The Egyptian Journal of Hospital Medicine (July 2017) Vol.68(1), Page 1035-1041

Adjusted Serum leptin and leptin Adiponectin ratio in correlation with Hyperemesis gravidarum

El zeneny A.H , Sayed A.M , Abdel hafez A.M and Hafez S.A.

Department of obstetrics and Gynecology, Faculty of Medicine, Ain Shams University ,Cairo ,Egypt

Abstract

Aim: to determine the level of serum leptin, adiponectin and leptin /adiponectin ratio in women with hyperemesis gravidraum and compare them with those with normal pregnancy in order to speculate their role in prediction and assessement of severity of the disease. **Patients and method :** This case control study was conducted at the department of Obstetrics and Gynecology, Ain-shams university maternity hospital. A total of 90 women are included in the study and are divided into two groups. Group A: Fourty -five pregnant women with hyperemesis gravidarum.. Group B : Fourty -five pregnant women with no hyperemesis gravidarum..the groups were compared for age, gestational age, body mass index,Leptin ,adiponectin, adjusted leptin level,,leptin to adiponectin ratio were calculated in each group. Primary outcome was the increase in adjusted leptin level in hyperemesis gravidarum group.

Results: leptin was found to be significantly high in the HG group (37.91± 6.42) , also Adjusted leptin level were found to be significantly higher in the hyperemesis gravidarum group(4.36± 1.26) than in the control group (P = 0.001) and adiponectin level were found to be lower in the HG (9.34±1.49) than in the control group. There was increase in leptin to adiponectin ratio as compared with severity of the disease. The maternal leptin level was positively correlated with gestational age in the HG group (r = 0.011, p= 0.944). Also the maternal adiponectin level was positively correlated with BMI in the HG group (r = 0.290 , p = 0.054). Etiology of the hyperemesis gravidarum is multifactorial. However we can postulate the adjusted leptin level as a good predictor for hyperemesis gravidarum.,alsoLeptin to adiponectin ratio can be used to determine severity of the disease.

Keywords: Hyperemsis gravidarum ;Adjusted leptin; Leptin; adiponectin ; leptin to adiponectin ratio.

1.Introduction

Nausea and vomiting is a common symptom of early pregnancy. Affecting up to 80 % of women. While the reported incidence of hyperemesis gravidraum is 0. 5-2. 0% [1] . Hyperemesis gravidarum [HG] is a significant but underappreciated illness of pregnancy. It is the most commen indication for admission to the hospital in the first half of pregnancy and second only to preterm labour as a cause of hospitalization overall. Hyperemesis gravidarum is a state characterized by intractable vomiting during pregnancy, leading to dehydration, ketonemia, electrolyte imbalance and weight loss[2]. Although recent researches say that the pathophysiology for hyperemesis gravidraum is not clear, it has been proposed that hormonal allergen as well as genetic factors, immunolgical, neuropsychosomotic,and metabolic factors may play a role in the etiology of hyperemsis gravidraum [3]. HG, like nausea and vomiting (NVP), typically occurs between the 4th and the 10th week of gestation, with resolution by 20 weeks of gestation. In approximately 10% of HG patients, symptoms will persist throughout pregnancy [4].

Leptin and adiponectin are the hormones that are secreated mainly by the adipose tissue to signal the status of body energy stores to the central nervous system.

Received:10/5/2017 DOI: 10.12816/0038205
Accepted:19/5/2017

As a signal of energy sufficiency, adequate leptin levels suppress feeding and permit energy-costly neuro endocrine functions [5].

Leptin is Is a circulating hormone which acts as an afferent satiety signal to regulate body weight and has a structure similar to that of cytokines. A relationship between leptin and hyperemesis gravidraum was originally based on the crucial role in reducing appetite and raising the consumption of energy by interacting with other factors such as cortisol, thyroid hormones and insulin [6].

Although the pathophysiology for hyperemesis gravidarum is not clear. maternal leptin level increases progressively during gestation. However, in other hypothesis, rapid increase in maternal leptin concentration disproportional to gestational age is a marker for hyperemesis gravidarum [7]. Adiponectin is a newly discovered hormone secreted by adipocytes, which constitutes a link between intraabdominal fat mass and the metabolic and cardiovascular complications of obesity. There is growing evidence that this protein is an important regulator of insulin sensitivity. Adiponectin suppresses hepatic glucose production [8].

Adjusted leptin levels is calculated by dividing maternal serum leptin level over gestional week. Leptin / adiponectin ratio is calculated by dividing the maternal serum leptin levels which show an increase in cases of hyperemesis gravidraum by the maternal serum adiponectin levels which show decrease in hyperemsis gravidraum. leptin / adiponectin ratio will be significantly (low or high) with hyperemsis gravidraum in the first trimester of pregnancy [9].

