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PROLACTIN AND HOSTILITY IN HOSPITALISED PATIENT AND HEALTHY WOMAN: A SYSTEMATIC REVIEW

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ABSTRACT
These maternal adaptations are the result of dynamic changes in key hormones during pregnancy and lactation, which act on neural circuits in the brain. Lactogenic hormones (for example, prolactin and its pregnancy-specific homolog, placental lactogen) are significant regulators of these processes, with receptors located in key brain areas controlling emotional behaviors and maternal reactions. Prolactin (PRL) receptors are most typically found in the hypothalamus, where females have the highest amounts of binding. It has been proven beyond doubt that the hypothalamus has a role in the control of aggressive behavior in humans. This notion is particularly plausible for women. However, some research suggests that there is no link between PRL levels and levels of rage or aggression. This could be due, at least in part, to the fact that the participants in the several research were of different sorts, as discussed in the following section. PRL is enhanced not only after giving birth, but also as a result of other occurrences. Increased PRL levels have been associated to a variety of factors, including but not limited to pregnancy, primary hyperthyroidism, medications, pituitary tumor, stress, anxiety, and pain. According to studies, hospitalized patients had greater prolactin levels than healthy people. Stress, depression, anxiety, and other mood disorders are all linked to high prolactin levels.

Keyword: *Breastfeeding; Hostility; Maternal; Prolactin*

INTRODUCTION

The transition to motherhood necessitates significant physiological and behavioral changes to promote the proper growth of kids while sustaining maternal health.[1] These maternal adaptations are caused by dynamic variations in important hormones during pregnancy and breastfeeding, which operate on neural circuits in the brain. Lactogenic hormones (e.g., prolactin and its pregnancy-specific homolog, placental lactogen) are crucial regulators of these processes, with receptors situated in critical brain areas mediating emotional behaviors and maternal reactions.[2]

Prolactin (PRL) receptors are most commonly found in the hypothalamus, which is also where the highest levels of binding occur in females. It has been demonstrated beyond a reasonable doubt that hypothalamus has a role in the regulation of aggressive behavior in humans.[3] Therefore, it is possible that PRL could be connected with aggressive behavior, particularly in females around the time of delivery when PRL levels are naturally at their maximum.[4]

This theory is especially probable for women. However, the results of some investigations suggest that there is no connection between PRL levels and levels of anger or violence. This might be attributable, at least in part, to the fact that the different studies had different types of participants, as will be covered in the following section. Not only is PRL high after giving birth, but it is also elevated as a result of other events. A number of causes, including but not limited to pregnancy, primary hyperthyroidism, medicines, pituitary tumor, stress, anxiety, and pain, have been linked to increased PRL levels.[5,6]

PRL levels are typically one-third higher in women than in males. It's possible that up to 10% of the population has PRL levels that are higher above the typical range. In addition, PRL fulfills various roles in the body in addition to those associated with lactation. For instance, PRL influences immunological function, reproductive behavior, the amount of sleep one gets, and the body's response to stress. According to the findings of certain studies, PRL is connected to both aggressive behavior in animals and hostile behavior in humans.[7]

It has been hypothesized that this association is caused by an adaptive mechanism referred to as "maternal aggression." The high levels of PRL that are normally observed in female mammals shortly after giving birth promote behavior in the mother that is protective of the newborn.[7] This article investigate the prolactin and hostility in hospitalised patient and healty woman.

METHODS

Protocol

The Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 criteria were adhered to throughout the course of this investigation. The things on this list served as the foundation for the regulations.

