Chapter 7

Posttraumatic stress disorder following complicated and uncomplicated pregnancies; prospective identification of incidence and risk factors

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Abstract

Objective: Stressful, life threatening situations can induce posttraumatic stress disorder (PTSD). As Preeclampsia (PE), the HELLP syndrome and preterm prelabor rupture of membranes (PPROM) are conditions threatening both maternal (HELLP/PE) and fetal health (HELLP/PE and PPROM) they might induce PTSD. We therefore prospectively investigated the incidence and risk factors for PTSD in women suffering from these conditions as compared with uneventful pregnancies.

Methods: Women with HELLP, PE, PPROM or uncomplicated pregnancies completed a PTSD questionnaire (PSS-SR) and a depression questionnaire (BDI-II) during pregnancy (pre-test) and six weeks postpartum (follow-up). Data regarding psychiatric history and indices of obstetric care were collected.

Results: We included 22 HELLP, 35 PE, 53 PPROM and 65 healthy pregnant women. The incidence of PTSD in follow-up test was found to be 11% for HELLP/PE and 17% for PPROM, which is significantly higher than the 3% in the uneventful pregnancies. The incidence of depression did not differ between complicated and uneventful pregnancies. A history of depression (β=.23), depressive symptoms during pre-test (β=.29) and infant death in the postpartum period (β=.29) explained almost 40% of the variance in post traumatic stress symptoms in a regression analyses.

Conclusion: The sequence of events accompanying pregnancies complicated by HELLP/PE or PPROM is associated with post traumatic stress symptoms in a substantial number of women, indicating that clinicians need to monitor maternal mental health in the postpartum period.
Introduction

Pregnancy can be complicated by disorders which are life-threatening for both fetus and mother. The most prevalent disorder is preeclampsia (PE), a condition characterized by hypertension and proteinuria. The HELLP syndrome is an acute, life threatening form of preeclampsia and consists of the symptoms Hemolysis, Elevated Liver enzymes, and Low Platelets. During HELLP and PE the fetal condition is endangered due to placental dysfunction and the risk of preterm birth. Clinical management consists of close monitoring of the maternal and fetal condition; the only treatment is termination of pregnancy by cesarean delivery or induction of labor. A third pregnancy complication that is life threatening for the fetus is preterm prelabor rupture of membranes (PPROM), a condition putting the fetus at risk most probably due to intra-uterine infections and premature birth. PPROM is managed with medication inhibiting uterine contractions and eventually antibiotics. In many cases of HELLP, PE and PPROM infants are born preterm and require prolonged management in a neonatal intensive care unit.

Extreme stressful, life threatening situations can induce long lasting and disabling anxiety-related complaints, labeled posttraumatic stress disorder (PTSD). Symptoms of PTSD consist of re-experiences of the stressful situation, avoidance of reminders of that situation and a persistent hyper-aroused state. The diagnosis of PTSD according to the DSM-IV, additionally requires that the threat elicits a subjective response of intense fear, horror or helplessness; that the symptoms persist for at least a month; and that the symptoms impair daily life functioning (1). PTSD commonly co-occurs with other psychiatric disorders, particularly major depressive disorder (2, 3).

The concept of PTSD was primarily developed in relation to battlefield experiences, violence, accidents and rape. In the last decade however, increasing attention has been devoted to childbirth as a possible traumatic event (4, 5). A limited number of studies have reported estimates of the prevalence of PTSD following childbirth, ranging from 0.0-5.9% between one and six months after childbirth (6, 7). More posttraumatic stress symptoms were observed following pregnancy and delivery complications like early pregnancy loss (8, 9), stillbirth (10), emergency cesarean delivery (11) and in mothers of premature infants (12, 13). As antenatal risk factors for postpartum PTSD have been indicated: previous mental health difficulties, previous traumatic childbirth and trait anxiety; perinatal risk factors are feelings of lack of control, intense emotional distress, lack of social support (14, 15).

PTSD might especially occur following PE, HELLP and PPROM, considering their life-threatening and uncontrollable character. An indication for this is found in an
retrospective exploratory study in Dutch PE patients, which estimated the incidence of PTSD following PE at 28% (16). Post traumatic stress symptoms following PE in this study were associated with gestational age and measures of peritraumatic psychological processes, such as distress, negative interpretation of symptoms and suppression of condition-related thoughts.

