Risk for postpartum depression in association with zinc, magnesium and calcium levels at delivery
Abstract

Postpartum depression is a serious illness that affects many newly delivered women. If not treated in time it may cause disturbances in the connection between the mother and her baby and even have consequences for the whole family. Today, some antenatal clinics in Sweden use screening questionnaires to identify women who suffer from the illness. Earlier studies have found elevated serum levels of calcium and decreased levels of magnesium among depressed patients. Studies have also found a connection between hypozincemia and depression, one study even with postpartum depression.

This study is a sub-study of the UPPSAT project, which is aimed to investigate correlates of postpartum depression. The current study focuses on serum levels of calcium, magnesium and zinc at delivery and their possible association with postpartum depression. No associations were seen between calcium or magnesium and postpartum depressive symptoms in our study, but it could be shown that higher levels of zinc at the start of the delivery were associated with depressive symptoms 6 weeks postpartum. The association was not statistically significant after controlling for possible confounders. Serum levels of zinc are affected by steroid hormones, metabolic parameters and inflammation, which is a known factor that triggers the delivery process. Despite the fact that the design of this study was not optional, and the zinc might be too sensitive a test as a marker for postpartum depression, the association of zinc levels and postpartum depression deserves further research.
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1. Introduction

1.1. Postpartum mood disorders

1.1.1. Postpartum blues

 postpartum blues is the most common post partum mood disorder, with a prevalence of 30-75%[1]. DSM IV describes post partum blues as a mild and transient form of depression, starting in the early postpartum period. It then lasts between a few hours and two weeks [2]. Common symptoms of postpartum blues are crying episodes, mild depression, anxiety, fatigue and emotional instability[3]. Because of the self termination of postpartum blues, no treatment is necessary[4]. If this mood disorder does not regress within 1-2 weeks after delivery or the woman experiences a severe depression early post partum, she should be considered having a postpartum depression[5].

1.1.2. Postpartum depression

13-20% of the newly delivered women experiences PPD[6]. Typical symptoms of PPD are sadness, anxiety, fear, fatigue and compulsive thoughts. In the DSM-IV, an episode of major depression after delivery is defined as 2 weeks or more of persistent: (1) depressed mood, or (2) loss of interest in daily activities and 4 associated symptoms (appetite disturbance, sleep disturbance, psychomotor agitation or slowing, fatigue, feelings of worthlessness or inappropriate guilt, poor concentration, and suicidal ideation) that onset within 4 weeks after childbirth. However, onset between three months and one year are commonly used timeframes[7][8].

The cause of PPD is unclear, but the hormonal differences in the puerperium may be part of the explanation. After delivery all women experience a rapid reduction of hormones, especially oestrogen and progesterone. Most women cope with this without developing PPD, but some seem to be extra sensitive to the reduction, and develop a depression. By simulating the hormonal reduction of the puerperium, researchers have shown that women with a history of PPD are more sensitive to these reductions[9].

Many studies investigating risk factors for PPD have been made, often with various conclusions. An earlier episode of depression, before or during pregnancy, has though been associated by many researchers as an important risk factor[10, 11]. Women who suffer from PPD are more likely to have a relative with a depression, suggesting family history of depression to be another risk factor[12]. Psychosocial factors such as feelings of social isolation, low socio-economic status and lack of social support are other risk factors for PPD,
Cigarette smoking and obesity, both associated with many diseases, are factors that influence the development of PPD too[11, 16].

Obstetric situations, such as preterm and low birth weight infants may also influence the risk of developing PPD[17]. Complications during labour has though shown not to contribute to the development of PPD[13]. Breastfeeding, comparing to bottle feeding with infant formula, reduces the risk of developing PPD[11].

PPD often goes undiagnosed[18], many women suffer from the disease in silence. In general, the sensitivity of a diagnose is increased when rating scales are used as a complement in an investigation. Edinburgh Postnatal Depression Scale is the most common tool used when screening for PPD[19]. It is a self-report form with 10 questions. In each one, the women can grade her symptoms between 1-3 according to severity leading to a final score of 0-30 points. Established cut-off scores in Sweden are 12 or more points for a high risk of postpartum depression.[20] Today EPDS is used in research and in some antenatal clinics to screen for PPD. If a score above cut-off is obtained, a wider investigation according to the DSM-IV criteria should be initiated as EPDS by itself is not enough to diagnose PPD. Screening with EPDS is often not used within the first two weeks after delivery according to the high prevalence of postpartum blues during this period.