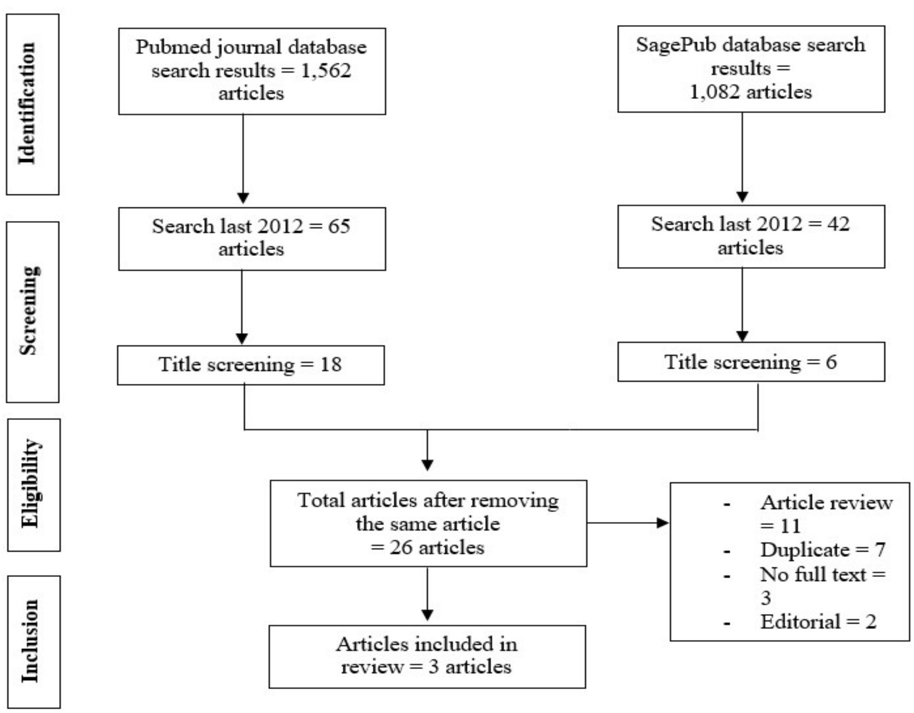

Figure 1. Article search flowchart

Eligibility Criteria

This systematic review was developed to assess literature on “prolactin”, “hostility”, “hospitalised patient” and "healty woman". These are the subjects that were thoroughly covered in the study under consideration. The following conditions must be met in order for your work to be taken into consideration: 1) In order to be accepted, articles must be written in English. 2) In order to be considered, the articles had to have been published after 2017, but before this systematic review was created. The following types of textual entries will not be considered for inclusion in the anthology: 1) Editorial letters, 2) submissions without a Digital Object Identifier (DOI), and 3) article reviews and submissions equivalent to those previously published in the journal.

Search Strategy

The search for studies to be included in the systematic review was carried out from December, 17nd 2022 using the PubMed and SagePub databases by inputting the words: "prolactin", "hostility", "hospitalised patient" and "healty woman". *("prolactin"[MeSH Terms] OR "prolactin"[All Fields] OR "prolactins"[All Fields] OR "prolactin s"[All Fields] OR "prolactine"[All Fields] OR "prolactinic"[All Fields]) AND ("hostile"[All Fields] OR "hostiles"[All Fields] OR "hostility"[MeSH Terms] OR "hostility"[All Fields] OR "hostilities"[All Fields]) AND ("hospital s"[All Fields] OR "hospitalisation"[All Fields] OR "hospitalization"[MeSH Terms] OR "hospitalization"[All Fields] OR "hospitalised"[All Fields] OR "hospitalising"[All Fields] OR "hospitality"[All Fields] OR "hospitalisations"[All Fields] OR "hospitalizations"[All Fields] OR "hospitalize"[All Fields] OR "hospitalized"[All Fields] OR "hospitalizing"[All Fields] OR "hospitals"[MeSH Terms] OR "hospitals"[All Fields] OR "hospital"[All Fields]) AND ("patient s"[All Fields] OR "patients"[MeSH Terms] OR "patients"[All Fields] OR "patient"[All Fields] OR "patients s"[All Fields]) AND "healty"[All Fields] AND ("womans"[All Fields] OR "women"[MeSH Terms] OR "women"[All Fields] OR "woman"[All Fields] OR "women s"[All Fields] OR "womens"[All Fields])* is used as search keywords.

Data retrieval

Following the completion of a literature review and an analysis of the titles and abstracts of previously published research, the author of the study revised the criteria for inclusion and exclusion in the study. The revised criteria are included in the additional materials that were provided with the study. This was done so that the breadth of the problem could be reduced, and so that it could be determined which elements required additional examination.

Following a review of other research that were conducted in a similar manner and published before, the author arrived at this verdict. During the process of creating the systematic review, it was decided that in order for a study to be considered for inclusion, it must satisfy all of the criteria that were established. This meant that we would only take into consideration research concepts that were capable of meeting each and every one of the standards. This was done in order to ensure that the evaluation would be as comprehensive as was humanly possible.

The goal of this activity was to collect information about each individual study, such as its title, author, publication date, place of the study's origin, research study design, and research components. It is possible to acquire data of this kind. The pieces of information listed below are just examples of those that could be gathered: You have a number of options available to you regarding the method in which this information is displayed to you, based on your preferences.

