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Circadian Variation of Zinc, Copper, Selenium, and Bromine in Human Milk

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Abstract

Introduction: Human milk undergoes dynamic modifications throughout lactation to optimally meet the dietary and immunological requirements of the growing infant, with variations of its composition also occurring throughout the day. Circadian variation in some bioactive components helps the development of the biological clock by passing on chronobiological information from mother to infant. This study aimed to identify the circadian variation of zinc, copper, selenium, and bromine in human milk during the postpartum period. **Methods:** Human milk samples were collected from a postpartum mother who was taking zinc and copper supplements. Milk samples were analysed using inductively coupled plasma mass spectrometry. Data on zinc, copper, selenium, and bromine concentrations were analysed using Microsoft Excel 2021 and reported descriptively to determine circadian variation. **Results:** The concentration of all four trace elements declined throughout the six months postpartum period with consistent fluctuations for bromine. Zinc, copper, and bromine possess the most similar circadian variation throughout the day with a 'V' shaped pattern, but selenium showed inconsistent circadian pattern over the first six months postpartum. The 'V' shaped pattern generally disappeared in the fourth, fifth, and sixth months. **Conclusion:** Circadian rhythms for zinc, copper, selenium, and bromine varied during the first six months postpartum. This may indicate a functional circadian clock regulating infants' biological development. Future studies should explore the factors influencing the development of fully functional circadian rhythmicity in infants.

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Introduction

Human milk contains nutritional components, antibodies, and hormones as important bioactive components for infant development. These components exhibit circadian patterns which aid the transfer of information from the mother to her newborn during the day and night. This aspect of knowledge of human milk has been referred to as "chrononutrition." The importance of chrononutrition of human milk includes the physiological impact on the establishment of regulation of the biological clock in infants. The variation between the time of expression and feeding may affect how well an infant's circadian clock and sleep homeostasis develop when they are breastfed (Italianer et al., 2020). The circadian rhythm of infants concerning metabolic clocks influences feeding behaviour such as time-restricted feeding as well as energy distribution throughout the day, which could also be therapeutic for metabolism including insulin responsiveness (Flanagan et al., 2021). The circadian cue from the mother is transferred to infants and involves hormones such as glucocorticoids and melatonin which play vital roles in metabolism, immunity, and sleep regulation (Caba-Flores et al., 2022). The homeostasis of glucocorticoids in stress response for example, particularly by cortisol exposure is linked with the development of autoimmune disease (Ramamoorthy & Cidlowski, 2016). Other components including fat, amino acids, and endogenous cannabinoids also exhibit diurnal variation (Caba-Flores et al., 2022). The optimal exposure to specific quality and quantity of nutritive and non-nutritive components in human milk corresponding to the time of the day may have biological significance in human biological clock coordination. Nevertheless, its long-term impact from early developmental exposure is unclear.

The transition from the womb to birth involves changes in the circadian rhythms of infants since the foetus in the womb is exposed to the physiological and metabolic rhythms of the mother. It was suggested that maternal milk after birth substitutes the exposure to nutrition and other bioactive components to regulate the circadian rhythms. For example, the optimal neurodevelopment in infants is partly attributable to the sensitivity to breast milk melatonin which highlights the role and impact of breastfeeding (Häusler et al., 2024). Breastfeeding practices are always superior to formula feeding despite the low breastfeeding rate worldwide. Globally, the costs of not breastfeeding are significant including 595,379 childhood deaths annually, and 98,243 maternal comorbidities and mortality from chronic diseases with the total estimated global economic losses between US$257 billion and US$341 billion (Walters, Phan, & Mathisen, 2019). In adults, it was suggested that chrononutrition promotes cardiometabolic health, but many knowledge gaps remain to be addressed in developing approaches for chronic disease prevention (Raji et al., 2024). Therefore, there was limited knowledge about chrononutrition in adults and infants which requires further research.

There are concerns about the adverse external circadian signals including mistimed exposure to hormones in breast milk which cause misalignment of temporal sequence which leads to susceptibility to poor infant development. The maturation of the biological clock in humans contributes to the development of synchronicity of cognitive and physical function in response to the demands of the environment (Wong et al., 2022). It is measured by patterns of hormone secretion and sleep pattern and the ability to adjust to external time cues, of which this aspect is poorly understood in the first year of life (Wong et al., 2022). The presence of trace elements in human milk as part of the optimal nutrition in infants particularly in the first six months after birth indicates the important requirement for healthy development. Nevertheless, the variation in its concentration is less understood. Zinc, copper, and selenium have been reported to vary in human milk over the postpartum period (Li et al., 2016). Bromine plays an important role in supporting the formation of the cell membrane, and its quantities in human milk are comparable to zinc but its variation over the postpartum period is unclear (McCall et al., 2014; Mohd-Taufek et al., 2016; Mohd-Taufek et al., 2024). Little is known regarding the circadian variation of these minerals and any changes over the postpartum period. This study aimed to investigate the circadian pattern of zinc, copper, selenium, and bromine in human milk throughout six months postpartum.

