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# Amyline Hormone, Leptin and Other Metabolic Hormones in Preterm Babies

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**Abstract:** Prematurity is a growing problem, advances in life supporting techniques have resulted in increased survival of more preterm neonates whom were expected to die before. Those preterm babies have several problems and on the top of these problems comes metabolism. Amylin is a recently discovered neuropeptide hormone from the calcitonin gene-related peptide. It is co-secreted with insulin in response to nutrient intake. Serum Leptin (the adipocyte derived hormone) shows a dramatic increase in its level after 34 wks of gestation due to rapid accumulation of fetal fat mass. Our objectives is to determine the levels of amylin, leptin and other metabolic hormones namely the cortisol and and insulin in preterm babies and to determine if there is any relationship between these hormones and adipo-insular axis or hypothalamic-adrenal axis compared to full term babies. The cord serum levels of amylin, leptin, insulin and cortisol in 30 preterm babies (gestational age of 32-36 wk) were compared to 15 full term babies (gestational age of 38-42 wK). The same serum levels (except amylin) were also rechecked on the 5th day of life only in the 30 premature babies group. The mean level of amylin in preterm babies (1.71±1.41 Pmol/L) was statistically highly significant (P<0.001) lower than that of full term babies (3.517±2.245 Pmol/L) .While the mean level of leptin hormone in the preterm group (5.937±4.15 ng/ml) was statistically higher than that of the full term babies (3.78±3.338 ng/ml) with P value of <0.044. The mean serum cortisol level in preterm group (5.366±6.24 ug/dl) was lower than that of the full term babies (15.3±9.096 ug/dl) which was highly significant statistically. The mean serum level of insulin in the preterm group (9.346±4.996 µIU) was higher than that of full term group (6.571±1.869µIU) but this was not statistically significant (P =0.099). When comparing the serum levels of leptin, cortisol and insulin in day 5 in the preterm group to the cord level of the full term group, the same relation was kept as in day 1 but all of them were statistically not significant. We conclude that the lower amylin level in preterm group is attributed to difference in blood glucose level and the lower level of cortisol in the same group is due to its correlation with gestational age indicating better response towards stress. However the lower level of leptin in full term group promotes food intake and preserves energy.

**Key words:** Amyline – Leptin – preterm babies.

## INTRODUCTION

Prematurity is defined as gestational age less than 37 weeks. Estimated incidence of prematurity is 10% of which 4% are less than 32 weeks of gestation[1].

Leptin hormone is an adipocyte derived hormone. It is involved in body weight regulation. A dramatic increase in serum leptin after 34 weeks of gestation associates the rapid accumulation of fetal fat mass during this period. It was noticed that there is decline in the level of leptin in full term neonates after delivery and this allows preservation of energy expenditure in these neonates; however, in preterm neonates, leptin level remains high[2].

Insulin is secreted by beta cells of pancreatic islands of Langerhans. It increases fat deposition and decreases lipolysis, glycogenolysis and gluconeogenesis[3]. Insulin has an indirect effect on leptin by by exerting a negative feedback on cortisol secretion[2].

Cortisol hormone is secreted from Zona Fasciculata of the adrenal cortex. It stimulates gluconeogenesis by decreasing glucose utilization, increasing protein catabolism and lipolysis[3]. It has a positive fecdback on the secretion of leptin[2].

Amylin is a recent hormone derived from the calcitonin gene related peptide. It is co-secreted with insulin from pancreatic beta cells in response to nutrient intake[4]. Amylin is a potent inhibitor of gastric motility and plays a role in controlling carbohydrate absorption by regulating the efflux from the stomach to the small bowel. In addition to this local effect, there is evidence that amylin has neuroendocrine effect influencing glycemic control, satiety and long-term energy homeostasis[5]. Amylin plays its satiating effect by direct activation of the prestema area where the

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nucleus of the solitary tract relays its effect to the higher brain structures controlling the appetite and inducing satiety. Hence the name; neuropeptide hormone[6].

