

The relationship between maternal postpartum psychological state and breast milk secretory immunoglobulin A level.

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Abstract

BACKGROUND: Maternal psychological state may influence the passive transfer of immune factors (e.g., immunoglobulin) via the mother's breast milk. **OBJECTIVE:** The aim of this study was to determine whether a correlation exists between mothers' postpartum psychological state and their breast milk secretory immunoglobulin A (SIgA) levels. **STUDY DESIGN:** Eighty-one mothers who delivered at an urban general hospital were included in our analysis. Two weeks after delivery, we measured their breast milk SIgA levels and simultaneously documented their psychological state using the Profile of Mood States (POMS), General Health Questionnaire (GHQ), and State-Trait Anxiety Inventory (STAI) scales. **RESULTS:** Breast milk SIgA levels were negatively correlated with negative POMS states (tension-anxiety, depression-dejection, anger-hostility, fatigue, and confusion). A negative correlation was also observed between SIgA levels and GHQ mental health ($r = -.625$, $P = .000$), and a similar negative correlation was observed with STAI trait and state anxieties. However, no correlation existed between breast milk SIgA levels and the positive POMS state (vigor). **CONCLUSIONS:** These results indicate that the maternal psychological state may affect the immune properties of breast milk.

Key Words

Secretory immunoglobulin A; Breast milk; Postpartum depression; Immunity, Maternally-acquired

INTRODUCTION

In the postpartum period, women are known to be at an increased risk of depression (Nagaturu, 2006; Dennis et al., 2006), which in extreme cases can lead to abuse of the newborn. It is well known that the human psychological condition influences the physiological state, with stress causing an increase in blood pressure. Recent reports have also suggested that the maternal psychological state may influence the composition of her breast milk (O'Connor et al., 1999; Groer et al., 2004, 2005a, 2005b, 2007). Interestingly, maternal breastfeeding provides numerous advantages to the mother and the newborn, including optimal nutrition, increased mother-infant interaction, prevention of sudden infant death syndrome (Gordon et al., 1999), restoration of maternal health after delivery, reduced risk of ovarian tumors or breast cancer (Aguilar et al., 2010), and the transfer of immune mediators to the newborn (Walker, 2010). These immune mediators include lactoferrin, lysozymes, lactoperoxidase, leukocytes, and immunoglobulin. Interestingly, high levels of secretory immunoglobulin A (SIgA) are detected in breast milk, as well as in tears, saliva, gastrointestinal mucosa, vagina, and bronchi (Tomasi, 1970, 1976). In these locations, SIgA prevents bacterial or viral infections and their related conditions, including tetanus, pertussis, *Diplococcus pneumoniae* infection, diphtheria, *Salmonella* infection, and dysentery (Tomasi, 1976; Lamm et al., 1995).

In addition to its immunoprotective role, SIgA is also a marker for mental stress, and various studies have examined the association between SIgA and various mental states (Lowe et al., 1985; Stone et al., 1994; Nakane et al., 1997, 1998; Tsujita et al., 2000; Tanaka et al., 2002; Vivian et al., 2003; Nagai et al., 2004; Shitami et al., 2004; Pawlow et al., 2005; Phillips et al., 2006; Campisi et al., 2012). In addition, several previous studies have observed an association between the mental status of postpartum women and SIgA levels in their breast milk. These studies have reported the association between breast milk SIgA levels and anger and vigor (Groer et al., 1994), the stressed and relaxed state (O'Connor et al., 1998), positive and stressful conditions (Groer et al., 2004), anxiety based on the State-Trait Anxiety Inventory (STAI) scores (Nagai, 2000), and fatigue (Groer et al., 2005b).

Given the relationship between patients' psychological states and their immune function, it has become clear that the nervous, endocrine, and immune systems work together to maintain homeostasis. When a patient experiences stress, endogenous opioids and amines are secreted by their hypothalamus, resulting in the release of corticotropin-releasing hormone by the hypothalamic-pituitary-adrenal axis, thereby increasing their plasma cortisol levels and decreasing cytokine production. This process subsequently decreases the patient's T-cell response and reduces their overall immune response (Irwin et al., 1987). In addition, psychological stress has been reported to affect the levels of natural killer cells (Poli et al., 2013) and IgA (De Andres-Garcia et al., 2012).