Materials and methods

In the present study, a total of 196 milk samples were collected from one postpartum mother as a case study. She consented to the study and collected the samples at her convenience throughout the six months postpartum, from June until November 2023. The samples were expressed using breast pumps and kept in breast milk plastic packaging, labelled with the date and time of the day, then stored in the freezer at -21˚C. The volume of milk samples in each pack was between 90mL to 150mL. The number of samples for each date selected varied depending on the availability, and only the days with samples from three sessions of morning, evening, and night were included. All milk samples were labelled once collected at different times of the day and were divided into three time intervals which were 4:00 to 11:59, 12:00 to 19:59, and 20:00 to 3:59. The time range was selected for a similar range of samples between each interval for morning, afternoon, and night sessions. The days with incomplete samples or labels, or with missing at least one session were excluded. The day postpartum included were randomly selected to represent each week of the month. A data collection form was completed by the participant for demographic information.

The analyses of milk samples have been conducted following the protocol described in the previously published article (Mohd Taufek et al., 2024). The details regarding instruments, procedure, and analysis were described. The developed and validated method has been used to analyse and report zinc, copper, selenium, and bromine concentration in human milk, and was analysed using the acid digestion method by inductively coupled plasma mass spectrometry at the Institute of Oceanography and Environment (INOS), University Malaysia Terengganu.

Results were analysed for descriptive analysis using Microsoft Excel version 2021, and reported as a case study. This study received ethics approval from the International Islamic University Malaysia (IIUM) Research Ethics Committee (IREC) (ID No.: IREC 2021-053).

Results and discussion

The participant in the case study was a healthy 39-year-old mother, who had neither medical illnesses nor chronic medications, practiced mild exercise three times a week, and took nutritional supplements of zinc and copper. Her height was 157 cm, with a weight from pre-pregnancy of 72kg, pre-delivery of 89kg, and post-delivery of 80kg. It was her first pregnancy and delivered a healthy male infant at 38 weeks of gestation via the caesarean method. She followed a normal diet per the Malaysian dietary guidelines for pregnant mothers.

A total of 196 expressed breast milk samples were collected from one participant as a case study. They were analysed and reported for zinc, copper, selenium, and bromine. As shown in Table 1, all trace elements exhibited the highest concentration in the first month compared to the later months. The mean concentration of zinc over the first six months of lactation dropped from 10,353 to 2,157 mcg/l. Generally, zinc showed the highest concentration in human milk compared to copper, selenium, and bromine. For copper, the mean concentration ranged from 309 to 999 mcg/l, which showed relatively small differences over the six months duration. The mean selenium concentration decreased gradually from 85 mcg/l to 27 mcg/l. The bromine concentration fluctuated across the six months with 1803 mcg/l in the first month and 1004 mcg/l in the sixth month.

Table 1: Concentration of Zn, Cu, Se, and Br over six months postpartum.

Trace element		Month postpartum					
		1	2	3	4	5	6
	No. of milk samples	18	55	45	26	31	21
Zn (µg/l)	mean ± SD	10353 ± 4353	3311 ± 975	3898 ± 758	2477 ± 922	2182 ± 611	2157 ± 781
	median (range)	8730 (4540-18300)	3080 (1670-6110)	3870 (1820-5280)	2590 (627-5450)	2100 (1190-3550)	2100 (1020-3580)
Cu (µg/l)	mean ± SD	999 ± 367	413 ± 126	505 ± 125	392 ± 232	309 ± 67	351 ± 131
	Median (range)	952 (482-1690)	384 (201-814)	503 (268-780)	351 (90.7-1360)	300 (184-461)	347 (152-610)
Se (µg/l)	mean ± SD	85 ± 58	27 ± 20	39 ± 21	16 ± 8	23 ± 16	27 ± 15
	Median (range)	72 (24-196)	20 (6-78)	45 (10-82)	16 (10-27)	17 (4-47)	22 (8-50)
Br (µg/l)	mean ± SD	1803 ± 640	764 ± 196	1075 ± 231	864 ± 228	666 ± 164	1004 ± 360
	Median (range)	1800 (926-2970)	716 (444-1350)	1070 (507-1640	847 (362-1360)	667 (363-1000)	999 (462-1880)

The time of the day influenced the concentration of zinc, copper, selenium, and bromine in human milk as shown in Figures 1, 2, 3, and 4. Diurnal variations were noticeable for all elements particularly in the first three months postpartum, indicated by the 'V' shaped pattern of the graphs. The concentration of these elements rose in the morning, dropped in the afternoon, and returned to a higher level at night. Nevertheless, the diurnal pattern was inconsistent and mostly disappeared from the fourth until the sixth month.

