



# Is there a connection between fecal and milk microbiota composition and function and perinatal depression? Rationale for future studies

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### Is there a connection between fecal and milk microbiota composition and function and perinatal depression? Rationale for future studies

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#### Abstract

**Introduction:** Coping with perinatal depression in healthcare systems worldwide has been so far more or less insufficient and there is a huge need of implementing new prevention and treatment options.

**Methods:** Literature review has been done to assess state of current knowledge on microbiome changes in perinatal period and form potential clinical implementation of these information.

**Results:** Intestinal microbiota can influence central nervous system functions and this relation seems bidirectional. The diversity of gut microbiota has emerged to play a significant role in the occurrence of mood and anxiety disorders, but this relationship is poorly understood in perinatal period. Studies have shown a reduced phylogenetic diversity and species richness of gut microbiota in depressed pregnant women, and a significant association between antibiotic exposure during the peripartum period and development of depressive symptoms. Even though breast milk is the fundamental source of microbes colonizing the infant's gut, there is very little known about possible human milk microbiota changes in depressed women. Our microbiome may be modulated by numerous circumstances, especially diet but no current microbiome-specific dietary recommendations exist.

**Conclusions:** Future research in the relationship between the gut microbiota, diet and PND holds tremendous potential to be integrated in clinical practice. The impact of breast milk microbiota on infant development and health could have important implications for early-life prevention of chronic conditions. Given that bacterial functions are conserved across taxonomic groups, incorporating microbial function biomarkers may be more productive than a purely taxonomic approach to understanding the microbiome in diseases.

**Keywords:** Perinatal depression; Microbiota; Diet; Pregnancy; Breastfeeding

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## Introduction

Coping with perinatal depression (PND) in healthcare systems worldwide has been so far more or less insufficient and a few areas in the field need particular attention. First and foremost, there is a huge need of implementing new prevention and treatment options for patients with PND as it can be fatal for mothers and lack of treatment of maternal depression may actually be the most harmful effect for infants [1]. PND is associated with disturbed mother-child bonding, neonatal complications such as premature birth, poor infant attachment, poor quality mother-child interactions, early childhood cognitive, emotional, motor and neural functioning developmental delays [2].

## Perinatal depression definition and needs

Several questions have to be considered in the research area of PND. To start with, there are same doubts regarding definition. In DSM-5 the diagnosis of major depressive disorder (MDD) in perinatal period utilizes the onset specifier “with peripartum onset” which is defined as the most recent episode occurring during pregnancy or in the four weeks after delivery [3]. However, according to Postpartum Support International (PSI) suffering often occurs during the first year following delivery [4]. In line with the above it was underlined that in clinical practice and research women with a depressive disorder onset within 12 months of birth are mostly classified as having „MDD, with postpartum onset” [5]. Additionally, there are clear data that peak time of new onset depression in the perinatal period is rather 2–3 months after delivery than 4 weeks [6]. Further, PSI supports a mentioned above specifier addition also to the mixed depression and anxiety disorder and obsessive-compulsive disorder as many postpartum women present with them [4]. Concurrently, a recent systematic review [7] found anxiety to be one of the strongest comorbidities with antenatal

depression. That is why future research should rather concentrate not only on depressive but also anxiety symptoms and in this paper, the term PND encompasses depression with/without anxiety symptoms that occur during pregnancy as well as in the first year postpartum.

Such defined PND affects an estimated 7% to 25% of women and there is a general agreement that the rates of MDD during the perinatal period range from 10 to 15% [8]. Approximately half of “postpartum” major depressive episodes (MDE) actually have onset in pregnancy [9], thus there is a huge need to screen as early as possible for PND as a prompt intervention can protect the well-being of the mother, baby and entire family. Importantly, existing treatment options are insufficient. Firstly, there is a huge problem with psychotherapy availability [10]. Secondly, the data regarding efficacy of antidepressants in pregnancy and long-term effects for the child is not clear [11]. And thirdly, despite the fact that antidepressants are mostly safe during lactation, their efficacy and acceptability in that period is not good enough [12].

Prevention, next to treatment, is another key component of handling PND. However, existing knowledge on the etiology of PND is incomplete what limits prophylaxis of this disorder. As stress and poor diet quality are some of the known risk factors of PND [7], and the diversity of the gut microbiota has emerged to play an important role in the occurrence of mood and anxiety disorders [13], it comes to mind that microbiota changes may play a role in the etiopathogenesis of PND.

