Persistence of anxiety symptoms after elective caesarean delivery

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Background

11.8% of expectant mothers in the UK undergo an elective caesarean delivery (ELCS) representing 92,000 births per annum. It is not known to what extent this procedure impacts mental well-being in the longer term.

Aims

This study sought to determine the prevalence and postpartum progression of anxiety and depression symptoms in women undergoing ELCS in Wales.

Method

Prevalence of depression and anxiety were determined in women at University Hospital Wales (2015-16; n = 308) through completion of Edinburgh Postnatal Depression Scale (EPDS; ≥ 13) and State-Trait Anxiety Inventory (STAI; ≥ 40) questionnaires one day prior to ELCS, and three postpartum timepoints for one year. Maternal characteristics were determined from questionnaires and, where possible, confirmed from NHS maternity records.

Results

Using these criteria the prevalence of reported depression symptoms was 14.3% (95% CI 10.9–18.3) one day prior to ELCS, 8.4% (95% CI 4.2–13.1) within one week, 8.6% (95% CI 4.5–13.2) within 12 weeks and 12.1% (95% CI 6.8-18.6) one year post partum. Prevalence of reported anxiety symptoms was 27.3% (95% CI 22.5–32.4), 21.9% (95% CI 15.8–28.7), 24.8% (95% CI 18.3–31.6) and 34.2% (95% CI 25.2-42.9) at these same stages. Prenatal anxiety was not resolved after ELCS more than one year after delivery.

Conclusions

Women undergoing ELCS experience prolonged anxiety postpartum which merits focused clinical attention.
Introduction

One in four pregnancies are impacted by stress, depression and/or anxiety with the risk of these conditions highest in women with a history of mental illness and those exposed to adverse circumstances (1-3). Antenatal depression is highly co-morbid with antenatal anxiety (4, 5) and both are risk factors for postpartum depression which can impair mother-infant interactions (6).

Antenatal depression and anxiety correlate with low birth weight (7-15), and difficulties in offspring including emotional and behavioural problems, cognitive impairment and psychopathology (16-20).

Understanding the causes and prevalence of mental health problems in pregnancy and the early postpartum period is important for clinical management. In 2015, we initiated a Medical Research Council (MRC) funded study to examine antenatal and postpartum maternal mood disorders in a local Welsh population focusing on women undergoing elective caesareans (ELCS). ELCS was chosen to maximise the efficient collection of biological samples, which will be described elsewhere. The proportion of hospital deliveries by caesarean section in Wales rose from 24% in 2002-03 to 26% in 2015-16 with 11.8% being elective (http://gov.wales/statistics-and-research/maternity-statistics) highlighting the increasing importance of studying this population.

Few studies report on the longer term progression of depression and anxiety symptoms in new mothers after a planned surgical delivery which may differ from other modes if requested, for example, due to fear of childbirth or previous experience of trauma (2). Moreover, during pregnancy and labour dramatic changes occur in the brain resulting in physiological and behavioural adaptations which enable women to cope with motherhood (21). Mothers delivering by elective caesarean do not undergo the physiological process of labour which may have longer term consequences. In this first report on the Grown in Wales (GiW) study, we determined antenatal and postpartum prevalence and progression of anxiety and depression symptoms reported by women undergoing ELCS using validated questionnaires, and examined the relevance of risk factors variously linked to antenatal depression and anxiety including a previous history of mental illness, alcohol, smoking, maternal age, parity, maternal BMI, education level and income (2, 5, 22-27). We included fetal sex as a potential predictor as some studies report that women who give birth to boys are more likely to suffer from postpartum depression (28, 29).
Methods

Study design and participants

Women were recruited at their pre-operative assessment one day prior to an ELCS between the ages of 18 to 45 with a singleton term pregnancy excluding fetal anomalies and infectious diseases by two research midwives between 1st September 2015 and 31st November 2016, recording indication for delivery mode. 355 women agreed to participate, 7 withdrew and 11 failed to complete the questionnaire (Figure 1).

Ethics

Full ethical approval for the study was obtained via the Wales Research Ethics Committee REC reference 15/WA/0004.