The aim of the study: first was to compare maternal serum adjusted leptin level (ALL; maternal leptin / gestational week) in the first trimester in women with HG and with levels in normal pregnancy. The second aim was to asses the relationship between leptin / adiponectin ratio with the severity and progression of the disease.

2. Study design

A case control study was conducted at the department of Obstetrics and Gynecology, Ain Shams university maternity hospital .

3. Pateints and methods :

Ninty first trimester pregnant women were enrolled : 45 women with hyperemesis gravidarum and 45 women without hyperemesis gravidarum..

Hyperemsis gravidarum was defined as excessive nausea and vomiting during pregnancy, leading to electrolyte imbalance, nutritional deficiency and losing more than 10 pounds or 5 % of the patient's body weight, and the presence of ketones in urine, increase in heart rate, low blood pressure.

The study and control groups were compared for age , gestational age, BMI ,ketones , Na , K , urea creatinine, AST,ALT as well as leptin and adiponectin levels.

It is found that the maternal leptin level increases progressively during gestation and that maternal adiponectin level decreases . It is hypothesized that rapid increase in maternal leptin concentration disproportional to gestational week is a marker for HG. Hence, we used a newly defined a new parameter by dividing maternal serum leptin level by gestational week. This new parameter is called adjusted leptin level (ALL). In this study also we calculated leptin to adiponectin ratio which palys an important role in determining the severity of the disease.this study was approved by the department of Obstetrics and Gynecology, Ain-shams university maternity hospital. Written informed consent was obtained from all subjects before enrollment in the study.

The blood was collected between 8:30 and 10:00 A.M. Serum samples were stored at -20°C .All analysis were performed within one month of collection. Serum leptin concentration were measured by enzyme-linked immunosorbent assay (ELISA) (DBG Leptin ELISA kits supplied from Diagnostic Biochem Canada Inc).Serum adiponectin concentartions were also measured byEnzyme - linked immunosorbent assay (Adiponectin ELISA Kits supplied from Orgenium laboratories, Finland.).

Statistical analysis was performed using IBM© SPSS© Statistics version 22 (IBM© Corp., Armonk, NY). Normally distributed numerical data were presented as mean and SD, and skewed data as median and interquartile range. Qualitative data were presented as number and percentage. Comparison of normally distributed numerical data were done using the Student *t* test. Categorical data were compared using the chi-squared test, when appropriate. A two-sided p-value <0. 05 will be considered statistically significant.

4. Results

The characteristics of both groups are showen in Table 1. BMI were significantly lower in HG group than in the control group (P = 0.001 ; table 1).

Table 1. The characteristics of the pateints with and without hyperemesis gravidarum (mean ± S.D.,median-range)

		Groups		T-Test		Sig.
		Group A	Group B	t	P-value	
Age	**Range**	18 - 33	18 - 36	-0.560	0.577	NS
	Mean ±SD	23.711 ± 3.533	24.133 ± 3.616			
Gestational age (Weeks)	**Range**	6 - 13	5 - 13	-1.749	0.084	NS
	Mean ±SD	9.067 ± 2.038	9.800 ± 1.938			
BMI Kg/m2	**Range**	16.3 - 24.4	17.8 - 25	-3.453	0.001*	HS
	Mean ±SD	19.709 ± 1.922	20.984 ± 1.564			

Leptin levels were significally higher in the HG group (37.91 ± 6.42) than in the control group. Adiponectin levels were lower in the HG group (9.34 ± 1.49) than in the control group. However, ALL was significally higher in the HG group than in control group. (4.36±1.26 ; table 2 & 3).

Table 2. Leptin and adiponectin of HG and control groups (mean ± S.D.)

		Groups		T-Test		Sig.
		Group A	Group B	t	P-value	
Leptin mug/ml	**Range**	19.3 - 49	12 - 29.4	16.134	<0.001*	HS
	Mean ±SD	37.911 ± 6.422	21.000 ± 2.864			
Adiponctinmug/ml	**Range**	7.2 - 13	10.3 - 15	-12.689	<0.001*	HS
	Mean ±SD	9.349 ± 1.490	12.711 ± 0.969			

Table 3. Adjusted leptin level of HG and control group (mean ± S.D).

ALL	Groups		T-Test	
	Group A	Group B	t	P-value
Range	2.08 - 7.88	1.15 - 3.16	10.634	<0.001*
Mean ±SD	4.369 ± 1.269	2.218 ± 0.479		

A significant positive correlation was found between ALL and gestational age (r = 0.749 , 0.001) . But there is no correlation between ALL and age ,BMI,. Also serum leptin level was negatively correlated with BMI(r = -0308 p = 0.040) and no correlation with gestational age ,age, Serum adiponectin level shows no correlation between age and gestational age and BMI (table 4).(table 5) (table 6).

Table 4: Correlation betwwen ALL and different variables.

