

# ASSOCIATION BETWEEN PRETERM BREASTMILK MELATONIN CONCENTRATION, MATERNAL NUTRITION AND PSYCHOSOCIAL FACTORS AT BIRTH (ProMote)

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## BACKGROUND

Melatonin in human milk is important for normal neurodevelopment and may contribute to better growth and development with long-term outcomes (Gombert & Codoñer-Franch, 2021). Melatonin detected in the fetus originates from the mother and the levels rise beginning at 24 weeks gestation, reaching a peak in the third trimester. During the first 3 months approximately the infant will experience a transient deficiency in melatonin, due to suboptimal melatonin production and immature circadian rhythmicity (D'Angelo, 2020). However, preterm birth leads to sudden interruption of transplacental transfer of melatonin that normally takes place during the last part of the pregnancy and provides the highest melatonin levels. Thus, preterm newborns have a delay in the rhythmic expression of melatonin with respect to full-term infants. Breastmilk is therefore the only source of melatonin for the infant, and especially the preterm neonate, during the first few months of life (Gombert & Codoñer-Franch, 2021).

Human milk melatonin likely derives from blood and the 24-hour human milk melatonin profile mimicks the melatonin levels changes in the blood. Thus, human milk melatonin productions are relatively low during daytime hours, elevating at night, and then peaks at around 03:00 (Quin et al., 2019). Melatonin concentration in human serum may increase after the consumption of melatonin containing food, or nutritional factors may modify melatonin production. In particular, in animal foods, the content of melatonin is higher in eggs and fish than in meat. In plant foods, the highest contents of melatonin is found in nuts, seeds and mushrooms are also rich in melatonin (Meng et al., 2017; Peuhkuri et al., 2012). Further, there is evidence that melatonin may regulate the mood or maternal mental health may contribute to interindividual variations in milk composition among mothers (Hausler et al., 2024; Meng et al., 2017).

On this ground, the main aim of this study is to explore the way maternal nutrition and psychosocial factors are associated with preterm breastmilk melatonin concentration.

