Title

The persistent pain experience after Caesarean section and its association with maternal anxiety and socioeconomic background.

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ABSTRACT

Background: Pain, both from the surgical site, and from other sources such as musculoskeletal backache, can persist after Caesarean delivery**.** In this study, of a predominantly socially deprived population we have sought to prospectively examine the association between antenatal maternal anxiety and socioeconomic background and the development of persistent pain after Caesarean section.

Methods: Demographic details and an anxiety questionnaire were completed by 205 women prior to elective Caesarean section. On the first post-operative day pain scores were recorded, and at 4 months the subjects were asked to complete a Brief Pain Inventory and an Edinburgh Postnatal Depression Score.

Results: Of 205 parturients recruited, 186 records were complete at the hospital admission phase, and 98 (52.7%) were complete at the 4 month follow up phase. At recruitment 15.1% reported pain. At 4 months 41.8% (CI 32.1%-51.6%) reported pain, of those, pain was a new finding in 35.7% (CI 26.2%-45.2%). Antenatal anxiety was not predictive of severity of new pain at 4 months (p= 0.439 for state anxiety, p=

0.516 for trait anxiety). However, 4 month pain severity did correlate with social deprivation (p= 0.011), post natal depression (p<0.001), and pain at 24 hours (p= 0.018).

Conclusion: Persistent pain after Caesarean delivery is common. Our findings do not support the use of antenatal anxiety scoring to predict persistent pain in this setting, but suggest that persistent pain is influenced by acute pain, post natal depression and socioeconomic deprivation.

***Keywords*:** Pain: persistent, chronic: Caesarean section: Anxiety: Socioeconomic deprivation: Post natal depression.

Introduction

Pain is complex, multidimensional and subjective. The International Association for the Study of Pain in 1994 described it as "an unpleasant sensory and emotional experience". When this occurs immediately, and for short duration after a defined tissue injury such as following surgery, this is defined as "acute", with the expectation that after a given length of time the tissue heals and the pain resolves. Pain failing to resolve can then be classed as persistent (chronic). The point at which the nomenclature changes is somewhat arbitrary, with both two [1,2] and three months being quoted [3]. Chronic Post-surgical Pain (CPSP) has been studied across the surgical spectrum, with extremely high incidences in some operations such as amputation (50 - 88%) and lower in others such as hip replacement (12%). Projecting these figures across populations suggests up to 100,000 UK and 1.5 million USA cases of CPSP are generated annually [3]. Even if the incidence of pain is low, if an operation is performed frequently, the absolute number of cases of CPSP will be high. So it is with Caesarean section, often quoted as the commonest surgical procedure worldwide, and one whose increasing use has prompted concerns over short and long term population morbidity [4].

The incidence of persistent pain after Caesarean section varies according to definitions and study design. A retrospective Scandinavian study found 12.3% at 10.2 months using "scar pain" as the end point [5], whilst Kainu and colleagues [1] questioning Finnish women at 12 months postnatally found 18% continued to experience "wound

site" pain. A prospective US study found an incidence of 9.8% at 8 weeks [6], which interestingly was similar in the Caesarean and the vaginal delivery populations, and went on to link severe acute post partum pain with a 2.5 fold increased risk of developing persistent pain and a 3 fold increased risk of postpartum (postnatal) depression. This relationship between poorly controlled acute pain and persistent pain is well described across the surgical specialties [7].

Other potential influences are less well elucidated. Whilst there is a recognition that psychosocial factors are important, the evidence is mainly in the acute setting, for example anxiety influencing acute postoperative pain [8]. Authors have recognised the difficulty of separating the anxiety experienced pre-operatively from a patient's normal psychological status [9].

The primary outcome of this present study was to define the incidence of new persistent pain after elective Caesarean section in a predominantly socially deprived urban Scottish population. Importantly we defined new persistent pain, as pain from any source present from the time of hospital discharge. This design allows for the capture of any pain source, for example musculoskeletal that may cause interference with a patient's daily activities and is a broader definition than those used in the above studies. The main secondary outcome was correlating antenatal anxiety with persistent pain (as defined above). Additional variables studied were: acute pain, socioeconomic status, and post natal depression.

