

Metabolic consequences of Polycystic ovary syndrome (PCOS)

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Endocrinology & Metabolism

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Date: 15/07/2016



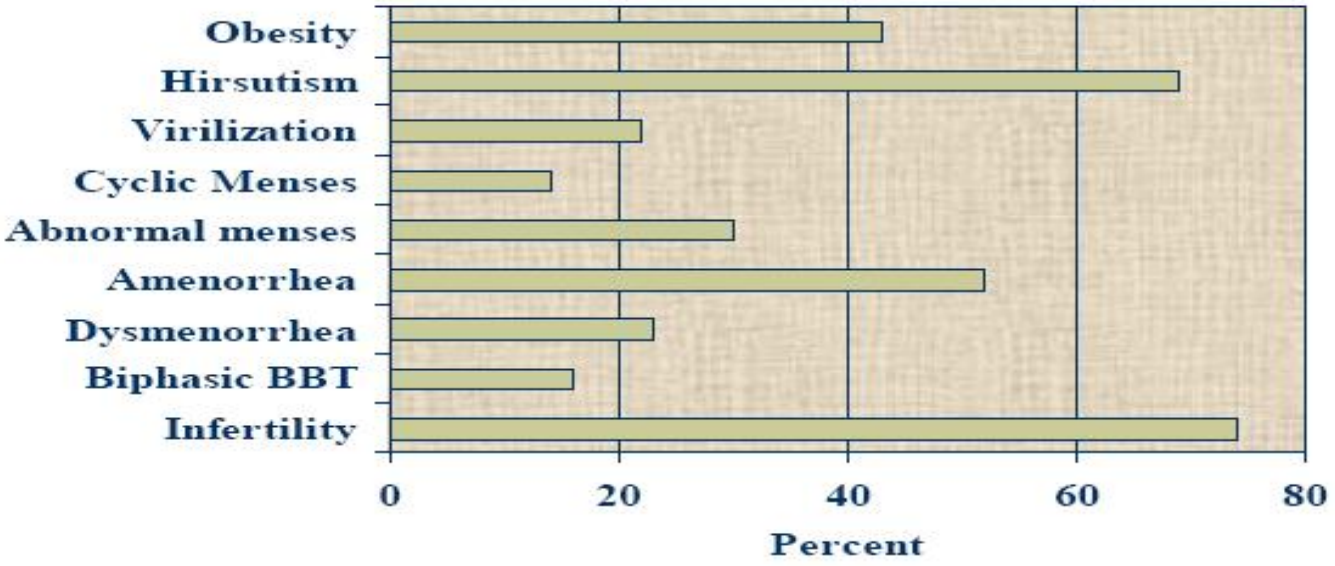
POLYCYSTIC OVARY SYNDROME



What is PCOS ?

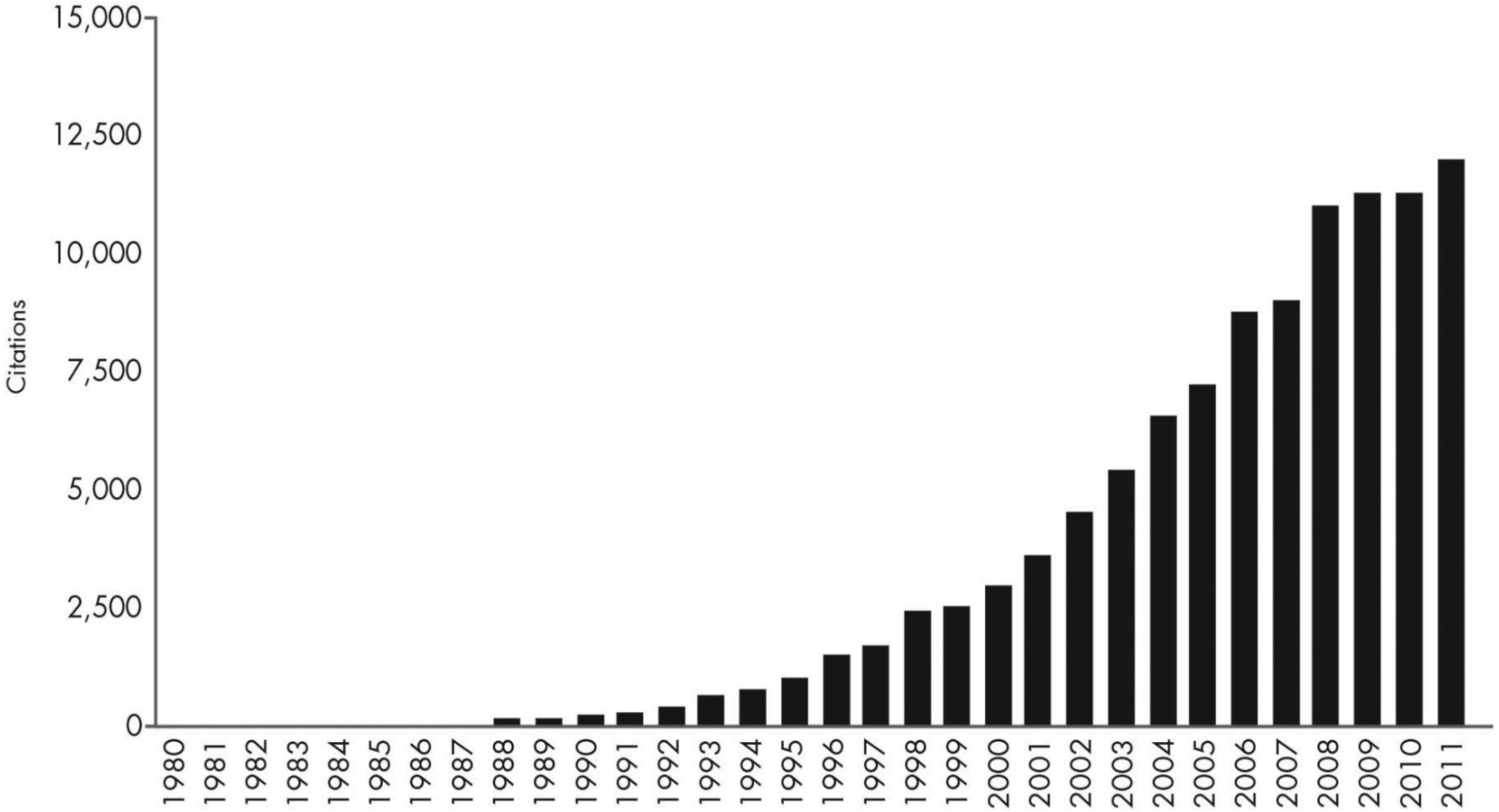
Stein and Leventhal in 1935

PCOS *Symptoms*



Goldzieher JW, et al: JCEM 22:325, 1962

A new field—Most extensively studied



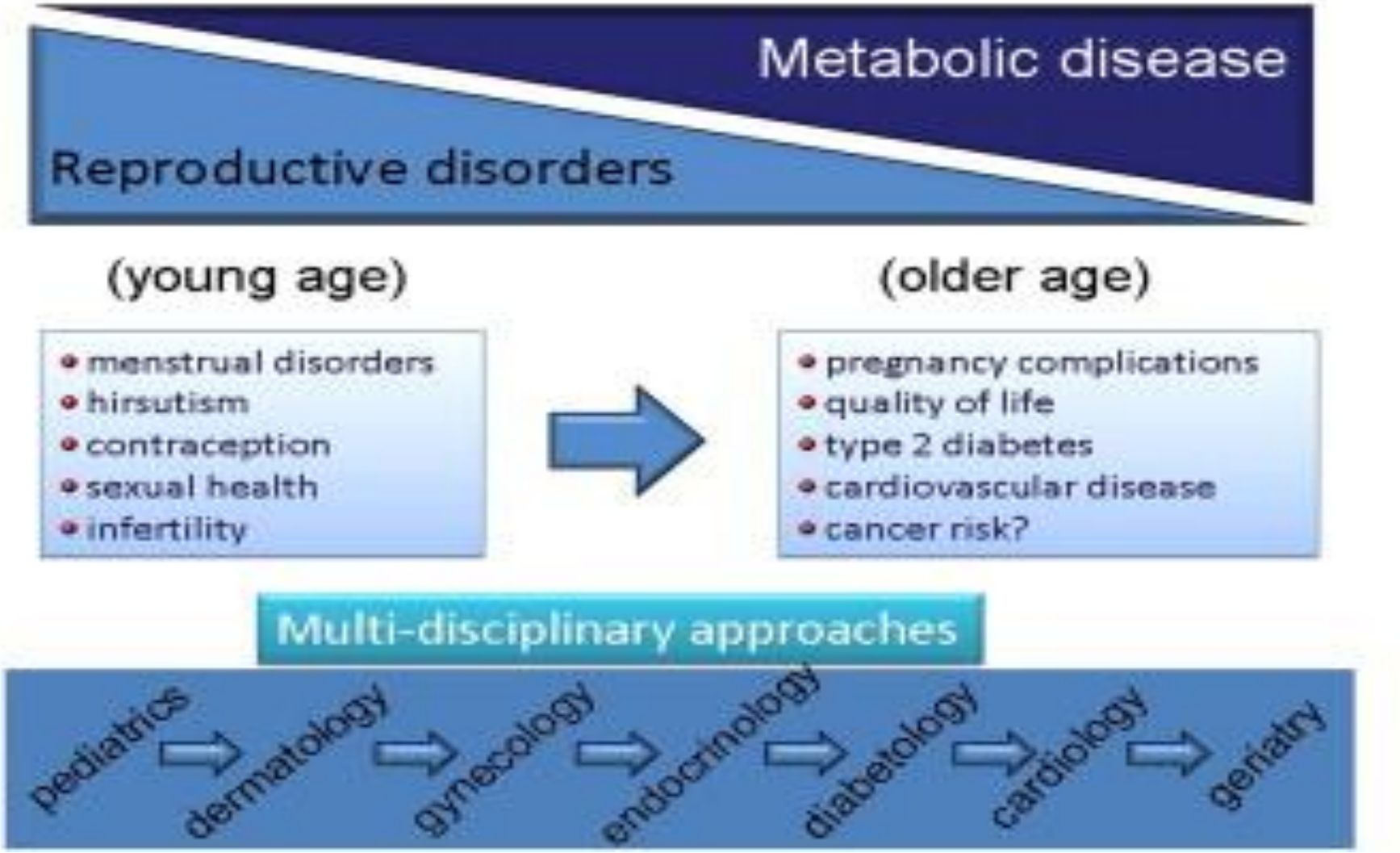
There are approximately 103,000 citations in a Web of Science (Thomson Reuters, New York, NY) Citation Report for 1980–2011 on the topics of PCOS or hyperandrogenism and hyperinsulinemia, insulin resistance, glucose intolerance, or diabetes mellitus. The annual citations have increased steadily from 1 in 1980 to approximately 12,000 in 2011