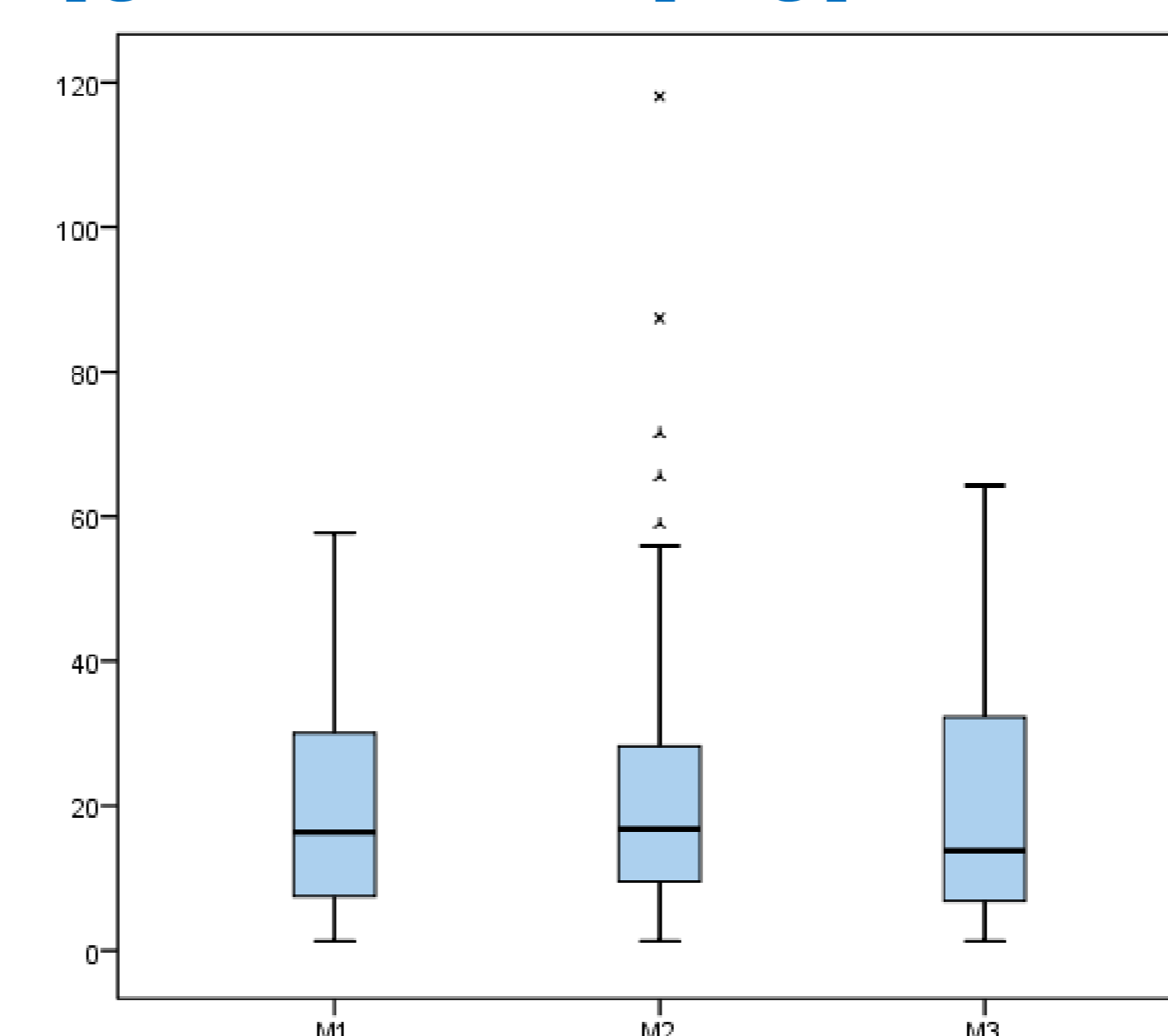
## METHOD

The study population includes 64 mothers and their preterm neonates (<37 weeks) hospitalized in the Neonatology Department / NICU of the University General Hospital of Heraklion, Crete. Mothers of preterm neonates were asked to collect 5-10 ml of nighttime breastmilk with the use of an electrical pump between 01:00-05:00 a.m. at three time points: 3rd-5th day (colostrum), 10th-14th day (transitional milk), and 20th-28th day (mature milk). The milk was collected in a sterile container and frozen immediately at -80°C until analysis. Melatonin levels were measured using an ELISA kit. Within the first 3 days after birth, the following maternal psychosocial factors were assessed: Depressive symptoms (Edinburgh Postnatal Depression Scale); Anxiety (The Spielberger State-Trait Anxiety Inventory for Adults); Family functioning (The Family Adaptability and Cohesion Evaluation Scales IV Package). Maternal nutrition according to factors that may affect levels of breastmilk melatonin were assessed.