The feeling of guilt and worthlessness as a mother are reasons why many women wait too long before they seek medical attention. The longer it takes before diagnose and start of treatment, the longer the depression of the mother may negative effect the relationship between her and her child. Screening for depression both during pregnancy and after is a way to detect women at risk, which could lead to informative dialogues, closer check-ups and earlier start of treatment if necessary.

1.1.3. Post partum psychosis
The post partum psychosis is the most severe post partum mood disorder. It is also the most unusual type, the prevalence is about 1-2 of 1000 women [21], [22]. According to DSM-IV, symptoms of post partum psychosis are illusions, hallucinations and disorganized speech and behaviour. At first, symptoms as sleep disturbances, irritability and restlessness may be the only signs of the disease. Earlier episodes of psychiatric illnesses, especially bipolar diseases, are overrepresented in women developing post partum psychosis[22]. Post partum psychosis starts between 48 hours and 2 weeks post partus[4]. The primary goal when detecting post partum psychosis is safety for the woman and her child because of the woman´s decreased judgement. A feared consequence of post partum psychosis is infanticide, a very rare event that can be further reduced if better guidelines for diagnose and treatment are developed[23].
Post partum psychosis is an acute emergency case that often requires immediate hospitalization. The alternatives when treating postpartum psychosis involves antipsychotics, litium and ECT. Litium may also be used as prophylaxis in women with a history of bipolar disease to decrease the rate of relapse[24]. Addition with estradiol in women with estradiol deficiency has shown a reversal of psychiatric symptoms, implicating it’s usage in treating post partum psychosis[25].

1.2. Calcium, zinc and magnesium
Calcium, zinc and magnesium are three substances responsible for many actions in the human body. Studies investigating eventual correlations between each substance and depression have been made, implicating an interest in these substances and their eventual impact on psychiatric disorders.

1.2.1. Calcium
99% of all calcium in the body is stored in the bones, most as hydroxyapatite crystals and less as mobilizable non crystalline calcium salts. 1% is distributed in ECF and soft tissues. In serum, Calcium is by 50% in its ionized form (Ca2+), the form that is biological active. The rest is either bound to organic acids, non organic acids or to a protein most common albumine. Calcium is elevated by Para Thyroid Hormone (PTH) through its direct effect on the kidneys reabsorption of Ca and through boneresorption. PTH also affects Vitamine D, resulting in elevated Calcium absorption from the intestines. Thanks to a negative feedback loop Calcium then inhibits further secretion of PTH[26].

In the synapsis of neurons, Calcium plays a crucial role. Neurotransmitters are stored in vesicles in the presynaptic terminals. When an action potential invades the presynaptic terminal, depolarization causes opening of voltage- gated Ca2+ channels leading to influx of Ca2+. This makes the vesicles with neurotransmitters fuse with the presynaptic membrane, releasing the transmitter in the synapsis to act on the postsynaptic neuron. A fall in free Ca in the plasma results in overexcitability of nerves and muscles and a rise in Ca depresses neuroexcitability. Thus hypocalcemia may lead to for example muscle spasm and hypercalcemia to cardiac arrythmias through depression of neuromuscular excitability of the heart[26].

Another effect of calcium is exocytosis of cells. The entry of Ca into secretory cells (because of stimuli leading to increased permeability to Ca) triggers e release by exocytosis. This release is important for the secretion of neurotransmitters by nerve cells and hormone secretion by endocrine cells. Calcium forms parts of the intercellular cement that holds
particular cells together through tight junctions. It also serves as a cofactor in several steps of the cascade of reaction leading to clotting of the blood[26].

It is known that serum Ca levels are increased in depression and decreased in recovery, though few studies are made on the subject. One study from Japan shows that patients with affective disorder have enhanced intracellular calcium response and that antidepressant drugs inhibit intracellular calcium signalling[27].