600 articles in QR of AE-PCOS

Diamanti-Kandarakis E , and Dunaif A Endocrine Reviews 2012;33:981-1030

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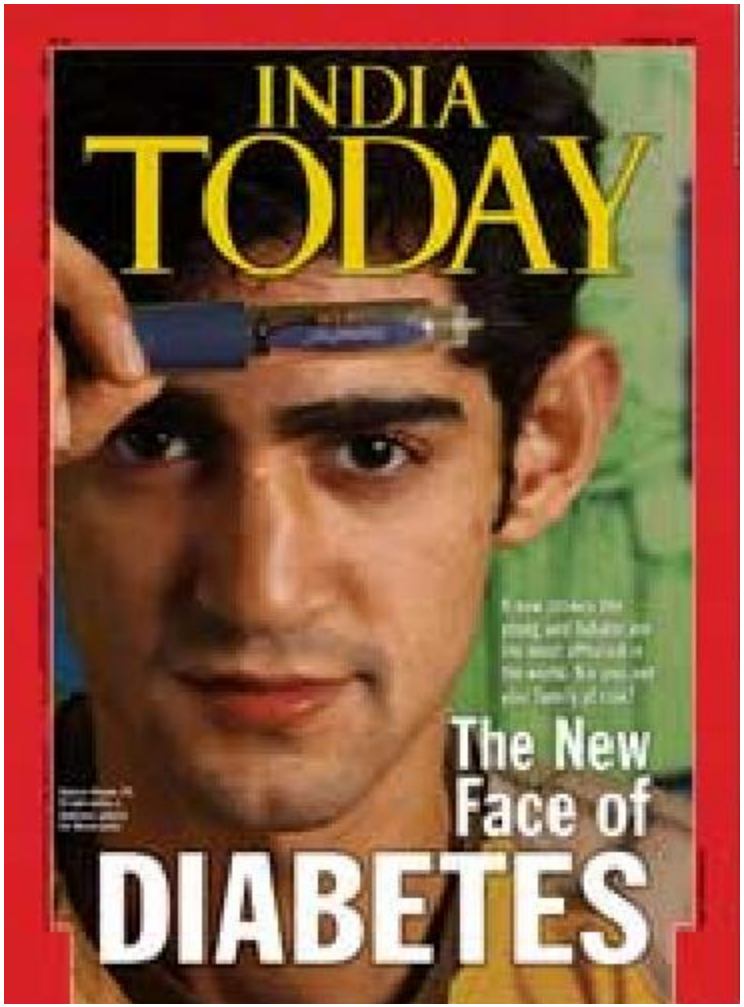
PCOS: *changing women's health paradigm*



Bart C.J.M. Fauser , Basil C. Tarlatzis , Robert W. Rebar , Richard S. Legro , Ada Consensus on women's health of polycystic ovary syndrome (PCOS): the Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Workshop Group

How common is PCOS ?

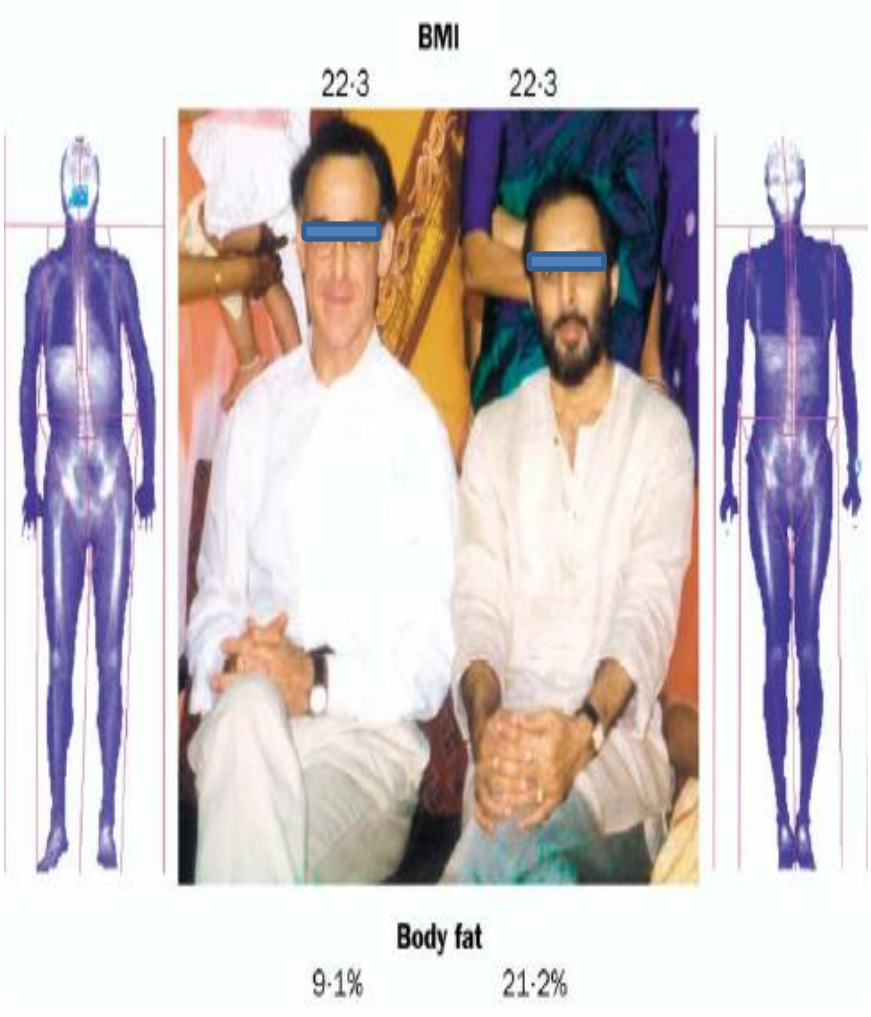
- PCOS affects 5-10% women in West
- 2-4% in Europe
- 19-21% in India ..parallel to DM prevalence



India
Diabetic capital ?
Parallels PCOS

India is also a **PCOS** capital

India vs. World



1. Elevated inflammatory markers
2. Insulin resistant
3. Central obesity
4. More fat mass
5. Less lean mass

How do you diagnose PCOS ?

PCOS Findings

Physical

- Obesity
- Hirsutism
- Acanthosis
- Abnormal menses
- Acne

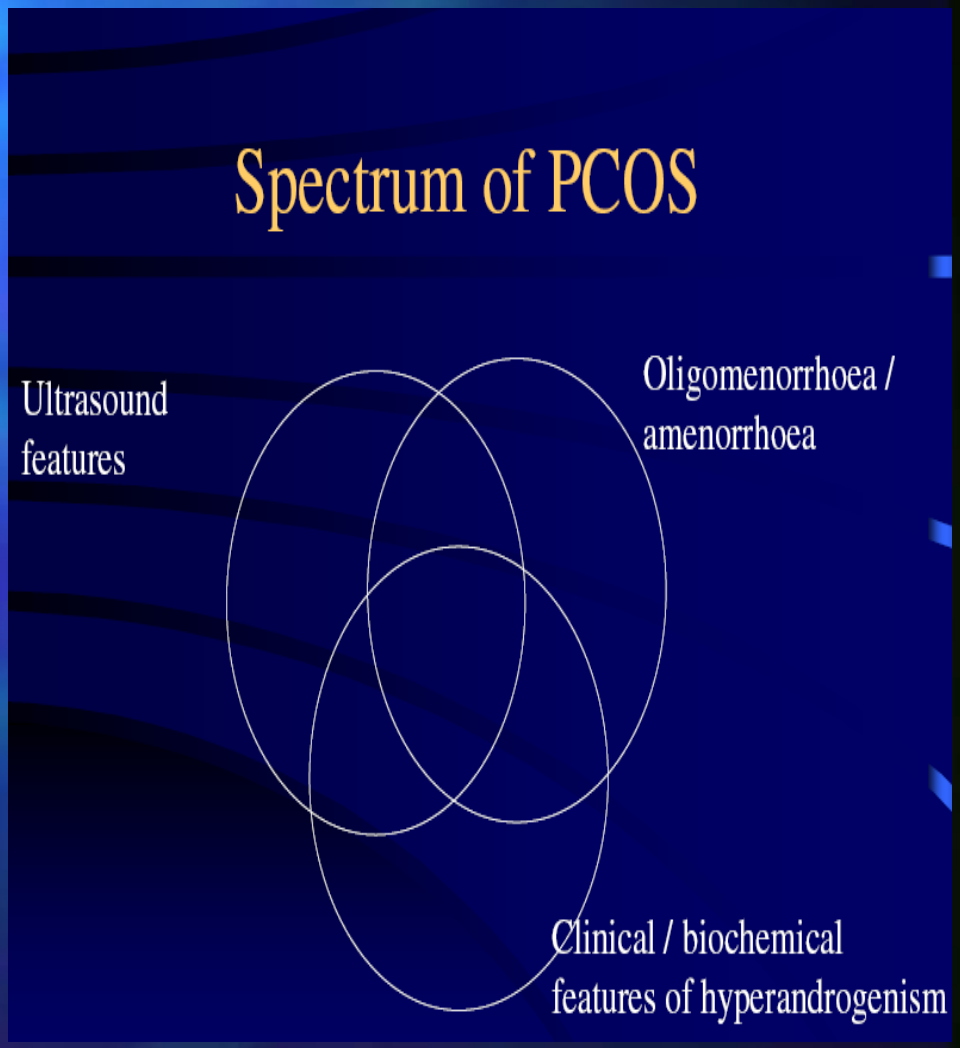
Biochemical

- ↑ Androgen
  - Testosterone
  - DHEAS
  - Androstenedione
  - 17OH progesterone
- ↓ SHBG
- ↑ LH
- Insulin/Glucose
- ↑ PAI-1
- ↑ Lipids