Methods

The design was a prospective longitudinal observational cohort study. Hospital Ethics Committee approval was obtained, the study was pre-registered on a trials database (ACTRN12610000926033), and informed written consent was obtained from each participant. Parturients scheduled for elective Caesarean section were given a study information leaflet the week prior to their scheduled date, and approached on admission to hospital and invited to participate by a researcher independent of the usual anaesthetic team. The only exclusion criteria were: parity>2; being unable to understand written English; and being unable to give legally valid consent.

Data collection was in three phases: on admission to the hospital on the morning before surgery with a researcher; 24 hrs after surgery with a researcher; and at 4 months after surgery by self completed postal questionnaire.

In the first phase, performed in a quiet, spacious pre-operative waiting area between 0830hrs and 0900hrs in the presence of the patient's birth partner, recruited subjects were asked to complete a Spielberger State-Trait Anxiety Inventory (SAIS) [10]. This tool seeks to separately define the degree of anxiety at the time of completing the score (state) and how anxious the subject is normally (trait). Each section has 20 items that the subject scores on a 4 point Likert scale giving a score in a range 20 to 80. The higher the score, the higher the anxiety, with a cut off point of 39 to 40 being suggested as indicating clinically significant symptoms. Also at this time they were asked whether they had any pre-existing pain (Yes/No) or were currently using analgesics (Yes/No). Also baseline demographic data were collected: postal code (which subsequently was converted to an area based deprivation score using SIMD 2012), age, parity, duration of surgery and grade of operating surgeon.

The SIMD 2012 (Scottish Index of Multiple Deprivation) [11] ranks the post code areas of Scotland by deprivation status from highest deprivation to lowest, i.e., the lower the rank number, the more deprived the area is. As this is an area deprivation score, it does not account for situations where for example a wealthier person is living in a high deprivation area, however it is commonly used and recognised as a useful tool for demographic study. The SIMD is a composite score of data from domains of income, employment, health, education, housing, access and crime.

At 24hrs post surgery the participants were visited by a researcher and asked to mark a 100mm visual analogue score (VAS) to record acute post operative pain levels.

In the last phase of the study, a postal questionnaire was sent out with a prepaid addressed reply envelope to the participant's registered home address at 4 months post delivery. This comprised of a Brief Pain Inventory (BPI) [12] and an Edinburgh Post Natal Depression Score (EPND) [13]. The BPI scoring system measures the presence of pain by a number of questions ranked from 0 to 10 for severity, and separately for interference with daily life. Each subject's score was calculated as an average of the score for each question, giving a possible range of 0 to 10. Presence of pain at four months was defined as a score greater than zero on the severity scoring questionnaire. The BPI also includes a pictogram of a human body for the participant to indicate where the main site of their pain is. The EPND score is widely used in research and in

clinical practice. It consists of 10 questions, each with 4 responses, which for the purposes of this study were converted into a 0 to 3 scale, giving a potential range of scores from 0 to 30.

The patients were asked to complete and return the questionnaire. In the event of no reply after 4 weeks, a duplicate questionnaire was sent out. No further attempts at contact were made if there was no response after these 2 mailings.

If subjects scored highly on either the EPND or BPI scores, as per the study protocol, the patient's General Practitioner was informed to ensure appropriate ongoing care.

A standardised anaesthetic technique was used. This incorporated spinal anaesthesia with hyperbaric 0.5% bupivacaine at a base dose of 2.5ml, which could be varied at the discretion of the attending anaesthetist between 2.25ml and 2.75ml. All participants received 0.3mg of intrathecal diamorphine. Surgery was commenced after a sensory block to at least the T4 dermatome bilaterally to cold, associated with a complete motor block at the hips was demonstrated. Fluid and vasopressor use was at the discretion of the attending anaesthetist, as was the management of inadequate blockade, however as this was entirely elective surgery, the expectation for supplementation of anaesthesia or conversion to general anaesthesia was low. A standard surgical approach was used with transverse skin and uterine incisions, and a standardised layered closure technique.