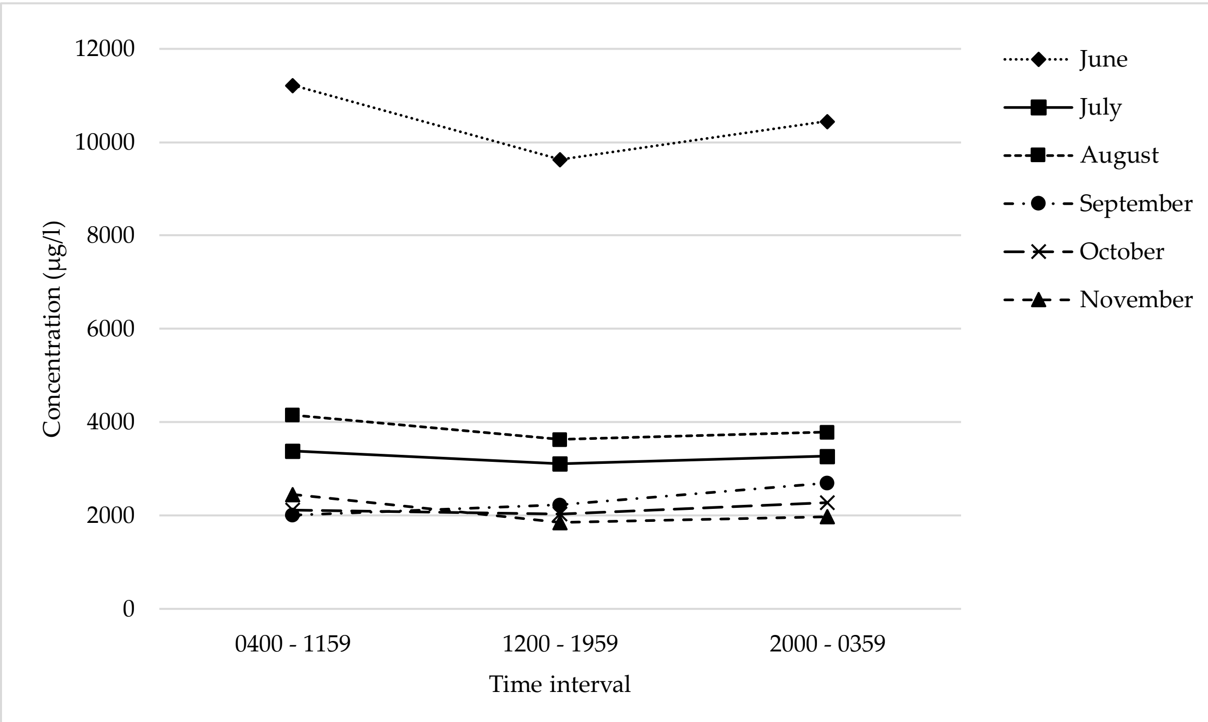

Fig. 1: Mean zinc concentration at three-time intervals during the 24 hours over six months postpartum.