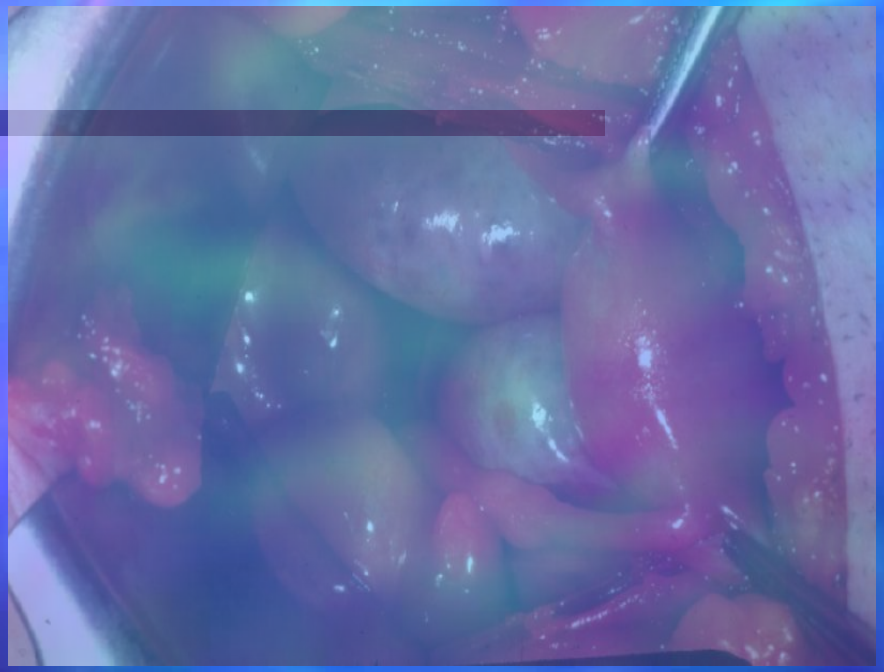
Ultrasound

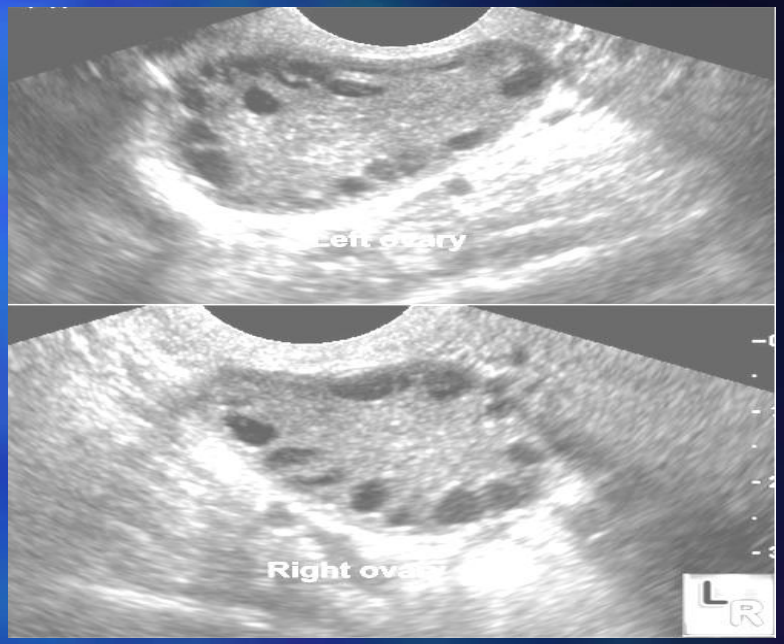
- Necklace sign
- ↑ Ovarian volume
- Antral follicle count
- Doppler blood flow changes

Spectrum of PCOS



Multiple necklace cysts





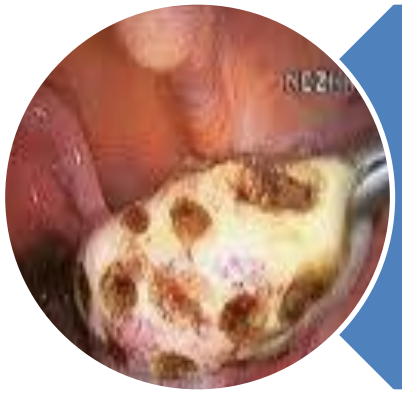
- Cysts are not must for diagnosis.
- They have no consequences

Original Article

Comparative evaluation of sonographic ovarian morphology of Indian women with polycystic ovary syndrome versus those of normal women

Sanjeed Ahmed, Shivani Pahwa[2], Chandan Jyoti Das[2], Farooq A Mir, Sobia Nisar[3], Majid Jehangir[4], Shameem Parveen[5], Aafia Rashid[6], Mohd Ashraf Ganie[1]

POLYCYSTIC OVARY SYNDROME



How does PCOS present?

The Dual Ordeal

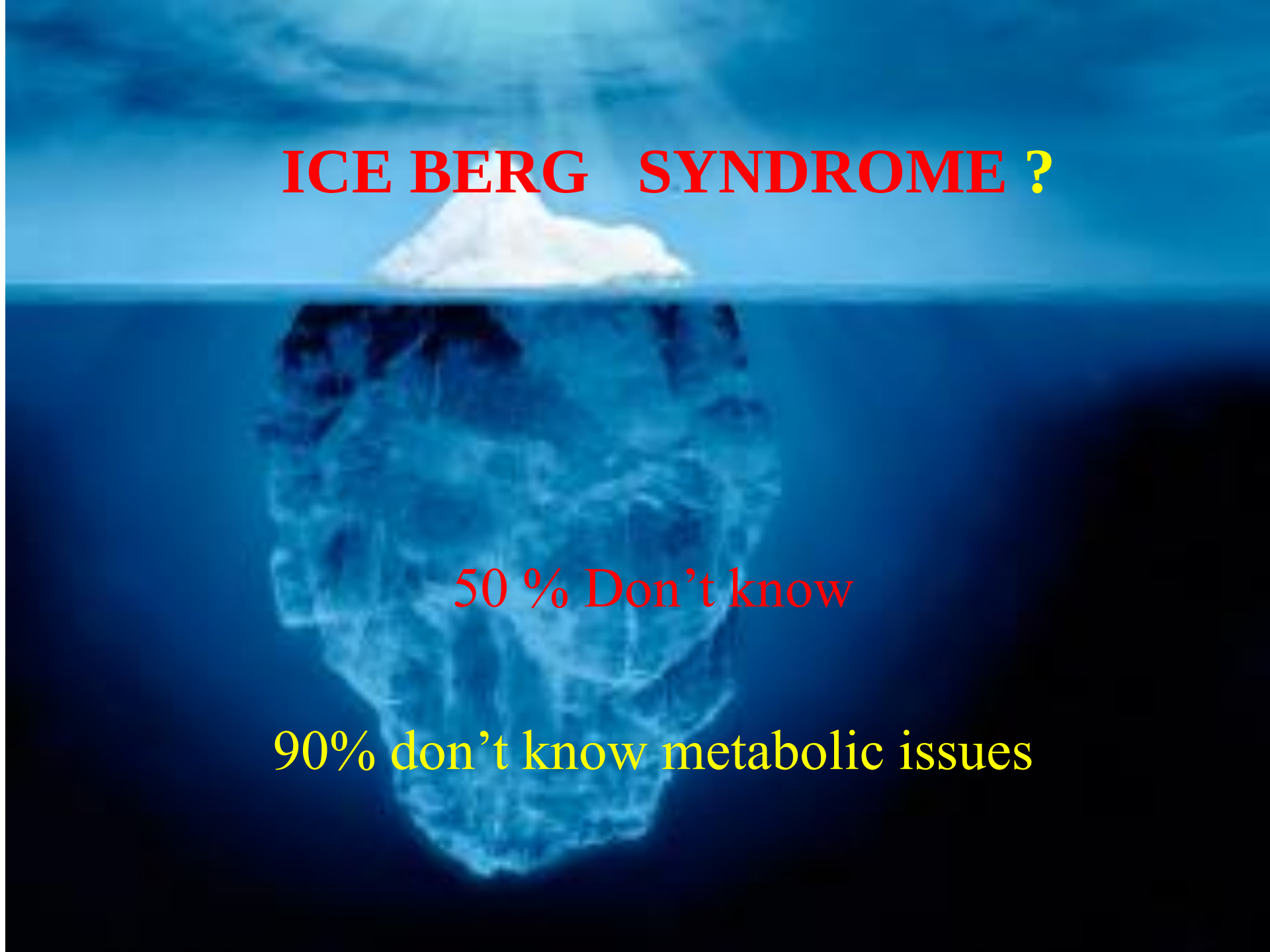
The Outlook

- Obesity
- Acne
- Hirsutism
- Alopecia

The inside story

- Cycle disturbances
- Infertility
- Insulin resistance
- Glucose intolerance
- Dyslipidemia
- Premalignant




ICE BERG SYNDROME ?
50 % Don’t know
90% don’t know metabolic issues

Menstrual disturbances

Normal cycles <35 days interval or >8 cycles in a year

T[redacted] Prevalence of menstrual dysfunction in PCOS

Study	Total no. PCOS	No. of PCOS patients with oligoamenorrhea	PCOS patients with oligoamenorrhea (%)[a]	No. of PCOS patients with eumenorrhea	PCOS patients with eumenorrhea (%)
Ferriman and Purdie, 1983	280	237	84.6	43	15.4
Conway *et al.*, 1989	556	395	71.0	139	25.0
Kiddy *et al.*, 1990	263	203	77.2	60	22.8
Ardaens *et al.*, 1991	144	105	72.9	39	27.1
Rajkhowa *et al.*, 1995	153	129	84.3		
Balen *et al.*, 1995	1741	1043	59.9	517	29.7
Falsetti and Eleftheriou, 1996	240	207	86.3	24	10.0
Khoury *et al.*, 1996	112	112	100.0	0	0.0
Talbott *et al.*, 1998	244	229	93.9	15	6.1
Carmina, 1998	332	290	87.3	42	12.7
Alborzi *et al.*, 2001	371	371	100.0	0	0.0
Williamson *et al.*, 2001	162	144	88.9		
Haddad *et al.*, 2002	146	120	82.2	26	17.8
Amer *et al.*, 2002	161	149	92.5	12	7.5
Glueck *et al.*, 2003	138	138	100.0	0	0.0
Orio *et al.*, 2003	100	100	100.0	0	0.0
Chang *et al.*, 2005	316	265	83.9	51	16.1
Hahn *et al.*, 2005	200	200	100.0	0	0.0
Total	5659	4437	78.4	968	18.1