Measures

The questionnaire (A1) completed at recruitment consisted of two assessments of perceived mood symptoms. Depression symptoms were assessed using the Edinburgh Postnatal Depression Scale (EPDS) (30) and trait anxiety was assessed using a subscale from the Spielberger State-Trait Anxiety Inventory (STAI) test (form Y-2) (31, 32). Questions on ethnicity (both parents), place of birth, age, weight (pre-pregnancy and current), income, mental health history and lifestyle were also included. Participants provided a sample of saliva in the morning at least 30 minutes after their last meal. Samples were kept at -80°C until cortisol concentration in µg/dL was determined in duplicate repeats by the Human Tissue Authority licensed Salimetrics at Anglia Ruskin University. Participants repeated the EPDS and STAI questionnaires within 7 days of delivery (P1), 10 weeks (P2) and one year (Y1) post partum. Women reporting high anxiety/depression scores postpartum were contacted by RP or NS to ensure access to appropriate help.

Additional data collected

Antenatal data were recorded from NHS maternity records including mental health history, medication taken during pregnancy and complications during the pregnancy for comparison with questionnaire data. Welsh Index of Multiple Deprivation (WIMD) 2014 scores were calculated from anonymised postcodes (http://wimd.wales.gov.uk). Delivery information, fetal and placental biometry were recorded, and biological samples collected.

Data analysis
Analyses were conducted using IBM Corp. Released 2013. IBM SPSS Statistics for Macintosh, Version 23.0. Armonk, NY: IBM Corp. Univariate analyses was performed to assess the relationships between maternal antenatal depression and maternal factors. Antenatal depression data was non-normally distributed and independent samples Mann-Whitney U test, Chi-squared test, Friedman test, Wilcoxon Signed Ranks test, independent samples Kruskal-Wallis test and Spearman’s rho correlations were used to analyse data. In tables results are displayed as n (%) for categorical variables and median (interquartile range; IQR) for continuous variables. Binary logistic regression was used to identify predictors of A1 EPDS scores ≥13. All data presented as bar charts are shown as mean ± SEM. P ≤0.05 were considered statistically significant.

**Results**

**GiW cohort**

The majority (91%; n = 308) of eligible GiW participants reported Caucasian ethnicity with 74% reporting Wales as their birth place (Table S1). To avoid potential confounders introduced by heterogeneous sampling in smaller cohort studies (33, 34), we focused on this group. One in four of these participants reported a mental health history on our questionnaires. Examination of NHS maternity records revealed an additional 12 participants with a history not recorded on their questionnaire (26% v. 30%, Table S2), which may reflect the concerns some women have about reporting their mental health history. Similarly, fewer women (6.2%) reported using antidepressants in pregnancy in our questionnaire compared to NHS maternity records on prescriptions (8.4%; Table S2), considerably higher than the prevalence reported in Wales between 2004 and 2010 (4.5%), already one of the highest rates in Europe (35).

**Prevalence of maternal depression symptoms prior to delivery**

EPDS scores of ≥13 predict an episode of clinical depression based on diagnostic criteria in the postpartum period (36-38). 14.3% of women scored ≥13 on the EPDS questionnaire completed just prior to birth (A1; 37-42 weeks of pregnancy; Table 1). McCabe-Beane et al. (39) further classified severity ranges in EPDS scores to identify no or minimal depression (EPDS 0-6), mild
depression (EPDS 7-13), moderate depression (EPDS 14-19) and severe depression (19-30).

Using these severity ranges, during pregnancy 44% of participants suffered from mild depression, 8% moderate depression and 3% severe depression.