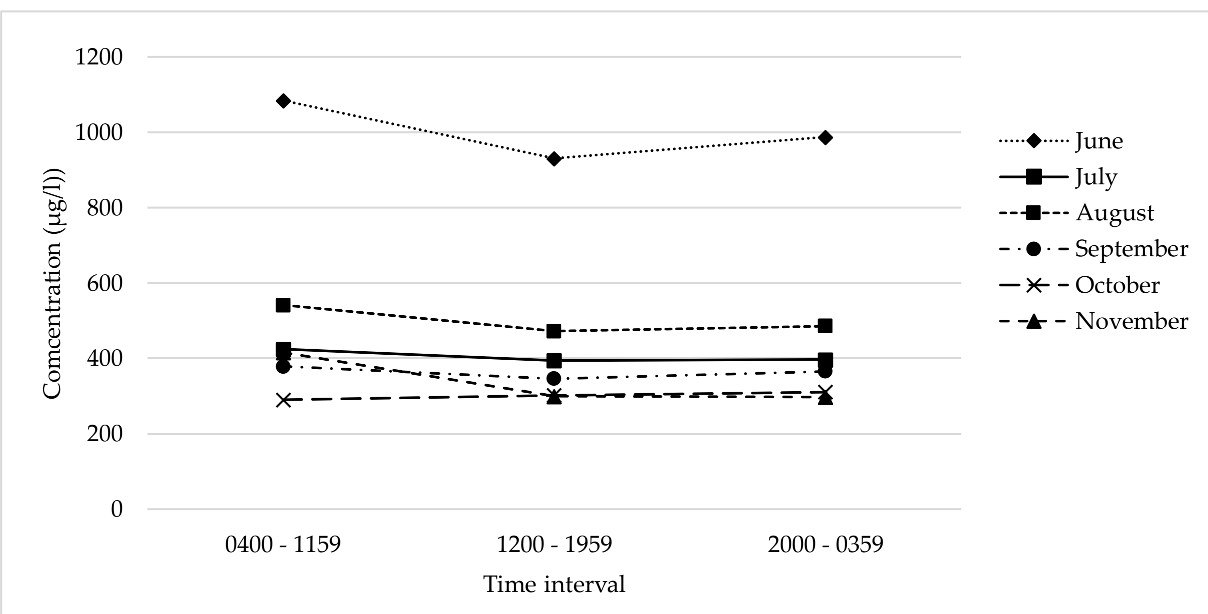

Fig. 2: Mean copper concentration at three-time intervals during the 24 hours over six months postpartum.

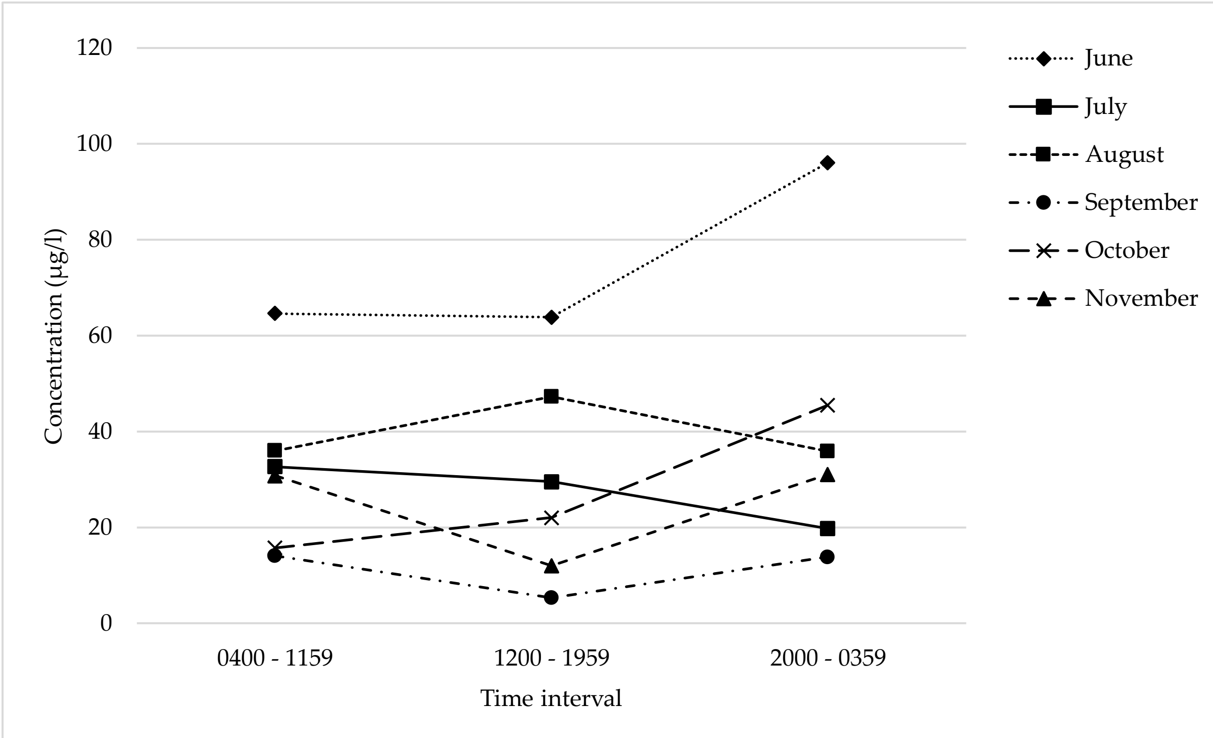

Fig. 3: Mean selenium concentration at three-time intervals during the 24 hours over six months postpartum.