Indicator of no egg shedding (Ovulation)- Infertility

Unwanted hair growth

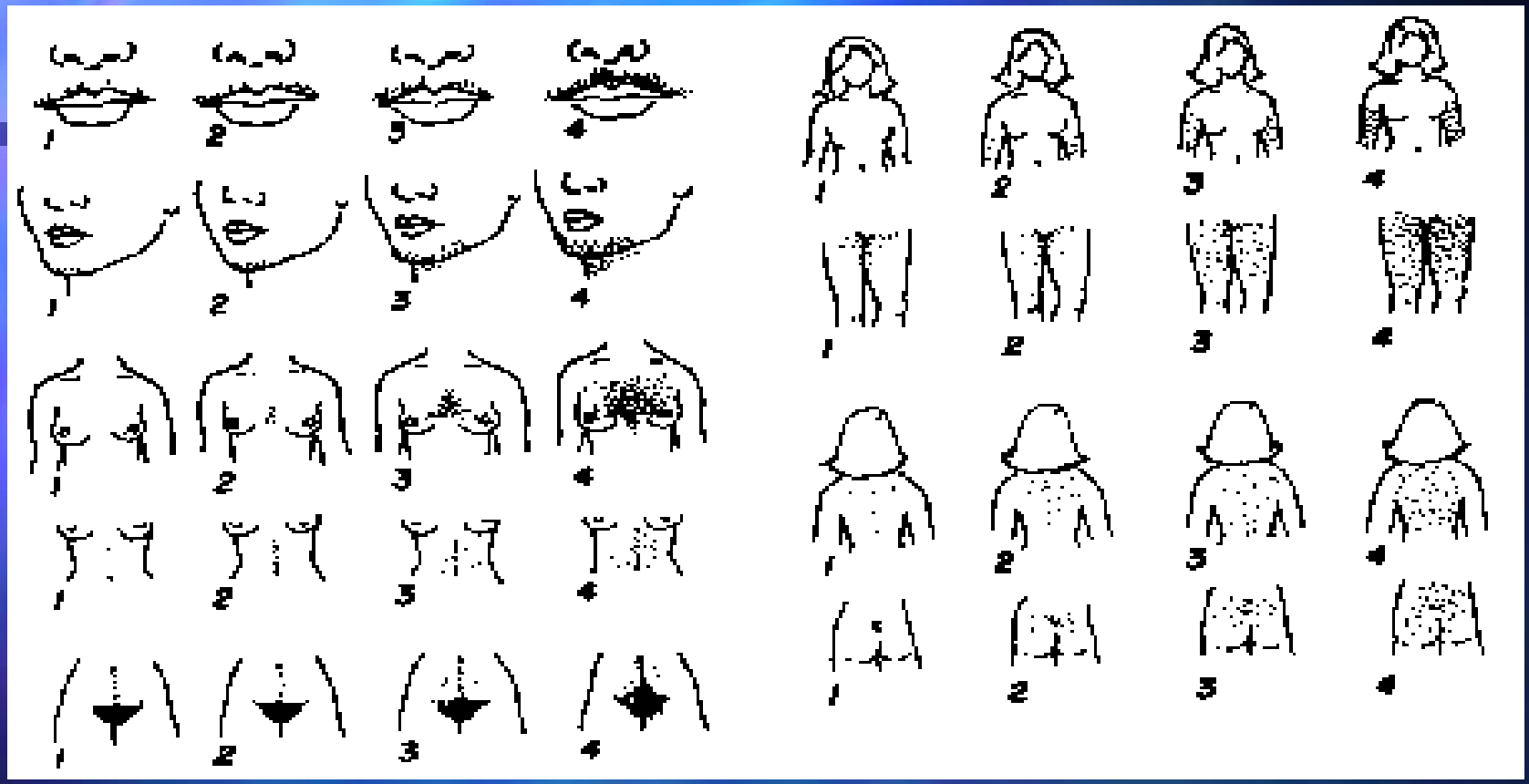








Hirsutism scoring



Modified Ferrima-Gallwy method 1930

Each area =1-4

Total score =36 Significant >8

Male pattern hair & Pimples









High male hormone (testosterone)

Velvety black Patchs (Acanthosis Nigricans)





High serum insulin levels (Insulin resistance)

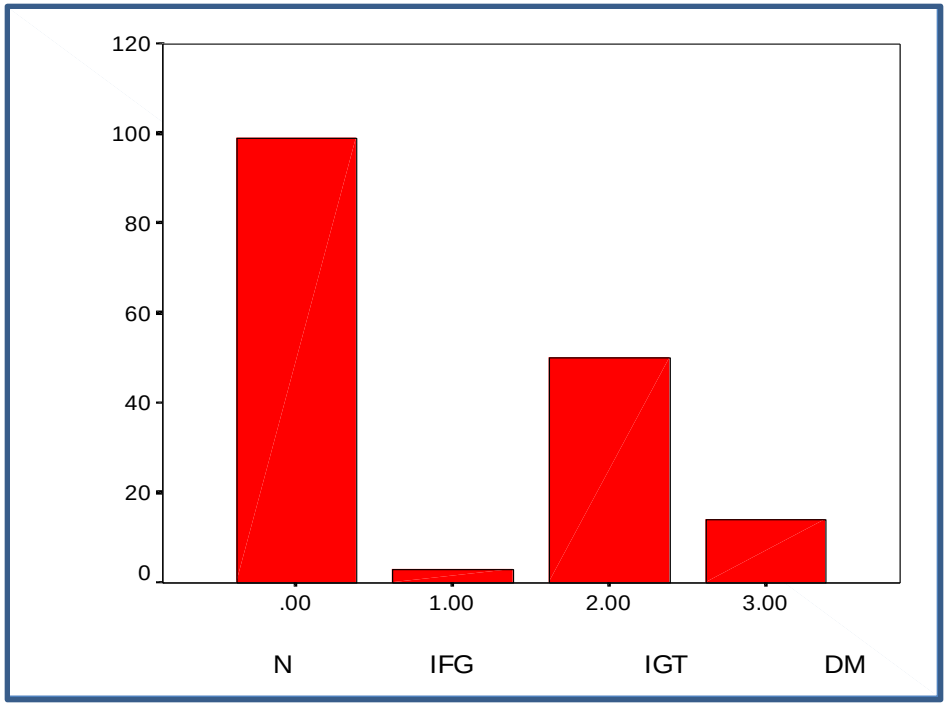
Metabolic abnormalities

- Obesity- CENTRAL
- High serum insulin (Hyerinsulinemia)
- High Blood sugar(Glucose intolerance /Diabetes)
- High cholesterol (Dyslipidemia)
- High uric acid (Hyperuricemia)
- Fatty liver (NASH)
- Heart problems (Coronary artery disease)
- Protein loss from Kidney (Premicroalbuminuria)
- Increased sleep problems (OSA)
- Strokes
- Hyperhomocystenemia
- CANCERS –breast, endometrium, ovarian

ORIGINAL ARTICLE

Prevalence of glucose intolerance among adolescent and young women with polycystic ovary syndrome in India

Ganie M. Ashraf*, M.L. Khurana*, M. Eunice*, N. Gupta*, S.N. Diwivedi**, M.S. Gulati***, A.C. Ammini*



Mean age of 23 years

Current PCOS Series
(Mean age =
years)
SKIM
DM
IG

Half have pre-diabetes or Diabtetes

- **DM 8.93% IFG 29.16% IFG 3.57%**

Reproductive Biology and Endocrinology

BioMed Central

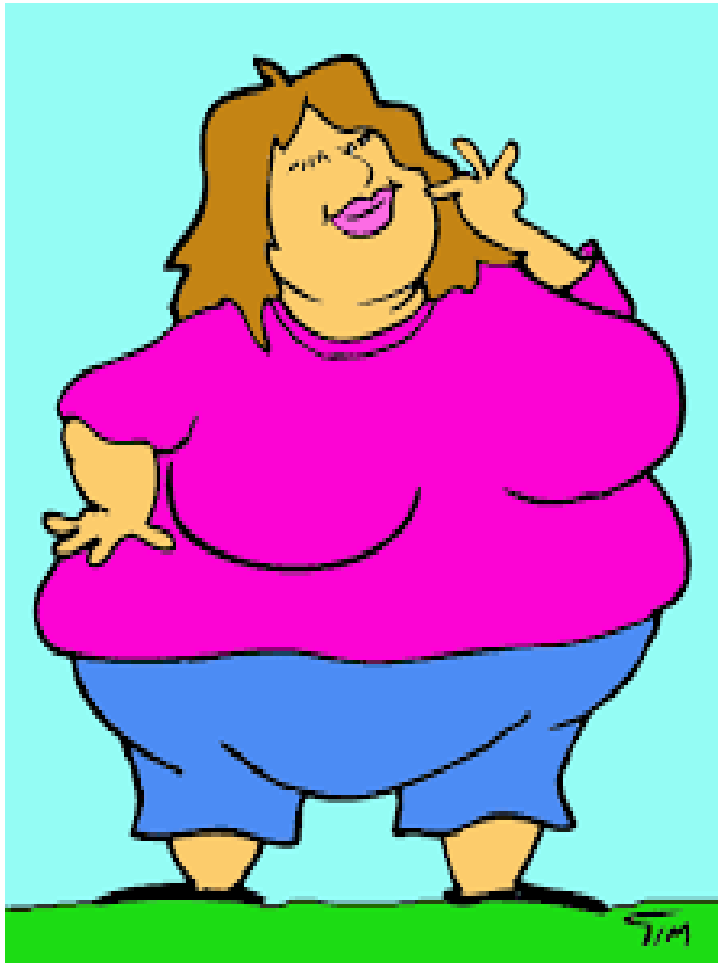
Research

Open Access

Prevalence of ultrasonography proved polycystic ovaries in North Indian women with type 2 diabetes mellitus

Ultrasonographic prevalence of PCO was higher in women with diabetes than in non-diabetic (61.0% vs. 36.7%)

