IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 15, Issue 6 Ver. XIV (June 2016), PP 48-51
www.iosrjournals.org

Estimation of Serum Insulin in Polycystic Ovarian Disease.

Dr. Lakshman Lal[1], Dr. Atima Bharti[2], Dr. Ila Jha[3]
[1]Professor And Head Of The Department, Dept. Of Biochemistry, MGM, Jamshedpur
[2]Assistant Professor, Dept. Of Obs & Gynae, RIMS, Ranchi
[3]Senior Resident, Dept. Of Obs & Gynae, MGM, Jamshedpur

Abstract
Aim: *To estimate the level of serum insulin in polycystic ovarian disease (PCOS). To compare the status of insulin resistance in obese and non-obese PCOS.*
Material And Method: *This study was conducted in the department of Biochemistry, Mahatma Gandhi Medical College, Jamshedpur. A total of 102 cases were studied. The study subjects were selected from patients visiting the out patient department of Obstetrics and Gynaecology. Age of the patients were between 14 and 45 years. Serum insulin and fasting plasma glucose were measured in these patients.*
Result: *The data and result obtained were statistically analyzed and arranged. 25.49% of the study population had impaired plasma glucose, while 74.50% of the patients had fasting blood glucose level <100 mg/dl. Increased insulin level ≥13μIU/dl was present in 73.52% of the population. Higher value of HOMA (Homeostatic model assessment) insulin resistance was found in 68.62% of study subjects. Fasting serum insulin in obese and non-obese patients was compared, which was statistically not significant P value – 0.5750. Status of insulin resistance in obese and non-obese patients was compared which was statistically insignificant.*
Conclusion: *In this study a quantitative study of serum insulin, fasting blood glucose (FBG) level was estimated in 102 patients of polycystic ovarian syndrome.*
Hormonal milieu in normal weight and obese women differs. Insulin resistance is common in PCOS women which is independent of obesity.
Keyords: *Serum insulin, polycystic ovarian disease, insulin resistance, hyperinsulinemia.*

I. Introduction

Polycystic ovarian syndrome (PCOS) is the most common endocrine disorder among women between the ages of 18 and 44 [1]. It affects 5% to 10% of this age group [2]. It is one of the leading cause of poor fertility [3] and metabolic syndrome[4]. Polycystic ovarian syndrome is known to the associated with insulin resistance in both lean and obese individuals. Insulin resistance in fact is felt to be a key feature in the reproductive and metabolic dysfunction of PCOS. There are numerous studies reporting the benefits of insulin sensitizing therapy.

The association of obesity with PCOS has been noted since the first description of PCOS in the 1930s [5]. Despite this finding the diagnostic feature of PCOS do not include obesity, but rather the diagnostic criteria include clinical or biochemical heperandrogenism, oligo-ovulation and presence of polycystic ovaries on ultrasound [6].

Associated conditions include type 2 diabetes, obesity, obstructive sleep apnoea, heart disease mood disorders and endometrial cancer [3]. Diagnosis is based on two of the following three finding: no ovulation, high androgen level and ovarian cyst [3]. PCOS has no cure [7]. Insulin resistance is a major feature of PCOS and is particularly prevalent in those women who are obese with 70-80% demonstrating insulin resistance and compensatory hyperinsulinemia [8]. Hyperinsulinemia is an important finding associated with the features of PCOS and addressing the hyperinsulinemia can be critical to the management of the disorder[9]. Serum insulin, Insulin resistance and homocysteine levels are higher in women with PCOS[10]. It is a multi system disorder with the primary problem lying in hormonal regulation in the hypothalamus, with the involvement of many organs. The term PCOD is used when there is ultrasonographic evidence. The term PCOS is used since there is a wide spectrum of symptoms possible and cysts in the ovaries are seen only in 15% of people [11].

II. Materials And Method

The present study "Estimation of serum insulin in polycystic ovarian disease" and compare insulin resistance in obese and non obese patients of PCOD was conducted in the department of Biochemistry, Mahatma Gandhi Medical College, Jamshedpur.
A total of 102 cases were studied. The study subjects were selected randomly from patients visiting the Outpatient Department Of Obstetrics And Gynaecology.
Inclusion Criteria

The diagnosis of PCOD is fulfilled by Rotterdam ESHRE / ASRM – Sponsored PCOS consensus criteria, when two of the following first three clinical features will be present[12].

