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# RELATIONSHIP BETWEEN INTRA-ABDOMINAL FAT AND OVULATION IN OBESE POLYCYSTIC OVARIAN SYNDROME PATIENT: A PROSPECTIVE STUDY IN INDIAN POPULATION

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**ABSTRACT** Obesity and PCOS is one of the major modifiable causes of fertility problems. The aim of our study was to compare the changes in body fat distribution between a group of anovulatory women with PCOS and obesity who resume ovulation (Ov+) to those who remain anovulatory (Ov-) undergoing a lifestyle modification programme.

60 anovulatory women with PCOS underwent a 6 month lifestyle modification programme. Body fat distribution was assessed by anthropometrics, ultrasonography, and multi slice abdominal CT scan at beginning, after 3 months and after 6 months and analysed statistically.

It was found from the study that-: The total group of Ov+ women lost more weight (6.7 versus 2% at 6 months, and abdominal fat(IAF) on CT (18.5 versus 1.04% at 3 months) compared with the total group of Ov- women, At 6 month the difference was 31% in Ov+ compared to 8% in Ov- .

The IAF on USG had reduced in Ov+ from baseline as 5.2% at 3month and as 12.2% at 6 month, in comparison Ov- showed reduction as 1.7% at 3 moth and 3.4% at 6 month.

In Ov+ women, there was a difference in loss of SAF (CT) between baseline and 3 months (7 versus 0 .8% ) compared with Ov- women. At 6 month the difference was 16% versus 3.2%.

SAF (US) had reduced in Ov+ from baseline as 7.7% at 3month and as 13% at 6 month, in comparison Ov- showed reduction as 1.2% at 3 month and 2.4% at 6 month.

It may be concluded that-: In anovulatory women with PCOS and obesity undergoing a lifestyle programme, Ov+ women lose more body weight and abdominal fat than Ov- women. Loss of IAF is more associated with resumption of ovulation.

**KEYWORDS :** subcutaneous abdominal fat / intra-abdominal fat/ovulation.

## INTRODUCTION

Overweight and obesity plays a major role in anovulation and that there occurs exponential increase in anovulation in relation to with increasing body weight [7, 6].

A Women is said to be having poly cystic ovarian syndrome if two of the following criteria is satisfied (Rotterdam consensus diagnostic criteria); [8]

1. Anovulation (women with cycle interval ≥6 months, women with cycles ≤42 days in whom ovulation could not be confirmed by ultrasound monitoring were considered anovulatory)
2. Hyperandrogenemia (clinically or biochemically)- serum testosterone level > 3.5 nmol/l or a free testosterone level > 62 pmol/l or when clinical hirsutism was present.
3. Polycystic ovary morphology on ultrasound and after other endocrine causes of anovulation were excluded.

Increased abdominal fat accumulation in obese PCOS women (waist hip ratio > 0.8) may lead to reproductive dysfunction and fertility problem, mainly anovulation [9,10].

Abdominal fat accumulation is an indicator of higher metabolic risk profile since it is associated with insulin resistance (IR) [11].

Hyperinsulinemia in women with obesity contributes to anovulation by increased ovarian androgen secretion leading to arrest of follicle growth [10, 12].

Loss of abdominal fat, on the other hand, is associated with resumption of menstruation and ovulation in obese women [13, 14].

## AIM OF THE STUDY

To study the Variation of body fat distribution by measuring IAF and SAF of a group of obese anovulatory women with PCOS who resumed ovulation(Ov+) to those who remained anovulatory(Ov-) after undergoing a lifestyle modification for a six month duration.

## MATERIALS AND METHODS

**SOURCE OF DATA:** The study was conducted in the Department of Physiology, Biochemistry, Obstetrics & Gynaecology & Radio diagnosis, SCB Medical College,Cuttack,Odisha,India.

**STUDY PERIOD:** September 2013 to September 2015

**STUDY DESIGN:** Prospective cohort study.

In this study, 60 anovulatory obese women were recruited from those attending the Obstetrics and Gynaecology OPD in S.C.B Medical College & Hospital,Cuttack between 2013 and 2015 basing upon the following Inclusion criteria and exclusion criteria.

### INCLUSION CRITERIA

BMI >29 kg/m2
Infertility≥1 year,
Age <35years

### EXCLUSION CRITERIA

1. Participant who had hormonal medications / metformin in the previous 3 months
2. Abnormal serum prolactin level
3. Abnormal thyroid hormone levels The subjects underwent life style modification programme for 6 month and evaluated for resumption of ovulation and measured for Intra-abdominal fat at 3 month and 6 month time.