Prospective studies on the incidence and risk factors for PTSD following pregnancies complicated by PE, HELLP and PPROM are lacking, even though the early hospital admission of women suffering from these diseases allows for prospective investigations. Data from prospective studies may allow physicians to identify women vulnerable to developing PTSD and may facilitate the development of interventions to prevent PTSD. We therefore performed a study in which we prospectively examined the incidence and risk factors for PTSD and depression following HELLP, PE and PPROM, and compared these to uneventful pregnancies.

Regarding the risk factors for PTSD we investigated a number of hypotheses. The first topic; is PTSD related to the disease of the mother or to the pre-term birth of the child? This was investigated by comparing the incidence of PTSD in patients suffering from HELLP /PE (pre-term birth + maternal threat) with patients with PPROM (pre-term birth alone). We hypothesized that the development of PTSD would be more related to the condition of the mother and therefore expected the highest incidences in the PE/HELLP group; 2) As the onset of PTSD has been associated with previous psychopathology (17), and considering the co-morbidity between PTSD and depression (2) we expected to find that a previous depressive episode and depressive symptoms during pregnancy are strong risk factors for PTSD; 3) Only a subgroup of women suffering from PE is found to develop PTSD symptoms (16), we therefore hypothesized that individual psychological factors are stronger risk factors for PTSD than objective obstetrical measures of threat.

Materials and methods

Participants

Women with PE, HELLP and PPROM were recruited in the obstetric clinic of the University Medical Centre Groningen between February 2005 and February 2008. PE and HELLP defined according to the criteria of the International Society for the Study of Hypertension in Pregnancy (18) and PPROM according to the ACOG practice bulletin on PPROM (19). A control group of healthy pregnant women with an uneventful pregnancy was recruited in a midwifery practice in Groningen from February 2005 till
May 2006. All women had singleton pregnancies and were native Dutch speakers. Exclusion criteria for all groups were pre-existing medical conditions (hypertension, cardiovascular or renal diseases, SLE, Diabetes Mellitus), or a history of intra-uterine fetal death (IUFD). All women gave written informed consent. Approval was obtained from the Medical Ethics Committee of the University Medical Center Groningen.

Procedure
Participants were tested during pregnancy (pre-test) and six weeks postpartum (follow-up). Upon admission, the hospitalized patients received information about the study and were asked to consider participation in the study within 24 hours. When they returned signed consent, they were contacted by the researcher and were tested as soon as possible, to prevent loss of participants due to delivery before testing. The participants in the control group were tested in their 38th week of pregnancy.

Measures
During the pre-test, participants completed a brief self-report measure of general demographic information. Information regarding psychiatric history was obtained in an interview, containing questions on the life-time presence of episodes of depressed mood or anhedonia, and regarding previous post traumatic stress symptoms. Questions were: ‘In the past, did you ever experience one or more periods: in which you felt depressed or down for most of the day or in which you lost interest in activities you usually enjoy?’; and ‘Have you ever witnessed or experienced a traumatic situation, (such as experiencing or witnessing a life-threatening situation, physical or sexual abuse, a disaster or serious accident) and has this experience affected you afterwards (e.g., with nightmares or intrusive thoughts)?’. Based on the answers to these questions 2 variables were constructed: 1) indication for a previous depressive episode (0 = absent; 1 = present); 2) indication for previous post traumatic stress symptoms (0 = absent; 1 = present). Data regarding current and past obstetric status were collected from the medical record.

During both test-sessions, the PTSD Symptom Scale self report questionnaire (PSS-SR) (20) and the Beck Depression Inventory, second edition (BDI-II) (21), were completed. The PSS-SR is a questionnaire containing 17 items corresponding to the 17 PTSD symptoms described in the DSM-IV. These items are rated using 4 point scales asking for the frequency with which each symptom occurred over the past month (0= never, 1 = once a week, 2 = -4 times a week, 3 = more than 5 times a week). The total PSS-SR score ranges from 0 – 51. The re-test reliability has been calculated .74 (20). In the
present sample the internal consistency was good ($\alpha = .86$ for the pre-test and $\alpha = .94$ for the follow up). The PSS-SR that was administered during the pre-test asked for PTSD symptoms in the past month that were related to any stressful event experienced before. The follow-up PSS-SR referred to PTSD symptoms in the past month that were specifically related to pregnancy and parturition. In addition, during follow-up assessment participants rated the extent to which they had felt fear, helplessness, or horror during the most shocking pregnancy-related event on three 100 mm Visual Analogue Scales (VAS).