PCOS- 50-60 % are OBESE





POLYCYSTIC OVARY SYNDROME

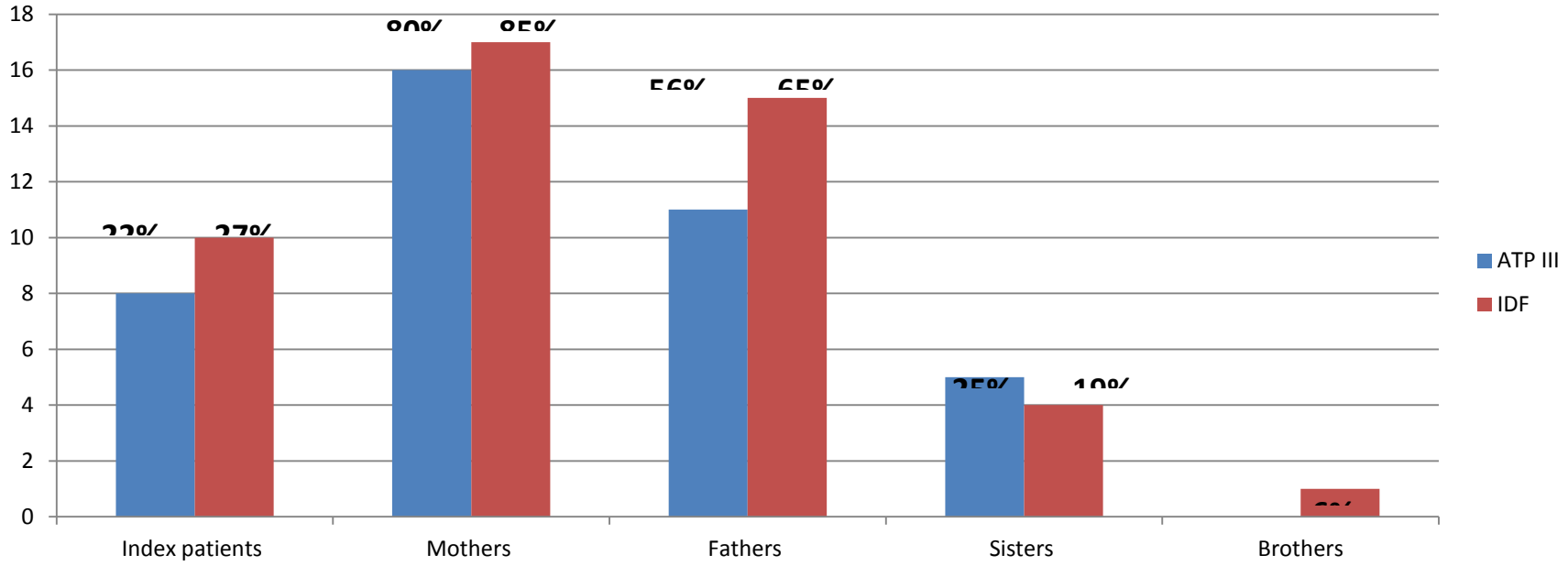
METABOLIC SYNDROME

Metabolic syndrome vs. PCOS

- The prevalence of MS in PCOS by IDF, WHO, ATP III and criteria were 50.0%, 47.3% and 23.68% respectively.
- ATP III criteria grossly underestimates the MS prevalence

Ganie M A, Kamili MMA et al Diabetes & CVD

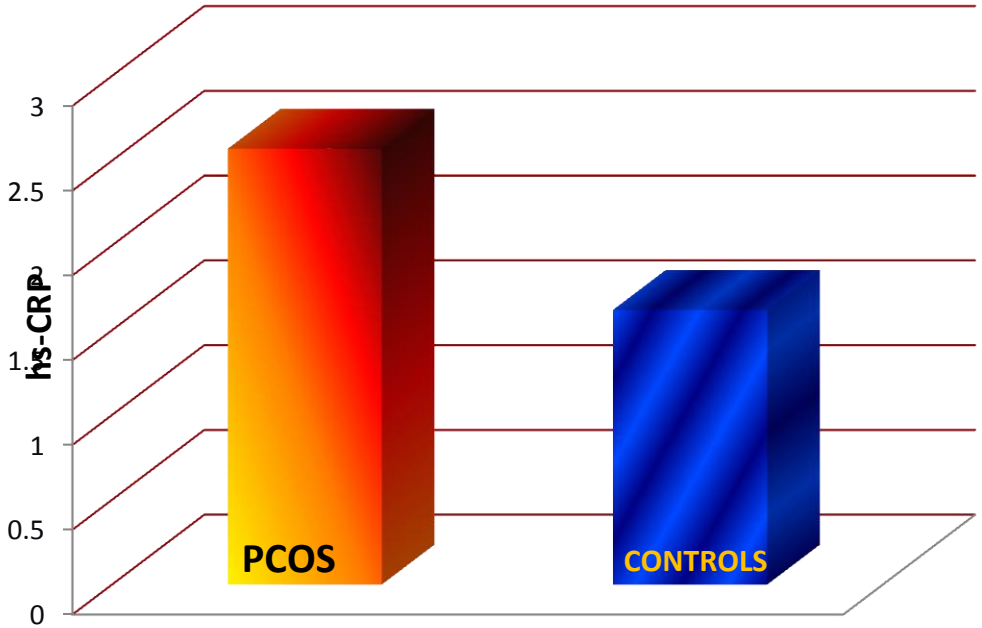
Prevalence of metabolic syndrome in subjects by ATP III and IDF definitions.



Original Article

Prevalence of metabolic syndrome in the family members of women with polycystic ovary syndrome from North India

Iram Shabir, Mohd Ashraf Ganie[1], Mohd Afzal Zargar[2], Dilafroz Bhat[3], Mohd Muzzafar Mir[3], Aleem Jan[4], Zaffar Amin Shah[5], Vicar Jan[6], Riyaz Rasool[7], Andleeb Naqati[2]



Elevated hsCRP/MCP-1 / Resistin / ICAM / PAI-1 with higher levels of adiponectin and F VIII levels

(Douhat s and Ganie MA IJF 2013 – IN PRESS

hs-CRP IN INDIAN PCOS

Pattern of urinary albumin excretion in normotensive young and adolescent Indian women with polycystic ovary syndrome

Mohd Ashraf Ganie, Khalid Jamal Farooqui, Mohd Ashraf Bhat, Mohammad Muzzafar Mir[2], Zaffar Amin Shah, Syed Douhath[1], Syed Hussain Mir[1], Fouzia Rashid[1], Shazia Naqshi[1], Mohd Ibrahim Masoodi[2], S. A. Zargar[3], Abdul Hamid Zargar[4]

Departments of Endocrinology, Nephrology, and Immunology and Molecular Medicine, Sheri-Kashmir Institute of Medical Sciences, Soura, Srinagar, Jammu and Kashmir, [1]Department of Clinical Biochemistry, University of Kashmir, Srinagar, Jammu and Kashmir, India, [2]Departments of Gastroenterology, and Clinical Biochemistry, Al Jouf, Aljouf University, KSA, [3]Sheri-Kashmir Institute of Medical Sciences, Soura, Srinagar, Jammu and Kashmir, [4]Department of Endocrinology, Sheri-Kashmir Institute of Medical Sciences, Soura, Srinagar, Jammu and Kashmir, India

A B S T R A C T

Objective: Polycystic ovarian syndrome (PCOS) is a clinically heterogeneous endocrine disorder affecting up to 4–8% of women of reproductive age. The aim of this study was to evaluate the presence of microalbuminuria in women with PCOS and study its correlation with the various metabolic, clinical, and hormonal parameters. **Materials and Methods:** A cross-sectional study involving 69 PCOS women was carried out in a tertiary care center hospital. The diagnosis of PCOS was made according to the Rotterdam

Elevated Coronary Artery disease risk



Atherosclerotic disease accounts for most of the excess mortality in patients with diabetes

Aggressive anti-atherosclerotic intervention is warranted in diabetics

GYNECOLOGICAL ENDOCRINOLOGY

http://informahealthcare.com/gye
ISSN: 0951-3590 (print), 1473-0766 (electronic)

Gynecol Endocrinol, Early Online: 1–4
© 2014 Informa UK Ltd. DOI: 10.3109/09513590.2014.924099

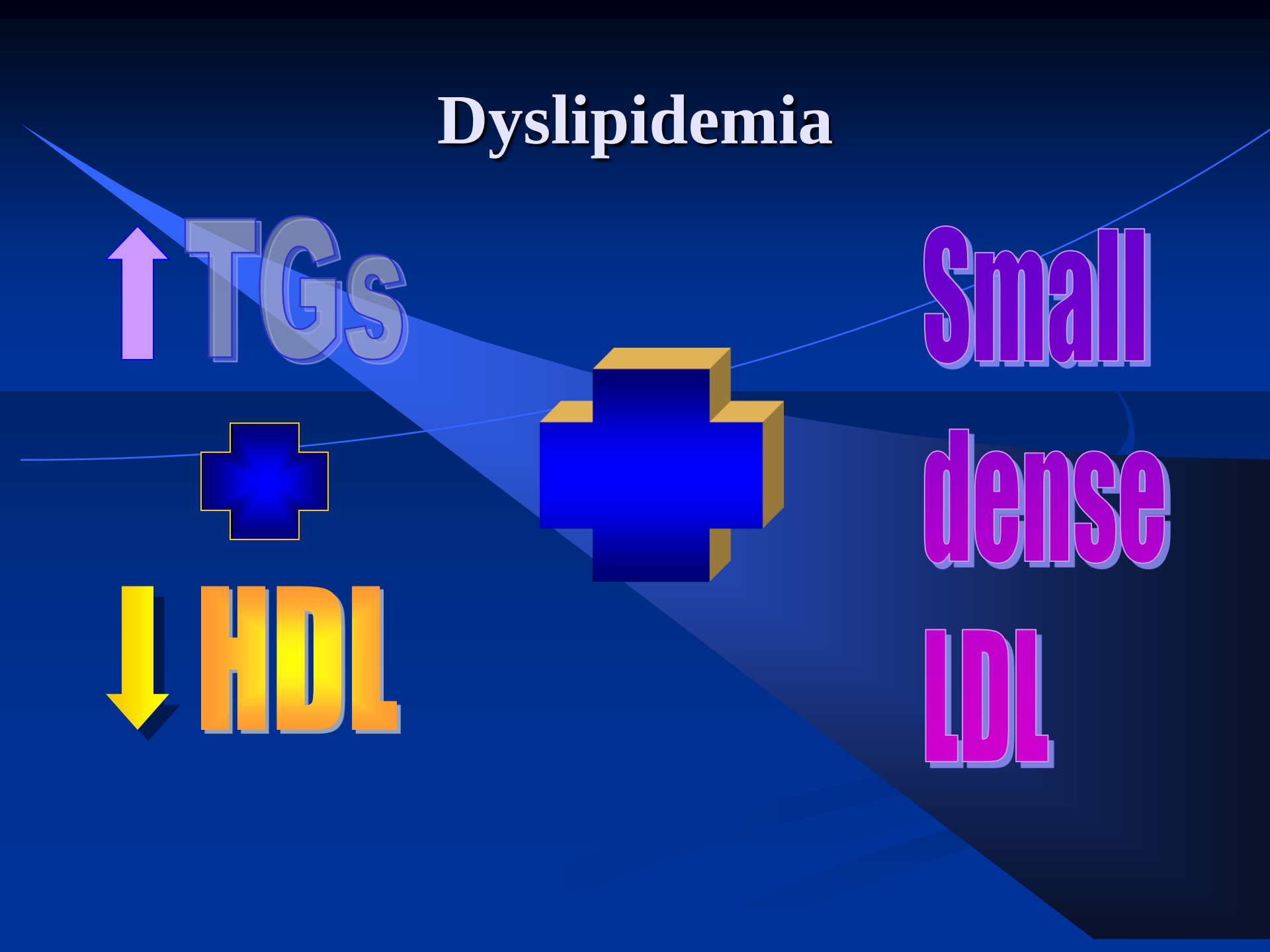
informa healthcare

ORIGINAL ARTICLE

High-sensitivity C-reactive protein (hs-CRP) levels and its relationship with components of polycystic ovary syndrome in Indian adolescent women with polycystic ovary syndrome (PCOS)

