Development, behaviour and temperament: a prospective study of infants conceived through in-vitro fertilization

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The development, behaviour and temperament of 65 singleton infants conceived through in-vitro fertilization (IVF) and 63 matched controls were compared at 1 year postpartum. Primiparous women were recruited during pregnancy and their infants’ development was assessed at 1 year. In addition, test-taking behaviour was evaluated by an examiner using the Bayley behaviour rating scale and mothers completed a behaviour problem checklist and temperament scale. Mental, motor, speech and social development were appropriate for age, with no significant group differences. While receptive language development was in the normal range, IVF infants scored lower than control infants. Across both groups, mothers reported low levels of behaviour difficulty and mean temperament ratings were in the general population range. There were no group differences in observed test-taking behaviour. However, IVF mothers rated their children at a higher level of behaviour difficulty and more reactive than the ratings given by control mothers. Overall, singleton children conceived through IVF demonstrate appropriate general development at 1 year of age. The higher reported behaviour difficulty experienced by IVF mothers may reflect their concerns about the well-being and adjustment of their child during the first year.

Key words: behaviour/children/development/IVF/temperament

Introduction

Assisted reproductive technologies, such as in-vitro fertilization (IVF), have been available for almost two decades and their use has increased rapidly over this period. In 1994, 1% of all births in Australia were the result of assisted conception (Lancaster et al., 1997). While available research indicates that the outcomes of these technologies are generally positive (Kovacs, 1996), recent published research and policy guidelines emphasize the need for further data on the growth and development of the children (Saunders et al., 1996), on the consequences for parents (Golombok et al., 1996), and on the psychosocial effects for both participants and offspring (National Health and Medical Research Council of Australia, 1996).

It is now well established that children conceived through IVF are at increased biological risk because of an increased likelihood of premature delivery and multiple birth (Rufat et al., 1994), of intrauterine growth restriction (Doyle et al., 1992; Wang et al., 1994), and a need for mechanical ventilation in the neonatal period (Leslie et al., 1992). Furthermore, these biological risks may combine with psychosocial risk factors, in particular impaired parenting ability secondary to unresolved issues about infertility and the stress of the IVF process itself, to contribute to poorer developmental outcomes and increased behaviour problems in the children (Mushin et al., 1986; Spensley et al., 1986; Cederblad et al., 1996). Studies to date of developmental and behavioural outcome for IVF children have produced mixed results but have mostly suggested that such outcomes are no worse for IVF children than those conceived naturally when allowance is made for differences in biological risk factors (Mushin et al., 1986; Morin et al., 1989; Halasz et al., 1993; Golombok et al., 1995, 1996; Cederblad et al., 1996). However, methodological problems, especially the lack of appropriate control groups, have limited an interpretation of the reported studies.

The aim of the present study was to evaluate parental adjustment and the parent–child relationship, as well as the child’s cognitive, behavioural, emotional and physical development up to 1 year after birth for families conceiving through IVF, compared with a naturally conceived control group whose mothers were of identical parity and similar age. The results presented in this report relate to the development, behaviour and temperament of singleton IVF children at 1 year.

Materials and methods

Sample

The IVF sample was recruited over a 3 year period (September, 1992–September, 1995) from the Royal North Shore Hospital IVF Clinic. Mothers and fathers, who were both genetically related to the child, were recruited during pregnancy for the longitudinal project which involved contact during pregnancy and at 4 and 12 months postpartum. All mothers met the following inclusion criteria: primiparous, singleton pregnancy, 28 years or older, living with the father of the child, and adequate English language skills to complete self-report measures and interviews.

Eligible couples were sent information about the study at 28 weeks of pregnancy and then telephoned to discuss their participation. The acceptance rate for IVF participants was 80% (n = 70). A control group from the same hospital that met the same inclusion criteria was also recruited, and their acceptance rate was 70% (n = 63). While women with twin pregnancies were also recruited for the...
longitudinal research, data on these mothers and children are not included in this report because of the special parenting and developmental issues related to multiple birth.