Based on these data, we speculated that the maternal psychological state might directly affect early childhood growth and development via the transfer of immune mediators in breast milk (Groer et al., 2004, 2005b; Nagai et al., 2000). Therefore, the objective of the current study was to investigate the association between postpartum maternal psychological states and SIgA levels.

METHODS

Participants

We included consecutive mothers who delivered at an urban general hospital in a prefecture adjacent to Tokyo, Japan. Mothers who decided to raise the infant exclusively using breast milk were selected from this population, and maternal age, family constitution, the clinical course from pregnancy to the postpartum period, and neonatal health were recorded for each included case.

No studies have reported an association between SIgA levels and pregnancy-induced hypertension or other chronic diseases; therefore, mothers with chronic conditions were not excluded. However, mothers with gestational diabetes were excluded, as this condition is known to affect the levels of SIgA in breast milk (Smilowitz et al., 2013). In addition, liver diseases are known to affect SIgA levels (Delacroix et al., 1982); therefore, mothers with liver diseases were excluded. Mothers who used tobacco were also excluded due to the possible effect on biochemical indices (Doni et al., 2013). Finally, only mothers with a body mass index (BMI) of 18.5–25 were included, as there is a known association between SIgA and BMI (Bachour et al., 2012) .

Ethical Considerations

The study was approved by the ethical review board of the Tsukuba University Graduate School, Human Science Graduate Course (approval number 478). Prior to participation, the significance, objective, and methods for this study were explained to all participants, who were also provided with an explanatory leaflet that reiterated this information. In addition, we explained that their refusal to participate would not affect their treatment and that they had the right to withdraw their consent at any time. At this point, written informed consent was obtained from each participant.

Investigation Methods

The medical records for all participants were handled by a nursing supervisor who was blinded to the study goals and testing strategies. This supervisor extracted various anonymized patient data from the clinical records of included patients on the second or third postpartum day, including the presence or absence of disease or smoking, family status, and

occupation.

Therefore, women who met the following inclusion criteria provided by the investigators were selected by the nurse supervisor from the clinical records at the second or third postpartum day; during the breastfeeding period; the presence or absence of disease; the presence or absence of smoking habit. No additional directives regarding feeding infants with breast milk were given to the participants. Two weeks after delivery, we confirmed that mothers had continued to exclusively breastfeed, administered the psychological questionnaires, and collected samples of the mother's milk at her home.

Documented Parameters

Physical checkup

To screen for infection, which is known to influence breast milk SIgA levels, we examined the participants for symptoms of pain, cracking, inflammation, mastitis, or changes at the vulvar orifice at the time of delivery. No participants exhibited any of these symptoms.

Profile of Mood States (POMS)

POMS is a questionnaire survey that measures subjective mood states over the previous week according to six criteria: tension-anxiety (T-A), depression-dejection (D), anger-hostility (A-H), vigor (V), fatigue (F), and confusion (C). This standardized questionnaire was originally developed by McNair et al. (1971), and was translated into Japanese by Yokoyama et al. (1990). The survey consists of 65 items (each scored on a scale of 0 to 4 points) that are used to evaluate several symptoms of “maternity blues” and postnatal depression. Higher scores indicate that the subject is experiencing stronger feelings.

General Health Questionnaire (GHQ)

The GHQ was developed by Goldberg to evaluate subjects' mental health (Goldberg 1978), and is considered effective for detecting and evaluating the magnitude of stress and neurological symptoms. The Japanese version was translated by Nakagawa et al. (1985), and is widely used in Japan. The GHQ scale comprises 28 items that are related to “physical symptoms,” “anxiety and sleeplessness,” “social life disabilities,” and “depressive tendencies.” This scale is widely used to evaluate mental status among various age groups and among postpartum women (Assarian, 2014; Grussu, 2014).

State-Trait Anxiety Inventory (STAI)

The STAI questionnaire assesses both state and trait anxiety, and was developed in 1970 by

Spielberger (1970) to evaluate anxiety while distinguishing between an anxious state at the time of assessment and an anxious personality trait. The questionnaire is comprised of 40 items, with a cumulative score ranging from 20 to 80 points; higher scores indicate greater anxiety. This scale is effective in evaluating postpartum mothers' psychological conditions (Tendais, 2014), and was translated into Japanese by Mizuguchi et al. (1991).