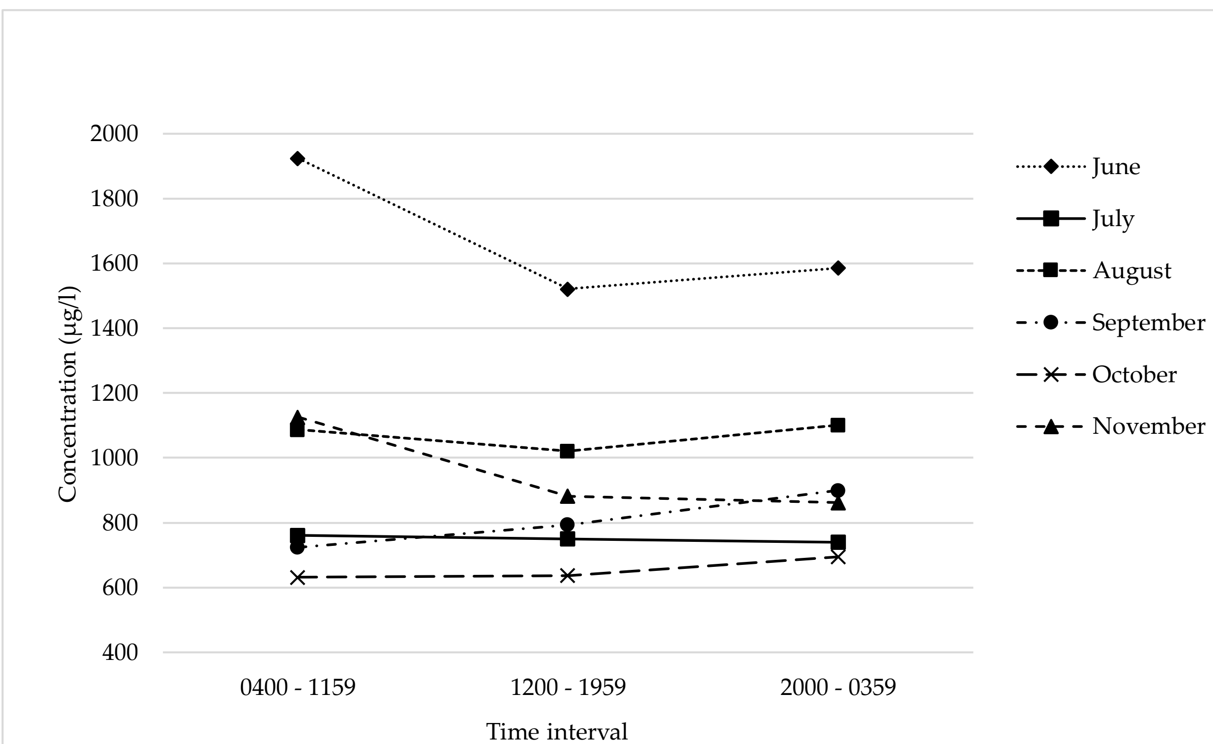

Fig. 4: Mean bromine concentration at three-time intervals during the 24 hours over six months postpartum.

The present study reported that variation of zinc, copper, selenium, and bromine from a case study exhibited a decreasing trend in concentrations over a six-month postpartum period. It has been reported worldwide that these minerals gradually decreased and fluctuated over the postpartum period (Hunt & Nielsen, 2009; Kim et al., 2012; Mohd-Taufek et al., 2017; Sabatier et al., 2019; Mandia et al., 2021). The decreased concentration could be due to the decrease in the levels of proteins including casein and whey in human milk that serve as ligands for zinc and copper (Fransson & Lönnerdal, 1983). Nevertheless, zinc has been reported to decline despite increased total protein in human milk in the second year postpartum (Perrin et al., 2017). It is unclear whether the specific protein changes are different in the first year as compared to the second year postpartum, which requires further investigation.

All minerals in the current study showed similar changes and dropped by about half of the initial concentration from the first month to the second month, then gradually decreased in later months. Zinc showed the highest concentrations in the first month postpartum ranging from 4,540 to 18,300 mcg/l. The results in the current study showed very high levels of zinc in the first month compared to other studies which reported the range of 400 to 11,900 mcg/L in term milk of 34 mothers (Sabatier et al., 2019), 900-7,800 mcg/L in preterm milk of 67 mothers (Kim et al., 2012), and 1,419-6,303 mcg/L in term milk of nine mothers (Mohd-Taufek, 2017). Copper concentration ranged from 201 to 1,690 mcg/L in the first and second months, which was higher than reported in other studies 111-926 mcg/L (Mohd-Taufek, 2017), and 130-1,000 mcg/L (Sabatier et al., 2019). This could be due to the supplements containing zinc and copper taken by the participant in our study.

Selenium despite showing the highest level in the first month (24-196 mcg/L) dropped to 6-28 mcg/L (second month) and then fluctuated consistently across the lactation month. Nevertheless, the concentration was relatively higher than those reported previously in the literature 10-22 mcg/L (first month) and 7-14 mcg/L (second month) (Mohd-Taufek et al., 2017), 6-24 (first and second month) (Sabatier et al., 2019). Selenium was found to be lower than recommended in the milk of mothers who delivered low birth-weight infants (Mandia et al., 2021). Nevertheless, our case study involved full-term milk. In Malaysia, the recommended intake of selenium in infants aged 0-5 months is 6 µg/day (Ministry of Health Malaysia, 2017). Our findings showed bromine concentrations of 926-2970 mcg/l (first month) and dropped to about half in the sixth month (462-1880 mcg/l). It demonstrated that relatively stable bromine concentrations are maintained throughout the six months of lactation. These concentrations are comparable to the previous studies which reported concentrations ranging from 834 to 1443 mcg/l of 16 donor milk collected at random lactation stages (Mohd-Taufek et al., 2016), and of 661-1026 mcg/l (first month) and 868-1387 mcg/l (second and third month) of preterm milk (Mohd-Taufek, 2017). Limited data are available regarding the biological importance of bromine in humans, but our findings indicated that bromine concentration is relatively high in human milk and is comparable to other minerals. It exhibits circadian rhythm which could further be investigated for its role in early infant growth and development. Bromine has been reported to be abundant in humans and is required for cell metabolism (McCall et al., 2014). The updated nutrient composition data of human milk is still greatly needed as it is paramount for the management of infant feeding, assessment of infant and maternal nutritional and health needs, and as a reference for infant formula development (Mandiá et al., 2021). Future studies should explore the specific role of bromine and its reference range to prevent deficiency and toxicity.