### LIFESTYLE PROGRAMME

All participants received individualized dietary advice aiming for reduction in calorie intake of at least 500 kilocalories/day and a total calorie intake within 1500 kilocalories/day. An individualized exercise programme was for each participant. Individual guidance consisted of visits every 2 weeks, during which body weight was measured.

### BMI MEASUREMENT

Body weight (kg), height (cm), BMI [weight (kg)/ (height in meters)$^2$], waist circumference (Wc) was measured at the narrowest part of the abdomen between the lower rib and the iliac crest.

### ABDOMINAL FAT MEASUREMENT

It was measured by using ultrasonography (US) and computed tomography (CT).

Ultrasound was performed using PHILIPS HD-7 machine at Dept. Of Radio diagnosis, S.C.B.M.C.H,Cuttack, with a 3.5 MHz convex-array

and 11 MHz linear- array abdominal transducer to measure IAF and SAF. All measurements were performed at the level of the Waist circumference. IAF measurements were performed in the midline and the right and left longitudinal lines (10 cm to the left and right of the midline, respectively) in a longitudinal plane. IAF was measured as the distance in cm from the anterior boundary of the lumbar vertebra and the peritoneal boundary of the anterior abdominal wall. SAF was measured in the midline, in a transversal plane at the level of the Waist circumference, as the distance in cm from the cutaneous boundary to the linea alba. Measurements were done at the end of a quiet expiration[16]

Using CT scan few slices were taken at the level of the umbilicus for the measurement of the IAF and the SAF. IAF and SAF volume was calculated by multiplying the IAF and SAF area of each slice with the slice thickness, and the mean volume of the slices was taken for analysis.[15]

All measurements were performed at RDC, SCB MCH by the 16 slice GE Bright speed MDCT scanner.

Pregnancy was excluded before each CT scan by a urine pregnancy test (UPT).

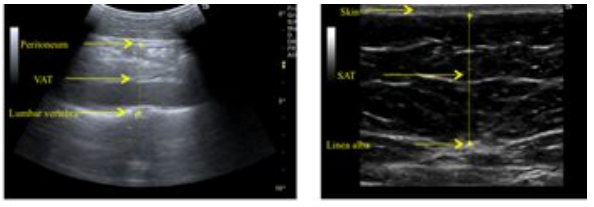
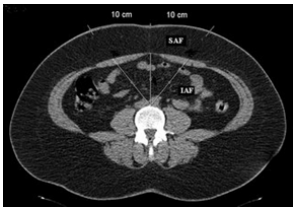



**Fig.1. Abdominal ultrasound showing the intra-abdominal fat (IAF=VAT) and the subcutaneous abdominal fat (SAF=SAT) measurements.**




**Fig, 2. CT scan showing the intra-abdominal fat (IAF) and the subcutaneous abdominal fat (SAF). The lines indicate the location of the distance measurement of IAF.**

## BIOCHEMICALASSESSMENT

Serum insulin was measured after an overnight fast at 0 , after 3 months and after 6 months of the lifestyle modification program.

## TEST FOR OVULATION

The subjects were evaluated for ovulation by basal body temperature (BBT) monitoring and TAS (Trans abdominal) & TVS (trans vaginal ultrasound scan ) at the end of 3 month and 6 month of life style modification . (TVS- in case of married females and TAS in case of unmarried ladies .TVS Ultrasound was performed using PHILIPS HD-7 machine at Dept. Of Radio diagnosis, S.C.B.M.C.H, Cuttack, with a 5 MHz TVS transducer. Features of ovulation in USG are, 1. Non-visualisation of previously visible dominant follicle and 2. Mild fluid in pouch of douglas.

## STASTICALANALYSIS

At the end of the lifestyle program, the participants were divided into two group those who had resumed ovulation (Ov+) and those who had not resumed ovulation (Ov-) Between-group comparisons were performed using an independent samples Student's t-test .The obtained data were analyzed by using a software statistical package for the social science (SPSS version 20). Frequency and descriptive analyses were used to describe the data. Paired samples t-test was also used to differentiate between two numerical data of two phases. Any difference or correlation was considered significant if p value less than 0.05 ($P<0.05$).

## RESULTS

Sixty anovulatory obese women with PCOS were included in the lifestyle programme and their baseline data were recorded. During the first 3 months, the five women conceived and five drop-outs left the programme, leaving 50 participants to measure and record the data at 3 months. Out of the 50 participants continuing the second 3 months of the lifestyle programme, the twenty women who resumed ovulation left the programme, leaving 30 participants to measure and record the data at 6 months.