Quality Assessment and Data Synthesis

The authors did their own independent evaluations of a subset of the research that was presented in the article titles and abstracts before making a decision on which papers should be studied. Then, the full texts of the studies that meet the inclusion criteria for the systematic review will be examined to determine which articles will be included in the review. This will be done so that the review may be as comprehensive as possible. This is done as an answer to the question, "Which studies are eligible for consideration in the review?"

RESULT

First study showed that women with lower prolactin had non-significantly elevated scores on two different anger measures, as well as one measure that measured trait temper. When comparing those with the highest and lowest 20% of prolactin levels, those with lower prolactin levels had non-significantly higher scores on trait temper and outward expression of anger, whereas those with higher prolactin levels had non-significantly lower scores on control of anger. These findings, despite the fact that they are not substantial, go against what was discovered in past research on this subject.[8]

Second study showed plasma prolactin was greater in individuals with MDD compared to controls (8.79 ng/mL against 7.03 ng/mL, respectively; $F = 4.528$, $p = 0.035$), as well as among females compared to men (9.14 ng/mL versus 6.31 ng/mL; $F = 9.157$, $p = 0.003$). Prolactin was found to have a correlation with a number of psychological symptoms, such as anxiety, aggression, and somatization, as well as with heart rate; however, this correlation did not exist with any other biometric measurements.[9]

Herceg, *et al* (2020)[10] showed 74.79% of patients (n=89) were found to have hyperprolactinemia, while the group that did not have hyperprolactinemia comprised 25.21% of the sample. There was a statistically significant difference in the negative subscale scores of the PANSS (p=0.0011), positive subscale scores of the PANNS (p=0.0043), general subscale scores of the PANSS (p=0.0226), and total scores of the PANNS (p=0.0003) when plasma prolactin levels and clinical features were compared between the groups.

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Result
Barry, 2014[8]	UK	Cross sectional	66 woman	High-prolactin women were not more hostile. After Bonferroni adjustment, women with lower prolactin had non-significantly higher state anger and trait temper scores. Lower prolactin levels were associated with higher trait temper, outward manifestation of anger, and control of anger scores. These non-significant findings contradict previous studies on this topic. Discussing future research and patient treatment.
Elgellaie, 2021[9]	Australia	Cross-sectional	120 woman	Plasma prolactin was greater in MDD patients than controls (8.79 ± 5.16 and 7.03 ± 4.78 ng/mL, respectively; F = 4.528, p = 0.035) and in females than males (9.14 ± 5.57 and 6.31 ± 3.70, respectively; F = 9.157, p = 0.003). Prolactin was associated with heart rate, anxiety, aggression, and somatization, but not other biometric variables.
Herceg, 2020[10]	Croatia	Cross-sectional	119 woman	74.79% of patients (n=89) were found to have hyperprolactinemia, while the group that did not have hyperprolactinemia comprised 25.21% of the sample. There was a statistically significant difference in the negative subscale scores of the PANSS (p=0.0011), positive subscale scores of the PANNS (p=0.0043), general subscale scores of the PANSS (p=0.0226), and total scores of the PANNS (p=0.0003) when plasma prolactin levels and clinical features were compared between the groups.

DISCUSSION

The acidophilic cells (lactotrophs) of the anterior pituitary gland are responsible for the production of prolactin, a polypeptide hormone that is inhibited in a tonic manner by dopamine in the hypothalamus. Prolactin's primary function is to stimulate the growth of the mammary gland and the production of milk while a woman is pregnant or nursing. However, prolactin has been shown to impact more than 300 other physiological processes. Notably, prolactin plays a fundamental part in the regulation of the stress response as well as the adaptability to stress.[3,11]

In addition to the brain, a vast variety of tissues located throughout the rest of the body also express PRL. Lactogens, which have a molecular weight of 23 kilodaltons, are too big to pass across the blood-brain barrier and exert central activities without the help of a transporter. The levels of prolactin in the cerebrospinal fluid mirror variations in the amount of prolactin that is circulating in the periphery of the body. Prolactin is brought into the brain from the periphery by means of a carrier-mediated transport pathway that can become saturated.[12,13]

Prolactin transport was once believed to be dependent on PRL expression inside the choroid plexus of the brain's ventricular system. However, new research have shown that prolactin transport does not rely on the PRL, but rather on a transport molecule that has not yet been discovered. Epithelial cells in the choroid plexus are thought to be responsible for the production of prolactin and its subsequent release into the cerebrospinal fluid, in addition to the actions of lactogens that are obtained from the periphery of the body and that take place in the brain.[14]