Mohd Ashraf Ganie[1], Saqib Hassan[2], Sobia Nisar[3], Nasir Shamas[2], Aafia Rashid[2], Ishfaq Ahmed[2], Syed Douhat[2], Syed Mudassar[4], Vicar M. Jan[5], and Fouzia Rashid[6]

Dyslipidemia



Sleep Apnea and PCOS

- Multiple groups have documented an increased risk RISK

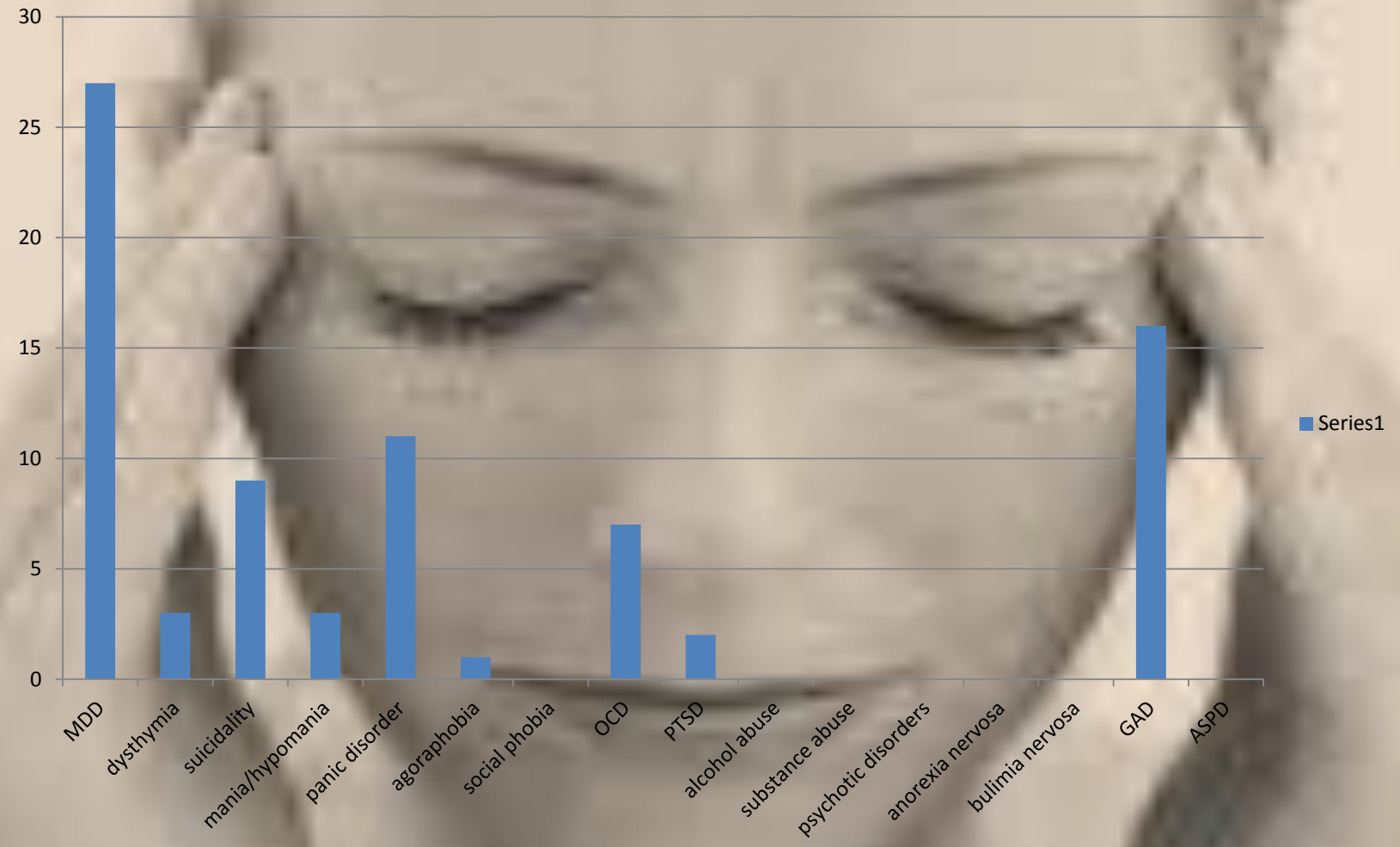
Fatty liver -30-40%

Cancers – uterus, breast

Body Image and Quality of Life in PCOS

POLYCYSTIC OVARY SYNDROME

PCOS and Stress/Psychiatric disorders



N=112 PCOS girls

72% have some psychiatric abnormality

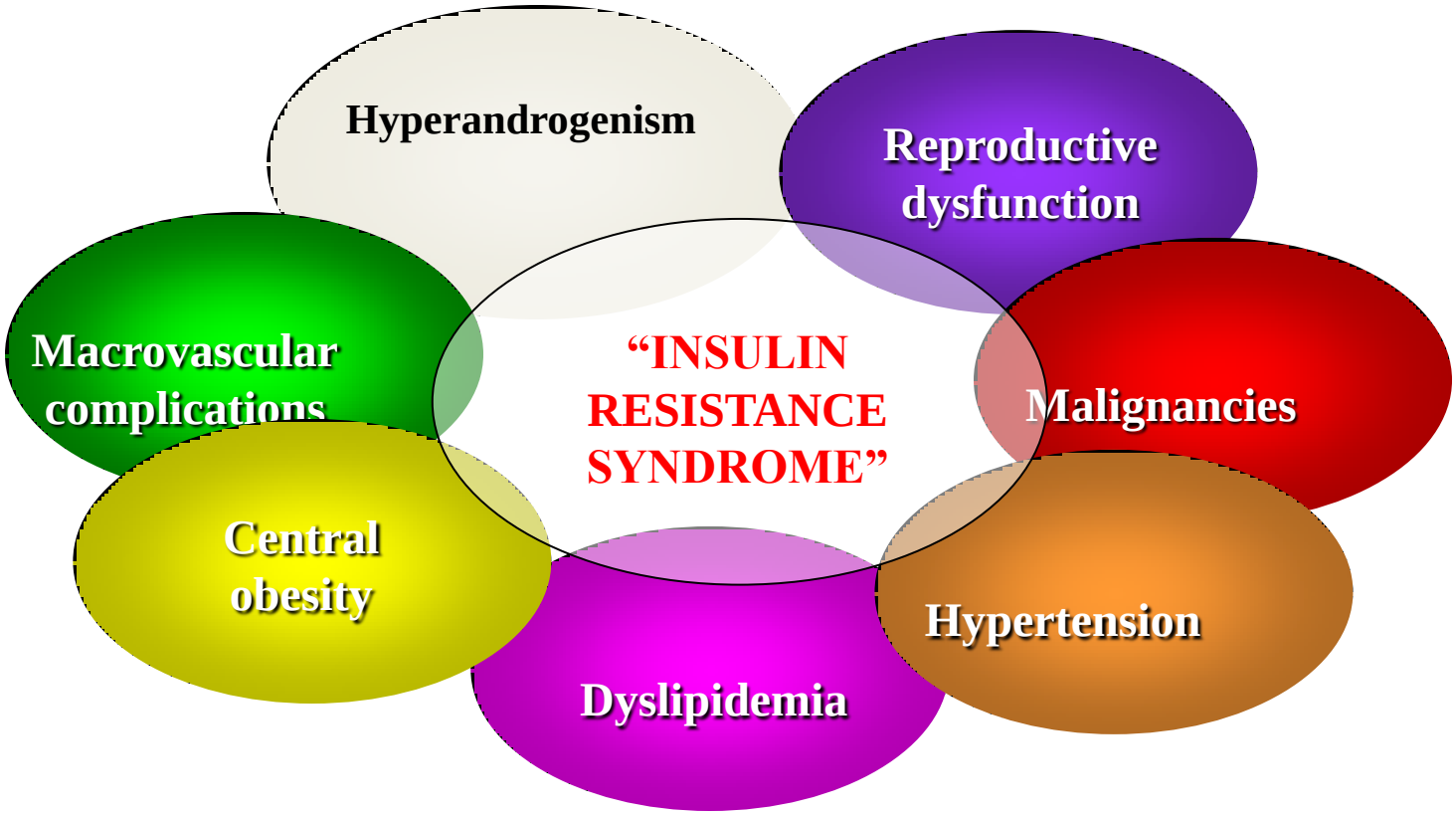
No eating disorder

Ganie M A et al 2010

Macrosomia- GDM



A Complex Metabolic Disorder

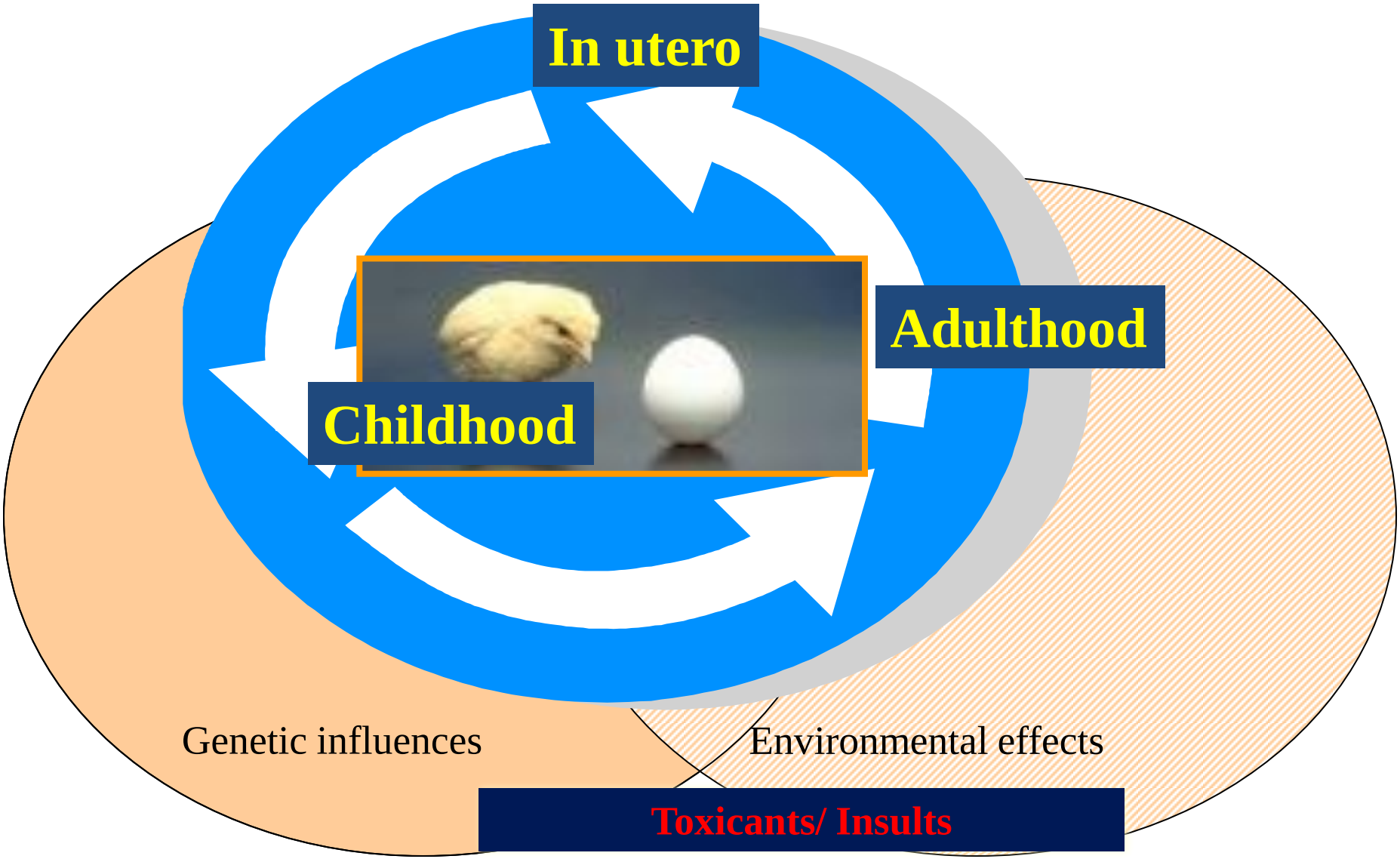


Original Article

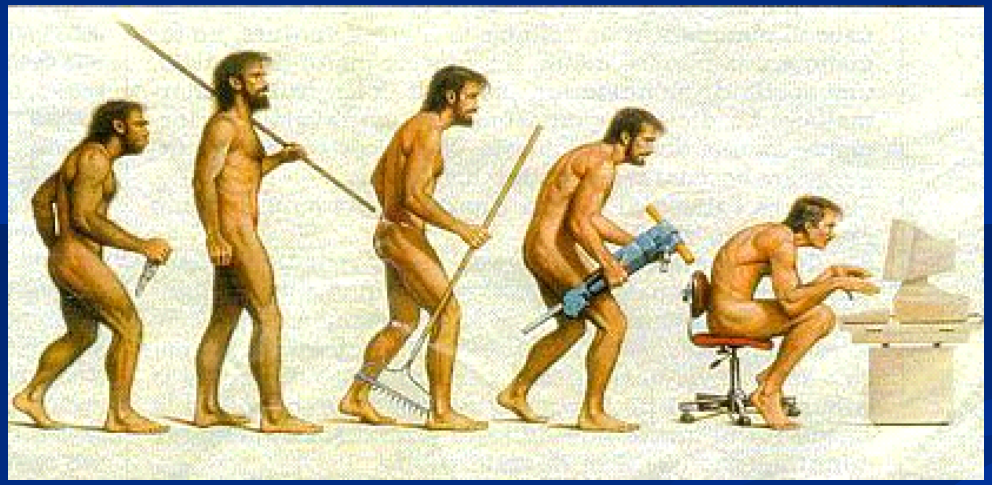
Prevalence of metabolic syndrome in the family members of women with polycystic ovary syndrome from North India

Iram Shabir, Mohd Ashraf Ganie[1], Mohd Afzal Zargar[2], Dilafroz Bhat[3], Mohd Muzzafar Mir[3], Aleem Jan[4], Zaffar Amin Shah[5], Vicar Jan[6], Riyaz Rasool[7], Andleeb Naqati[2]

Cause -???- Multiple factors –LIFETSYLE DISORDER