The total group of Ov+ women lost more weight (6.7 versus 2% at 6 months, $P = 0.018$,) and abdominal fat (IAF) on CT (18.5 versus 1.04% at 3 months, $P = 0.025$ ) compared with the total group of Ov- women. At 6 month the difference was 31% in Ov+ compared to 8% in Ov- .

The IAF (US) had reduced in Ov+ from baseline as 5.2% at 3month and as 12.2% at 6 month, in comparison Ov- showed reduction as 1.7% at 3 moth and 3.4% at 6 month.

In Ov+ women, there was a difference in loss of SAF (CT) between baseline and 3 months (7 versus 0 .8%, $P =0.031$) compared with Ov- women. At 6 month the difference was 16% versus 3.2%.

SAF (US) had reduced in Ov+ from baseline as 7.7% at 3month and as 13% at 6 month, in comparison Ov- showed reduction as 1.2% at 3 moth and 2.4% at 6 month.

**TABLE – 1: Baseline Parameters of 60 study subjects**

| CATEGORY | MEASUREMENTS |
|---|---|
| Age | 26.33 |
| BMI(kg/m$^2$) | 39.8+5.5 |
| IAF(US) in cm | 5.7 |
| SAF(US) in cm | 7.7 |
| WC | 116±17 |
| IAF(CT)incm$^3$ | 194±57 |
| SAF(CT) incm$^3$ | 999±55 |
| FASTING INSULIN | 189(29-534) |

*p value < 0.05, statistically significant.

***TABLE- 2: Characteristics of 50 Study subjects divided into those who resumed ovulation (Ov+) and those who remained anovulatory (Ov-) at the end of 3 months.***

| CATEGORY | Ov+)N=20 | Ov-)N=30 |
|---|---|---|
| AGE | 26.9±3.0 | 28.5±9.4 |
| BMI | 31.8±4.2 | 37.9±5.2 |
| IAF(US) in cm | 5.4 | 5.6 |
| SAF(US) in cm | 7.1 | 7.6 |
| WC | 110±15 | 114±12 |
| IAF(CT) cm$^3$ | 158±24 | 192±60 |
| SAF(CT) cm$^3$ | 928±21 | 991±170 |
| FASTING INSULIN | 156 | 184 |

*p value < 0.05, statistically significant

***TABLE- 3: Characteristics of 30 study subjects divided into those who resumed ovulation (ov+) and those who remained anovulatory (ov-) at the end of 6 month***

| CATEGORY | (Ov+) N=22 | Ov-) N=8 |
|---|---|---|
| AGE | 27.89±1.9 | 29.1±3.2 |
| BMI(kg/m$^2$) | 30.3±2.1 | 36,8±2.4 |
| IAF(US)cm | 5.0 | 5.5 |
| SAF(US)cm | 6.7 | 7.5 |
| WC | 104±8 | 114±18 |
| IAF(CT)cm3 | 132±18 | 178±92 |
| SAF(CT)cm$^3$ | 839±23 | 967±24 |
| FASTING INSULIN | 119 | 160 |

*p value < 0.05, statistically significant

***Diagram- 1: Changes in study parameters in ov+ and ov- group in 6 month.***

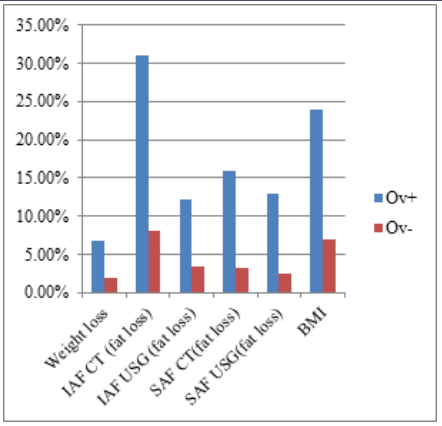
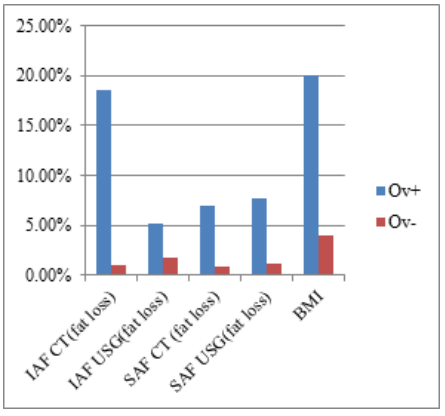



***Diagram - 2: Changes in study parameters in ov+ and ov- group in 3 month.***




## DISCUSSION

Loss of abdominal fat is associated with resumption of menstruation and ovulation in obese women with polycystic ovary syndrome (PCOS) undergoing a weight loss program.