At 1 year postpartum the participation rate was 93% \((n = 65)\) for the IVF group and 98\% \((n = 62)\) for the control group. Following contact during pregnancy, three IVF families moved out of the metropolitan area, one withdrew due to concerns over confidentiality and one because of time constraints. One control family withdrew, and of the 62 remaining, two completed the questionnaire measures only, not attending for interview or assessments at 1 year due to time constraints.

### Developmental measures

#### Mental and psychomotor development

The Bayley scales of infant development, 2nd edition (BSID II) was administered to each child (Bayley, 1993). Separate mental (MDI) and psychomotor (PDI) development index scores were derived, each with a mean of 100 and SD of 15.

#### Language development

The Receptive–Expressive Emergent Language Test, 2nd edition (REEL-2) was administered through a semi-structured interview with the mother and direct observation of the child (Bzoch and League, 1991). The REEL-2 is a method for assessing emergent language skills in the first 3 years. It yields receptive (carrying out actions on request, listening to others’ speech) and expressive (range of babble, use of first words) language ages from which quotient scores are calculated.

#### Social development

The Socialization domain from the Vineland Adaptive Behaviour Scales (Sparrow et al., 1984) was administered to provide a measure of social development as indicated through the infant’s developing responsiveness to others and in play (shows interest in other children and adults, joins in simple games, responds if praised). This measure was completed using a semi-structured interview format with each child’s mother.

#### Behavioural measures

##### Test-taking behaviour

After each child was tested with the BSID II mental and psychomotor scales, the Bayley Behaviour Rating Scale (BRS) was completed by the examiner based on observed behaviour during testing. Item raw scores were clustered to yield three factor scores (percentile ranks): motor quality, orientation/engagement, and emotional regulation, and a total score. Percentile ranks were then classified as follows: within normal limits, >25th percentile; questionable, 11th–25th percentile; non-optimal, 1st–10th percentile.

##### Behaviour problems

A downward adaptation of the behaviour checklist (BCL) assessing the child’s current problem behaviours (Richman et al., 1982) was completed by mothers. The checklist included 13 items which covered eating (appetite and food fussiness), sleeping (settling at bedtime, waking at night, sleeping with parent to settle, day sleeping), activity, independence (ability to occupy self in play, clinginess, demands for attention), behavioural control, and mood (manageable, tantrums, happiness). Mothers chose one of three or four response options reflecting the severity of the behaviour problem. Higher scores indicated more problematic behaviour. A summary question was also included which asked if there was any behaviour, on the checklist or otherwise, which was considered to be a problem by the mother and this was answered with a yes/no response.

### Temperament

Mothers also completed a Short Temperament Scale for Toddlers (STST) developed through the Australian Temperament Project (Prior et al., 1989). There are six factor scores reflecting temperament dimensions as follows: approach, cooperation–manageability, persist-ence, rhythmicity, distractibility and reactivity. Three factors (approach, cooperation and reactivity) are averaged to produce an overall easy/difficult scale score (EDS). Prior et al. (1989) have reported significant relationships for toddlers and preschool aged children between the EDS and a range of concurrent behaviour problems (sleep, temper tantrums, crying, mood swings), as well as future behavioural adjustment.

### Statistics

The data were analysed using the statistical package SPSS version 6.1 (Norusis, 1994). Most of the analyses were performed using multivariate analysis of variance (MANOVA) to deal with more than one dependent variable at a time. As is recommended following such analyses, the relative contribution of each dependent variable to the multivariate effect was assessed by investigating the standardized discriminant function coefficients (Haase and Ellis, 1987). Univariate analyses were also examined when following up the results of multivariate analyses. Where only one dependent variable was in an analysis, the univariate analysis of variance was used (ANOVA) for continuous variables and logistic regression for dichotomous outcomes.