**Aim of the Work:** The aim of this work is to determine the levels of Amylin, leptin and other metabolic hormones namely cortisol and insulin in preterm neonates to establish the relationship of these hormones with both adipo-insular axis and hypothalamic=adrenal axis compared to full-term neonates.

## MATERIALS AND METHODS

This study is a case-control cross-sectional which was conducted in Neonatal intensive care unit at Ain Shams University Hospital, Cairo in the period June2006 to August 2006 . Newborn babies were divided into two groups. Patient group (Group 1) comprised 30 preterm neonates (gestational age 32-36 wk). Second group was the control group (Group 2) comprised 15 full term newborn babies (gestational age 37-41 wk).

All babies were subjected to full history taking including prenatal, natal, and postnatal histories with thorough clinical examination. Routine lab tests e.g. CBC, C-reactive protein, electrolytes, random sugar, and blood culture were done to all participant newborns.

Both groups of newborns were subjected to simultaneous assessment of blood glucose level, amylin , cortisol, insulin, and leptin in cord blood; while the premature group ONLY (Group 1) were subjected to another simultaneous assessment of blood glucose level, cortisol, insulin and leptin on DAY 5 of life. Collection of blood in day 1 was done through the umbilical cord while a venipuncture under complete aseptic technique was used in day 5 to collect blood. Hormonal levels were determined using immunoassay techniques.

Statistical analysis of obtained data was carried out using SPSS version 11.5 to determine mean values with standard deviation and correlation coefficient .

## RESULTS AND DISCUSSIONS

**Results:** There was no statistical difference between both groups regarding sex distribution (in preterm group 1,there was 16 M and 14 F while in full term group 2,there was 7 M and 8 F).

As shown in Table 1, the amylin level in day 1 was statistically lower in preterm babies GROUP 1 (1.721 ± 1.41 Pmol/l) when compared to full term newborns GROUP 2 (3.517± 2.245 Pmol/l) with p value of <0.001. We found also significant correlation between amylin level in day 1 for the preterm GROUP 1 and serum glucose level being the higher the glucose level the higher the amylin level (r= 0.417 and p = 0.043) as seen in Figure 1.

**Table 1:** Shows comparison between preterm group (cases) and full term group (controls) regarding amylin level in cord blood

| Hormone | Pre-terms (cases) | Full term(Controls) |
|---|---|---|
| Mean Amylin Level Pmol/l $\overline{X}$ | -1.721(Pmol/l) | 3.517(Pmol/l) |
| Standared deviation | +/-1.410 | +/-2.245 |
| P — | <0.001 | |

(HS) P is significant if < 0.05

The insulin level of preterm babies "GROUP 1" in both days 1 (9.346± 4.996 µIU) and day 5(7.833± 2.717 µIU) was higher than in full term babies "GROUP 2" (6.571± 1.869 µIU) in day 1 but this difference was not statistically significant (Table 2). Also the difference between the two levels in days 1 and 5 among the premature GROUP 1 was not statistically significant.

The mean level of serum leptin in the premature newborns "GROUP 1" in day 1 (5.937± 4.15 ng/ml) was statistically higher than the mean serum leptin level in the full term newborns "GROUP 2" in day 1 (3.78± 3.338 ng/ml) with p value of < 0.044 as shown in Table 3. Although the serum leptin level in day 5 for the premature newborns "GROUP 1" (4.753 ± 3.776 ng/ml) is still higher than that of full term newborns " GROUP 2" mentioned above but this difference was not statistically significant with p value of < 0.448. The decrease in serum leptin level from day 1 to day 5 in the preterm GROUP 1 was not statistically significant (p = 0.102).

The study also showed that the higher the leptin level the lower the glucose level in both days 1 and 5 in the premature GROUP 1 and in day 1 for the full term GROUP 2 but this correlation was not statistically significant.