Evolution of Obesity:



- >10,000 B.C. : last Ice age ended
- 7,000 B.C. : Wheat cultivated
- 1900 A.D. : Coca Cola
- 1960s : Fast foods/McDonald
- 1970s (1980) : TV
- 1980s (1990) : Computer, video games



Environmental ‘Endocrine Disruptors’ (EDs)

Industrial

Unintentional



Intentional

Pharmaceutical

Male equivalent ?

- Brothers and sons of PCOS SUBJECTS – high prevelance of Metabolic syndrome
- PCOS variants also occur in sibs of subjects
- Syndrome XX (Dunaif 2005)
- Sex-limited Reaven's syndrome



Management

Focuses to reverse
–basic pathophysiology ??

1.Lifestyle modification
2.Insulin sensitizers – Metformin /Glitazones
3.Anti-androgens-Flutamide, Spironolactone
4.Anti-obesity- Sibutramine,Orlistat
5.Ovulating agents – Clomiphene , Letrozole
6.Others-inositol, acupuncture, Chinese medicine etc

Prevention is the Key

If we work out the burden and its cost on health care- Enormous

Editorial

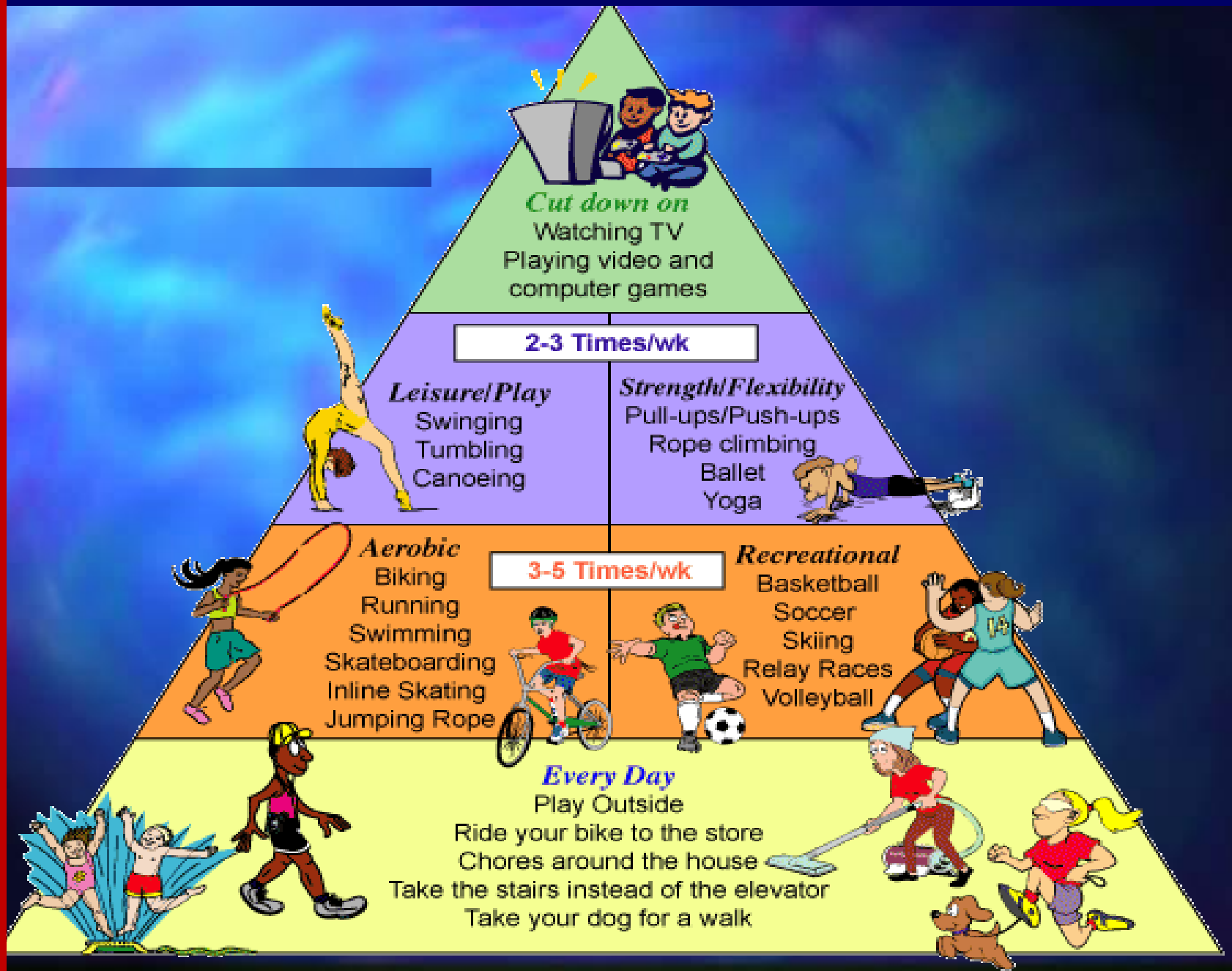
Polycystic ovary syndrome – A metabolic malady, the mother of all lifestyle disorders in women – Can Indian health budget tackle it in future?