### Results

Despite efforts to match groups for maternal age, the mothers who conceived through IVF were significantly older than the control mothers at 34.5 years \((SD = 3.0)\) versus 31.9 years \((SD = 2.4)\) \([t(125) = 5.43, P = 0.000]\), as were IVF fathers with a mean age of 37.4 years \((SD = 5.6)\) compared to control fathers at 34.8 years \((SD = 4.8)\) \([t(125) = 2.78, P = 0.006]\). Both groups had a high proportion of mothers who had completed tertiary education; 40 and 52\% for IVF and control groups, respectively. There were no significant group differences based on highest level of maternal education achieved across three categories; 3–6 years of high school, professional diploma/certificate, or university degree. However, there was a trend towards more variability within the IVF group \([\chi^2(2, n = 127) = 5.05, P = 0.080]\). In addition, significantly more children in the control group compared to the IVF group \([95 versus 78%, respectively, \chi^2(1, n = 127) = 7.26, P = 0.007]\) were from families where English was the only language spoken.

The trend towards group differences in maternal education, as well as the differences in maternal age and languages spoken at home, most likely reflect a larger, more demographically varied referral area for the specialist IVF clinic than for the hospital. Since these social factors may impact on child function, maternal age, level of education and use of English as a primary language were entered as covariates in subsequent analyses of developmental and behavioural outcomes.

Child characteristics are shown in Table I. There were no differences between groups based on gender. All infants were seen at a mean age of 13 months, ranging from 10.4 to 15.6 months and corrected for prematurity \((<37 completed weeks of gestation)\). Although there was no significant difference in
Development and behaviour of IVF infants

Table I. Comparisons of in-vitro fertilization (IVF) and control children on perinatal and neonatal characteristics: age, gestation, birthweight and neonatal nursery (NN) admission

<table>
<thead>
<tr>
<th>Child characteristics</th>
<th>IVF group</th>
<th>Control group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 65)</td>
<td>(n = 62)</td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>34 (52)</td>
<td>32 (52)</td>
<td>ns</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>31 (48)</td>
<td>30 (48)</td>
<td>ns</td>
</tr>
<tr>
<td>Age (months)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>39.1</td>
<td>39.8</td>
<td>0.039</td>
</tr>
<tr>
<td>SD</td>
<td>1.9</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>32–42</td>
<td>35–42</td>
<td></td>
</tr>
<tr>
<td>Prematurityb, n (%)</td>
<td>6 (9)</td>
<td>3 (5)</td>
<td>ns</td>
</tr>
<tr>
<td>Birthweight (g)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>3291.7</td>
<td>3489.6</td>
<td>0.036</td>
</tr>
<tr>
<td>SD</td>
<td>598.1</td>
<td>437.7</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>1300–4535</td>
<td>2525–4530</td>
<td></td>
</tr>
<tr>
<td>LBW, n (%)</td>
<td>5 (8)</td>
<td>0</td>
<td>0.026</td>
</tr>
<tr>
<td>NN admission , n (%)</td>
<td>12 (19)</td>
<td>4 (7)</td>
<td>0.041</td>
</tr>
<tr>
<td>NN admission in days</td>
<td>Mean</td>
<td>2.3</td>
<td>0.014</td>
</tr>
<tr>
<td></td>
<td>SD</td>
<td>6.9</td>
<td>0.6</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>0–34</td>
<td>0–3</td>
</tr>
</tbody>
</table>

Tests were used to compare group means on continuous variables and \( \chi^2 \)-tests were carried out to compare group proportions for categorical variables.

\( ^b \)Premature = born \(<37 \) weeks of gestation.

\( ^c \)LBW = low birthweight (\(<2500 \) g).

\( ^d \)NN = admission to a level III or level II neonatal nursery care unit.

\( ^* \)ns = not significant.

The proportion of IVF (9%) versus control infants (5%) born prematurely, IVF infants were born earlier on average at 39.1 weeks, compared with the control group’s gestational mean of 39.8 weeks \([t(125) = –2.09, \ P = 0.039]\). Their mean birthweight was also lighter \([t(125) = –2.12, \ P = 0.036]\), and five IVF babies were low birthweight \(<2500 \) g \(\chi^2 (1, n = 127) = 4.96, \ P = 0.026\), whereas no controls were in this range. It can be seen in Table I that there was more likelihood of admission to a level III or level II neonatal nursery for IVF newborns \(\chi^2 (1, n = 127) = 4.16, \ P = 0.041\) and their mean length of stay was longer \([t(64.88, n = 127) =2.53, \ P = 0.014]\). Seven of the 12 IVF babies admitted to a neonatal nursery were born at term and had shorter stays than the premature infants whose admissions ranged from 14 to 34 days. Of the four control infants admitted to a neonatal nursery, one was premature and all admissions were short, from 1 to 3 days.