1.2.2. Zinc
Zinc is a trace element in the human body involved in cell division and differentiation through its influence on DNA replication and protein synthesis[28]. Because of this, a deprivation of zinc leads to a retardation of growth[29]. Other known clinical manifestations of zinc deficiency is dermatitis, hair loss, delayed wound healing and depressed immunity. Zinc is essential for the function of over 100 enzymes, one of them superoxide dismutase which is a protector against oxidant stress and free radical damage. Zinc is also a part of Zinc fingers, a structure that helps binding of hormones and proteins on regulatory regions of genes[30].

Zinc has a regulatory function of neurons by moving into the cells through gated membrane channels, acting like an ionic signal[31]. In the brain, the highest amounts of Zinc is thought to be found in the cerebral cortex and the limbic structures (eg hippocampus, amygdala)[28, 32]. The cells of these areas store and release zinc but also glutamate, hence the term “gluzinergic” neurons[33]. Zinc modulates the excitability of neurons through effects on glutamate and GABA receptors. [31]. It may also be involved in synaptic plasticity[34]. A deprivation of dietary zinc can influence the homeostasis of zinc in the brain leading to brain dysfunctions (learning impairment and alterations in mental function and behaviour) and even seizures[35].

Dietary zinc is absorbed in the duodenum and jejunum and then active transported into the portal blood. In serum, zinc is by 98% protein-bound form, 1- 2% low molecular weight ligand-bound form and a very small fraction as free Zn$^{2+}$[36, 37]. The biggest amount of exchangeable zinc in serum is bound to albumin, though rat experiments show that albumin is not involved in the transport of zinc into the brain[38]. The next biggest amount of exchangeable zinc is bound to amino acids such as histidine and cysteine[39]. Studies have shown that the uptake of zinc in the brain and other tissues was enhanced by infusion of L-histidine[40].

Both animal experiments and clinical data suggests that a hypozincemia can be linked to depression[41]. A study in Poland has investigated the relationship between Zink and
postpartum depression leading to the conclusion that a decrease in serum Zink correlates to a higher frequency of postpartum depression [42].

1.2.3. Magnesium
Most of the magnesium in the body is stored in bones and teeth, but some is present in muscles and extracellular fluids. In serum, magnesium is by 20% bound to albumin. Magnesium is important in many enzymatic functions, in particular those involved in carbohydrate metabolism. It is also part of the transcription and replication of DNA, translation of mRNA and in calcium-channel function[43].

There are animal experimental tests showing that a magnesium deficiency induce depression in the test animal[44]. The effect Magnesium has on different affective disorders is though under discussion. Both decreases and increases have been monitored in different affective-like mood disorders[45]. The same study that showed a relation between hypozincemia and postpartum depression did not find the same relations between postpartum depression and Magnesium[42].

1.3. Aim
The aim of the UPPSAT project is to investigate correlates of postpartum depression in Sweden. For the current sub-study the aim is to investigate if the serum levels of calcium, zinc and magnesium at delivery are associated with postpartum depressive symptoms.

2. Methods
This study is part of the UPPSAT project which is a population based cohort study made in Uppsala. The study was conducted at the department of Obstetrics and Gynecology at Uppsala University Hospital. The county of Uppsala has a population of 323 270 inhabitants. Uppsala University Hospital is responsible for all the delivering women in this county and also surrounding counties in high-risk pregnancies[8].

2.1. Study population
Between November 2006 and May 2007 all newly delivered women who gave birth at Uppsala University Hospital were contacted by their midwife or a midwife assistant and asked if they wanted to take part in a longitudinal study about maternal, paternal and infant wellbeing. Exclusion criteria for participating in the study were (1) inadequacy to communicate in Swedish, (2) women with their personal data kept confidential and (3) women with intrauterine death or with infants immediately admitted in the neonatal intensive care unit. The mothers that fulfilled the criteria for the study received oral and written information about the aim of the study and written consent was obtained. 5 days after delivery
the participating women completed a self-administered structured questionnaire containing the Edinburgh Postnatal Depression scale (EPDS). 6 weeks and 6 months after delivery new questionnaires were sent to the women by mail with instructions to complete and then send the questionnaires back[8].

2.2. Outcome measures
The questionnaires given to the women included structured questions about lifestyle, physical and psychological health, history of gynecologic and obstetric experiences and the Swedish version of EPDS[19, 20]. A cut of score of 12 was used for all three time-points, 5 days, 6 weeks and 6 months.