The circadian changes were present in daily concentrations of zinc, copper, selenium, and bromine in human milk. Zinc concentration demonstrated the 'V' shaped pattern with higher concentration in the morning and at night for the first, second, and third months postpartum (Figure 1). Copper showed a similar trend in concentration in the first three months of postpartum compared to the later months (Figure 2). A previous study reported that diurnal variation demonstrated no significant differences between the concentrations of zinc and copper in the morning and at night (Silvestre et al., 2000). For selenium, the 'V' shaped pattern was noticeable in the first, fourth, and sixth months, despite there being only slight differences in its concentrations (Figure 3). Bromine showed a slightly 'V' shaped pattern in the first and third month postpartum with no obvious pattern for other months (Figure 4). For selenium and bromine, the inconsistent circadian pattern may suggest that the time of day may not be a major factor in influencing biological rhythm in infants. Overall, we speculate that beyond three months postpartum, the time of day may not be considered as the major factor for zinc, copper, selenium, and bromine in human milk to regulate the circadian pattern physiologically due to a better maturation of the infant body system. These aspects may be related to the knowledge of the respective biological roles such as nutritional and immunological as part of chronological development in humans.

Trace elements may influence circadian nutrition adaptation, although the mechanisms are not clearly understood, unlike melatonin and other hormones which affect sleep patterns and metabolism during the day and night. Other bioactive components that exhibited significant circadian variation include tryptophan, fats, triacylglycerol, cholesterol, iron, cortisol, and cortisone which may also influence their respective role in the biological clock (Italianer et al., 2020). Trace elements which are also involved in the metabolisms of cells and tissues may affect the growth and development of infants, particularly during the first year of life. Zinc deficiency is associated with abnormalities in humoral and cell-mediated immunity that increase the risk of infection and liver disease (Tuerk & Fazel, 2009). Copper is involved in all organs and systems, such as the hematologic and neurologic systems, cardiovascular, cutaneous, and immune systems, and its deficiencies are more common than previously reported (Altarelli et al., 2019). Selenium is associated with cardiovascular disease, of which selenoproteins are involved in oxidative stress, redox regulation, thyroid hormone metabolism, calcium flux, and microRNA regulation (Shimada, Alfulaij & Seale, 2021). Bromine plays a crucial role in brain metabolism and tissue development (Canavese et al., 2006; McCall et al., 2014). The mechanisms of these elements involved in the circadian rhythm of physiological and biological processes during the day and night are poorly understood. We propose that to a certain extent, these elements could influence the regulation of circadian-related activities including body temperature, hormonal secretion, sleep-wake cycle, food intake, mood, and cognitive and physical performance in infants (Montaruli et al., 2021; Wong et al., 2022). For example, this aspect could lead to dietary approaches for addressing persistent cardiometabolic health inequities by designing and implementing flexible and feasible interventions in real-world settings (Raji et al., 2024). The knowledge regarding the chrononutrition dimension on health will be the key to quantifying the true impact of the infant's temporal eating pattern on health.

Our findings supported the suggestion that human milk is optimally formulated to communicate the time of the day with infants through chrononutrition. However, modern practices of pumped and stored milk (e.g. chilled or frozen) may cause infants to ingest mistimed milk, affecting circadian rhythm development (Hahn-Holbrook et al., 2019). It is important to explore whether the expressed breast milk practice may influence sleep problems and physiological adaptation of infants to the environment as well as any adverse health outcomes resulting from disruption of circadian-matching milk. Similarly, infants receiving formula milk may be affected differently by the absence of chrononutrition in formula as compared to human milk mistimed milk. Nonetheless, the essential roles of bioactive components in human milk, although pumped and stored are superior to formula for healthy development of infants. Little is known about circadian-match stored milk, of different weeks and months postpartum which meets the needs of infants' development.