Correlations		
Variables	ALL	
	r	P-value
Age	-0.118	0.440
Gestational age (Weeks)	0.749	<0.001*
BMI kg/m^2	-0.253	0.094

Table 5: Correlation between Serum leptin level and different variables

Correlations		
variables	Leptin mug/ml	
	r	P-value
Age	-0.074	0.631
Gestational age (Weeks)	0.011	0.944
BMI kg/m^2	-0.308	0.040*

Table 6: Correlation between serum adiponectin level and different variables

Correlations		
variables	Adiponctinmug/ml	
	r	P-value
Age	**0.190**	0.211
Gestational age (Weeks)	0.057	0.712
BMI kg/m^2	0.290	0.054

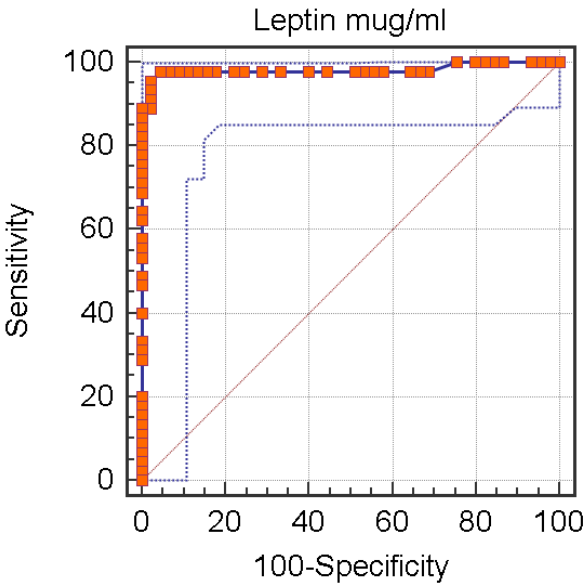

Fig. 1. Roc curve for the serum leptin level at hyperemesis gravidarum cases.

The calculated cut-off value for the serum leptin was 24.3 sensitivity and specifity were 97.78% and 95.56% respectively (fig . 1)

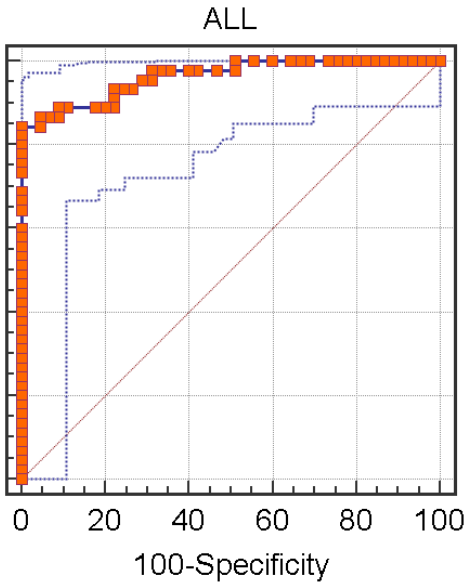

Fig. 2. ROC curve for the adjusted leptin level at hyperemesis gravidarum cases.

The calculated cut-off value for the ALL was 3.16 . Sensitivity and specifity were 84.44 % and 100% respectively (fig. 2).

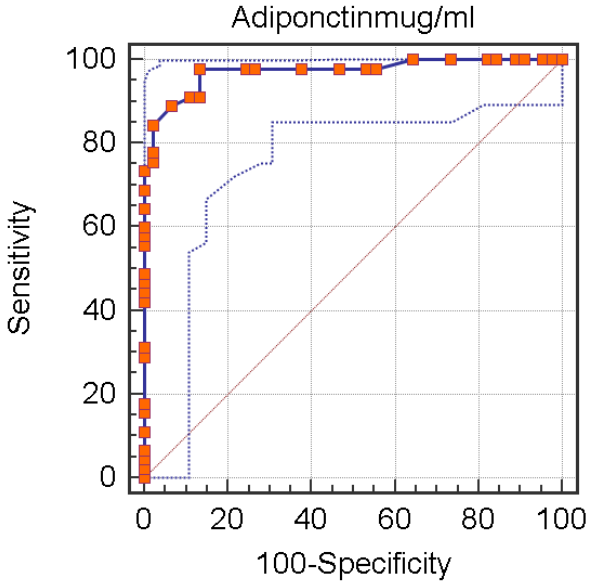

Fig. 3. ROC curve for the serum adiponectin level at hyperemesis gravidarum cases. The calculated cut-off value for the serum adiponectin level was 12 .Sensitivity and specifity were 97.78% and 86.67% respectively.