2.3. Blood samples
In the UPPSAT study, one blood sample was collected from all women delivering at Uppsala University Hospital between November 2006 and May 2007. This was in conjunction with the routine intravenous catheterization before delivery. After receiving the blood samples they were coded and stored at 4 C for a maximum of 24 hours (depending on the time of the day when the sample was collected) and then centrifuged. After centrifugation the sera was stored at – 70 C. The blood samples of the women who chose not to participate in the study were discarded[8].

2.4. Analysis of Ca, Mg and Zn
The blood samples were analyzed at the laboratory of Uppsala university Hospital. Calcium (reagent: 1125621, Roche Diagnostics, Mannheim, Germany), magnesium (reagent: 11489330; Roche Diagnostics) and zinc (reagent: 17255; Sentinel Diagnostics, Milano, Italy) measurements were performed on an Architect Ci8200 analyzer (Abbott Laboratories, Abbott Park, IL, USA) and reported using SI units. The total coefficient of variation (CV) for the assays were 0.9% at 2.2 mmol/l and 1.2% at 2.9 mmol/l for calcium, 1.4% at 0.9 mmol/l and 0.9% at 1.7 mmol/l for magnesium and 4.5% at 14.4 µmol/l and 6.0% at 6.4 µmol/L for zinc.

2.5. Statistical analyses
For the statistical analyses SPSS version 18.0 was used. Statistical significance was set at a p-value of <0.05. For the current sub-study of the UPPSAT project, women who were smoking and women consuming alcohol during pregnancy were excluded. This is because alcohol and tobacco may influence the concentrations of calcium, magnesium and zinc and therefore the results of the study. A case is defined as a woman who scored above cut off score in any of the three questionnaires (5 days, 6 weeks or 6 months).
Differences in the study variables between cases and controls were examined with the Mann-Whitney U-test. Possible correlations of calcium, zinc and magnesium levels with each other, BMI, age of the woman and duration of gestation were assessed separately among cases and controls using the Spearman Correlation Coefficient.

Finally, a multivariate linear regression model was used with the EPDS score as the outcome variable and calcium, zinc, magnesium and possible confounders (BMI before pregnancy, Age and duration of gestation) as predictor variables. The EPDS score at five days, six weeks and six months after delivery were used in the model after logarithmic transformation, in order to account for non-normality.

3. Results
In total, one blood sample, written consent as well as at least one completed questionnaire were available for 365 women. 26 women who reported cigarette smoking or alcohol use during pregnancy were excluded from the analysis because of their possible impact on the levels of calcium, zinc and magnesium. This left 339, women to be included in the analyses. Finally, of all the blood samples taken, 189 were problematic to analyze, most likely because they were not stored in optimal conditions. Therefore these women were also excluded, leaving 150 women to be included in the analyses.

Table 1 shows the number of completed questionnaires at 5 days, 6 weeks, 6 months and over all. These are shown together with percentage of women with self-reported depression, mean, range and standard deviation of EPDS score. Over all, 150 women completed one or more questionnaires of three possible. 25 women screened positive in the EPDS (cut off \( \geq 12 \)) in one or more of the three questionnaires while 125 women screened negative at all three occasions.

Table 2 shows the distribution of anthropometric, obstetric and calcium, zinc and magnesium variables among cases and controls. There were no statistical significant associations between these variables and case/control status.

In Tables 3a and 3b, the Spearman Correlation Coefficients between calcium, magnesium and zinc and the continuous variables that might act as possible confounders among cases and controls respectively are displayed. Zinc levels at delivery were negatively associated with maternal BMI before pregnancy among cases but not controls. Duration of gestation was nearly statistical significant correlated to calcium with the control group but not the case group. Correlations at a p-value level of \(< 0.25\) among cases were observed between Zinc and
Magnesium. In the control group correlations were observed at a p-value of < 0.25 between: Magnesium and BMI, zinc and BMI and zinc and duration of gestation.