Breast Milk (SIgA) Collection and Analysis

Immediately after breastfeeding, 5–10 mL of breast milk was manually collected into a polypropylene container by an experienced researcher. Samples were immediately transported (at 4°C) to a laboratory where they were stored at –30°C. The same researcher thawed the samples and centrifuged them (6,000 rpm for 15 min) using a TOMY SRX -201 centrifuge to obtain the supernatant, and SIgA levels were analyzed using an enzyme immunoassay (MBL Co., Ltd.) and a DU640 spectrophotometer (Beckmann-Coulter).

Data Analysis

The association between the mother's characteristics (e.g., age and number of pregnancies) and breast milk SIgA levels were analyzed using the t-test. To verify the validity of the analysis without separating the data from primiparous and multiparous mothers, the Mann-Whitney test was used to analyze whether there were differences in the POMS, GHQ, and STAI scores and breast milk SIgA levels based on the number of previous deliveries. Univariate analysis was used to determine the relationship between the psychological state and breast milk SIgA levels using Spearman's rank correlation coefficient test (2-tailed). The Shapiro-Wilk test was used to confirm the nonparametric distribution of our data ($P < 0.05$). SPSS version 17 for Windows was used for statistical analysis, and the significance level was set at 5%.

RESULTS

Among the 101 women who were invited to participate, 81 (80.1%; 40 primiparae, 41 multigravidae) agreed to participate in this study, and their characteristics are listed in Table 1. The average maternal age was 32.7 ± 4.45 years, and 72 subjects underwent a vaginal delivery (88.9%), while 9 underwent cesarean sections (11.1%). There was no significant difference in the mode of delivery, bleeding, or neonatal birth weight between the primiparous and multigravid women, although the multigravid women had significantly longer labor times.

The relationship between breast milk SIgA levels and the mother's age and number of pregnancies

The subjects were divided into two groups: those who were younger or older than the mean age (32 years). However, there was no significant difference between the SIgA levels in mothers who were ≥ 32 years old (1599.2 ± 660.9 $\mu\text{g/ml}$) and those in mothers < 32 years old (1783.1 ± 707.3 $\mu\text{g/ml}$) ($P = 0.228$). In addition, no significant difference was observed in the breast milk SIgA levels when primiparous women (1772.1 ± 628.8 $\mu\text{g/ml}$) were compared to multigravid women (1614.2 ± 741.9 $\mu\text{g/ml}$) ($P = 0.301$).

The relationship between breast milk SIgA levels and psychological scores

The POMS, STAI, and GHQ scores, as well as SIgA levels, are listed in Table 3. Although we separately analyzed the POMS items (which measures both positive and negative mood states), no significant differences were observed when the primiparae and multigravid women were compared. Therefore, we concluded that there was no significant relationship between the psychological scores and the number of pregnancies.

A weak negative correlation was observed between the breast milk SIgA levels and all negative POMS states (T-A, D, A-H, F, and C). However, no correlation was observed between the breast milk SIgA levels and the positive POMS state (V). A strong negative correlation was observed between the GHQ score and the breast milk SIgA levels ($r = -0.625$, $P = 0.000$), while a weak negative correlation was observed between the breast milk SIgA levels and the STAI state anxiety score ($r = -0.334$, $P = 0.004$) and the STAI trait anxiety score ($r = -0.430$, $P = 0.000$) (Table 4).

DISCUSSION

Questionnaire Scores

Although the questionnaires that we used have been translated into Japanese, the validity of the translated tools has previously been established. Although no previous study has reported mean STAI state or trait anxiety scores during the second postpartum week, the mean trait anxiety scores (39.6 ± 9.6) have been reported during the first puerperal month (Sato, 2006), and these were similar to the scores that we observed in our study. According to Matsuoka et al. (2001), the mean maternal POMS scores during puerperal days 3–10 were as follows: T-A = 11.1 ± 7.13 , D = 4.6 ± 7.30 , A-H = 2.0 ± 3.8 , V = 14.2 ± 7.16 , F = 6.3 ± 4.26 , and C = 4.3 ± 3.82 . However, as they did not report data for the second puerperal week, their scores cannot be accurately compared to the scores obtained in our current sample. Nevertheless, a comparison of mean POMS scores indicated that the mothers in our study had slightly lower T-A and V scores, as well as higher A-H, F, and C scores. Among the general Japanese population, the mean subscale scores for Japanese women are as follows: T-A = 7.1, D = 4.5,

A-H = 5.0, V = 8.7, F = 7.6, and C = 5.6 (Yokoyama et al. 1994). Postpartum women are thought to more psychologically stressed, with strongly negative states that are combined with high vigor scores.