It has been shown that resumption of ovulation in anovulatory women with obesity undergoing weight loss is mediated by improvement of IR and decrease in free androgen levels [17, 18, [10].

Abdominal fat consists of Intra-abdominal fat (IAF) and subcutaneous abdominal fat (SAF). In study subjects with obesity who lost weight, loss of IAF had a greater beneficial effect on IR than loss of SAF [19].

Specifically loss of IAF is required for improvement of IR, decrease in androgen levels and resumption of ovulation[21]

In anovulatory women it is found that more than 5% loss of body weight is required for resumption of ovulation [1,13,17].

Similar to our one, study conducted by Huber-Buchholz et al., 1999; Thomson et al., 2008 indicated that loss of abdominal fat is associated with resumption of ovulation.

Early and consistent loss of IAF over a 6-month period is associated with resumption of ovulation. Previous studies in different patient populations have shown that during the initial period of calorie restriction, preferential loss of IAF occurs which correlates signific antly with improvement in IR and resumption of ovulat ion[19,22]

In this study, anovulatory obese women with PCOS on resumption of ovulation were associated with more weight loss and loss of abdominal fat. Similar results were found by Kiddy et al., 1992; Guzick et al., 1994; Clark et al., 1995; Holte et al., 1995; Huber-Buchholz et al., 1999.

In the present Study the Ov+ women lost 18.55% abdominal fat during the lifestyle program, as compared with 1.04% loss of fat at 3 month and 31% vs 8% at 6 month as compared with Ov- .

These results Coincide with study conducted by Walter K.H. Kuchenbecker, Henk Groen, Sophie J. van Asselt, Johanna H.T. Bolster, J. Zwerver).

In our study there was loss of IAF and improvement in IR which coincides with study conducted by Caroll et al).[20]

This study shows that in anovulatory women with PCOS and obesity participating in a lifestyle programme, resumption of ovulation is associated with early and consistent loss of IAF. The most likely mechanism of resumption of ovulation after loss of IAF during a lifestyle programme is improvement of insulin resistance and lower free androgen levels.

## CONCLUSION

1. Life style modification and dietary management leads to loss of abdominal fat and weight loss significantly which positively affects ovulatory status of an obese PCOS woman.
2. PCOS is a growing problem among the reproductive age group women and can be modified through life style and dietary changes could prevent impending fertility issues.

## ABBREVIATION

IAF =Intra-abdominal fat
SAF =Subcutaneous abdominal fat
IR =Insulin resistance
USG =Ultrasound
CT = Computed tomography
Ov+ =Resumed ovulation
Ov - =ovulation not resumed