## Microbiota in mental health problems

When it comes to microbiota, the gastrointestinal tract contains the densest and the best-known microbial community that plays critical roles in the function and development of several physiological processes [14] thus being

the most commonly studied in the context of health and diseases. Human milk microbiota is, however, much less known than gut one. As milk microbiota demonstrates a high degree of inter-individual variability affected mainly by maternal factors [15] and the bacteria found in the infant gut most resemble the bacteria from their own mother [16], studying mother's milk microbiota in disease may add useful knowledge to preserve offspring's health. All the more that following a dose of microbes at birth, breast milk is the next fundamental source of microbes colonizing the infant's gut [17]. On that account, it is absolutely worth to study not only gut but also milk microbiota in PND.

Up to date, the relationship between microbiome and mood is poorly understood in perinatal period. The research in the field is more complex as a shift of maternal intestinal microbial composition takes place across physiological pregnancy [18]. However, it was found that pregnant women reporting higher depressive symptoms had reduced phylogenetic diversity and species richness of the intestinal microbiota and there was an increase in the dominant *Faecalibacterium* in this group of patients [19]. Additionally, a significant association between antibiotic exposure during the peripartum period, and development of depressive symptoms up to 2 months after delivery was demonstrated [20]. The relationship between microbiota and PND was also indirectly confirmed in a human randomized control trial of the probiotic *Lactobacillus rhamnosus* HN001 influence on depressive and anxiety symptoms in pregnancy (Probiotics in Pregnancy Study; [21]). Regrettably, there is very little known about possible human milk microbiota changes in depressed women in first year postpartum. Since breastfeeding is the preferred mode of feeding an infant [22], the above question seems to be an interesting area for future research. Furthermore, the lactation period may provide a new target for devising novel tools to human milk dysbiosis and thereby reduce the

risk of noncommunicable diseases, including mental health problems in offspring.

Alas, most studies on microbiome have identified bacterial population shifts, not providing any functional insights into these communities. Results from to date gut microbiota studies have demonstrated that microbial ecosystems are more conserved at functional than at taxonomic level, suggesting that some species might interchange in terms of functional attributes. Thus, function and metabolites may be better biomarkers for health-disease states than microbiota composition [23]. To sum up, there is a need to study not only composition but also function of microbiota in PND. It is worth considering incorporating short chain fatty acids (SCFAs) level analysis to assess microbiota function in future studies. The suggestion has been made upon the fact that SCFAs are the most representative metabolites of bacterial fiber anaerobic fermentation [24]. Interestingly, a depletion of the most common SCFAs, butyrate, acetate and propionate, was reported in MDD patients [25], and administration of them was shown to alleviate symptoms of depression in mice [26]. However, results supporting the antidepressant potential of SCFAs are not yet consistent enough to be translated into medical practice.

## Conclusions

Considering that maternal health plays a key role in the development of microbiota as well as in the neurodevelopment of a child [27], characterizing the composition and function of gut and milk microbiota during pregnancy and lactation seems to be an important step in developing microbiota modulating interventions in humans. To recapitulate, future research in the relationship between the intestinal and milk microbiota, diet and PND holds tremendous potential to be integrated in clinical practice to improve screening, diagnosis, prevention, and treatment (diet, pre-

or probiotics). Thus, the aim of future studies may be to evaluate the depression and anxiety symptoms in pregnant and postpartum women concurrently with the fecal and breast milk microflora composition and SCFAs level as a source of functional assessment.

Based on the above, my long-term research objectives are to improve our knowledge about the gut and milk microbiota changes during perinatal period in relation to depression and anxiety and to widen a range of possible prophylaxis and treatment options for PND with regard to both women and children. Future directions may include studying the joint effects of the perinatal microbiota changes and depression on the infant microbiota.

Altogether, these data confirm that the whole range of circumstances needs to be considered in perinatal care; and further, that depressive and anxiety symptoms in perinatal period demand interdisciplinary approach. What is the role of microbiota in PND etiology? May changes of microbiota be biomarkers of PND? Is there a place for dietary interventions in women within perinatal period?

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