Characteristics of women scoring < 13 with those scoring ≥ 13 on the EPDS scale

In a univariate analysis, women scoring ≥ 13 on the A1 EPDS questionnaire reported a lower level of education ($P = 0.028$) and lower family income ($P = 0.029$) consistent with a lower average WIMD score (Table S3). High scorers had a higher BMI at booking (27.5 v 26.0; $P = 0.012$) and reported higher levels of smoking ($P = 0.033$) but not higher levels of drinking ($P = 0.243$), were more likely to have a mood disorder history (NHS maternity records; $p < 0.001$) and a higher A1 STAI score ($P < 0.001$). Some studies report that depressed mothers have higher antenatal cortisol levels while others report no association (40). We found no association between salivary cortisol provided the morning before the ELCS and EPDS score at A1 ($P = 0.976$; Table S3). Fetal sex ratio, gestational age, placental weight, birth weight, custom birth weight centile and head circumference was similar between the high and low EPDS scorers.

Predictors of EPDS ≥ 13

Binary logistic regression was undertaken to identify variables that predict an A1 EPDS ≥ 13. Variables entered into multivariate model 1 (Table 2) were those significantly associated with A1 EPDS ≥ 13 in the univariate analysis (Table S3), as well as potential risk factors identified in the literature (alcohol, age, parity and fetal sex). Multicollinearity amongst independent variables was assessed and found within income and education. Consequently, income was excluded from the model. Model 1 was found to be significant with $\chi^2(12) = 122.88$, $P < 0.001$, and Nagelkerke $R^2 = 0.62$, identifying significant predictors of A1 EPDS ≥ 13 to be A1 STAI total, fetal sex and education-left before GCSE. A second binary logistic regression to produce model 2 (Table 2) was then undertaken, with non-significant variables in model 1 at $P \geq 0.1$ removed. Model 2 was significant with $\chi^2(8) = 120.02$, $P < 0.001$, explaining 60.9% of the variation in A1 EDPS scores (Nagelkerke $R^2$), only a slight decrease in fit from model 1. Model 2 identified significant predictors of A1 EPDS ≥ 13 to be A1 STAI total, mental health history, fetal sex and education-left before
GCSE. A one point increase in STAI total and a fetal sex of female compared to male increased the odds of A1 EPDS ≥ 13 by a factor of 1.34 and 2.86, respectively. Additionally, an education that ended before GCSE compared to postgraduate education, and a mental health history compared to no history increased the odds of having an A1 EPDS > 13 by a factor of 7.04 and 3.15, respectively.

**Prevalence and progression of postpartum depressive symptoms**

Mean completion of questionnaire P1 was 4.2 days post partum (range 1-33, SD 3.8), P2 was 69.1 days (range 40-112, SD 13.8) and Y1 was 405.8 days (range 353-561, SD 45.3) (Figure S1). There was no difference in P1 EPDS score (6.0 v. 6.0; \(P = 0.981\)) between participants completing questionnaires in hospital and or from home. Prevalence of EPDS ≥ 13 at P1, P2 and Y1 was 8.4%, 8.6% and 12.1%, respectively (Table 1). Some studies report that women who give birth to boys are more likely to suffer from postpartum depression and anxiety (28, 29). In the GiW cohort, postpartum EPDS and STAI scores were similar between mothers delivering boys and those delivering girls. However, salivary cortisol showed a relationship to gender with mothers delivering boys having significantly higher levels the day before their ELCS (\(P = 0.004\); Table S6).

A total of 108 participants (35%) completed questionnaires at A1, P1 and/or P2 and Y1, allowing the direct comparison of the progression of depressive symptoms (Figure 1A). A Freidman test showed a significant difference in EPDS scores antenatally and postnatally (\(\chi^2(3) = 9.161, P = 0.027\)). Post hoc analysis using Wilcoxon signed-rank test with Bonferroni correction showed maternal EPDS scores to be significantly higher in late pregnancy compared with postnatal week 1 (7 v. 6; \(Z = -2.791, p = 0.005\)) and 10 weeks after delivery (7 v. 5; \(Z = -3.546, P < 0.001\)), similar to previous studies (Table 1). Postnatal year one scores were significantly higher than 10 weeks after delivery (5 v. 6; \(Z = -2.522, P = 0.012\); Figure 1).

