smoke during pregnancy about the detrimental effects of smoking on their unborn babies and the later health problems that can occur in childhood. Measures taken to reduce maternal smoking should help to reduce related neonatal, infant and maternal morbidity and improve long-term health outcomes. The results will be considered for use in health promotion as part of smoking cessation programs in antenatal clinics in this area. Maternal smoking forms an ideal target for intervention and there is a need for more resources for existing smoking cessation campaigns in order to achieve higher cure rates. Prevention of smoking early in pregnancy, especially heavy smoking, is an immediate public health challenge for young women living in the Merseyside area. The results from this work have lead to the concept of using a Venn diagram approach as an intervention tool for demonstrating attributable risk for asthma and obesity among children in relation to maternal cigarette smoke exposure. By combining these risk categories for child health outcomes, the extent of child ill health may be better represented visually in relation to maternal cigarette smoke exposure. Application of Venn diagrams to illustrate these associations may be useful for deterrent programmes.

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