Table 4 shows the results of the linear regression models with EPDS score at six weeks postpartum as the outcome variable and calcium, magnesium, zinc and possible confounders as predictor variables. EPDS score was introduced as the outcome variable after logarithmic transformation in order to account for non-normality. In these analyses, adjustments were made for maternal BMI before pregnancy, maternal age and duration of gestation. Zinc levels are positively correlated with EPDS score at six weeks postpartum (Model 1), but the correlation becomes statistically non-significant when controlling for all possible confounders (Model 5). Respective regression models with EPDS at 5 days or 6 months postpartum did not shown any statistically significant association with zink, magnesium eller calcium levels.

Table 1. Number of completed questionnaires (N), percentage of mothers with self-reported depression (%) when cut off score of 12 points and Mean, Range and Standard Deviation (SD) of the EPDS score at the three points postpartum.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>% screened pos</th>
<th>Mean EPDS</th>
<th>Range EPDS</th>
<th>SD EPDS</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 days</td>
<td>111</td>
<td>13,5</td>
<td>5,85</td>
<td>20</td>
<td>4,903</td>
</tr>
<tr>
<td>6 weeks</td>
<td>122</td>
<td>9,8</td>
<td>5,57</td>
<td>18</td>
<td>4,182</td>
</tr>
<tr>
<td>6 months</td>
<td>101</td>
<td>7,9</td>
<td>4,66</td>
<td>17</td>
<td>3,905</td>
</tr>
<tr>
<td>Over all</td>
<td>150</td>
<td>16,7</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Anthropometric, obstetric and Ca/Zn/Mg variables in 25 cases of self-reported depression and 125 controls.

<table>
<thead>
<tr>
<th>Variable (years) (median, mean ± SD)</th>
<th>Cases</th>
<th>Controls</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (median, mean ± SD)</td>
<td>31,0, 31,0 ± 6.3</td>
<td>31,0, 30,9 ± 3.6</td>
<td>0.129</td>
</tr>
<tr>
<td>BMI before pregnancy (kg/m2) (median, mean + SD)</td>
<td>24,3, 24,4 ± 4.2</td>
<td>22,8, 23,6 ± 4.1</td>
<td>0.366</td>
</tr>
<tr>
<td>Ca (mmol/l) (median, mean ± SD)</td>
<td>2.33, 2.33 ± 0.06</td>
<td>2.33, 2.32 ± 0.10</td>
<td>0.203</td>
</tr>
<tr>
<td>Mg (mmol/l) (median, mean ± SD)</td>
<td>0.82, 0.83 ± 0.06</td>
<td>0.82, 0.81 ± 0.08</td>
<td>0.323</td>
</tr>
<tr>
<td>Zn (µmol/l) (median, mean ± SD)</td>
<td>10,30, 12,20 ±8,14</td>
<td>10,41, 11,08 ±3,81</td>
<td>0.428</td>
</tr>
<tr>
<td>Duration of gestation (days) (median, mean + SD)</td>
<td>282, 280 ± 8</td>
<td>282, 281 ± 10</td>
<td>0.559</td>
</tr>
</tbody>
</table>

* Mann-Whitney U-test

Table 3a. Spearman Correlation Coefficients for serum Ca, maternal age, BMI before pregnancy, duration of gestation and serum Zn and Mg among the 25 cases and respective p-value.
### Table 3b. Spearman Correlation Coefficients for serum Ca, maternal age, BMI before pregnancy, duration of gestation and serum Zn and Mg among the 125 controls and respective p-value.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Age</th>
<th>BMI</th>
<th>Duration of gestation</th>
<th>Mg</th>
<th>Zn</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ca</td>
<td>-0.064(0.788)</td>
<td>0.015(0.946)</td>
<td>0.203(0.331)</td>
<td>-0.106(0.613)</td>
<td>0.148(0.481)</td>
</tr>
<tr>
<td>Mg</td>
<td>-0.193(0.415)</td>
<td>-0.114(0.614)</td>
<td>-0.136(0.516)</td>
<td>0.282(0.172)</td>
<td></td>
</tr>
<tr>
<td>Zn</td>
<td>-0.205(0.385)</td>
<td>-0.477(0.025)</td>
<td>0.069(0.742)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 4. Linear regression models for variables associated with self-reported postpartum depression 6 weeks after delivery.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
<th>Model 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc</td>
<td>1,0398**</td>
<td>1,0387**</td>
<td>1,0387*</td>
<td>1,0387*</td>
<td>1,0336</td>
</tr>
<tr>
<td>EPDS Magnesium</td>
<td>1,1712</td>
<td>1,1595</td>
<td>1,2092</td>
<td>1,9309</td>
<td></td>
</tr>
<tr>
<td>EPDS 6 weeks</td>
<td>0,9637</td>
<td>0,4724</td>
<td>0,8428</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of gestation</td>
<td>1,001</td>
<td>1,003</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1,0131</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>0,995</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p- value < 0,1 borderline significant