Because the groups differed on these perinatal and neonatal measures, these variables had to be taken into account when comparing the groups on developmental and behavioural outcomes. Since the perinatal and neonatal variables were correlated, it was not necessary to use all of them as covariates. In order to select a non-redundant set of covariates, preliminary analyses were carried out with the developmental and behavioural outcomes as dependent variables and the perinatal and neonatal covariates as independent variables (with and without group as an independent variable). Two of these, infant birthweight and days spent in neonatal nursery care, demonstrated a unique, significant relationship with the developmental and behavioural outcomes. None of the other perinatal and neonatal variables added significantly to these covariates. They were, therefore, included as covariates in all subsequent analyses together with the social demographic covariates of maternal age, maternal level of education and use of English as a primary language.

Development
Mean scores on measures of development and results of statistical comparisons are summarized in Table II.

<table>
<thead>
<tr>
<th>Developmental measures</th>
<th>IVF group</th>
<th>Control group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 65)</td>
<td>(n = 62)</td>
<td></td>
</tr>
<tr>
<td>MDI Mean</td>
<td>102.4</td>
<td>103.2</td>
<td>ns</td>
</tr>
<tr>
<td>SD</td>
<td>8.3</td>
<td>7.0</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>82–118</td>
<td>82–118</td>
<td></td>
</tr>
<tr>
<td>PDI Mean</td>
<td>90.4</td>
<td>89.5</td>
<td>ns</td>
</tr>
<tr>
<td>SD</td>
<td>14.8</td>
<td>15.5</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>60–110</td>
<td>56–118</td>
<td></td>
</tr>
<tr>
<td>Receptive language RQ</td>
<td>Mean</td>
<td>94.3</td>
<td>99.0</td>
</tr>
<tr>
<td>SD</td>
<td>8.1</td>
<td>9.1</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>77–108</td>
<td>77–117</td>
<td></td>
</tr>
<tr>
<td>Expressive language EQ</td>
<td>Mean</td>
<td>89.4</td>
<td>91.0</td>
</tr>
<tr>
<td>SD</td>
<td>7.1</td>
<td>8.5</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>77–108</td>
<td>77–117</td>
<td></td>
</tr>
<tr>
<td>Socialization score</td>
<td>Mean</td>
<td>100.8</td>
<td>101.4</td>
</tr>
<tr>
<td>SD</td>
<td>3.0</td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>92–109</td>
<td>94–107</td>
<td></td>
</tr>
</tbody>
</table>

^a Univariate \( F(1,117) = 7.76, \text{ SDF} = 0.88 \).

IVF = in-vitro fertilization; MDI = mental development index; PDI = psychomotor development index; RQ = receptive quotient score; EQ = expressive quotient score; ns = not significant.

Development
Mean scores on measures of development and results of statistical comparisons are summarized in Table II.

Mental and psychomotor development
Multivariate analysis of MDI and PDI results revealed no significant differences between groups in mental and psychomotor development [Wilks’ lambda = 0.99, \( F(2, 116) = 0.29, \ P = 0.747\)]. The mean mental indices of 102 and 103 for the IVF and control infants, respectively, were in the average range compared to the Bayley test mean of 100. Although both groups’ mean PDI (90 for IVF infants and 89 for controls) were in the average range, they were two-thirds of one SD below the test mean. More variability was also apparent in PDI results across the groups, with SD of 15 and 16, compared to 7 and 8 for MDI results. A total of 34% of the IVF children and 45% of controls had a PDI of \(<85\), and 12% of both groups were \(<70\), in contrast to only one infant from each group with an MDI of \(<85\).