Data Analysis

Sample size was calculated by assuming the predominant source of pain would be surgical (wound) and the incidence in this study would lie within the range of the two previously mentioned Scandinavian studies [1, 5] of 12% to 18%. Taking the midpoint of 15%, with the corresponding 95% confidence interval of 8% to 22%, using a normal approximation to the binomial distribution, the required sample size was 100. The study design and the population characteristics were expected to produce a high drop out rate at 4 months estimated to be 50%, thus the target recruitment figure was set at 200.

The main outcome measure was the presence of new pain at 4 months. This was defined as a score greater than zero on the BPI severity questionnaire of pain (from any site) present from hospital discharge in a participant who had reported no pre-

existing pain on the antenatal questionnaire. Importantly the questionnaire was not restricted to wound or abdominal pain and was able to capture pain from all sites, e.g. musculoskeletal.

For secondary endpoints, continuous variables were compared between those that did and did not have pain at 4 months by t-tests or Mann-Whitney tests depending on the distribution. The Chi-squared test or Fisher's exact test, as appropriate were used to test for any differences in the distribution of categorical variables, in particular socioeconomic status, between those that do and do not have pain at 4 months. Linear regression was used to model predictors of pain (BPI) severity at 4 month and logistic regression for the presence of pain as the outcome. Baseline anxiety scores, socioeconomic status and pre-operative pain were adjusted for in each model.

To allow for sub group analysis of wound pain only, the pictogram (body maps) from the BPI questionnaire were assessed by 2 researchers independently. The subject was classed as likely to be experiencing wound pain if both researchers felt the markings on the pictogram were closely related to the surgical site. The potential limitations of this are commented upon in the discussion section.

Analyses were performed using SAS software (Enterprise Guide 5.1). Statistical significance was accepted when $p<0.05$.

Results

205 subjects were recruited in total. 19 of these were not able to be analysed for reasons including non return or inadequate completion of the form, patient's delivery status changing to emergency (for example, if beginning to labour), or it subsequently becoming clear that the subject did not meet the inclusion criteria- most commonly struggling with written English. Of the remaining 186 questionnaires, 98 were returned at 4 months giving a response rate of 52.7%. General anaesthesia was employed once to convert from a spinal anaesthetic that was beginning to fail due to unexpectedly prolonged surgery. This patient did not return the 4 month questionnaire.

Baseline data:

Data are mean (SD), n (%), n/N (%), or median (IQR), unless otherwise shown.

insert table 1 here

insert table 2 here

insert table 3 here

The study group was drawn from an area of high social deprivation, and includes a migrant and transient population which is recognised as a factor influencing reduced returns at four months. With 6505 postcode areas, and 1 being the most deprived, the median of 2222 in our study indicates a high level of deprivation.

28(15.1%) recorded "yes" when asked pre-operatively if they were experiencing pain, although only 16 (8.6%) were taking analgesics. Indicating perhaps a reluctance to medicate during pregnancy or that pain was mild in nature.

The BPI four month pain results show the mean (SD) severity score was 1.38 (1.99), and for the interference score was 1.39 (2.32), suggesting the population pain burden is low. The primary outcome measure of incidence of new pain at four months was 35.7% (with a 95% CI of 26.2%, 45.2%). Including the group that reported preoperative pain the incidence rises to 41.8%.