In the present study, PTSD diagnosis at follow-up was based on a symptom profile reflected by the PSS-SR and VAS scores that was consistent with the DSM IV criteria. For this we used the criteria as used in the study of Engelhard et al. (16). More specifically, pregnancy-related PTSD was considered to be present when participants: 1) scored 80 or more on one of the VAS for horror, fear or helplessness (subjective stress, DSM-IV A2 criterion); 2) reported at least 1 re-experiencing, 3 avoidance and 2 hyperarousal symptoms on the PSS (DSM IV, B, C, and D criterion, respectively). Symptoms were considered present if an item was rated 2 (‘2 – 4 times a week’) or more; 3) obtained a total PSS-SR score of 18 or higher (severity, DSM IV F criterion). It should be noted that the time criterion of 4 weeks (DSM IV E criterion) was met because follow-up assessment was at six weeks postpartum. For PTSD diagnosis at pre-test, a similar classification was used, with the exception of the A2 subjective stress criterion because VAS ratings were not obtained.

The BDI-II (21) is a self-report measure of depressive symptoms during the preceding two weeks. It consists of 21 items containing four statements that reflect increasing symptom severity (scoring 0-3 per item). The total score ranges from 0 to 63. The BDI-II is found to have good psychometrical properties (21-23). The internal consistency in the current sample was good ($\alpha = .88$ for the pre-test and $\alpha = .91$ for the follow up). In the present study, participants completed the BDI-II during pre-test as well as follow-up. A cut-off score of 21 was used as this is the criterion for a moderate depression according to the BDI manual (21). In addition, a cut-off score of 15 was used in order to compare the present results with those reported by Engelhard et al. (16). Furthermore, the BDI total symptom scores were compared.

**Statistical analysis**

Statistical analyses were performed with SPSS 14.0. Alpha was set at 0.05. Group comparisons involved three groups: 1) HELLP/PE, 2) PPROM and 3) Control (uneventful pregnancies). For the dichotomous data, Chi$^2$ analyses were used.
Exploration of the continuous data revealed that the BDI and PSS scores were not normally distributed. Therefore, for group comparisons non-parametrical Spearmans rho, Kruskal-Wallis or Friedmans tests were employed. In order to identify risk factors for PTSD and depression in the patient groups, hierarchical multiple regression (HMR) analyses were performed on the BDI and PSS sum scores. Where appropriate, non-normally distributed variables were square-root transformed to meet assumptions of normality, linearity and homoscedasticity.

Results

In the period between January 2005 and January 2008 we included 199 participants. Four women did not meet the inclusion criteria (1 previous hypertension, 1 chronically ill, 1 addicted, and 1 previous IUFD), and 2 women were too sick to perform the pre-test during hospitalization. Eighteen women from the patient-group refused to participate in the post-test of whom 14 were not motivated, without giving a specific reason for that, and 4 women did not want to participate because they lost their child in the postpartum period. The remaining 175 women consisted of 22 HELLP, 35 PE, 53 PPROM and 65 healthy pregnant women. Demographic and obstetrical characteristics are shown in table 1. The patients and control groups differed in all obstetrical indices, as expected. Furthermore, the control group was slightly but significantly older, and had higher levels of education relative to the patients. In contrast to all other groups, none of the patients with HELLP was unemployed. Women with PPROM had a significant higher number of previous pregnancies and deliveries. As the HELLP and PE groups did not differ in their obstetric characteristics, they were pooled into one group for further analysis, labeled “HELLP/PE”.
Incidence and severity of PTSD and Depression

Table 2 shows the incidence of PTSD and depression at six weeks postpartum. A Pearson Chi$^2$ test indicated an association between diagnosis and the incidence of PTSD (Chi$^2=6.499$, df =2, p=.039). The incidence of PTSD was significantly higher in the PPROM groups than in the control group (Chi$^2=6.677$, df =1, p=.01). There were no significant differences in PTSD incidence between the HELLP/PE and the PPROM groups (Chi$^2=9.972$, df =1, p=.324). Irrespective of cut-off point, the three groups did not significantly differ with respect to incidence of depression.