**p- value <0,05 significant

### 4. Discussion

The results of his sub-study of the UPPSAT study shows no statistically significant differences in the concentrations of zinc, magnesium or calcium levels at delivery among women reporting depressive symptoms at some point during the first 6 months postpartum and controls. When looking into specific time-points postpartum, women reporting depressive symptoms at 6 weeks postpartum had higher zinc levels at delivery than respective controls. This difference is mostly brought about by two individuals who scored high in the EPDS 6 weeks postpartum and also had very high zinc levels at delivery, presumably after consumption of vitamin supplements. When accounting for other variables associated with postpartum depression the results become statistically not significant.
To our knowledge this is the first study trying to investigate the association between levels of zinc, magnesium and calcium at delivery and the subsequent risk for the development of postpartum depression. The association between zinc levels and postpartum depression status has been investigated in one other study, which showed low zinc levels among subjects with ongoing postpartum depression[42]. This study had nevertheless a different design, with a cut off-score of 9 and above in EPDS, which was answered at 3 and 30 days after delivery. The blood samples were also taken at 3 and 30 days after delivery, all at the same time of the day, thus controlling for fluctuations during the day.

The monoamine hypothesis of depression describes that a deficiency of monoamines such as serotonin might be the cause of major depression. New studies reveal that inflammation may be part of the process and that accepted antidepressants beyond their effects on monoamines also affect the state of inflammation[46]. The development of inflammatory processes has in experiments on rats shown that inflammation leads to an accumulation of zinc in different body compartments including the inflamed area[47]. As a result of this accumulation blood levels of zinc fall and may lead to hypozincemia. This could explain why earlier studies have shown that people with an ongoing major depression are more likely to have lower levels of zinc in the blood than non depressed individuals.

Inflammation, with the associated excretion of prostaglandins, is one of the established factors that leads to the start of the delivery process. When the delivering women arrive at the delivery ward, this inflammatory process is ongoing, and may have already affected zinc levels.

Estrogen is a hormone involved the menstrual cycle. Its levels rise during pregnancy, men after delivery, all women experience a great fall in estrogen levels. A sensitivity to this fall of estrogen is suggested to be the reason why some women develope PPD and some do not[9]. One study showed that zinc levels fluctuate during the menstrual cycle with high levels during ovulation and low levels at the time of menstruation. [48], correlating with the fluctuations of estrogen. It is plausible to speculate that estrogen affects the association between zinc and risk for postpartum depression, as there are inter-individual variations in how estrogen levels zinc levels interact, especially during pregnancy and the early puerperium. In further studies, it would be useful to control for estrogen levels.

Among the strengths of the UPPSAT study are its longitudinal, population based design including a large number of delivering women and the fact that depressive symptoms were assessed at three times postpartum. Limitations include possible sub-optimal blood sampling technique and storage for the specific analyses, as well as the fact that blood sampling was performed during the delivery process, at different times of the day and with some women
having eaten while others not. Zinc, magnesium and calcium levels are fluctuating, both by time of days as well as by food intake. Zinc levels, for example, decrease after a meal[49]. Blood sampling at the same times postpartum as the assessment of the depressive symptoms was performed would have been optional, but was unfortunately impossible due to administrative reasons.

In conclusion, the results of this study indicate that higher levels of zinc at the start of delivery are associated with a greater risk of developing depressive symptoms 6 weeks after delivery. The association is not statistically significant once potential confounders are controlled for. Because zinc is affected by many variables such as inflammation, hormonal differences and food intake, it may be too sensitive to act as a marker of the risk of developing postpartum depression. More research, with studies having strict criteria for the time of blood sampling and storage are needed to investigate the association between zinc, inflammation, hormonal levels and postpartum depression.
References