The main secondary outcome was comparing those with and without pain at 4 months against their pre-operative anxiety scoring. Taking a division between non-anxious and anxious at the 39 to 40 mark shows that our cohort (scoring a median of 40 on the state questionnaire) can be described as anxious.

insert figure 1 here

insert figure 2 here

Figure 1 and figure 2 show that there was no difference between those in pain at four months and those with no pain at four months for either state or trait anxiety scores. For state anxiety the mean (SD) for those with pain was 39.2 (11.36) compared to 39.4 (9.59) for those without pain giving a p-value of 0.9292. Trait anxiety results were 33.5 (8.20) and 34.3 (8.19), p =0.6540 for "pain" and "no pain" groups respectively.

insert table 4 here

Linear regression (table 4) shows that the only predictor variables for pain at four months were: being more socially deprived (comparing highest with lowest on SIMD score); having a higher VAS score at 24hrs post operatively, and being more at risk of post natal depression on the EPND score (completed at four months). Logistic regressions (table 5) were performed with the dependent factor of presence/absence of pain at four months and independent factors of anxiety scores, socioeconomic status and preoperative pain. Sensitivity analyses were run on this model using the two extremes of (1) imputing the missing data as "without pain at 4 months" and (2) imputing the missing data as "with pain at 4 months". This shows that our main secondary outcome of anxiety remains non-significant in all scenarios suggesting the results are not influenced by the response rate of the 4 month questionnaire.

Insert table 5 here

Of the 41 subjects reporting pain at 4 months, a pictogram assessment was possible in 40. The researchers interpreted the site of pain as wound (surgical) in 12 (30%). Thus the estimated incidence of wound pain in the whole cohort is 12 of 98 or 12.2%. Sub-analysing these 40 parturients, we compared the wound pain subjects with the non-wound pain subjects for anxiety and found: mean (SD) state anxiety scores of 41 (13.6) and 38.5 (10.44), for wound and non-wound respectively, p=0.5714. Trait anxiety was similarly non-significant at 32.3 (9.35) and 33.9 (7.85), p=0.6103.

Discussion

Our main finding is that the incidence of persistent pain, four months after Caesarean section is high. Even after excluding those subjects who were experiencing pain pre-operatively, over a third of our cohort reported pain. At a population level, both the severity of, and the degree to which pain interfered with normal activities were low, though this obviously masks significant problems for some individuals. Our definition of pain is a broad one, so this study captures surgical site, abdominal, and other ongoing sources such as musculoskeletal pain. The BPI questionnaire included a diagram for the subjects to record the site of pain, however there is a degree of subjectivity in the interpretation of where exactly the patient intended their mark to represent, and these results should be viewed cautiously. Within the limitations of this method, our cohort has an incidence of persistent wound pain after Caesarean of 12.2%, suggesting approximately twice as many women experience non-wound pain as experience wound pain.

The two most comparable studies investigating surgical pain [1,5], whilst using different timescales, found incidences of pain of 12% and 18%, which is consistent with our wound pain estimate. Our study differs by including all sites of pain persisting from hospital discharge, which we believe represents an important outcome for patients.

The main predefined secondary end point of the study was to compare anxiety levels for those with and without pain at four months, and this was found to be non-significant both for state and trait anxiety. This finding was replicated when the subgroup of wound pain subjects were analysed separately. The expectation of this scoring system is that trait (or the propensity for anxiety) is a relative constant whereas state anxiety will identify the patient's current anxiety level. This has been demonstrated in relation to surgical operations by Auerbach [14] where only the state component fell significantly between pre and post- operative periods (from 39.29 to 32.46). The findings confirm that high levels of anxiety are common prior to Caesarean section, as they are for other surgical operations, but anxiety scoring, at least with this measure is not a useful predictor of persistent pain. In this respect, the null hypothesis: that there is no difference in antenatal anxiety between those that have and those that have not new pain at 4 months after Caesarean Section is confirmed. However, two of the pre-operative variables, i.e. socioeconomic status and VAS score at 24hrs did show an influence on persistent pain, which adds to the findings of others [7,8,9] and suggests potential avenues for predicting or indeed

influencing, problems. As an example, Breivik [15] describes how high quality acute pain management reduced persistent post surgical pain in Norwegian surgical patients. The influence of deprivation is likely to be more complex, but is consistent with findings from the general population that there are significant associations between pain and socioeconomic disadvantage[16] . It is possible that deprived women have less social support and other barriers that make it more difficult for them to access medical or physiotherapy services. Our findings suggest that improvements in persistent pain may come from service providers understanding and overcoming some of the socioeconomic problems experienced by parturients.