The sum scores of the PSS-SR, BDI during pregnancy and follow-up are depicted in Table 3. Kruskall-Wallis testing of the BDI scores during pre-test indicated a significant association with diagnosis. Posthoc testing indicated that the HELLP/PE group differed from the controls (Z = -2.33, p=0.020). Comparison of the follow-up PSS-SR scores in the three groups indicated no significant differences (Chi$^2=5.286$, df =2, p=.072). A post-hoc Mann-Whitney U-test indicated a significant difference between HELLP/PE and controls (Z=-2.33, p=0.020). The follow-up BDI scores did not differ between the three groups. Scores on the BDI and PSS-SR during follow-up were found to correlate strongly (Spearman's rho =.780, p<.001), and 9 of the 17 women (53%) with PTSD also had a co-morbid depression.

Risk factors for PTSD and Depression in the clinical sample

As the death of a child in the postpartum period is extremely stressful and can induce ‘grief associated depressive symptoms’ we investigated the effect of the death of a child on the incidence of depression and PTSD. The results, summarized in Table 2 & 4, indicate that the incidence of depression and PTSD, as well as sum-scores of the PSS-SR and BDI were significantly higher in women who had lost their child (all p<.01). Subsequently, we investigated if hospitalization of the child at time of follow-up influenced the diagnosis of PTSD and depression. The incidences of PTSD and depression did not differ significantly between both groups (data not shown).

Finally, we investigated the contribution of psychological and obstetric risk factors to the PSS-SR and BDI scores at follow up using 2 hierarchical linear regression analyses.
As we hypothesized that psychiatric history and BDI scores during pregnancy were the strongest risk factors for PTSD and depression postpartum (see introduction), these variables were entered in the first step (Psychiatric history was dichotomized, i.e., 0 = no history; 1 = history of depression). In the second step variables indicative for the wellbeing of both mother and child were added, to investigate if these variables explained variance additive to the history of depression and pretest BDI scores, i.e. death of child (0 = living child; 1 = child died before follow-up), hospital admission of the child during follow-up assessment (0 = child at home; 1 = child in hospital), birth weight, diagnosis of mother (0= HELLP/PE; 1= PPROM), cesarean delivery (0 = no CD; 1 = CD). BDI and PSS-SR scores were skewed and therefore square root transformed (SQRT). The results are shown in table 6 & 7. The model for SQRT PSS-SR explained 29% of the variance in the first step, and an additional 10% in the second step, resulting in a model explaining 39% of the variance. Significant risk factors were a high SQRT BDI score during pre-test (β=.33), indication for a previous depressive episode (β=.23) and the death of the child (β=.29). The other indicators for maternal or child well-being significantly contributed to the model in the first period but not in the second period. The model for SQRT BDI explained 38% of the variance in the first step, and addition of the second step increased R² with 6% (p=.032), yielding a total of 44%. Significant risk factors in this model were the SQRT BDI during pre-test (β=.42), indication for a previous depressive episode (β=.30) and death of the child (β=.21).

**Table 2.** Number (%) of women with PTSD and Depression in the HELLP/PE, PPROM and Control groups at 6 weeks postpartum in the total group, and in the subgroup of the participants with living children.

<table>
<thead>
<tr>
<th></th>
<th>HELLP/PE (n = 57)</th>
<th>PPROM (n = 53)</th>
<th>Control (n = 65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTSD</td>
<td>11%</td>
<td>13%</td>
<td>2%</td>
</tr>
<tr>
<td>BDI&gt;15</td>
<td>18%</td>
<td>26%</td>
<td>9%</td>
</tr>
<tr>
<td>BDI&gt;20</td>
<td>12%</td>
<td>24%</td>
<td>10%</td>
</tr>
<tr>
<td>PSS-SR pre-test</td>
<td>11%</td>
<td>15%</td>
<td>7%</td>
</tr>
<tr>
<td>PSS-SR post-test</td>
<td>30%</td>
<td>39%</td>
<td>9%</td>
</tr>
</tbody>
</table>

*Significantly different from all other groups (Pearson Χ²=6.499, df=2, p=0.039)

**Table 3.** BDI and PSS-SR sum scores (25-th -75-th percentile) for women with HELLP/PE, PPROM and uncomplicated pregnancies during pre-test and post-test.