- Clinical or biochemical evidence of hyperandogenism.
- Chronic anovulation
- Polycystic ovaries on imaging.
- Age 14 - 45 years
- Female
- Should be fasting for at least 12 hours.
- Should readily agree to participate in the study with an informed consent.

Exclusion Criteria:-

- Any major systemic illness.
- Congenital adrenal hyperplasia.
- Hyperprolactinemia
- Thyroid dysfunction
- Functional hypothalamic amenorrhoea
- Non-co-operative patients.

Study Tools :-

- Collection of blood samples : An overnight fasting blood with caution to avoid hemolysis and contamination.
- Diagnosis of cases by modified Rotterdam ESHRE / ASRM – sponsored PCOS consensus criteria.
- Fasting plasma glucose was evaluated with the help of fully automated chemistry analyzer BECK MAN COULTER AU480.
- Fasting serum insulin was evaluated with the help of ENZYME LINKED IMMUNO SORBENT ASSAY (ELISA).

The blood sample was collected in a plain vial and allowed to clot for serum insulin estimation. A part of drawn blood was put in the fluoride vial (containing sodium fluoride and potassium oxalate) plasma to estimate glucose level. The serum and plasma were analyzed on the same day using fully automated chemistry . Fasting blood glucose was categorized into normal (<100mg/dl), Prediabetes (100-125 mg/dl) and diabetes (>126 mg/dl), according to 2003 American Diabetes association (ADA) 2006.

CALCULATION OF HOMA – IR

HOMA (Homeostatic model assessment) has been widely employed in clinical research to assess insulin sensitivity. It is calculated by the product of the fasting values of glucose (expressed as mg/dl) and insulin (expressed as µu/ml) divided by a constant 405.

HOMA IR = Insulin x Glucose ÷ 405.

It should be noted that HOMA and fasting insulin values increase in the insulin resistant patients while the Glucose / Insulin ratio decreases. The reference range for fasting insulin is 2.6 – 24 µu/ml. HOMA >1.9 indicates insulin resistance.

Observation And Result – Table I

Distribution of cases according to FPG

FPG	NUMBER OF PATIENTS	PERCENTAGE
≥ 1oo mg/dl	26	25.49
< 100 mg/dl	76	74.50
TOTAL	102	100.0

25.49% of the study population had impaired blood glucose.

Distribution Of Cases According To Fasting Insulin Level – Table Ii

INSULIN	NUMBER OF PATIENTS	PERCENTAGE
Increased ≥13µIu	75	73.52
Normal <13µIu	27	26.47
TOTAL	102	100.0

Hyperinsulinemia was present in 73.52% of the study population.

Distribution Of Cases According To Insulin Resistance – Table Iii

HOMA IR	NUMBER OF PATIENTS	PERCENTAGE
Present HOMA IR >1.9	70	68.62
Absent HOMA IR <1.9	32	31.37

TOTAL	102	100.0

Higher value of HOMA IR was found in 68.62% study subjects.

Comparision Of Status Of Fasting Serum Insulin In Overweight / Obese And Non-Obese Pcos Patients- Table Iv

SERUM INSULIN	NORMAL WEIGHT PCOS (NUMBER)	OVERWEIGHT/OBESE PCOS (NUMBER)
NORMAL	11	16
RAISED	21	54
TOTAL	32	70

Analyzed using FISCHER'S TEST
P value – 0.5750 (Not significant)

Comparision Of Status Of Insulin Resistance In Overweight/Obese And Non-Obese Pcos Patients - Table V

HOMA	NORMAL WEIGHT PCOS (NUMBER)	OVERWEIGHT/OBESE PCOS (NUMBER)
NORMAL	12	20
RAISED	20	50
TOTAL	32	70

III. Discussion

Present study was done to determine the prevalence of elevated serum insulin levels in patients with PCOS as well as to compare insulin resistance in obese and non-obese PCOS patients. The prevalence of Insulin resistance is compared to that reported by Kalra et al [13].