Our study also showed that the higher the body weight among the full term newborns "GROUP 2" the lower is the serum leptin level and this correlation was statistically significant (r= - 0.2 and p = 0.026) as seen in Table 4 and Figure 2 . The same correlation was found in the premature GROUP 1 when correlating leptin level in day 1 to the birth weight of these babies (Figure 3).

The mean level of cortisol of the premature newborns "GROUP 1" in day 1 (5.366 ± 3.24 µg/dl) was lower than that of the full term GROUP 2 in day 1 (15.3 ± 9.096 µg/dl) and this difference was highly

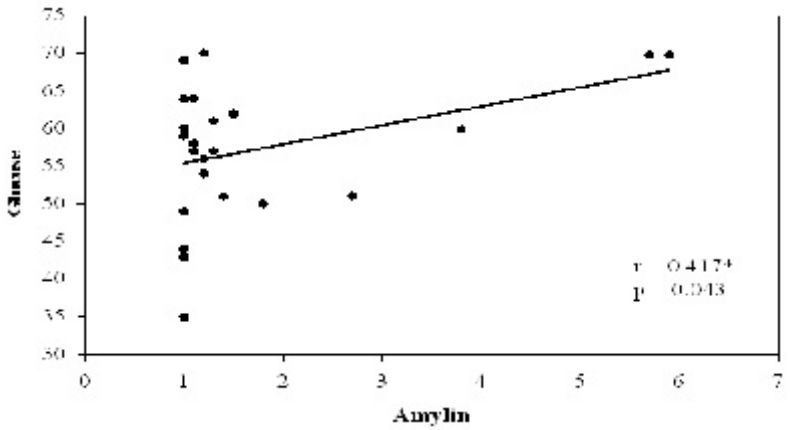


**Fig. 1:** Scattered curve showing the correlation between amylin hormone level and glucose level in Preterm neonates

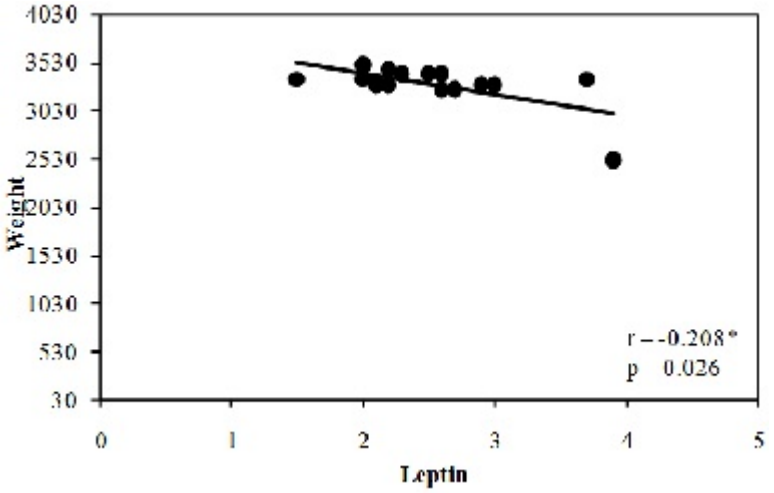


**Fig. 2:** Scattered chart showing the correlation between gestational weight and leptin hormone level in full term neonates(r=0.208&P=0.026)