The PRL belongs to the class 1 cytokine receptor superfamily and is made up of the prolactin-binding extracellular domain, a 24 amino acid long transmembrane domain, and an intracellular domain. Additionally, the PRL is a member of the superfamily of cytokine receptors. However, the receptor is connected with the Janus kinase 2 (JAK2) kinase, despite the fact that it does not have any intrinsic tyrosine kinase activity.[15]

The binding of prolactin to the extracellular domain of the receptor causes dimerization of the receptor and activation of JAK2. This, in turn, sets off a signaling cascade that results in the phosphorylation of signal transducer and activator of transcription 5 (pSTAT5) and its subsequent translocation to the nucleus, where it has the ability to have targeted effects on gene transcription. Both the STAT5a and STAT5b isoforms, which are identical to one another, are frequently co-expressed in many types of tissues.[15]

Although STAT5a is the primary mediator of prolactin receptor signaling in some tissues, such as the mammary gland, STAT5b is essential for prolactin action in the hypothalamus of the brain, which is where PRL is extensively expressed. The immunostaining for pSTAT5 can detect phosphorylation of both STAT5 isoforms. This technique has been used extensively to demonstrate prolactin-induced activity in multiple brain regions, including those known to regulate maternal behaviors. In order to detect prolactin-induced activation in the brain, immunostaining for pSTAT5 can detect phosphorylation of both STAT5 isoforms.[16,17]

The period of time referred to as motherhood is accompanied by significant alterations in both a woman's body and her behavior, which eventually contribute to the healthy growth of her kids. At least in part, the activities of prolactin have been related to these behaviors, and the actions in question take place on the MPOA and PVN. It is interesting to note that Prlr signaling is also elevated in numerous other areas of the maternal brain, such as the MeA, which are known to be crucial for controlling elements of maternal behavior; however, it is unknown what function prolactin plays in these locations.[7]

This argument is particularly plausible in the case of females. However, the findings of other studies imply that there is no connection between PRL levels and levels of anger or aggression. This is the conclusion that can be drawn from the findings. As will be discussed in the following section, this disparity could be attributed, at least in part, to the fact that the various studies used a diverse range of people. This topic will be further explored in the following paragraph. In addition to being enhanced as a result of giving birth, PRL levels can also be brought up by other life experiences. Increased PRL levels have been associated to a variety of factors, including but not limited to pregnancy, primary hyperthyroidism, medications, pituitary tumor, stress, anxiety, and pain.[5,6]

In most cases, the PRL levels of females are approximately one third higher than those of males. There is a possibility that as much as ten percent of the population has PRL levels that are significantly higher than the average range. In addition to its functions related to lactation, PRL also performs a variety of other important functions throughout the body.

For example, PRL affects how well the immune system works, how people behave when it comes to reproduction, how much sleep they get, and how their bodies react when they are stressed. PRL is linked to hostile conduct in people as well as aggressive behavior in animals, as indicated by the findings of a number of research.[7]

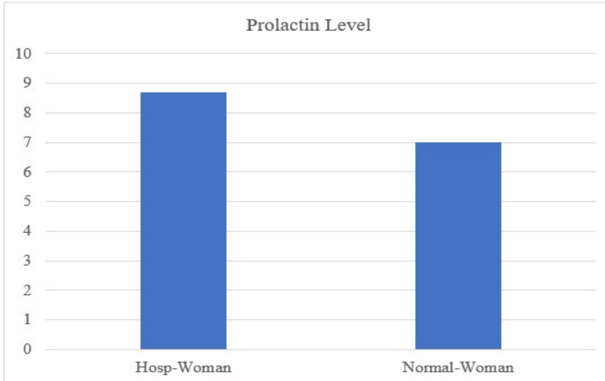

Figure 2. Prolactin level in hospitality patient and normal woman

Patients with hyperprolactineemia who took bromocriptine felt less depressed and anxious. These mood improvements may have been caused by a drop in prolactin levels and/or a return to normal gonadal function.[8,18,19] However, this study wasn't made to figure out which of these factors had the biggest effect on mood. Most people agree that depression is linked to a high level of prolactin, but the way this happens needs to be figured out. Hyperprolactinemia seems to be the most likely cause of depression on its own. But changes in the amount of gonadal steroids may cause depressive symptoms in people with hyperprolactineemia. A negative relationship between depression scores and estrogen levels in hyperprolactinemic patients suggests, as was already thought, that low estrogen levels may have an effect on the mood of hyperprolactinemic women.[19–21]

CONCLUSION

Research shows that the prolactin levels of patients in the hospital are higher than those who are normal. High prolactin levels are associated with stress, depression, anxiety, and other mood disorders.

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