Post natal depression, measured at four months, also correlated with persistent pain. The relationship here is likely to be complex and bi-directional. So persistent pain might lead to depression, depression might predispose to persistent pain, or the two conditions might share common causality. A large Australian study of a mainly affluent population found a similar trait anxiety score of 35.1 (compared to 33 in our study) [17]. Here the end point was postnatal depression, and antenatal anxiety using Spielberger was a predictor of this only when the statistics were unadjusted for cofounders. A UK study found that antenatal anxiety measured by the Crown-Crisp Experiential Index independently predicted postnatal depression [18]. As persistent pain and postnatal depression seem closely linked, it is possible that tools to predict post natal depression, may also capture those at risk of persistent pain. In this respect, Milgrom and colleagues [19] found that antenatal depression, a prior history of postnatal depression, and a low level of partner support were the strongest independent predictors of scoring highly on the EPND questionnaire.

The main strength of this study was its prospective nature, in contrast to the retrospective nature of some of the initial work in this field. This allowed us to accurately collate in-hospital data contemporaneously and test anxiety scoring and acute pain scoring as predictors of pain. Our main limitation is the relatively low response rate at four months, though this was predicted and sensitivity analyses give our conclusions validity. Future study design might benefit from using a researcher to visit and interview the subjects at home rather than relying on a postal questionnaire. Our study was designed to look at depression and pain concurrently at 4 months. For many women, post natal depression may occur soon after delivery, and resolve by 4

months. We cannot therefore exclude the possibility that early and resolved post natal depression may also influence persistent pain.

Importantly the observational nature of this study means that whilst it is clearly valid to link those thought to have wound pain (12.2%) with Caesarean delivery, causation between Caesarean section and all sources of pain at 4 months is not assumed. The non- wound pain subjects (29.6%) are presumed to be predominantly experiencing musculoskeletal pain. Whilst backache is well recognised post-partum regardless of delivery mode, the available literature would suggest that backache alone does not account for the high persistent pain incidence in our cohort. For example, a study investigating post partum backache and epidural use [20] found that pain from this source rapidly fell to 14% (in the epidural group) by 6 weeks . An area of future research might be to compare the persistent pain experience after Caesarean section with that after vaginal delivery using the same methodology.

In summary, persistent pain is more common after Caesarean section than previously recognised with contributions both from wound (surgical site) and other sources such as musculoskeletal. For most the pain is mild, with minimal interference with daily tasks. It is not associated with pre-operative anxiety, but is influenced by acute pain, socioeconomic status and post natal depression.

Acknowledgements

We are grateful to the NIAA for the awarding of a “small project grant” to help with postal costs.

We are grateful to Dr E. McGrady from the Princess Royal Maternity, Glasgow, UK, for the donation of research fund resources to support the statistical analyses.

Neither of the above sources of funding had any role in the design or conduct of the trial.

We are grateful for Dr Alex McConnachie, of the Robertson Centre, Glasgow for additional statistical support.

The study was preregistered with the ANZCTR trial registry ACTRN12610000926033, accessible on line at http://www.anzctr.org.au/.