Language development
A multivariate effect for group on language scores was found [Wilks’ lambda = 0.93, \( F(2, 116) = 4.05, \ P = 0.020\)], and it accounted for 7% of the variance beyond that accounted for by the covariates. Further inspection of the language results,
in particular the standardized discriminant function coefficients, showed that the multivariate effect of group was mainly due to a difference in receptive language scores (SDF = 0.88, see Table II). This difference favoured the control group with a higher mean receptive quotient score (RQ) of 99 (SD = 9) in comparison to the IVF group mean of 94 (SD = 8). There was no significant difference in expressive language development between IVF and control children, with mean expressive quotient score (EQ) of 89 (SD = 7) and 91 (SD = 9) respectively. There was also little difference between groups in score variability within language areas. Based on studies with the REEL-2, Bzoeh and League (1991) support the view that 90% of children will achieve at plus or minus one age interval from their chronological age. This translates into quotient scores of 83–117 for the age range represented and both the IVF and control groups’ mean receptive and expressive language scores were in this range.

Social development

There was little variability in social development between 1 year old IVF infants and controls \[F(1, 117) = 0.25, \ P = 0.620\]. The mean socialization standard score of 101 (SD = 3) obtained by both groups was right on the average compared to the test mean.

Behaviour

Test-taking behaviour

Since only a small number of children fell into the non-optimal or questionable range on each of the Bayley BRS factors, these categories were combined to examine group differences between normal and non-optimal test-taking behaviour. Logistic regression was carried out controlling for the same covariates used in multivariate analyses of the developmental data. There were no significant differences between groups in behaviour during testing based on examiner observations, for the total rating [Wald $\chi^2(1) = 0.409, P = 0.523$] or for the factor scores of orientation and engagement [Wald $\chi^2(1) = 0.579, P = 0.447$], emotional regulation [Wald $\chi^2(1) = 0.021, P = 0.884$] and motor quality [Wald $\chi^2(1) = 0.031, P = 0.859$]. The non-optimal category represents raw scores from the 1st to 10th percentile based on the test norms, and an expected proportion of children (9% of the IVF group and 8% of controls) were in this range for each factor score and for the total score.

Behaviour problems

Analysis of variance revealed a univariate group effect on the BCL total score \[F(1,119) = 5.51, P = 0.021\]. Examination of group means revealed that IVF mothers rated their 1 year olds at a higher level of behavioural difficulty than control mothers rated their children, and, although significant, this group effect explained only a small amount of the variance (4%) beyond that accounted for by covariates. Mean BCL scores were 6.5 (SD = 2.9) for the IVF group and 5.1 (SD = 2.7) for the controls out of a possible maximum score of 28. A score >10 on the BCL for the pre-school age group is considered problematic. In this study, only five IVF infants and two control infants scored >10, which is consistent with a low level of behavioural difficulty. However, significantly more IVF mothers than control mothers, 35 versus 16% respectively, affirmed that one of their child’s behaviours was a problem for them [Wald $\chi^2(1) = 7.82, P = 0.005$]. According to the odds ratio estimate produced by the logistic regression, they were four times more likely to respond yes (OR = 4.22; CI 95%, 1.47, 6.96).

Temperament

On the STST, both groups had mean temperament factor scores in the average range, when compared to Australian general population norms. There was, however, a multivariate effect for group [Wilks’ lambda = 0.87, $F(6,112) = 2.684, P = 0.018$], which accounted for 13% of the variance in the dependent variables. Inspection of the standardized discriminant function coefficients revealed that this effect was mainly due to the reactivity factor (SDF = –0.93). IVF mothers rated their infants significantly higher than control mothers rated their infants on this temperament factor, which encompasses irritability, moody reactions and activity. A small number of children, six IVF infants and two controls, fell into the difficult temperament range, based on the average of approach, cooperation and reactivity. A logistic regression indicated no group difference in the proportions of children with difficult temperament [Wald $\chi^2(1), = 2.68, P = 0.102$].

Discussion

The findings of this study are both reassuring and positive. They reveal no differences in mental, motor, social and expressive language development or in test-taking behaviour between 1 year old children conceived by IVF in comparison and other firstborn singleton children. Some differences were found in receptive language development and maternal reports of behaviour problems and temperament, although when compared to available population norms, IVF children still achieved within the normal range.