<table>
<thead>
<tr>
<th></th>
<th>HELLP/PE (n = 57)</th>
<th>PPROM (n = 53)</th>
<th>Control (n = 65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDI score pre-test</td>
<td>14.0 (8.5-18.5) #</td>
<td>12.0 (7.5-14.0)</td>
<td>10.0 (7.5-13.5)</td>
</tr>
<tr>
<td>BDI score post-test</td>
<td>9.0 (6.5-14.5)</td>
<td>9.0 (3.0-14.0)</td>
<td>8.0 (5.0-12.0)</td>
</tr>
<tr>
<td>PSS-SR pre-test</td>
<td>12.0 (3.0-20.0)</td>
<td>11.0 (2.5-19.5)</td>
<td>7.0 (0.0-15.0)</td>
</tr>
<tr>
<td>PSS-SR post-test</td>
<td>13.0 (8.0-20.0) *</td>
<td>9.0 (4.0-21.5)</td>
<td>9.0 (6.0-15.0)</td>
</tr>
</tbody>
</table>

# Significantly different from control in Mann-Whitney U-test (Z=-2.476, p=0.012)

*Significantly different from control in Mann-Whitney U-test (Z= -2.33, p=0.020).

**Table 4.** Number (%) of Women with PTSD and Depression, and PSS-SR, BDI scores (median, 25-th -75-th quartile) at six weeks postpartum in women with pregnancy complications, as a function of the death of their child.

<table>
<thead>
<tr>
<th></th>
<th>Living child (98)</th>
<th>Child died (12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTSD</td>
<td>11%</td>
<td>50%</td>
</tr>
<tr>
<td>BDI&gt;15</td>
<td>13% (13%)</td>
<td>75% (75%)</td>
</tr>
<tr>
<td>BDI&gt;20</td>
<td>7% (7%)</td>
<td>42% (42%)</td>
</tr>
<tr>
<td>PSS-SR score</td>
<td>16.0 (6.0-17.2) *</td>
<td>24.4 (18.2-37.5)</td>
</tr>
<tr>
<td>BDI score</td>
<td>5.0 (2.5-12.4)</td>
<td>16.1 (9.8-30.2)</td>
</tr>
</tbody>
</table>

*significant different between women with a living child or those whose child died in the postpartum period.

**Table 5.** Number (%) of Women with PTSD and Depression, and PSS-SR, BDI scores (median, 25-th -75-th quartile) at six weeks postpartum in women with pregnancy complications, as a function of the death of their child.

As we hypothesized that psychiatric history and BDI scores during pregnancy were the strongest risk factors for PTSD and depression postpartum (see introduction), these variables were entered in the first step (Psychiatric history was dichotomized, i.e., 0 = no history; 1 = history of depression). In the second step variables indicative for the wellbeing of both mother and child were added, to investigate if these variables explained variance additive to the history of depression and pretest BDI scores, i.e. death of child (0 = living child; 1 = child died before follow-up), hospital admission of the child during follow-up assessment (0 = child at home; 1 = child in hospital), birth weight, diagnosis of mother (0= HELLP/PE; 1= PPROM), cesarean delivery (0 = no CD; 1 = CD). BDI and PSS-SR scores were skewed and therefore square root transformed (SQRT). The results are shown in table 6 & 7. The model for SQRT PSS-SR explained 29% of the variance in the first step, and an additional 10% in the second step, resulting in a model explaining 39% of the variance. Significant risk factors were a high SQRT BDI score during pre-test (β=.33), indication for a previous depressive episode (β=.23) and the death of the child (β=.29). The other indicators for maternal or child well-being significantly contributed to the model in the first period but not in the second period. The model for SQRT BDI explained 38% of the variance in the first step, and addition of the second step increased R² with 6% (p=.032), yielding a total of 44%. Significant risk factors in this model were the SQRT BDI during pre-test (β=.42), indication for a previous depressive episode (β=.30) and death of the child (β=.21).
Chapter 7

Our results should be considered in the light of several strengths and weaknesses. Strong points of this study are the prospective, longitudinal design, the use of a control group with uneventful pregnancies, and the assessment of both depression and PTSD. Limitations of this study are the use of self report questionnaires and the retrospective assessment of the experiences of the women during hospitalization. The high level of education in the control group might also be a confounder, as a high IQ is found be a protective factor regarding the onset of PTSD (24). However, the incidence of PTSD in the control group was comparable with the 2.1% found in the first echelon of obstetric care in the Netherlands (14). This study included a representative sample of the Dutch population, indicating that such confounding probably did not occur.

