

**Impact of Zinc to Copper ratio and Lipocalin -2  
in Obese Patients Undergoing Sleeve Gastrectomy.**

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## **Impact of Zinc to Copper ratio and Lipocalin -2 in Obese Patients Undergoing Sleeve Gastrectomy.**

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Obesity represents tremendous threat to health globally. WHO conveyed that over 10% of the world's population were classified as obese in 2016, which signifies 3-fold increase in frequency of obesity since 1975. Laparoscopic Sleeve Gastrectomy (LSG) has proved to be an effective procedure for achieving considerable weight loss with significant improvement in obesity-related comorbidities.

A possible role of trace elements in the pathogenesis of obesity has been largely ignored. In particular zinc (Zn) and Copper (Cu) are crucial TE, that act as structural ions in hormones, proteins and receptors and cofactors in various enzymatic reactions. It has been theorized that balance between Zn and Cu has an influence on antioxidant mechanisms and development of associated comorbidities. Nevertheless, few studies have systematically evaluated TE in morbidly obese patients undergoing bariatric surgery.

Lipocalin 2 (Lcn2), also known as NGAL (neutrophil gelatinase-associated lipocalin), Lcn2 is adipokine that belongs to lipocalin family. It is a 25- KD  $\alpha$ -glycoprotein originally identified in human neutrophils. Lcn2 overexpression in adipose tissue stimulates the production of pro-inflammatory cytokine as interleukin 6 (IL-6) and receptor activator of NF- $\kappa$ B ligand.

The aim of the current study primarily was to investigate the value of zinc to copper ratio as possible biomarker of TE imbalance in morbidly obese subjects undergoing LSG. Secondly to correlate it with lipocalin 2 (Lcn2) with respect to Anthropometric measurements and other metabolic markers prospectively.

### **Study design**

### **CONSORT 2010 Flow Diagram**

**Enrollment**

Assessed for eligibility (n= 120 )

## **Materials and methods:**

### **Recruitment**

Morbidly obese subjects attending clinic at Surgery department for laparoscopic sleeve gastrectomy Alexandria University Hospitals.

#### **Pre-assignment Details**

adult morbidly obese subjects were included age above 20 years, BMI above 40

Suffering from comorbidities as hypertension, DM, dyslipidemia.

Assigned participants were clinically evaluated for comorbidities as hypertension, DM, dyslipidemia.

As well as signs of nutritional deficiency as anemia, brittle nails.

### **Group Information**

one group of participants eligible for laparoscopic sleeve gastrectomy were assigned according to their will to participate in study.

#### **Period of evaluation:**

First visit: preoperative for clinical assessment of participants, determine BMI and waist circumference and withdrawal of serum blood sample

Second visit: within one month after surgery to make sure that no complication occurred after surgery.

Third visit: nine months postoperative for revaluation of participants, determine BMI and waist circumference, and withdrawal of a serum blood sample

#### **Number of participants at initiating the period of study.**

They were 120 morbidly obese subjects.

#### **Number of participants at the end of the period of study.**

They were 107 subjects, 13 obese subject withdraw from study as they didn't come during follow up period after 9 months.

Participants according Sex (69 females, and 38 male), with the mean age of  $41.6 \pm 8.9$  years. The mean preoperative BMI was  $47.43 \pm 5.4 \text{ kg/m}^2$ . Then, they were evaluated 9 months after LSG.

### **Preoperative and Postoperative Clinical characteristics and metabolic variables in studied subjects.**

	Preoperative	9 months postoperative	P
Body weight (Kg)	$129.7 \pm 12.1$	$93.4 \pm 13.6$	0.0013*
BMI ( $\text{kg/m}^2$ )	$47.43 \pm 5.4$	$35.7 \pm 3.8$	0.0052*
Waist circumference (cm)	$130.00 \pm 4.68$	$91.82 \pm 3.73$	0.001*

Systolic BP (mmHg)	146.0±17.0	132.0±11.0	0.001*
Total cholesterol (mmol/L)	5.85 ± 0.41	4.64 ± 0.31	0.035*
Triglycerides (mmol/L)	2.20 ± 0.23	1.92 ± 0.24	0.106
HDL cholesterol (mmol/L)	1.23 ± 0.19	1.39 ± 0.2	0.041*
LDL cholesterol (mmol/L)	3.37 ± 0.23	2.97 ± 0.21	0.022*
HOMA-IR	2.64 ± 1.3	1.44 ± 0.81	0.013*
S. Leptin (ng/ml)	102.87 ± 49.16	33.47 ±12.76	0.0001*
CRP (mg/L)	8.4±5.91	3.2±2.98	0.001*
Lipocalin 2 (µg/L)	107.24±36.8	51.6±12.73	0.001*
Albumin (g/dl)	4.05±0.21	3.91±0.29	0.113

\*Statistically significant at (p≤0.05).

#### **Outcome measures:**

primarily was to investigate the value of zinc to copper ratio as possible biomarker of TE imbalance in morbidly obese subjects undergoing LSG.

For detection of presence of micronutrient deficiency in morbid obesity in form of zinc to copper ratio and re-evaluate it after loss of weight

Secondly to correlate it with lipocalin 2 (Lcn2) with respect to Anthropometric measurements and other metabolic markers prospectively.

As zinc to copper ratio is considered as biomarker of micronutrient status; therefore, correlate it with other biomarkers of inflammation (lipocalin 2) and other parameters as BMI, FBG to determine if micronutrient status improve after weight loss or not

**Time frame:** 9 months.

#### **Follow-up and outcome parameters:**

All studied subjects will be followed up for early postoperative complications (within the first month) as Bleeding or Leak. Then they will be reviewed after 9 months postoperatively for assessment of anthropometric measurements, control of preoperative comorbidities, and manifestations of TE deficiencies (anemia, hair loss, teeth problems, edema. etc.).

### **Anthropometric parameters**

Body mass index (BMI) and waist circumference will be measured preoperative and 9 months postoperative.

### **Biochemical parameters**

Fasting blood samples will be collected from participants prior to surgery and nine months postoperative, after overnight fast and divided into two tubes; EDTA for complete blood count, the rest into plastic tubes and serum sample.

Serum glucose and Total cholesterol, HDL- cholesterol, LDL- cholesterol, and triglyceride, total protein and Albumin. Serum iron (Fe), and ferritin.

Serum insulin, Ceruloplasmin, Zn and Cu levels, CRP and lipocalin-2 (Lcn2) .

### **Statistical analysis**

All data will be analyzed with Statistical Package for the Social Sciences version 20 software (SPSS, Inc., Chicago, IL). Results will be displayed as mean  $\pm$  SD. Paired Student's t-test used to compare the data pre-operative and nine months postoperative. The chi-squared test used for category variables. Spearman correlation coefficient used to detect the correlation between different variables. Statistical correlations calculated by Pearson's correlation test.  $P < 0.05$  is considered significant.

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