All participants in this study were recruited from a cohort booked for an ELCS. In an independent samples Kruskal-Wallis test, there was no significant difference in late antenatal EPDS scores between participants with varying indications for ELCS (\(P = 0.914\), Figure 1B). Similarly, there was no significant difference in postnatal week 1 (\(P = 0.947\)), postnatal week 10 (\(P = 0.424\)), or postnatal year one (\(P = 0.597\)) EPDS scores.
Prevalence of anxiety symptoms

Trait anxiety was assessed using a subscale from the STAI test (form Y-2). Scores ≥ 40 indicate clinically significant symptoms of anxiety (41) while > 44 indicates major anxiety (42). There was no difference in STAI scores (30.0 v 32.0; \( P = 0.573 \)) between participants completing questionnaires in hospital or at home. Prevalence of STAI ≥ 40 at A1, P1, P2 and Y1 was 27.3%, 21.9%, 24.8% and 34.2%, respectively (Table 1). The prevalence of major anxiety symptoms (STAI > 44) at A1, P1, P2 and Y1 was 12.0%, 14.8%, 17.0% and 17.9%, respectively.

Characteristics of women scoring < 40 with those scoring ≥ 40 on the STAI scale

In contrast to EPDS depression scores, a univariate analysis did not reveal any association between a STAI score ≥ 40 and education, family income, BMI or smoking. There was no association between salivary cortisol provided the morning before the ELCS and STAI score at A1 (\( P= 0.5; \) Table S4). Only mental health history (NHS maternity records; \( P < 0.001 \)), type of mental health history (\( P = 0.009 \)) and a higher A1 EPDS score (\( P < 0.001 \)) were significantly associated.

Progression of anxiety symptoms

Anxiety scores significantly differed between time points (\( \chi^2(3) = 10.047, P = 0.018; \) Figure 1C). Post hoc analysis using Wilcoxon signed-rank test with Bonferroni correction revealed that this was not a consequence of decreased maternal anxiety scores after delivery as there was no difference between the antenatal score and postnatal scores either in week 1 (\( P1; Z = -1.678, P = 0.093 \)) or in week 10 (\( P2; Z = -0.907, P = 0.364 \)). This finding was in contrast to majority of studies that report a decline in anxiety symptoms after delivery (Table 1). Furthermore, postnatal year one scores were significantly higher compared with postnatal week 1 (34 v. 32; \( Z = -2.810, P = 0.005 \)) and postnatal week 10 scores (34 v. 34; \( Z = -2.966, P = 0.003 \)) indicating increasing anxiety symptoms. Reported anxiety symptoms did not differ by indications for ELCS either before delivery (independent samples Kruskal-Wallis test; \( P = 0.518 \)) or after delivery at P1 (\( P = 0.975 \)), P2 (\( P = 0.634 \)) or Y1 (\( P = 0.611 \)) (Figure 1D) suggesting that prolonged anxiety was not a consequence of a specific indicator.
To examine the possibility that anxious women were more likely to return questionnaires, participants’ characteristics of responders and non-responders were compared (Supplemental Table S5). Non-responders were more likely to report a lower educational attainment (P = 0.001), lower household incomes (P < 0.001) and had a lower WIMD score (P < 0.001), were younger (P < 0.001) and more likely to smoke (P = 0.002) than responders but there were no differences in antenatal scores for depression, anxiety or mental health history.

Taken together, these data demonstrate that women who undergo an ELCS delivery experience prolonged anxiety lasting more than one year.

**Discussion**

Our study findings on women in Wales delivering by ELCS mirrored the high prevalence of both depressive and anxiety symptoms in late pregnancy reported for other populations (Table 1). While depressive symptoms decreased after delivery, that symptoms of anxiety reported prenatally did not resolve with the safe delivery of a child. This raises the possibility that the physiology of a laboured pregnancy is important in ameliorating pregnancy-related anxiety, with implications for maternal welfare and the mother’s growing relationship with her baby.