## REFERENCES

1. Kiddy DS, Hamilton-Fairley D, Bush A, Short F,Anyaoku V, Reed MJ,Franks S. Improvement in endocrine and ovarian function during dietary treatment of obese women with polycystic ovary syndrome. Clin Endocrinol (Oxf) 1992;36:105–111.
2. Carroll S, Dudfield M. What is the relationship between exercise and metabolic abnormalities? A review of the metabolic syndrome. Sports Med 2004;34:371–418
3. Clark AM, Ledger W, Galletly C, Tomlinson L, Blaney F, Wang X, Norman RJ. Weight loss results in significant improvement in pregnancy and ovulation rates in anovulatory obese women. Hum Reprod 1995;10:2705–2712.
4. Guzick DS, Wing R, Smith D, Berga SL, Winters SJ. Endocrin econsequences of weight loss in obese, hypera ndrogenic, anovulatory women. Fertil Steril 1994;6 1:598–604.
5. Huber-Buchholz MM, Carey DG, Norman RJ. Restoration of reproductive potential by lifestyle modification in obese polycystic ovary syndrome: role of insulin sensitivity and luteinizing hormone. J Clin Endocrinol Metab 1999;84:1470–1474
6. Jorge E. Chavarro, M.D., Sc.D.,1,2 Janet W. Rich-Edwards, M.P.H., Sc.D.,2,3,4 Bernard A. Rosner, Ph.D.,2,5 and Walter C. Willett, M.D., Dr.P ; Protein intake and ovulatory infertility; Am J Obstet Gynecol. 2008 Feb; 198(2): 210.e1–210.e7.
7. Rich-Edwards JW1, Goldman MB, Willett WC, Hunter DJ, Stampfer MJ, Colditz GA, Manson JE.; Adolescent body mass index and infertility caused by ovulatory disorder.; Am J Obstet Gynecol. 1994 Jul;171(1):171-7.
8. Human Reproduction, Volume 19, Issue 1, 1 January 2004, Pages 41–47, https://doi.org/10.1093/humrep/deh098;; Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS)
9. B M Zaadstra, J C Seidell, P A Van Noord, E R te Velde, J D Habbema, B Vrieswijk, and J Karbaat; Fat and female fecundity: prospective study of effect of body fat distribution on conception rates.; BMJ. 1993 Feb 20; 306(6876): 484–487.
10. R Pasquali, A Gambineri, U Pagotto; The impact of obesity on reproduction in women with polycystic ovary syndrome; BJOG: An International Journal of Obstetrics & Gynaecology, Volume 113, Issue 10, Version of Record online: 7 JUL 2006
11. Jean-Pierre Després, professor,a Isabelle Lemieux, PhD student,b and Denis Prud'homme, professor; Treatment of obesity: need to focus on high risk abdominally obese patients; BMJ. 2001 Mar 24; 322(7288): 716–720.
12. D Willis H Mason C Gilling-Smith S Franks; Modulation by insulin of follicle-stimulating hormone and luteinizing hormone actions in human granulosa cells of normal and polycystic ovaries; The Journal of Clinical Endocrinology & Metabolism, Volume 81, Issue 1, 1 January 1996, Pages 302–309, https:// doi.org/10.1210/jcem.81.1.8550768
13. Huber-Buchholz, MM, Carey, DG, Norman, RJ. Restoration of reproductive potential by lifestyle modification in obese polycystic ovary syndrome: role of insulin sensitivity and luteinizing hormone. Journal of Clinical Endocrinology and Metabolism. 1999;84:1470–1474.
14. Lisa J Moran,Grant Brinkworth, Manny Noakes, Robert J Norman; Effects of lifestyle modification in polycystic ovarian syndrome;AJOG; 2006;Volume 12, Issue 5, Pages 569–578
15. Kuchenbecker WK1, Groen H, Zijlstra TM, Bolster JH, Slart RH, van der Jagt EJ, Kobold AC, Wolffenbuttel BH, Land JA, Hoek A ;The subcutaneous abdominal fat and not the intraabdominal fat compartment is associated with anovulation in women with obesity and infertility.; J Clin Endocrinol Metab. 2010 May;95(5):2107-12. doi: 10.1210/jc.2009-1915. Epub 2010 Mar 3.
16.. Stolk RP, Wink O, Zelissen PM, et al. Validity and reproducibility of ultrasonography for the measurement of intra-abdominal adipose tissue. Int J Obes Relat Metab Disord 2001;25:1346-1351.
17. Guzick DS, Wing R, Smith D, Berga SL, Winters SJ. Endocrine consequences of weight loss in obese, hyperandrogenic, anovulatory women. Fertil Steril 1994;61:598–604.
18. Holte J, Bergh T, Berne C, Wide L, Lithell H. Restored insulin sensitivity but persistently increased early insulin secretion after weight loss in obese women with polycystic ovary syndrome. J Clin Endocrinal Metab;1995;80:2586–2593.
19. Park HS, Lee K. Greater beneficial effects of visceral fat reduction compared with subcutaneous fat reduction on parameters of the metabolic syndrome: a study of weight reduction programmes in subjects with visceral and subcutaneous obesity. Diabet Med

2005;22:266–272.
20. Carroll S, Dudfield M. What is the relationship between exercise and metabolic abnormalities? A review of the metabolic syndrome. Sports Med 2004;34:371–418.
21. Walter K.H. Kuchenbecker1,8,*, Henk Groen2, Sophie J. van Asselt1,Johanna H.T. Bolster1, J. Zwerver3, Riemer H.J. Slart4, Erik J. vd Jagt5,Anneke C. Muller Kobold6, Bruce H.R. Wolffenbuttel 7,Jolande A. Land1, and Annemieke Hoek ; In women with polycystic ovary syndrome and obesity, loss of intra-abdominal fat is associated with resumption of ovulation; Human Reproduction, Vol.26, No.9 pp. 2505–2512, 2011
22. Goodpaster BH, Kelley DE, Wing RR, Meier A, Thaete FL. Effects of weight loss on regional fat distribution and insulin sensitivity in obesity. Diabetes 1999;48:839–847.