Interestingly, the mean GHQ score for Japanese women in the general population is 3.1 ± 3.1 (Nakagawa, 1985). According to Yoshida et al. (2003), the mean GHQ score 1 year after birth is 6.7 ± 5.5 , which is marginally greater than the mean score in our study (6.1 ± 4.3), although both scores are noticeably greater than the mean score in the general female Japanese population. Unfortunately, no studies have evaluated GHQ scores in the 2 weeks postpartum; thus, systematic comparisons to our data cannot be made. The characteristics of our subjects cannot be determined, although we can infer that their psychological states were more negative compared to those that are experienced by approximately one-half of the general female Japanese population. In previous studies, it has been reported that the duration of labor (≥ 30 h) and bleeding during parturition (≥ 800 mL) increases the fatigue experienced by women in the postpartum period. However, the duration of labor (498.2 ± 448.9 min) and bleeding during parturition (390.1 ± 252.3 mL) that our subjects experienced were within the normal ranges. Therefore, it appears that these factors had a minimal effect on our subjects' fatigue, and that our data are representative of puerperal women. However, differences in external factors (e.g., the availability of a childcare support system) may complicate the extrapolation of our data.

The relationship between breast milk SIgA levels and psychological scores

Interestingly, we observed that breast milk SIgA levels were negatively correlated with various negative POMS states (T-A, D, A-H, F, and C), although no correlation was observed with the positive (V) state. This result suggests that breast milk SIgA levels are more strongly influenced by negative maternal psychological conditions compared to positive conditions. This conclusion is consistent with the results of Groer (2004), who surveyed mothers 4–6 weeks after birth and observed a positive correlation between breast milk SIgA levels and the POMS A-H score. In addition, Nagai (2000) found that lower breast milk SIgA levels were correlated with anxiety among mothers 4 days after delivery, and Groer (2005b) has stated that maternal fatigue is associated with a decrease in breast milk SIgA levels. However, unlike Groer, we observed a negative correlation between feelings of anger and SIgA levels. Interestingly, it is known that women in the postpartum period encounter several factors that affect their psychological state (Nezu 1996, Kabeyama *et al.* 1985, Sato *et al.* 2003); therefore, a complex combination of various different psychological factors may account for our divergent results. It is also possible that a response to a positive POMS state may be more difficult to detect, compared to that induced by a negative POMS state.

Breast milk SIgA levels were also negatively correlated with the STAI trait and state

anxiety scores. This result confirms the report by Nagai (2000), who also suggested that higher maternal anxiety leads to lower breast milk SIgA levels. In addition, we also observed a strong negative correlation between breast milk SIgA levels and GHQ scores, which would support the assumption that a negative maternal psychological condition results in lower breast milk SIgA levels. This association between breast milk SIgA levels and the GHQ score was more significant compared to the association with the negative POMS states. This difference may be related to the fact that the POMS and STAI scales express moods or feelings, whereas the GHQ scale expresses the level of the subject's general mental health, and is also used as an inventory to screen for neurosis. Therefore, GHQ measures stronger negative emotions compared to the POMS or STAI, and these strong negative emotions might be more strongly correlated with breast milk SIgA levels.

Stress reaction and SIgA

SIgA is a key component of the body's immune system, preventing bacterial and viral infections by neutralizing the toxins and enzymes that they produce; therefore, an increase in SIgA levels indicates that the immune system is reacting to a physical stress. However, recent reports have also indicated that changes in SIgA levels are also associated with psychological stress (Martinez et al., 2011; Campos et al., 2013). However, the SIgA measurements that were obtained in most of these studies were based on serum and saliva specimens, and few studies have examined breast milk SIgA levels as an indicator of psychological stress. One exception is the study by Kawano et al. (2009), who reported that similar decreases are observed in saliva and breast milk SIgA levels, which might indicate that breast milk SIgA levels could be used to evaluate the mother's psychological state.