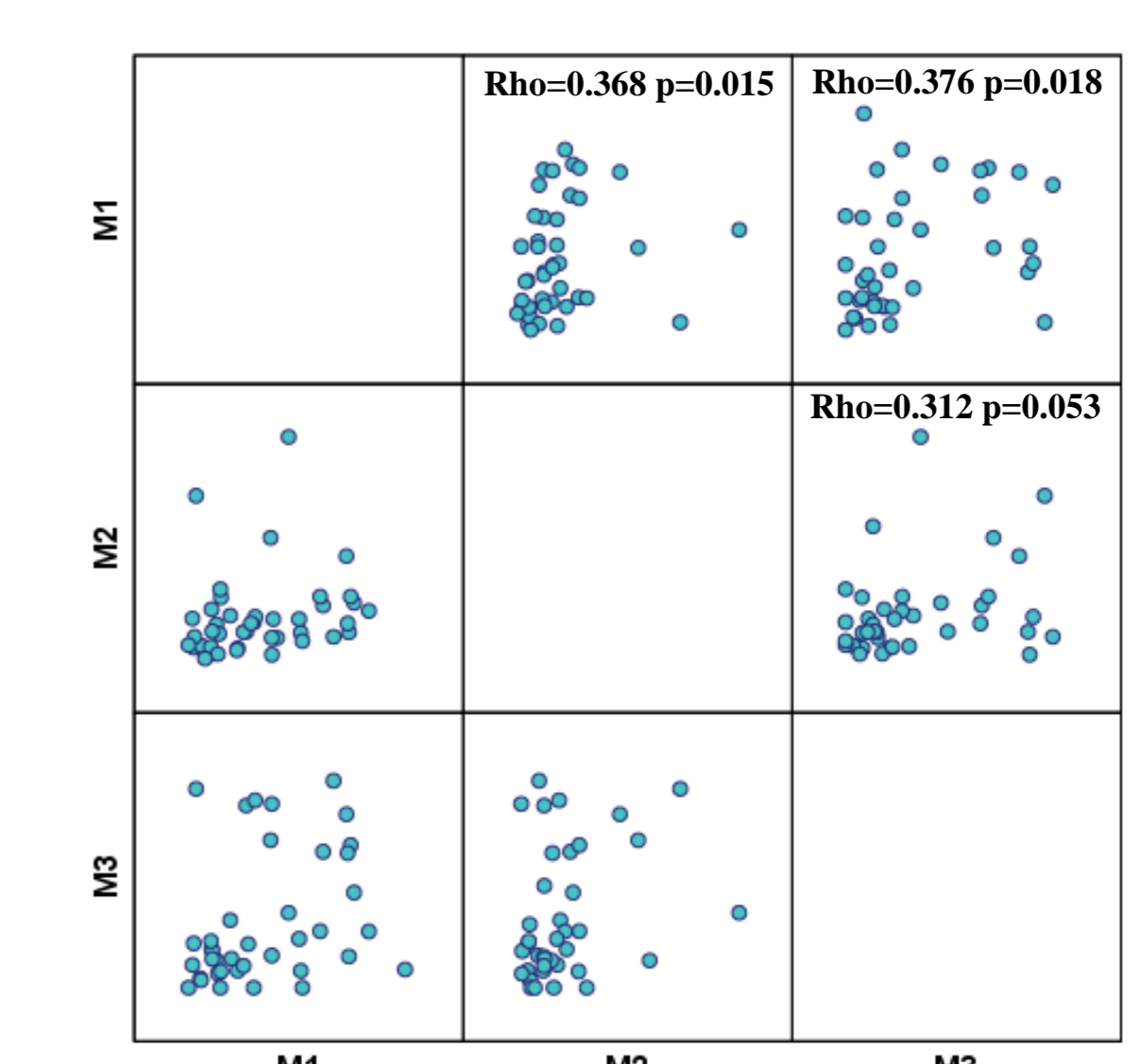
## RESULTS

In all, 64 mothers provided breast milk samples at three different postpartum time points, selected to capture the dynamic changes in breast milk composition during the transition from colostrum to mature milk: the 3rd–5th day (n=55, Mean [SD]=19.7 [14.7]), the 10th–14th day (n=47, Mean [SD]=24.3 [22.7]), and the 20th–28th day (n=42, Mean [SD]=21.5 [19.4]). Preliminary findings indicate that maternal postnatal depression and anxiety levels and melatonin in colostrum breast milk may be positively associated. Sample size restrictions and low daily consumption of selected food items led to inconclusive findings.

### Human milk melatonin concentration (pg/ml) at three sampling points.



### Correlation of melatonin concentration (pg/ml) at three sampling points.



### Parental characteristics

	Mother		Father	
	Mean	SD	Mean	SD
Age (years)	34.1	6.8	37.7	7.3
		%		%
Education				
Compulsory		5.7		21
Secondary		33.3		41
Tertiary		61		38.1
Origin				
Greek		92.6		93.8
Other		7.4		6.3
Marital status				
Married		71.4		
Other		23.2		

**Gestational Age**  
Mean (SD); 33.7 (2.2)  
**Infant sex**  
Male; 52%, Female; 48%

### Maternal diet (portions per day)

	Mean	SD
Eggs	0.3	0.4
Fish (120g)	0.1	0.1
Cereal (1 cup)	0.5	0.6
Grapes (10 berries)	0.2	0.7
Cherries (10 pcs)	0.4	1.5
Strawberries (10 pcs)	0.1	0.4
Nuts (a handful)	0.5	0.8
Tomatoes (1 pc)	0.6	0.5
Peppers (1 pc)	0.2	0.3

### Adjusted association of human milk melatonin (pg/ml) at three sampling points with maternal depression and anxiety<sup>1</sup>

	Colostrum		Transition milk		Mature milk	
	B-coeff.	95% CI	B-coeff.	95% CI	B-coeff.	95% CI
Depression	1.97	(0.47, 3.46)	-0.39	(-3.82, 3.02)	-0.55	(-3.87, 2.76)
Anxiety	0.16	(-0.34, 0.66)	0.21	(-0.94, 1.38)	-0.24	(-1.31, 0.83)

Linear regression models, adjusted for maternal age at delivery, educational level and gestational age (completed weeks)

## CONCLUSION

Although the sample size is relatively small, these findings indicate a potentially significant relationship between maternal depression/anxiety and melatonin secretion in breast milk. Higher states of postnatal depression and anxiety were significantly related to higher melatonin levels.



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