Alterations in circadian rhythm can lead to chronic pathologies and are influenced by a complex phenotype. The concept of chronotypes has been raised based on the bi-directional influences of the rest-activity circadian rhythm and sleep-wake cycle in chronic pathologies and disorders based on the interindividual differences in adults (e.g. morning, neither, and evening types) (Montaruli et al., 2021). However, the maturation in circadian rhythm in adults is different and adjustments could be easier to regulate the physiological processes compared to infants. Early life dysregulation of circadian rhythm has been linked to adult-onset cardiovascular disease, musculoskeletal issues, predisposition to diabetes, and mood disorders (Wong et al., 2022). Sleep disruption during infancy and childhood is common and causes psychosocial and behavioural issues. It has been proposed that the circadian clocks occur at the molecular level, with a set of clock genes organised in a system of interlocked transcriptional–translational feedback loops that coordinate physiological functions throughout the day that impact the cardiovascular system, energy metabolism, immunity, hormone secretion, reproduction and other systems (Pilorz, Helfrich-Förster & Oster, 2018). Therefore, further research is required to understand the association of early human development of circadian rhythm, the role of breastfeeding, and chrononutrition.

Our findings are not applicable to be generalised in the population since the limitation is only one participant was included in a case study. A bigger number of participants is recommended to reflect the population data on these elements and explore whether concentration is correlated with certain health parameters. The participant in our study was taking zinc and copper supplements during lactation, which may have altered the concentrations; thus, the data must be interpreted carefully. However, our findings can act as a reference for future studies to identify the importance of circadian changes in trace element concentration and how they reflect the health outcomes in the Malaysian population. It also serves as the basis to investigate the factors regulating trace elements circadian pattern, and the differences of pattern occurring after three months of lactation.

Conclusion

The trace elements zinc, copper, selenium, and bromine concentration in human milk exhibited a 'V' shaped pattern indicating the presence of functional circadian rhythm, particularly in the first three months postpartum. The gradual decrease in zinc, copper, selenium, and bromine concentration in the first six months postpartum may influence the circadian variation of these minerals. The role of chrononutrition of these minerals in the early lactation stages requires further investigation to confirm its developmental importance in infants.

Authors contributions

NHMT, ASMS & JB designed the study and collected samples and data. HNHM, AZA, and ARFN analysed the samples and data. All authors wrote and reviewed the manuscript.

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Ethical approval statement (if applicable)

This study received ethics approval from the International Islamic University Malaysia (IIUM) Research Ethics Committee (IREC) (ID No.: IREC 2021-053).

Informed consent statement (If applicable)

Informed consent was obtained from the participant included in the study.

Conflict of interest

NHMT, HNHM, ARFN, AZA, ASMS & JB declare that there is no competing interest in this research.

Declaration of generative AI and AI-assisted technologies in the writing process

Not applicable.

References

Altarelli, M., Ben-Hamouda, N., Schneider, A., & Berger, M. M. (2019). Copper deficiency: causes, manifestations, and treatment. Nutrition in Clinical Practice, 34(4), 504-513.

Caba-Flores, M. D., Ramos-Ligonio, A., Camacho-Morales, A., Martínez-Valenzuela, C., Viveros-Contreras, R., & Caba, M. (2022). Breast Milk and the Importance of Chrononutrition. Frontiers in Nutrition, 9, 867507. https://doi.org/10.3389/fnut.2022.867507

Canavese, C., De Costanzi, E., Stratta, P., & Sabbioni, E. (2006). A role for bromine deficiency in sleep disturbances of long-term dialysis patients. American Journal of Kidney Diseases, 48(6), 1018-1019.

Flanagan, A., Bechtold, D. A., Pot, G. K., & Johnston, J. D. (2021). Chrono-nutrition: From molecular and neuronal mechanisms to human epidemiology and timed feeding patterns. Journal of Neurochemistry, 157(1), 53–72. https://doi.org/10.1111/jnc.15246

Fransson, G. B., & Lönnerdal, B. O. (1983). Distribution of trace elements and minerals in human and cow's milk. Pediatric Research, 17(11), 912-915.

Hahn-Holbrook, J., Saxbe, D., Bixby, C., Steele, C., & Glynn, L. (2019). Human milk as "chrononutrition": implications for child health and development. Pediatric Research, 85(7), 936-942.

Häusler, S., Lanzinger, E., Sams, E., Fazelnia, C., Allmer, K., Binder, C., ... & Felder, T. K. (2024). Melatonin in Human Breast Milk and Its Potential Role in Circadian Entrainment: A Nod towards Chrononutrition?. Nutrients, 16(10), 1422.

Hunt, C. D., & Nielsen, F. H. (2009). Nutritional aspects of minerals in bovine and human milks. In Advanced Dairy Chemistry: Volume 3: Lactose, Water, Salts and Minor Constituents (pp. 391-456). New York, NY: Springer New York.

Italianer, M. F., Naninck, E. F., Roelants, J. A., van der Horst, G. T., Reiss, I. K., Goudoever, J. B. V., ... & Vermeulen, M. J. (2020). Circadian variation in human milk composition, a systematic review. Nutrients, 12(8), 2328.