The study was approved by the West of Scotland Research Ethics Committee 4 **,** Research & Development Management Office NHS Greater Glasgow & Clyde**,**West Glasgow Ambulatory Care Hospital **,**Dalnair Street, Glasgow **,**G3 8SW

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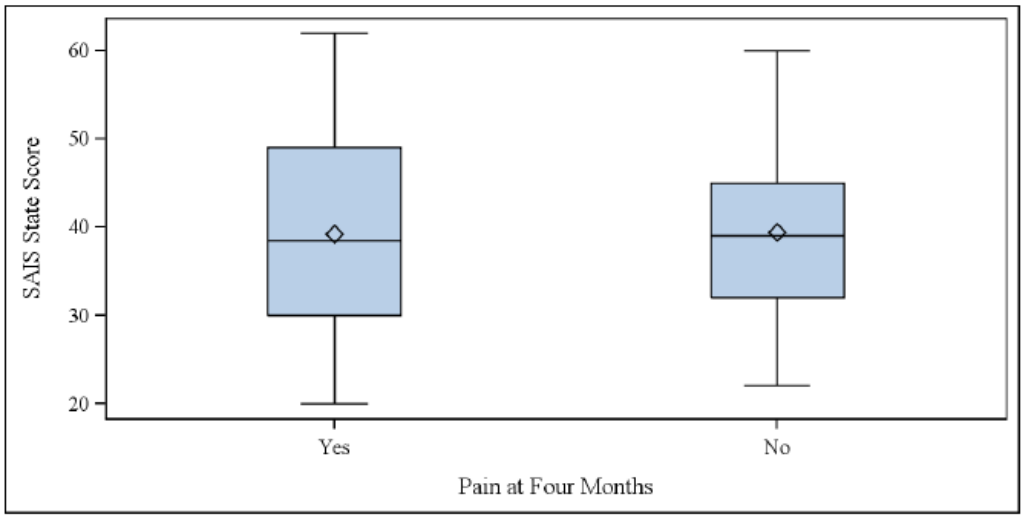
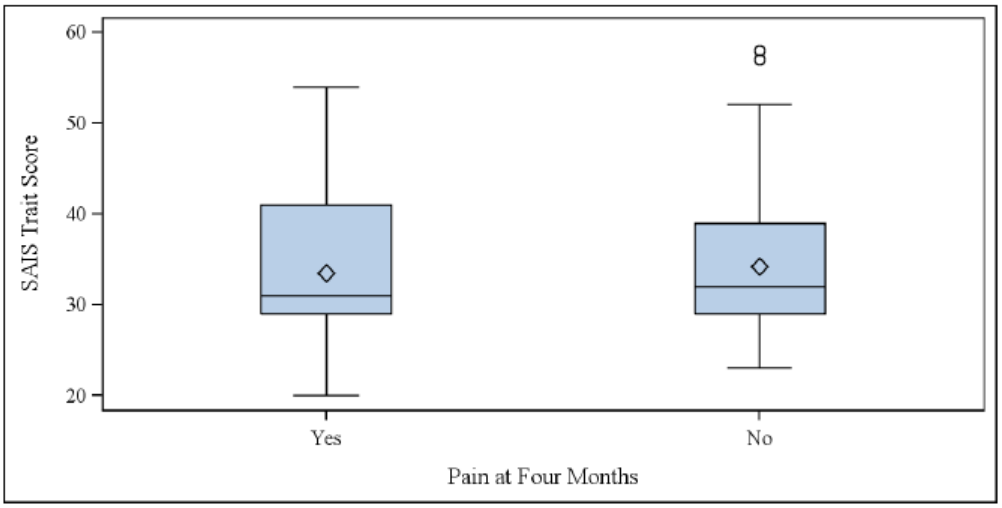

SAIS State Score
60
50
40
30
20
Yes
No
Pain at Four Months


60
50
40
30
20
SAIS Trait Score
8
Yes
No
Pain at Four Months

Legend for figures

Figure 1

TITLE: Presence of pain and SAIS state anxiety score.

LEGEND: Spielberger Anxiety Inventory State score (SAIS State) for those with and without pain at 4 months

Figure 2

TITLE: Presence of pain and SAIS Trait anxiety score.

LEGEND: Spielberger Anxiety Inventory Trait score (SAIS Trait) for those with and without pain at 4 months