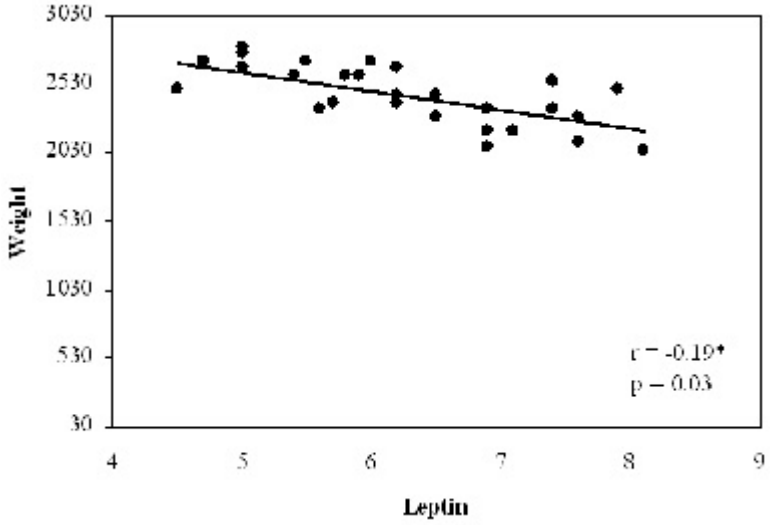


**Fig. 3:** Scattered chart showing the correlation between gestational weight and leptin hormone level in preterm neonates

**Table 2:** Shows comparison between insulin level in preterm cord blood and full term cord blood & between insulin level in preterm day 5 and full term cord blood.

| Hormone | Preterms(Cases) | Fullterm(Controls) | P |
|---|---|---|---|
| | 1st sample (cord blood) | (cord blood) | |
| Mean level of Insulin | 9.346 µIU | 6.571 µIU | 0.099 |
| +/- SD | +/-4.996 | +/-1.869 | (NS) |
| | 2nd sample (5th day) | (cord blood) | |
| Mean level of Insulin | 7.833 Miu | 6.571 µIU | 0.152 |
| +/- SD | +/-2.717 | +/-1.869 | (NS) |

P is significant if < 0.05

**Table 3:** Shows comparison between leptin level in preterm cord blood and full term cord blood & between leptin level in preterm day 5 and full term cord blood.

| Hormone | Preterm group(Cases) | Fullterm group(Controls) | P |
|---|---|---|---|
| | (cord blood) | (cord blood) | |
| Mean level of Leptin | 5.937 ng/ml | 3.78 ng/ml | <0.044 |
| +/- SD | +/-4.15 | +/-3.338 | (S) |
| | 2nd sample | (cord blood) | |
| Mean level of Leptin | 4.753 ng/ml | 3.78 ng/ml | <0.448 |
| +/- SD | +/-3.776 | +/-3.338 | (NS) |

**Table 4:** Shows the correlation between gestational weight and leptin hormone level in full term neonates (cord blood)

| Full term | Weight | Peptin | R | P | |
|---|---|---|---|---|---|
| Mean | 3370 gram +/- | 3.78 ng/ml | -0.2 | 0.026 | S |
| +/- SD | 154.46 | +/- 3.3 | | | |

statistically significant with p value of <0.001. The mean level of cortisol of the premature GROUP 1 rises in day 5 to (12.656 ± 2.23 µg/dl) but still lower than the day 1 level of the full term GROUP 2 with no statistically significant difference (p = 0.229) as seen in Table 5.

**Discussion:** Metabolic disturbance is one of the leading causes of death among preterm newborns. Their high rate of catabolism, utilization of their limited fat stores, failure to gain weight properly and susceptibility to hypo and hyperglycemia, all have been assumed to have link with abnormal hormonal levels in preterm neonates that plays some role in energy expenditure and metabolism[7].

Blood glucose is the major energy source for all tissues, and maintaining a normal glucose homeostasis is critical for efficient energy metabolism. Glucose homeostasis depends on interplay of endocrine and metabolic or enzymatic processes that control glucose uptake and utilization, as well as glucose production during periods of fasting and feeding to ensure a continuous supply. Premature infants and low birth weight babies have slightly lower glucose levels than full term infants[8].

