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### RESEARCH ARTICLE

#### ASSESSMENT OF INSULIN RESISTANCE INDEX (HOMA-IR) AND LIPID PROFILE AMONG SUDANESE WOMEN WITH GALLSTONES.

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HOMA-IR, Insulin resistance, Lipid profile, Gallstones and Sudan.

#### Abstract

The aim of this study was to assess insulin resistance index (HOMA-IR) and lipid profile level in Sudanese gallstones (GSs) patients and their association with study variables. In case control study 80 clinically diagnosed GSs patients were recruited, and 80 apparently health age matched women as control group. Fasting insulin, glucose and lipid profile (TC, TG, HDL-C and LDL-C) were measured using TOSOH-311<sup>®</sup> and Mindray-380<sup>®</sup> analyzers. IR-index was calculated using HOMA-IR formula.

Obese postmenopausal women had higher GS (62.5%). HOMA-IR, TC, LDL-C and TG level were significantly increased in Sudanese women with GS than control group  $p=0.000$ ,  $0.000$ ,  $0.000$  and  $0.000$  respectively. Significant positive associations between TC, LDL-C and HOMA-IR were observed  $p=0.001$ ,  $r=0.437$  and  $p=0.001$ ,  $r=0.419$  respectively. BMI also showed positive association with TC, TG and LDL-C. In conclusion, Sudanese females with GSs had higher HOMA-IR, TC, TG and LDL-C. Obesity may be the first risk factor of GS in Sudanese women. Thus could lead to GSs pathogenesis especially in postmenopausal.

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#### Introduction:-

GSs remain an important public health problem, due to its extraordinary frequency [1]. GSs account of 10% to 15% in western population compared with 20% to 30% in developing countries, which attributed to carbohydrate rich diet and life style. Females are more vulnerable to GSs than male thus described as disease of fat, fertile, over forty and female [2]. GSs are composed mainly of cholesterol, bilirubin, and calcium salts, with smaller amounts of protein and other materials [3,4,5,6]. There are three types of GSs [7]: Pure cholesterol stones, pigment stone and mixed composition stones [8]. Moreover, high biliary protein and lipid concentrations are risk factors for the formation of gallstones [9]. Therefore, many factors contribute in developing gallstone as genetic, obesity and body fat distribution [10], rapid weight loss [11] and diabetes [12]. Estrogen is considered to be the obvious reason for the gender difference [13]. Female predominance is obvious, particularly at a young age, thus, the gender difference narrows with increasing age, particularly after menopause [14].

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Insulin resistance (IR) is defined where a normal or elevated insulin level produces an attenuated biological response [15,16]. Physiologically, Insulin is driving metabolic processes in the fed state [17], excess secretion may contribute to IR [18]. IR play a curtail role in the pathogenesis of GD favoring the production of cholesterol supersaturated bile and altering gallbladder function [19]. Based on our observation of vast change of Sudanese life style especially during gestational period, we hypothesized that, HOMA-IR associated with GS in obese Sudanese women.

### **Materials and methods:-**

A case control study was conducted in Ibin Sina hospital, Sudan it is specialized hospital in the region, which serves the majority gallstone patients in Khartoum capital of Sudan. Of rottenly admitted patients 80 women (23 - 70 year of age) were enrolled from January to March 2017. Based on following criteria that might influence study parameters estimation (DM, CVD and/or statin drugs) were excluded. Moreover, 80 apparently health as control were matched. Fasting (5ml) venipuncture blood specimen was withdrawn under aseptic condition. Plasma and serum were obtained after centrifugation of blood at 3000 rpm for 5 min and stored at -20°C till used.

### **Ethical consideration:-**

The study was approved from local ethics committee of Al-Neelain University. All subjects gave their written informed consent considering the aims of the study and participate. Samples and clinical information's were used anonymously.

### **BMI calculation:-**

Anthropometric data including weight and height were measured thus body mass index (BMI) was calculated using weight (Kg) divided by height squared (m<sup>2</sup>) formula.

### **Estimation of glucose and lipid profile:-**

Brief according to manufacturer blood glucose and lipid profile (Cholesterol, Triglycerides, LDL-C and HDL-C) level were measured by fully automated chemical analyzer Bs-380®.

### **Estimation of insulin:-**

Brief according to manufacturer ST AIA-PACK IRI site immunoenzymometric assay was used. Insulin bound with monoclonal antibody immobilized on a magnetic solid phase and enzyme-labeled monoclonal antibody in the test cups. The magnetic beads were washed to remove unbound enzyme-labeled monoclonal antibody and were then incubated with a fluorogenic substrate, 4-methylumbelliferyl phosphate (4MUP). The amount of enzyme-labeled monoclonal antibody that binds to the beads was directly proportional to the insulin concentration.