**Maternal depression decreases after delivery**

14.3% of our mothers reported significant symptom of depression prior to delivery and this number decreased to 8.4-8.6% after delivery, similar to other studies using the same EPDS questionnaire cut-offs. As with other studies, we found higher reported antenatal depression symptoms in pregnant women with lower family incomes, lower education qualifications and higher BMIs at their first antenatal booking (2). In the final model of the binary logistic regression in which non-significant predictors were removed (Table 2), low educational attainment, fetal sex, mental health history and A1 STAI score remained significant predictors of EPDS score. Female sex increased the odds of a higher EPDS score at A1 and mothers delivering girls had significantly lower salivary
cortisol levels on the morning before their ELCS. Although we found no association between salivary cortisol and STAI score, more anxious mothers are already known to start the day with lower cortisol values than those with lower anxiety (43). To our knowledge this is the first report of an association between fetal sex and prenatal depression symptoms in a Western population.

**Maternal anxiety remains elevated after delivery**

One in four GiW mothers reported significant symptoms of anxiety before their ELCS. In contrast to other studies, mothers with STAI ≥ 40 prenatally remained highly anxious throughout the 12 months of the study and the overall prevalence of women reporting anxiety symptoms did not significantly reduce after delivery with one in three women reporting significant symptoms one year after a safe delivery. This was not explained by anxious mothers being more likely to return questionnaires as there were no differences in antenatal STAI scores between responders and non-responders. A study in Norway reported higher maternal distress before an ELCS compared to other modes of delivery and, while symptoms reduced somewhat 6 months after delivery, they were still higher than for other modes (44) suggesting a link between this mode of delivery and anxiety. The majority of women in our study were undergoing an ELCS as a consequence of a prior caesarean delivery or a previous traumatic delivery. However, we did not observe a correlation between anxiety scores and indications for surgical delivery that might be anticipated if women’s anxiety stemmed from a previous experience of trauma. STAI scores were similar across all indicators ($P = 0.423$) both before delivery and at all subsequent timepoints. A key difference between ELCS and other modes of delivery is labour. Labour is initiated by a complex series of physiological and hormonal changes which women undertaking an ELCS do not experience. Dramatic changes occur in the brain resulting in physiological and behavioural adaptations that enable the prospective mother to cope with her new situation. A key hormone facilitating parturition is oxytocin which has been shown in other mammals to play a critical role in the reduction of fear and anxiety postpartum (21). One possibility is that women remain anxious after ELCS because they do not undergo normal exposure to oxytocin, which could potentially be treated. Recognising and treating anxiety is important because untreated anxiety may impair maternal attachment and harm infant neurodevelopment.
**Study limitations**

The prevalence of depression, risk factors and progression of symptoms from antenatal to postpartum time points in our GiW study compares well with previous studies on Western populations using the same EPDS questionnaire with similar time points and cut-offs (Table 1). However, previous studies report that anxiety symptoms resolve after delivery whereas they remained elevated in the GiW women.

We had a higher than expected attrition rate after delivery. Our original study design was based on women remaining in hospital for 3-4 days after their ELCS allowing our research midwives to contact them directly but a change in hospital procedure meant many of our mothers went home only one day after delivery and had to return questionnaires by post which may explain the lower response. Although there were demographic differences between responders and non-responders there were no differences in antenatal scores for depression, anxiety or mental health history which reassures us that maternal mood was not a factor in the failure to return questionnaires.

A major limitation of this study is that we cannot say confidently that prolonged anxiety is a consequence of delivering by ELCS rather than a laboured birth because we did not recruit a cohort of women delivering by other modes to control for our specific population in Wales. There are a number of alternative explanations for our observation. Given the association between previous history of mood disorder and anxiety, the women delivering by ELCS may be more likely to have an ongoing anxiety disorder, although we would anticipate some evidence for this from the indications for surgical delivery. Welsh mothers may be more anxious than other populations or anxiety may be increasing in the general population. As in our study, women who have planned caesareans are more likely to be older than women delivering by other methods (45) and older mothers are known to have significantly higher rates of depression than younger mothers (46, 47) which could also contribute to increased anxiety. A larger population study comparing different modes of delivery within the same population will provide important context for our observation. Nonetheless, it is a major concern that one in three women report significant symptoms of anxiety over a 12 month period when they are caring for their infants.
A further weakness of our study is the lack of population diversity. 83.7% of population in the Cardiff local authority area (Stats for Wales 2017) and 84.7% of residents in Cardiff (2011 census data) were recorded as Caucasian. 91% of our eligible participant were Caucasian which may be explained because we only recruited English-speaking participants. It is now critically important to ask whether other ethnicities experience prolonged anxiety after ELCS.