Kim, S. Y., Park, J. H., Kim, E. A. R., & Lee-Kim, Y. C. (2012). Longitudinal study on trace mineral compositions (selenium, zinc, copper, manganese) in Korean human preterm milk. Journal of Korean Medical Science, 27(5), 532.

Li, C., Solomons, N. W., Scott, M. E., & Koski, K. G. (2016). Minerals and trace elements in human breast milk are associated with Guatemalan infant anthropometric outcomes within the first 6 months. The Journal of Nutrition, 146(10), 2067-2074.

Mandiá, N., Bermejo-Barrera, P., Herbello, P., López-Suárez, O., Fraga, J. M., Fernández-Pérez, C., & Couce, M. L. (2021). Human milk concentrations of minerals, essential and toxic trace elements and association with selective medical, social, demographic and environmental factors. Nutrients, 13(6), 1885.

McCall, A. S., Cummings, C. F., Bhave, G., Vanacore, R., Page-McCaw, A., & Hudson, B. G. (2014). Bromine is an essential trace element for assembly of collagen IV scaffolds in tissue development and architecture. Cell, 157(6), 1380-1392.

Ministry of Health Malaysia (2017). Recommended Nutritional Intake for Malaysia. https://hq.moh.gov.my/nutrition/wp-content/uploads/2023/12/FA-Buku-RNI.pdf

Mohd Taufek, N.H. (2017). Essential trace element analysis of human breast milk. The University of Queensland. https://doi.org/10.14264/uql.2017.477

Mohd-Taufek, N., Cartwright, D., Davies, M., Hewavitharana, A.K., Koorts, P., Mcconachy, H., Shaw, P.N., Sumner, R., & Whitfield, K. (2016). The effect of pasteurization on trace elements in donor breast milk. J Perinatol, 36, 897–900. https://doi.org/10.1038/jp.2016.88

Mohd Taufek, N. H., Mohmad Sabere, A. S., Mohamad Jamahari, U. S., Amran, N. B., Fata Nahas, A. R., & Bidai, J. (2024). Variation of bromine concentration as an essential trace element in human milk over lactation stages. Journal of Pharmacy, 4(1), 68–73. https://doi.org/10.31436/jop.v4i1.257

Montaruli, A., Castelli, L., Mulè, A., Scurati, R., Esposito, F., Galasso, L., & Roveda, E. (2021). Biological rhythm and chronotype: new perspectives in health. Biomolecules, 11(4), 487.

Perrin, M. T., Fogleman, A. D., Newburg, D. S., & Allen, J. C. (2017). A longitudinal study of human milk composition in the second year postpartum: implications for human milk banking. Maternal & Child Nutrition, 13(1), e12239.

Pilorz, V., Helfrich-Förster, C., & Oster, H. (2018). The role of the circadian clock system in physiology. Pflügers Archiv-European Journal of Physiology, 470, 227-239.

Raji, O. E., Kyeremah, E. B., Sears, D. D., St-Onge, M. P., & Makarem, N. (2024). Chrononutrition and Cardiometabolic Health: An Overview of Epidemiological Evidence and Key Future Research Directions. Nutrients, 16(14), 2332. https://doi.org/10.3390/nu16142332

Ramamoorthy, S., & Cidlowski, J. A. (2016). Corticosteroids: mechanisms of action in health and disease. Rheumatic Disease

Clinics, 42(1), 15-31.

Sabatier, M., Garcia-Rodenas, C. L., De Castro, C. A., Kastenmayer, P., Vigo, M., Dubascoux, S., ... & Affolter, M. (2019). Longitudinal changes of mineral concentrations in preterm and term human milk from lactating Swiss women. Nutrients, 11(8), 1855.

Shimada, B. K., Alfulaij, N., & Seale, L. A. (2021). The impact of selenium deficiency on cardiovascular function. International Journal of Molecular Sciences, 22(19), 10713.

Silvestre, M. D., Lagarda, M. J., Farré, R., Martínez-Costa, C., Brines, J., Molina, A., & Clemente, G. (2000). A study of factors that may influence the determination of copper, iron, and zinc in human milk during sampling and in sample individuals. Biological trace element research, 76, 217-227.

Tuerk, M. J., & Fazel, N. (2009). Zinc deficiency. Current Opinion in Gastroenterology, 25(2), 136-143.

Walters, D. D., Phan, L. T., & Mathisen, R. (2019). The cost of not breastfeeding: global results from a new tool. Health Policy and Planning, 34(6), 407-417.

Wong, S. D., Wright Jr, K. P., Spencer, R. L., Vetter, C., Hicks, L. M., Jenni, O. G., & LeBourgeois, M. K. (2022). Development of the circadian system in early life: maternal and environmental factors. Journal of physiological anthropology, 41(1), 22.