Insulin resistance was calculated using Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) index equations.

$$\text{HOMA-IR} = \text{fasting serum Insulin } (\mu\text{U/ml}) \times (\text{fasting plasma glucose (mmol/L)/22.5})$$

### **Statistical analysis:-**

Statistical analyses were performed using SPSS version 21.0 (SPSS Inc, USA). Descriptive statistics are reported as percentage and Mean±SD. Independent *t*-test was employed to compare two independent groups. Person's correlation was used to correlate between study parameters and variables. *P*-value ≤0.05 was considered statistically significant.

### **Results:-**

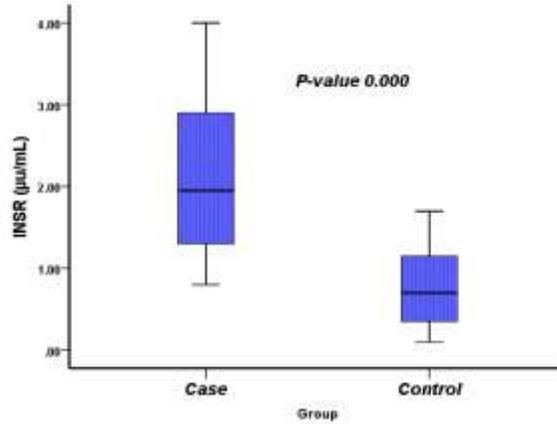
The analyses of frequency showed that, gallstones are more common in postmenopause 62.5% than premenopausal 37.5% Sudanese women. Moreover, the majority of GS women were overweight 42.5, obese 21.3 and normal weight 36.2 which presented in table 1.

Comparison analysis revealed that, mean level of HOMA-IR, TC, TG and LDL were significantly increases with *p*-value= (0.000, 0.000, 0.000 and 0.000) respectively presented in fig.1 and 2.

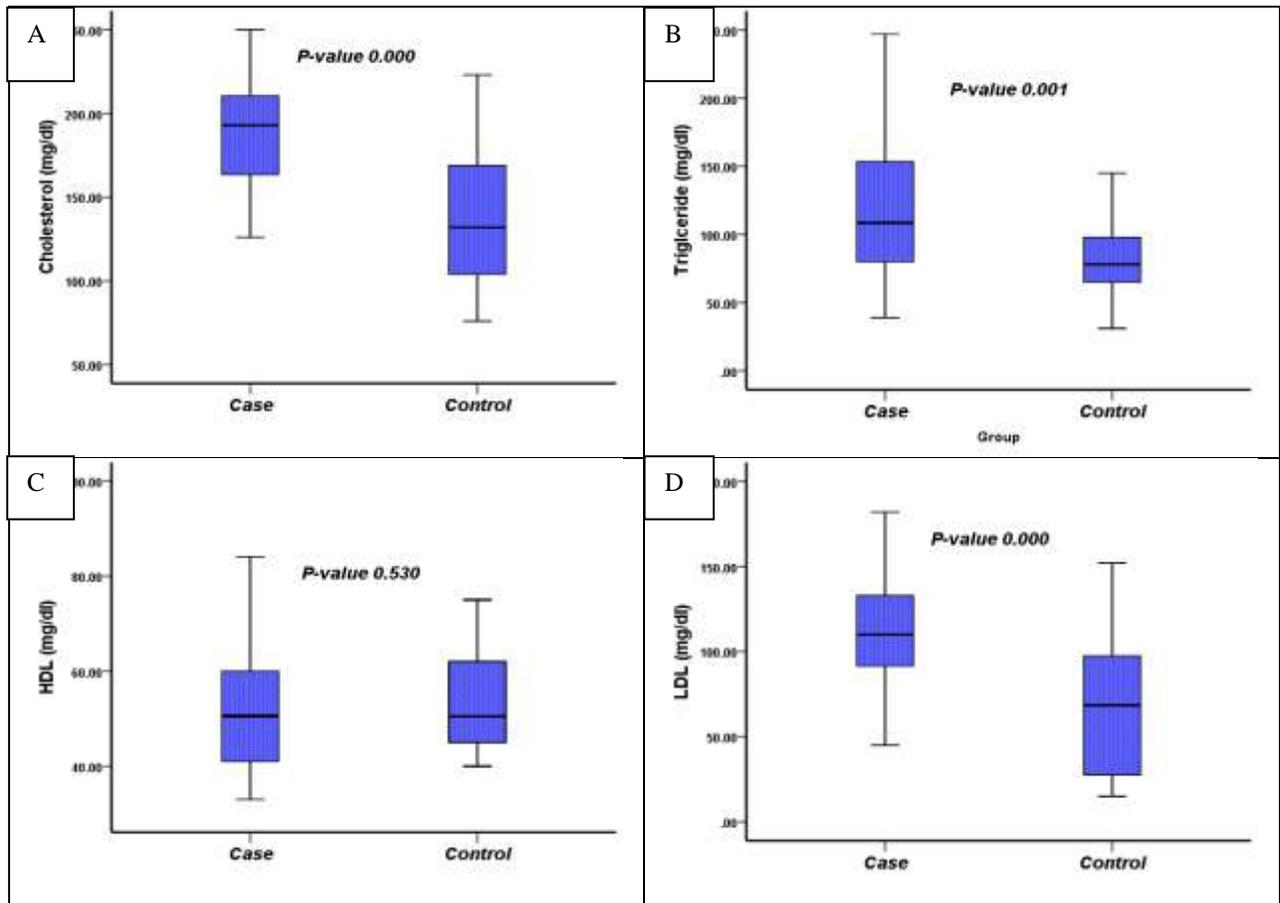
Dot blot regression analyses showed that, HOMA-IR positively correlate with TC (R= 0.437, P= 0.001), LDL-C (R= 0.419, P= 0.001) while no correlation was observed with TG (R= 0.206 P= 0.067). Moreover BMI positively correlate with TC (R= 0.483, P= 0.000), TG (R= 0.465, P= 0.000) and LDL-C (R= 0.424, P= 0.001) presented in fig.3.