5. Discussion

The endocrine factors are the primary cause for HG, although it is likely that the causes of Hyperemesis gravidarum are multifractorial and may involve immune, metabolic, placental, psychological and other factors [10] .Estimates of the incidence of HG vary from 0.3 to 1.5% of all live births, with most authors reporting an incidence of 0.5%.[11]. Hyperemesis gravidarum may be non severe or severe occurs in the form of signs and symptoms including, severe vomiting, weight loss, tachycardia hypotension, dry furred tongue, loss of skin elasticity, It is rarely encountered to see severe signs of jaundice, hyperpyrexia , albuminuria, peripheral neuritis, Wernickes encephalopathy due to vitamin B deficiency which is characterized by diplopia, nystagmus, disorientation, delusions and then coma. Death is due to hepatorenal failure[12]. Maternal serum leptin level were found to be significally high in the HG group as compared with the control group. This is also the case for other studies[13,14] In our study the adjusted serum leptin levels have been found significantly high in the HG group. Moreover, the present findings have shown that women with HG had significantly lower BMI than those with normal pregnancies,these agrees with other studies[15] .According to our study maternal serum adiponectin levels were found to be lower in the HG group as compared with control group ,which agrees with **Fell *et al***. study[16].According to our study leptin to adiponectin ratio shows highly significant progressive increase in HG group as compared with the control group which indicates that leptin to adiponectin ratio increases with the severity of the disease and can be used to determine the severity of the disease. This agrees with another study [17].

According to our results, the cutoff value for the ALL is 3.16. When this value exceeds 2.5 in the first trimester,the nausea and vomiting will be severe.the cutoff value for leptin was 24.3 ng/ml and for adiponectin was 12 µg/ml .Our study also showed that the best cutoff value for leptin to adiponectin ratio was 2.26 as it increases with severity of the disease[17]

References

[1] Kirk E, PapGeorghiou AT, Condous G *et al*. (2006): Hyperemesis gravidarum : is an ultrasound scan necessary. Hum Reprod J.,21:2440- 42.

[2] Goodwin TM, Studd J, Tan SL and Chervenak FA (2006): progress in obestatrics and gynacelogy. Elsevier publishing: Pp:49-64

[3] Karaca C, Guler N, Yazar A *et al*. (2009): Is lower socio-economic status a risk factor for *Helicobacter pylori* infection in pregnant women with hyperemesis gravidarum? Turk J Gastroenterol .,15: 86–89.

[4] Gadsby R, Barnie-Adshead AM and Jagger C (2006): A prospective study of nausea and vomiting during pregnancy. Br J Gen Pract., 43: 245–248.

[5] Bates SH, Dundon TA, Seifert M *et al* . (2004): Signal transducers and activators of transcription family of protein 3 signaling is required for the neuroendocrin regulation of energy expenditure by leptin. The Ampenditure diabetes association, 53: 3067-63.

[6] Considine RV and Caro JF (2008): Leptin: genes, concepts and clinical perspective. Horm Res .,46: 249–256.

[7] Enriori PJ, Evans AE, Sinnayah P etal. (2007): Leptin concentration in pregnancy., 5:181–94

[8] Combs TP, Berg AH, Obici S *et al*. (2001): Endogenous glucose production is inhibited by the adipose derived protein acrp 30. J clin invest., 108: 1875- 81.

[9] Mantzoros CS, Dunaif A, Flier J (2004) : Leptin concentrations in pregnancy. *J Clin Endocrinol Metab*., **82**: 1066

[10] Danzer H, Braustein GD, Rasor J *et al*. (2000): Maternal serum human chorionic gonadotropin concentrations and fetal sex prediction. Fertil Steril., 34: 336–340.

[11] Kallen B (2005): Hyperemesis during pregnancy and delivery outcome: a registry study. Eur J Obstet Gynecol Reprod Biol., 26: 291–302.

[12] Wayne R.Cohen N, Benian A *et al*. (2000): Leptin levels in women with hyperemesis gravidarum. Int J Gynaecol Obstet., 84: 162–163.

[13] Arslan EO, Cengiz L, Arslan M (2008): Hyperemesis gravidarum and correlation with serum leptin levels. Inter J Gynecol Obstetrics, 83: 187–88.

[14] Miami, A.Sivan, G, Whittaker PD (2010). Sinha Leptin in human pregnancy: the relationship with gestational hormones. Am J Obstet Gynecol. , 179:1128–32.

[15] Demir B, Erel TC, Haberal A *et al*. (2006). Adjusted leptin level (ALL) is a predictor for hyperemesis gravidarum. Eur J Obstet Gynecol Reprod Biol ., 124:193–196.

[16] Fell DB, Dodds L, Joseph KS *et al*. (2006): Risk factors for hyperemesis gravidarum requiring hospital admission during pregnancy. Obstet Gynecol., 107:277.

[17] Miroslav V, Oda N, Imamura S *et al*. (2009): The ratio of leptin to adiponectin can be used as an index of metabolic disorder. Metabolism ,57:268–73