Amylin and insulin are produced by β cells of Langerhans in response to hyperglycemia and through two complete different mechanisms. On the other hand, counter-regulatory hormones like cortisol and glucagon aim to elevate blood glucose when it declines below normal levels. Amylin lowers glucose level through different mechanisms; first by acting centrally to induce satiety, also it diminishes glucagon and digestive enzymes secretion and finally by restraining rate of gastric emptying and thus control nutrient appearance and postprandial glucose concentration[6].

We found statistically higher level of amylin in full term GROUP 2 babies when compared to premature GROUP 1 and we found also the higher the glucose level the higher the amylin level in both groups. We postulate that this statistically significant difference in amylin level between both groups is attributed to the difference in blood glucose level between the two groups being higher in full term babies. Kariamkonda[4] found similar results when serum amylin level was higher among a group of infants of diabetic mothers when compared to healthy newborns and they assumed that the higher level of blood glucose to which IDM babies were exposed stimulated release of amylin hormone . In the same way, Fineman[9] studied amylin level in a group of IDM babies and found a higher level of amylin hormone in babies born to mothers with poorly controlled diabetes and assumed that this might be caused by high level of glucose which again agrees with the fact that amylin hormone is secreted in response to hyperglycemia[9].

Although not statistically significant, insulin level was higher among the premature GROUP 1 in both days 1 and 5 when compared to full term GROUP 2

**Table 5:** Shows comparison between cortisol level in preterm cord blood and full term cord blood & between cortisol level in preterm day 5 and full term cord blood

| Hormone | Preterm group (Cases) | Fullterm group (Controls) | P |
|---|---|---|---|
| | Cord blood | Cord blood | |
| Mean level of cortisol | 5.366 µg/dl | 15.3 µg/dl | <.001 |
| +/- SD | +/-6.24 | +/-9.096 | (HS) |
| | ($2^{nd}$ day sample) | (Cord blood) | |
| Mean level of cortisol | 12.656 µg/dl | 15.3 µg/dl | 0.229 |
| +/- SD | +/-2.23 | +/-9.196 | (NS) |

due to increase need of insulin in premature babies to enhance glycogen and protein storage and spares fat stores in these smaller babies.

Leptin is a hormone which has been the focus of many researches over the last two decades. It plays a role in metabolism and energy expenditure. Higher levels of leptin reduces food intake, increases energy expenditure and hence weight loss, It is now clear that leptin is involved in glucose metabolism and functions as a metabolic and neuroendocrine hormone[10].

The present study showed that serum leptin level was higher among preterm GROUP 1 when compared to full term GROUP 2 in day 1 and this difference was statistically significant. This is in agreement with Schubring who found higher level of leptin among preterm infants than in full term ones and then a decline of its level in preterm infants with improvement in feeding and weight gain[11]. The lower level in full term infants coincides with preservation of energy expenditure and increase in body weight while the higher level in preterm neonates might contributes to their poor feeding and poor weight gain and this coincides with the role of leptin in energy expenditure and weight gain[10].

In our study, there was no statistically significant difference in correlating serum leptin with glucose level. Most probably, it seems that the role of leptin in controlling blood glucose level is indirect. The role of leptin is more evident in affecting satiety and energy expenditure and this mechanism may in turn affects blood glucose level.

In our study, cortisol level was highly statistically significant to be lower in premature GROUP 1 when compared to full term GROUP 2. The level of cortisol in preterm infants shows ascending pattern and got higher by day 5 but still lower than full term day 1 level but no statistically significant difference at this time. Jonetz *et al*[12] detected the same finding of increase in cortisol level with age and this was attributed to maturation of adrenal cortex and probably better response to stress as the age advances[12]. Another study showed that premature babies had lower basal cortisol level in response to stress when compard to full term newborns exposed to the same stress[13]

We can conclude that there is a highly complex process involving the interaction of metabolic hormones and their roles in the regulation of glucose homeostasis, weight gain and growth of newborns whether preterm or full term babies. Further studies are needed to assess the maturation of these hormones with age in relation to body metabolism and growth and probably discovery of new hormones interacting with these recent hormones.

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