A third weakness of the study was the use of questionnaires which are inherently subjective. To counteract misreporting, we compared questionnaire responses with data recorded within NHS maternity records. More mothers reported smoking and drinking in the questionnaires whereas fewer accurately reported their mood history and antidepressant drug history. We did not consult GP records and it is possible that more information may be missed from maternity records due to participants being reluctant to disclose due to concerns around stigmatisation or midwives not being appropriately trained to ensure they ask the questions correctly, factors that must be considered for all studies of this type.

In summary, a major concern that we identified in this study was the high prevalence of reported anxiety symptoms in women undergoing ELCS that do not resolve after delivery. One in four women before delivery and one in three women one year post partum reported concerning symptoms indicating a failure of anxiety symptoms to resolve despite the safe delivery of a child. This is in contrast to previous reports on natural deliveries and emergency caesareans where the prevalence of reported anxiety symptoms reduce after birth (48). Future work should address how we support these high risk women post partum to attenuate their symptoms improving longer term outcomes for them and their children.

Abbreviations

GiW: Grown in Wales; ELCS: elective caesarean section; EPDS: Edinburgh Postnatal Depression Scale; STAI: State-Trait Anxiety Inventory; BMI: body mass index; WIMD: Welsh Index of Multiple Deprivation; SSRI: Selective serotonin reuptake inhibitor.

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Author Contributions
RMJ and ABJ designed the study. ABJ, NS and AR collected data. ABJ and KS recorded and analysed data supported by LS and I G-M. SMG analysed data using regression models. WIMD score and statistical analysis was supported by WW. KS generated figures and tables, RMJ wrote the manuscript and all authors contributed to the final manuscript. All authors read and approved the final manuscript as submitted.

Conflict of Interest Statement
The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethics approval and consent to participate
Informed consent was obtained from participants following a verbal explanation of the study and provision of an information leaflet to read. Those who expressed an interest in joining the study completed the consent form. Participants were free to withdraw from the study at any time.
Availability of data and material

The data that support the findings of this study are available from The Grown in Wales Study but restrictions apply to the availability of these data, which were collected under ethical restrictions and are not publicly available. Anonymised data are, however, available upon reasonable request from the Grown in Wales Study Chief Investigator, Professor Rosalind John.

Figure 1: Progression of symptoms and indications for ELCS

A) Progression of reported depression symptoms in participants who delivered by ELCS and completed questionnaires at A1, P1 and/or P2 and Y1 (n = 108). EPDS scores at postnatal week one and week 10 were significantly lower compared to late pregnancy EPDS scores for all participants. EPDS scores at postnatal year one was significantly higher than in week 10.

B) Reported depression symptoms in pregnancy according to indication for elective caesarean section for 308 women who delivered by ELCS. Bar chart showing participants indication for elective caesarean section relative to antenatal depression scores as measured by the EPDS. ‘Previous caesarean” covered elective and emergency procedures. Reason for ‘maternal choice’ was not recorded. ‘Other’ included prolapse, macrocephaly, severe endometriosis, failure to progress, GDM, maternal disorder (unspecified), high BMI, bicorunate uterus, IVF/previous recurrent miscarriage, fetal growth restriction, previous neonatal death and large-for-gestational age.

Depression scores were not significantly different for participants’ indication for section.

C) Progression of reported anxiety symptoms in participants who delivered by ELCS and completed questionnaires at A1, P1 and/or P2 and Y1 (n = 108). For all participants, STAI scores did not significantly increase or decrease between antenatal A1 score and postnatal time points P1 or P2. STAI scores at postnatal year one was significantly higher than in week 1 and week 10.

D) Reported anxiety symptoms in pregnancy according to indication for elective caesarean section. Bar chart showing participants indication for elective caesarean section relative to antenatal
anxiety scores as measured by the STAI. Anxiety scores were not significantly different for
participants’ indication for section.

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