The incidence of PTSD in our sample was somewhat lower than found by Engelhard et al, who reported an incidence of 28% PTSD following preterm PE and preterm birth. The study of Engelhard et al. differed from this study with respect to its design (retrospective vs. prospective) and the timing of measurement (14 months postpartum (SD=3.5), vs. six weeks postpartum). This retrospective assessment of post traumatic stress symptoms might have induced an overestimation of symptoms, which might explain the higher incidence reported in this study. The incidence of PTSD in the control group was comparable with the 2.1% found in the first echelon of obstetric care in the Netherlands (14), underlining that PTSD may also occur after uncomplicated pregnancies and deliveries. The incidence of depression in the postpartum period in women with living children is within the normal range for depression in the postpartum period (period prevalence of 7.1%), (25). In general the year prevalence of depression in the postpartum year is somewhat higher than in non-pregnant women (26). The slight decrease in depressive symptoms in the postpartum period has been reported before (27) and is probably related to a decrease the level of worrying following the birth of a healthy child.

PTSD was as frequent in women with PPROM as in women suffering from PE or HELLP, contradicting our hypothesis. These findings are in accordance with those of Engelhard, reporting no difference in incidence of PTSD in women with PE or pre-term birth (16). All together, these data suggest that complications that affect the child (i.e. pre-term birth) more than the disease of the mother may predispose PTSD following pregnancy complications.

Significant risk factors for both PTSD and depression were high BDI scores during hospitalization, a self reported previous depressive episode and the death of the child in the postpartum period. Risk factors such as cesarean delivery and hospitalization of the child during follow-up did not significantly contribute to the regression models. These
findings are in line with the conclusion of the review of Olde et al. on PTSD following childbirth, indicating that obstetric interventions might be associated with PTSD but are not conditional, as PTSD may also develop following spontaneous, uneventful vaginal deliveries (1). The existing data on PTSD and depression following stillbirth and stillbirth or perinatal death (9-14) and illustrate the major impact of losing a child in the postpartum period. However, according to the DSM-IV, depression should not be diagnosed here, as the symptoms may be accounted for by bereavement (1). It must be noted though, that this bereavement criterion is subject of serious debate (28, 29). The very existence of this criterion could be a reason to consider the psychological reactions as a ‘normal’ emotional response. However, certain results of this study indicate that the emotional reaction in these women might not be monitoring, as a half of the women with depression also developed co-morbid PTSD; b) both previous depression as well as depressive symptoms are risk factors for the development of the death of a child, indicating that some of the depressions are rebound or pre-morbid depression, both of which need serious attention regardless of their cause.

As these pregnancy complications can induce post traumatic stress symptoms in some women, we suggest clinicians to be aware of these pathologic responses, not only to improve maternal mental health but also for the improvement of the quality of the development of the child, as PTSD and depression influence maternal attachment and infant development (30, 31). Moreover, a new pregnancy can reactivate unresolved post traumatic stress symptoms, which might contribute to undesirable pregnancy outcomes (32, 33). The latter is also a reason to seriously evaluate psychiatric symptoms in women who have lost their child. The results of this study suggest that women vulnerable for PTSD following complicated pregnancies by PE, HELLP and PPROM can induce post traumatic stress symptoms in a substantial number of women. Depression was not found to be a specific reaction to these complications. A history of depression, depressive symptoms during pregnancy and the death of the child in the postpartum period were found to explain almost 40% of the variance in post traumatic stress symptoms. The relatively high incidence of PTSD in this group of women indicates that the clinicians’ attention for maternal mental health is
needed and that researchers should develop and study proper, easily employable instruments for screening and monitoring of PTSD following pregnancy complications.
PTSD following Complicated Pregnancies
Reference List


