

## ORIGINAL ARTICLE

## MATERNAL SERUM HEPcidIN AND ITS IMPACT ON DIFFERENT MODES OF DELIVERY

Tabinda Najeeb, Saba Abrar, Nosheen Wasee\*, Faiza Sheikh

Department of Physiology, Baqai Medical University, Karachi, \*Karachi Medical and Dental College, Karachi, Pakistan

**Background:** Hepcidin production is affected by multiple stimuli including iron status of the body, erythropoiesis, hypoxia and inflammatory conditions. This study was conducted to assess the effect of maternal hepcidin concentration on the different modes of delivery and maternal age groups. Cord blood hepcidin was also compared with neonatal gender. **Methodology:** The present study is observational type and conducted in Baqai Medical University from Sep 2015 to Mar 2016. To carry out the study, 25 healthy full-term pregnant females were included along with the cord blood samples. Five (5) ml blood was drawn from females and infants. Serum hepcidin were measured in both mothers and cord blood by using ELISA. Kruksal Wallace test was performed to observe the difference in hepcidin levels in females with different modes of delivery and with different age groups. Difference in neonatal hepcidin on the basis of gender was analyzed by Mann Whitney U test. **Results:** There was no significant difference between the maternal hepcidin values who delivered vaginally or underwent emergency or elective caesarean sections ( $p=0.871$ ); however maternal age showed significant difference with maternal hepcidin ( $p=0.022$ ). Neonatal hepcidin value did not vary on the basis of gender ( $p=0.475$ ). **Conclusion:** Mode of delivery is independent of maternal and neonatal hepcidin levels. There were no differences gender-wise, whereas maternal age had effects on hepcidin levels of women.

**Keywords:** Hepcidin, ELISA, Caesarean sections, Modes of delivery, Kruksal Wallace test, Mann Whitney U test

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## INTRODUCTION

Hepcidin is a peptide hormone, mainly secreted from liver as a preprohormone, comprising 84 amino acids. Later, it goes 2 enzymatic cleavage, first it converts to 60–64 residue prohepcidin and then to 25 amino acid peptide hormone which is the active form.<sup>1</sup> Hepcidin controls the iron absorption from enterocytes and also its release from macrophages, spleen and hepatocytes by binding, internalizing and degrading the Ferroporin (Fpn), the only transporter of iron in mammals thus decreasing the iron levels.<sup>2,3</sup>

Hepcidin production is affected by multiple stimuli including iron status of the body, erythropoiesis, hypoxia and inflammatory conditions.<sup>4</sup> Apart from the hepatocytes, other organs also produce little amount of Hepcidin including intercalated disc area of heart, beta cells of pancreas and epithelial cells of tubules and ducts of kidneys but their significance is not known.<sup>5,6</sup>

During the course of pregnancy, maternal hepcidin gradually declines from first to third trimester which enhances the iron absorption to meet the maternal and growing neonatal demands for erythropoiesis especially in the third trimester.<sup>7</sup> Mode of delivery is found affected by hepcidin levels at the time of birth. Its levels are found highest in females who delivered vaginally as compare to other means of child birth.<sup>8</sup> The aim of to present study is to evaluate the effect of maternal hepcidin concentration on different modes of delivery in local population of Gadap Town, Karachi

and assess the age-wise comparison of maternal hepcidin at the time of birth and to observe the neonatal hepcidin levels on the basis of gender difference.

## SUBJECTS AND METHODS

This was an observational and comparative study, and the study population consisted of 25 full-term pregnant women and their healthy full-term babies. These women were admitted in Fatima Hospital, Karachi at the time of delivery and gave written consent for study. The inclusion criteria for the study were: full-term healthy pregnant women of any age, parity, and gravida without any co-morbidity. Women were excluded if they had doubleton pregnancy, assisted reproduction, stillbirth, iron deficiency anaemia or gestational diabetes.

Maternal venous blood was collected at the time of hospital admission and venous cord blood was collected just after the birth. The anthropometric measurements of mother and neonates were recorded as published previously.<sup>9</sup> The study was carried out from Sep 2015 to Mar 2016 after getting the approval from Ethics Committee of Baqai Medical University, Karachi.

Maternal and cord serum Hepcidin levels were measured for active Hepcidin 25 form by using commercially available competitive enzyme linked immunosorbent assay (ELISA) methods (Sunlong Biotech Co. Ltd., Hangzhou, Zhejiang, China).

SPSS-22 was used to analyze the data. Distribution of the data was checked by using Shapiro

Wilk test, median [interquartile range] was used as descriptive statistics because the data contained non-parametric variables. Kruksal Wallace test (an analogue of ANOVA for non-parametric variables/skewed distribution) was applied to observe the hepcidin concentration with different modes of delivery and age-wise distribution of mothers. Mann Whitney U test was used to compare means between Hepcidin levels of girls and boys, and  $p \leq 0.05$  was considered statistically significant.

## RESULTS

Hepcidin levels were measured in ng/ml. Kruskal Wallace test was used to observe the difference in mean hepcidin levels at the time of child birth with different modes of delivery, i.e., vaginal, elective and emergency C-section. Maternal Hepcidin was taken as test variable, while mode of delivery was used for group variable. There were no significant differences in hepcidin concentration among the modes of delivery ( $p=0.87$ ) (Table-1).

Hepcidin levels were compared across different age groups ranging from 17 to 40 years. Higher hepcidin levels were observed in group 2 ( $8.32 \pm 1.45$ ) and lowest levels were seen in group 3 ( $5.07 \pm 2.17$ ) having more miscarriages and multiple parities. Kruksal Wallace test showed significant results ( $p=0.022$ ) (Table-2).