**Table 3.1:-** Age and BMI distribution of GS patients

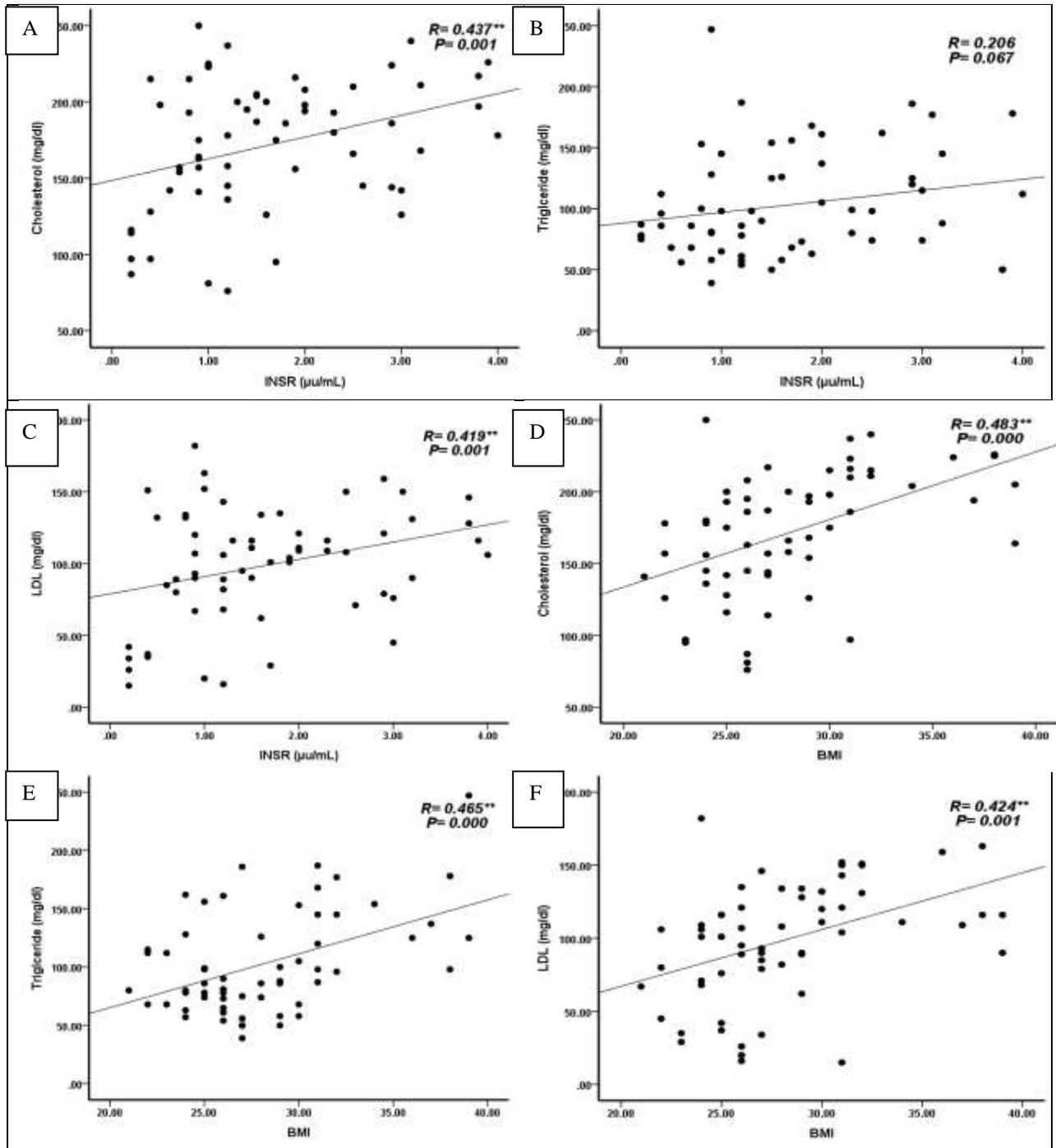
Variables	Frequency (%)
Age <48 years	30 (37.5%)
Age >48 years	50 (62.5%)
BMI 18.5 - 26	29 (36.2%)
BMI 26 - 30	34 (42.5%)
BMI >30	17 (21.3%)