The authors in their study, association of obesity and Insulin resistance with dyslipidemia in Indian PCOS women have reported 76.9% prevalence of insulin resistance. Insulin levels are significantly higher in overweight/obese patients as compared to normal weight. The proportion of patients showing insulin resistance in normal weight and overweight/ obese is comparable. Also the difference between mean HOMA in overweight/ obese and normal weight is statistically insignificant. This indicates that insulin resistance in PCOS women is independent of obesity. Our result is in accordance to the study by Andrea Duneif et al [14]. The authors have inferred that women with PCOS have a distinct disorder of insulin action not secondary to obesity. Decreased insulin sensitivity has been demonstrated in lean and obese women suggesting that the disorder is intrinsic to PCOS. But the degree of resistance is high in obese women as the insulin level is greater in obese.

Women with PCOS, independent of obesity are insulin resistant and have compensatory hyperinsulinemia as a result of their disorder [15]. However, higher value of insulin as stated above in overweight/ obese patients indicate, that excessive body weight in PCOS exacerbates or hastens the complications of the disease.

A majority of women with PCOS are insulin resistant and / or are obese. Their elevated insulin levels contribute to cause the abnormalities seen in the hypothalamic – pituitary – ovarian excess that leads to PCOS. Hyperinsulinemia increases GnRH pulse frequency, leutinizing hormone over follicular stimulating hormone dominance, increased ovarian androgen production [4], decreased follicular maturation and decreased sex hormone binding globulin, all these steps contribute to the development of PCOS. Insulin resistance is a common finding with a normal weight as well as over weight women [1, 10].

Since the report by Burghen et al [16] in 1980 that PCOS was associated with hyperinsulinemia , it has become clear that syndrome has major metabolic as well as reproductive morbidities. Burghen and Colleague [16] reported that women with the common hyperandrogenic disorder, PCOS has basal and glucose stimulated hyperinsulinemia compared with weight matched control women, suggesting the presence of insulin resistance.

The presence of hyperinsulinemia in PCOS women, independent of obesity was confirmed by a number of groups world wide [17,18]. Hughesdon [19], reported however that upon careful examination of ovaries from PCOS women, small islands of hyperthecosis were usually present. This morphologic change was more extensive in insulin resistant PCOS women, suggesting that hyperinsulinemia had an impact on ovarian morphology as well as on function [20].

Insulin resistance is an important defect in the pathogenesis of Non-insulin dependant diabetes mellitus (NIDDM) [21]. In the presence of peripheral insulin resistance, pancreatic B-Cell insulin secretion increases in a compensatory fashion. NIDDM develops when the compensatory increase in insulin level is no longer sufficient to maintain euglycemia [22]. Hyperinsulinemia can result from decrease in insulin clearance as well as from increased insulin secretion. Indeed decreased insulin clearance is usually present in insulin resistant states since insulin clearance is receptor mediated and acquired decrease in receptor number and/ or function are often present in insulin resistance secondary to hyperinsulinemia and / or hyperglycaemia [23].

There is considerable evidence that hyperinsulinemia, noted in majority of women with PCOS, contribute to the reproductive and metabolic dysfunction of the condition, but whether insulin resistance is a primary defect in PCOS is not clear. Women with PCOS and obesity have an increased rate of conversion to type 2 diabetes in a recent long term study [24]. Therefore management of insulin resistance is imperative and has been shown to delay the onset of diabetes [25, 26].

IV. Conclusion

PCOS is associated with insulin resistance in the majority of cases with or without obesity but insulin resistance is increased in obese individuals. As obesity is present in a majority of patients with PCOS, with a significant risk of developing type 2 diabetes mellitus, insulin resistance is a reasonable therapy target in PCOS treatment paradigm.