Afterwards, the post-hoc test was applied that gave multiple pair-wise comparison and significant result was obtained in between group 2 and 3 with  $p=0.02$  (Figure-1).

In Table-3, neonatal hepcidin was compared in 25 newborns on the basis of gender by using Mann Whitney U test, assuming equal variance by Levene's test, the median showed statistically insignificant higher concentration in girls as compare to newborn boys ( $p=0.48$ ).

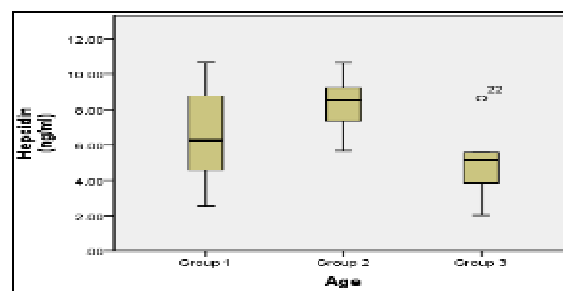
**Table-1: Hepcidin concentration in pregnant females with different modes of delivery**

Variable	Mode of Delivery	n	Mean $\pm$ SD (ng/ml)	Median [IQR] (ng/ml)	p
Maternal Hepcidin Concentration	Vaginal	18	6.88 $\pm$ 2.47	7.04 [8.62]	0.87
	Elective C-section	4	7.32 $\pm$ 1.36	7.56 [3.09]	
	Emergency C-section	3	7.08 $\pm$ 3.06	8.93 [7.25]	

**Table-2: Age-wise comparison of maternal hepcidin at the time of child birth**

Variable	Age	n	Mean $\pm$ SD (ng/ml)	Median [IQR] (ng/ml)	p
Maternal Hepcidin Concentration	Group 1	8	6.55 $\pm$ 2.77	6.27 [4.84]	0.02*
	Group 2	11	8.32 $\pm$ 1.45	8.53 [2.19]	
	Group 3	6	5.07 $\pm$ 2.17	5.15 [2.93]	

\*Significant. Ages: Group 1=17–24 years, Group 2=25–32 years, Group 3=33–40 years



Group 1: 17–24 years (n=8), Group 2: 25–32 years (n=11), Group 3: 33–40 years (n=6)

**Figure-1: Hepcidin concentration in pregnant females with different age groups**

**Table-3: Gender-wise comparison of neonatal Hepcidin concentration**

Variable	Gender	n	Mean $\pm$ SD (ng/ml)	Median [IQR]	P
Neonatal Hepcidin Concentration	Girl	8	74.51 $\pm$ 8.93	76.25 [13.63]	0.48
	Boy	17	71.69 $\pm$ 15.16	70.06 [22.49]	

## DISCUSSION

In the present study, serum hepcidin levels in full-term pregnant females were assessed to clarify the role of hepcidin in different modes of childbirth and the impact of maternal age on hepcidin concentration. Cord hepcidin levels were also evaluated to observe any effect of neonatal gender on serum hepcidin concentration of newborn. Hepcidin concentration was found insignificantly higher in elective C-section as compare to emergency or vaginal mode of delivery. These findings are in contrast with Rehu<sup>8</sup>, who have observed high hepcidin concentration in vaginally delivered group. The difference in findings could be due to the small number of observation in present study. Rehu explained that the reason of higher hepcidin levels in vaginally delivered could be due to active labour that involves inflammatory cytokines<sup>8,10</sup> as active labour is a physiological stress which enhances acute phase protein and hepcidin is one of the acute phase protein<sup>11</sup>. Gyarmati<sup>12</sup> in her studies found the highest hepcidin concentration in females who underwent elective C-section as compared to the females who underwent vaginal birth. These results are in concordance to our findings.

Hepcidin levels were found to vary in pregnant females of different age groups. The higher levels were found in age group 25–32 years of age, and lower in age group 33–40 years of age. Cao *et al*<sup>13</sup> in his study observed the hepcidin levels in young pregnant teens, aged 13–17 years and in that age group. He observed five times higher hepcidin levels in pregnant teens for normal BMI whereas Chelchowska *et al*<sup>14</sup>, reported hepcidin levels in non-smoking mothers aging from late twenties to middle thirties and found slightly higher values than ours. Basu *et al*<sup>15</sup> and Flynn *et al*<sup>16</sup> reported

the nearest range of hepcidin levels in non-anaemic and non-obese healthy mothers similar to our age group 2 respectively.

The neonatal hepcidin values differed insignificantly; girls had higher levels whereas newborn boys had lower levels of hepcidin. Young *et al*<sup>17</sup> observed somewhat lower concentration of hepcidin in neonates as compare to the present study. Hepcidin values in neonates are found to be gestational age specific. In preterm infants, its values are quite low, reflecting the need of iron in newborn, whereas in term healthy infants, Lorenz *et al*<sup>18</sup> observed higher values in uncomplicated, iron repleted newborns, indicating that neonates in our study though are not anaemic but might have decreased iron stores.

## CONCLUSION

Maternal hepcidin concentration has no effect on different modes of delivery. It does not have differences with respect to gender of neonates. Maternal age has influenced on maternal hepcidin concentration. The study may further be extended in future with bigger sample size to find the effect of maternal hepcidin on modes of birth as well as other aspects related to it.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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## Address for Correspondence

**Tabinda Najeeb**, Senior Lecturer, Department of Physiology, Baqai Medical University, 51, Deh Tor, Gadap Road, Super Highway PO Box 2407, Karachi-74600, Pakistan. **Cell:** +92-324-8083053  
**Email:** tabindanajeeb@baqai.edu.pk

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