**Fig.3.1:-** Comparison of HOMA-IR in case (GS patients) versus control group.



**Fig.3.2:-** Comparison of lipid profile (TC, TG, HDL-C and LDL-C) in case (GS patients) versus control group.



**Fig.3.3:-** Dot blot regression of A, B and C: HOMA-IR with TC, TG and LDL-C while D, E and F: BMI with TC, TG and LDL-C.

**Discussions:-**

The association of GS and metabolic abnormalities including obesity, diabetes, dyslipidemia and hyperinsulinemia previously have been studied [1,2,11–16]. Moreover, hypothesis that GS is a member of the metabolic syndrome has proved [17–19]. Therefore, the aim of present study was to assess HOMA-IR and lipid profile in GS patients and their correlation with study variables.

In the present study, it was observed that, postmenopausal Sudanese women (62.5%) had GS more than premenopausal (37.5%) approximately 1.7: 1 fold. Moreover, overweight GS patients account for (42.5%) followed by obese (21.3%) and normal weight (36.2%). In developing countries like Sudan, change in life style and carbohydrate diet especially during gestational, could partly be contributed factors in pathogenesis of GS. Indeed GS is disease of 4F, fat, fertile, female and over forty [2,20].

The results of present study provide evidence that, mean HOMA-IR was significantly increased in GS patients when compared with control group with p-value 0.000. In fact that IR plays a crucial role in abnormalities of glucose and lipid metabolism, thus lead to metabolic abnormalities such as GSs [16, 20]. Since exact mechanisms that IR leads to GSs formation are not clear. Researchers proved direct of hyperinsulinemia on hepatic lipid metabolism. Therefore increase risk of GSs in IR subjects [20]. In contrast insignificant difference was observed in HDL-C level. There have been multiple studies demonstrating the positive association between TC, TG, LDL-C and HOMA-IR in GS disease [18,19]. Hereby we also found that, HOMA-IR positively correlate with TC, TG and LDL-C while no correlation was observed with HDL-C. IR increasing cholesterol synthesis, hepatic uptake of LDL-C and associated with lower HDL-C [20]. Therefore these findings indicate that, IR and hyperlipidemia increase risk of GSs formation especially in our population.

It is important to note that, we test the relationship between BMI and lipid profile (TC, TG, LDL-C and HDL-C). Furthermore our regression analyses revealed positive correlation between BMI, TC, TG and LDL-C. A number of studies have observed positive association between BMI and hyperlipidemia in GSs patients [10, 20]. Therefore obese women with hyperlipidemia may be more vulnerable to GSs formation. In fact that, obesity is well-established as major risk factor for developing GSs, by increasing hepatic secretion of cholesterol [14].

### **Conclusions:-**

The data of present study suggested that, Sudanese females with GS had higher HOMA-IR, TC, TG and LDL-C. HOMA-IR and BMI have positive linear association with hyperlipidemia. Obesity may be the first risk factor of GSs in Sudanese women, thus may be predisposing factors of GSs pathogenesis in our population. HOMA-IR and lipids monitoring could help to diagnose of related complications and thus use of preventive therapeutic intervention. Further study is recommended focusing on nutritional diet, life style and GDs formation.

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### **Conflicts of interest:-**

Authors declare no conflicts of interest exist.

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