Bibliography

[1]. Teede H, Deeks A, Moran L (2010). "Polycystic ovarian syndrome: A complex condition with Psychological, reproductive and metabolic manifestation that impacts on health across the lifespan. BMC. Med 8 (1): 41. doi;10.1186/1741-7015-8-41.
[2]. How many people are affected or at risk of PCOS? http://www.nichd.nih.gov. 2013-05-23. Retrieved 13 March 2015.
[3]. Polycystic ovary syndrome (PCOS) condition information. American college of Obstetricians & Gynaecologists (2011). Polycystic ovary syndrome
[4]. Mayo clinic staff (04 April 2011). Polycystic ovary syndrome- mayo clinic.com retrieved 15 November 2015.
[5]. Stein IF ML. Amenorrhoea associated with bilateral polycystic ovaries. Am J obstet Gynaecol 1935; 29: 181-191.
[6]. The ESHRE/ASRM-Sponsored PCOS. Consensus workshop group. Revised 2003 consensus on diagnostic criteria and long term health risk related to polycystic ovary syndrome. Fertil Steril. 2004; 81: 19-25.
[7]. http://www.nichd.nih.gov. Is there a cure of PCOS? 2013-05-23. Retrieved 13 March 2015.
[8]. Deugarte CM, Bartolucci AA et al. Prevelence of insulin resistance in the polycystic ovary syndrome using the homeostasis model assessment. Fertil Steril 2005; 83: 1454-60.
[9]. Kathleen M Hoeger. Curr obes Rep (2012) syndrome: insulin sensitizing therapy.1: 191-198.
[10]. Nafiye Y, Sevtap K et al (2010) the effect of serum and intrafollicular insulin
[11]. resistance parameters and homocystine levels of nonobese, non
[12]. hyperandrogenemic polycystic ovary syndrome patients on in vitro
[13]. fertilization outcome. Fertil, steril 93 (6): 1864-9.
[14]. heterogeneity Hum. Reprod. Update 7 (1): 3-7.
[15]. Revised 2003 consensus on diagnostic criteria and long-term health risk
[16]. related to polycystic ovary syndrome. Rotterdam ESHRE/ASRM. Sponsored
[17]. PCOS consensus workshop group. Fertil Steril 2004; 81:19-25.
[18]. Kalra A, Nair S, Rai L, Indian J Med Sci 2006; 60: 447-53.
[19]. Dunaif A, Segar KR, et al. Diabetes 1989; 38: 1165-74.
[20]. Chang RJ, Nakamura RM et al. Clin Endocrinol metab 1983; 57: 356.
[21]. Burghen GA, Ginen JR et al. 1980. Corelation of hyperandrogenism with hyperinsulinsm in polycystic ovarian disease. J Clin Endocrinol metab 50: 113-116.
[22]. Pasquali R, Venturoli S, 1982 Insulin and C-peptide levels in obese patients with polycystic ovaries. Horm metab Res 14: 284-287 Cross ref, medline.
[23]. Shoupe D, Kumar DD 1983 Insulin resistance in polycystic ovary syndrome. Am J Obstet Gynecol 147: 588-592.
[24]. Hughesdon PE 1982 Morphology and morphogenesis of the Stein-leventhal ovary and of so called "Hyperthecosis". Obstet Gynecol surv 37: 59-77 Cross ref medline.
[25]. Dunaif A, Hoffman AR et al 1985. The clinical biochemical and ovarian morphologic features in women with acanthosis nigricans and masculinization. Obstet Gynecol 16: 545-552.
[26]. Kahn CR 1994 Insulin action, diabetogenesis and the cause of
[27]. Type-II diabetes. Diabetes 43: 1066-1084 Cross ref medline.
[28]. Bergman RN 1989 Toward physiological understanding of glucose tolerance. Minimal model approach. Diabetes 38: 1512-1527 Cross ref medline.
[29]. Marshall S 1985 Kinetics of Insulin receptor internalization and recycling in adipocytes shunting of receptor to a degradative pathway by inhibitors of recycling. J Biochem 260: 4136-4144 medline.
[30]. Gambineri A, Patton L, et al. Polycystic ovary syndrome is a risk factor for type 2 diabetes:results from a long term prospective study. Diabetes diabetes 2012 June 14.
[31]. Knowler WC, Barrett Connor E et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002; 346: 393-403.
[32]. Tuomilehto 2, Lindstorn J et al. Prevention of type 2 diabetes mellitus by changes
[33]. in lifestyle among subjects with impaired glucose tolerance, N Engl J Med 2001; 344: 1343-50.