However, aside from psychological stress, other factors can also affect the immune system. These factors include age and body mass index (Bachour et al., 2012), smoking (Waszkiewicz et al., 2012; Doni et al., 2013), exercise (Groer et al., 2009; Walsh et al., 2011), chronic diseases (e.g., gestational diabetes) (Smilowitz et al., 2013), and infectious diseases (Fetherston et al., 2006). Therefore, these factors must be duly considered if SIgA levels are used to evaluate stress, and further studies are needed in this area.

Our results support the concept that a healthy and enjoyable postpartum (as experienced by the mother) results in increased passive immunity being transmitted to the infant through the mother's breast milk. Conversely, SIgA in breast milk may also be used to evaluate postpartum mothers' psychological states and stresses, thereby providing a useful tool for investigating postpartum depression.

Limitations

Several limitations must be considered when interpreting our results. First, all our subjects

were of a single nationality (Japanese) and were recruited from a single medical facility. Second, we excluded subjects with allergic or immunological diseases. Third, we were unable to compare our data regarding the mental state of women in the second postpartum week, given the lack of previous research in this period. Therefore, unidentified confounders may have affected our analysis.

CONCLUSION

In conclusion, we assessed the maternal postpartum psychological state using the POMS, GHQ, and STAI scales, while simultaneously evaluating the mothers' breast milk SIgA levels. Our results indicate that the maternal postpartum psychological state affects breast milk SIgA levels, which are an important component of the passive immunity that is passed from the mother to the newborn. This data provides evidence that negative maternal feelings may reduce the transmission of immune factors to the newborn infant via the mother's breast milk. Therefore, it is important to provide mothers with an environment that supports their psychological health during the postpartum period.

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Table1. Population characteristics of the participants

		Total (n=81) No. (%)	Primiparae (n=40,49.4%) No. (%)	Multigravidae (n=41,50.6%) No. (%)	P Value
Characteristics					
Age(Mean±SD)		32.7±4.45	31.2±4.2	34.1±4.3	n.s
Type of delivery	Vaginal	72(88.9)	36(90.0)	36(87.8)	} n.s
	Cesarean	9(11.1)	4(10.0)	5(12.2)	
Delively situation(Mean±SD)	Delivery time(minutes)	498.2±448.9	661.5±536.38	329.9±245.1	0.000
	Bleeding(ml)	390.1±252.3	406.0±282.39	384.1±226.5	} n.s
	Neonatal birth weight(g)	2990.0±385.8	2929.2±303.9	3051.7±444.5	

Analysis for Age and Type of Delivery were conducted with a t-test.

Table2. Relationship between the mother's background -age, delivery experience- and breast milk SIgA levels

		breast milk SIgA levels	P value
Age	Aged 32 and over	1599.2 ±660.9	n.s
	Less than 32 years old	1783.1 ±707.3	
delivery experience	Primiparae	1772.1 ±628.8	n.s
	Multigravidae	1614.2 ±741.9	
Student t-test			

Table3. POMS, GHQ, and STAI score and breast milk SIgA levels and Comparison of a primipara and a multiparous woman

	POMS					GHQ		STAI		Mother's milk
	tension-Anxiety	Depression-Dejection	Anger-Hostility	Vigor	Fatigue	Confusion		Trait anxiety	State anxiety	SIgA (μg/ml)
Primiparae	9.8±4.7	5.3±6.3	5.6±5.4	11.7±5.4	9.3±5.7	7.2±3.5	6.4±4.4	39.2±9.3	41.0±10.2	1772.8±628.8
Multigravidae	7.7±6.4	5.7±7.0	6.8±6.2	11.1±6.5	7.3±5.4	6.0±3.6	5.7±4.2	38.8±9.7	39.3±10.1	1669.7±735.6
Total	8.6±5.7	5.5±6.7	6.2±5.8	11.4±6.0	8.3±5.6	6.6±3.6	6.1±4.3	39.0±9.4	40.1±10.3	1691.6±689.5

Mann-Whitney test

$P \leq 0.01$

Table4. Relationship between breast milk SIgA levels and POMS, GHQ and STAI

breast milk SIgA levels		
POMS	tension-Anxiety	-0.327*
	Depression-Dejection	-0.356*
	Anger-Hostility	-0.392*
	Vigor	0.231
	Fatigue	-0.352*
	Confusion	-0.394**
GHQ		-0.625**
STAI	Trait anxiety	-0.430*
	State anxiety	-0.334*
Spearman's rank correlation		*P<0.05 **P<0.01