The mental development results obtained are consistent with other studies that have found no decrement in development for older IVF children compared to matched controls (Morin et al., 1989; Brandes et al., 1992; Halasz et al., 1993). It has been noted that the mean motor score is in the lower range of average for both groups in the current study. Some of this is due to the revised norms of the Bayley scales, not used in previous studies, and some is possibly due to cultural factors specific to the age group studied. Ongoing longitudinal research in this country with a similar sample also indicates lower motor scores in infancy, catching up to the test mean by 3 years of age (L.Leader, personal communication). This pattern may be related to the age of walking as there is a cluster of items on the motor scale related to standing and walking independently around the 12 to 13 month level. This observation, however, needs further exploration with a larger more representative Australian sample.

Social development results were obtained through a semi-structured interview with mothers where responses were interpreted and scored by the interviewer. No differences were found between IVF and control group 1 year olds in their developing responsiveness interpersonally and in play.
sociable responding has been reported for older IVF children compared to control groups by van Balen (1996) and Halasz et al. (1993). These previous findings were based on a cluster of items from a maternal completed behaviour questionnaire and an observational test item, respectively, and may not be as robust as those reported here.

The results were mixed in this first study to examine language development, in addition to motor and mental outcomes for children conceived through IVF. There were no differences in emergent expressive language development between IVF 1 year olds and their matched controls, but the IVF infants were less strong in receptive language. However, both the effect and absolute difference were small. There was no impact on Bayley mental scale results, which include several language items at this age, and practical implications for day-to-day function were not indicated. The possible causes, however, remain unclear, and these findings need cautious interpretation and replication in further studies. It may reflect the impact of biological factors on social interaction during the first year, as these children were also rated as temperamentally more difficult. Parenting influences may also be relevant here, although research to date, comparing families who have conceived through IVF and natural conception control families, has indicated no differences on ratings of mother–child interaction (Coplin et al., 1995; Golombok et al., 1996). There was a growing expectation in the research to find more advanced expressive language amongst IVF children, in comparison to their peers. Both Morin et al. (1989) and Halasz et al. (1993) found that IVF children were more interested in producing vocal sounds during testing than control children, although this may be more closely linked to their findings of increased sociability at an older age, than to differences in language competency.

While there were no differences in the proportion of IVF infants and controls with maternal reported behaviour or temperament scores in the ‘clinical’ range, mothers who conceived through IVF did tend to report more behaviour problems and more difficult temperament than control mothers. Behavioural ratings have been described as both a function of the mother and the child but as more objective than a direct reflection of maternal attitudes (Ghodsi et al., 1985). Weaver et al. (1993) suggest that IVF parents may experience an underlying anxiety in their parental roles as reflected through overprotective attitudes. The current study is part of a larger longitudinal project, and results to date lend support to this notion, that IVF mothers experienced more anxiety about their baby’s well-being during pregnancy and they had a lower sense of self-efficacy in care-giving at 4 months postpartum compared to other mothers from a similar background (McMahon et al., 1996; McMahon et al., 1997). Certainly lower maternal self-efficacy has been associated with perception of more child difficulty (Gross et al., 1994), and it is possible that early anxiety about child well-being combined with a lower sense of competence during the first year is associated with a higher maternal report of problem behaviours among IVF infants compared to matched controls. Halasz et al. (1993) examined temperament and found no differences between IVF and comparison singleton 2 year old children. It is also plausible that these early perceptions of more infant difficulty by IVF mothers, in comparison to mothers from a similar background, fade during the second year as maternal concerns about child well-being resolve and confidence in care-giving increases.

Overall these results are reassuring for both parents and professionals alike, as few differences were found between the development, behaviour and temperament outcomes for children conceived through IVF and children from a similar background at 1 year of age. The practical significance of those differences identified remains unclear, partly because they are within the normal range and because they may not be sustained. Further follow up studies will no doubt provide clarification. To the extent that these differences may reflect the anxiety of IVF mothers about their children’s well being, sensitivity on the part of professionals to their concerns is indicated during the first postpartum year.

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