M. Ashraf Ganie, Sanjay Kalra[1]

Department of Endocrinology, Sher-I-Kashmir Institute of Medical Sciences, Soura, Srinagar, Jammu and Kashmir, [1]Department of Endocrinology, Bharti Hospital and BRIDE, Karnal, Haryana, India

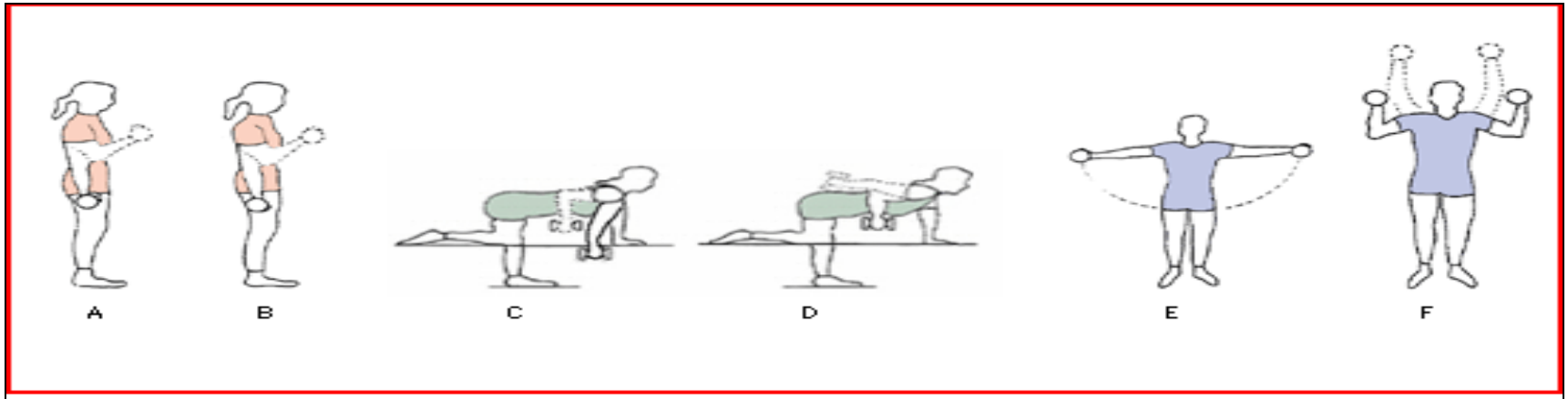
POLYCYSTIC OVARY SYNDROME

Physical Activity Pyramid



30 minutes brisk walk daily

Upper Body Exercise



Upper body weight routine (A) Curls/palms up (B) Reverse curls/palms down (C) Bent knee over rows (D) Tricep kick-backs (E) Side lift (F) Military press

Yoga- MAY HELP

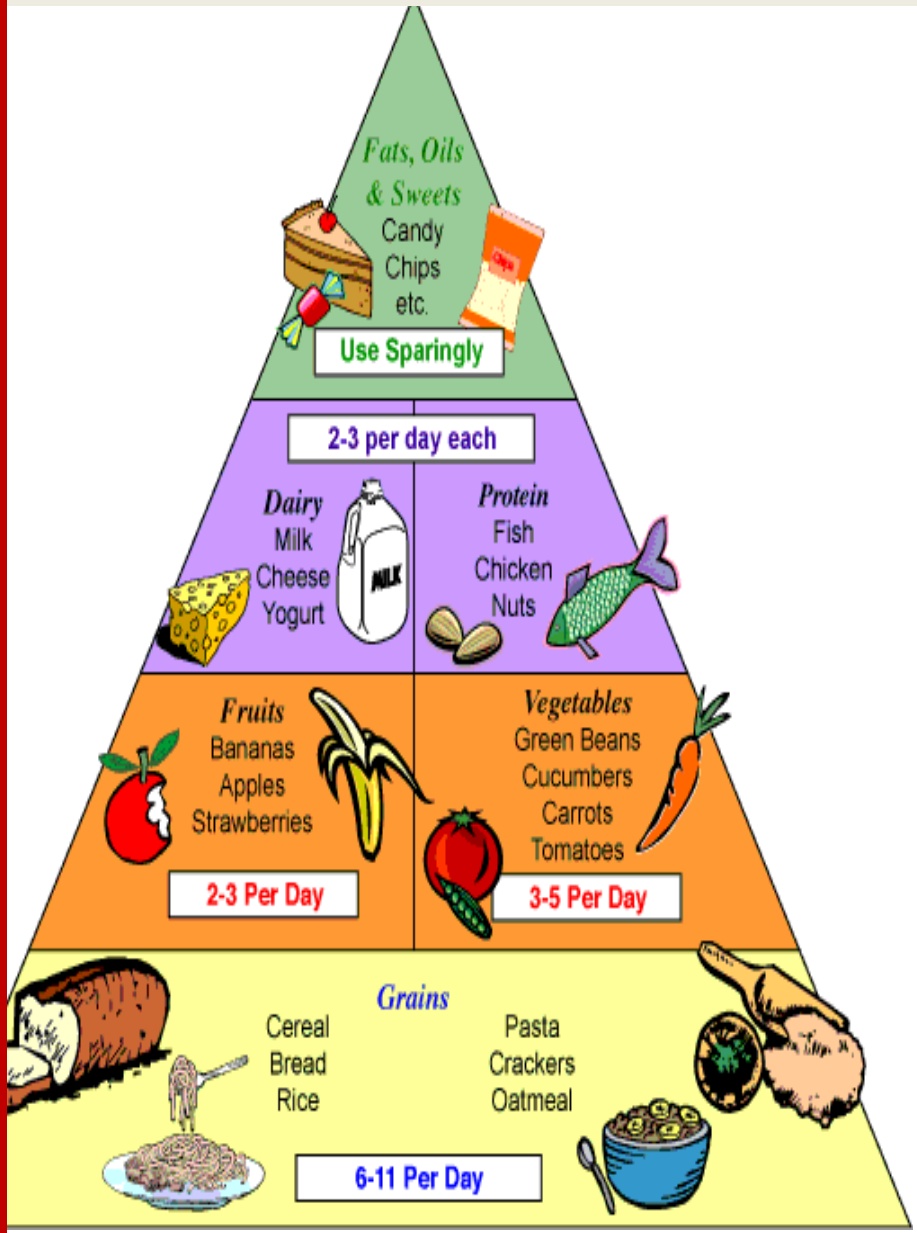
Dietary advice

- Qualified dietician
- Low fat /low carbohydrate
- High protein
- High fibre
- According to your BMI /Weight

5-10 % WEIGHT LOSS

POLYCYSTIC OVARY SYNDROME

Food Pyramid





Menstrual regulation/ Fertility

- MEDROXYPROGESTERONE ACETATE: 5 to 10 mg/day for 10 to 14 days monthly.
- OCP – Mala D/ Ovral etc.

Conception – Clomifene -=90%
IVF

Androgenic Symptoms

Hirsutism, acne, and alopecia

COSMETIC TREATMENT :

- depilatories, waxing, shaving for hirsutism
- laser hair removal and electrolysis.
- Side effects: treatment-site irritations.

ANTIANDROGENS.

- Spironolactone, at a dose of 25 to 100 mg twice daily, is the most commonly used antiandrogen because of its safety, availability, and low cost.
- Because of the increased risk of teratogenicity, contraception is recommended when patients are using antiandrogens .
- Spironolactone 100/ flutamide 25/ finasteride 5 found equally effective.

ORAL CONTRACEPTIVES:

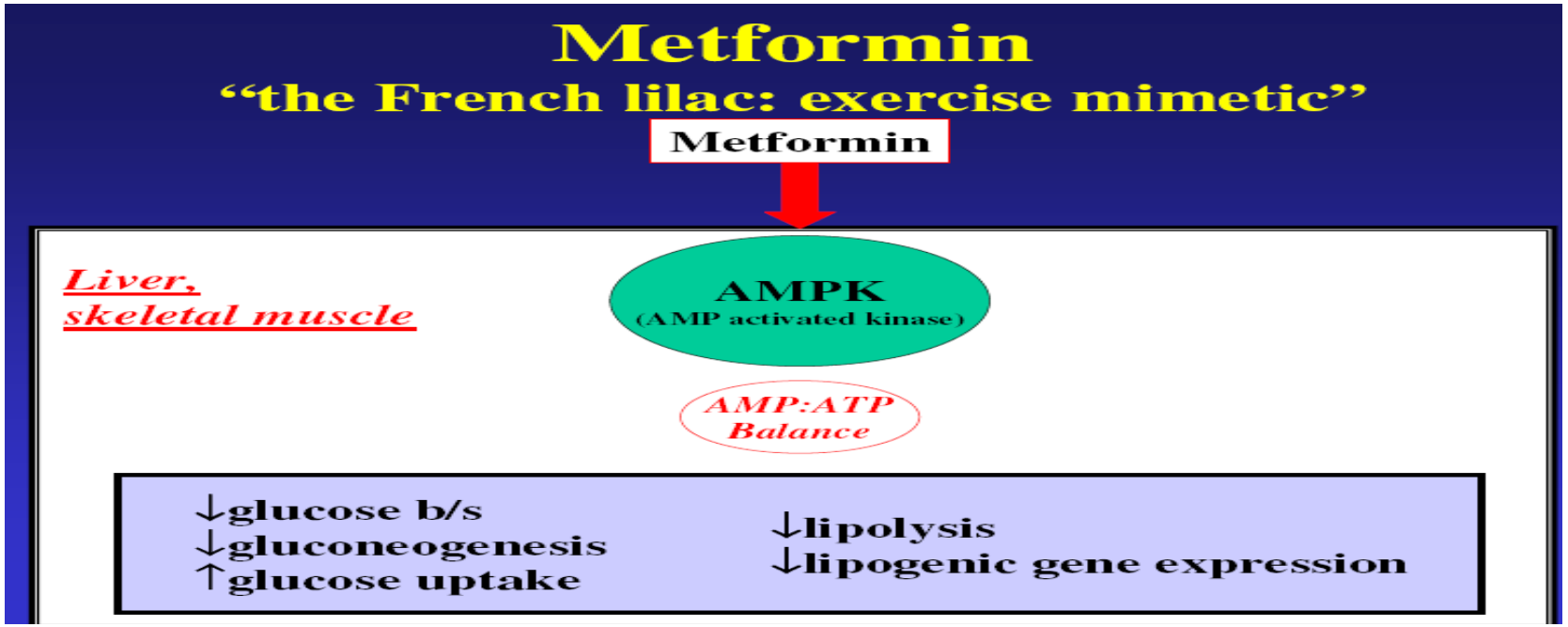
- Estrogen and progesteron/antiandrogen combination are the primary OCP used in combination of hirsutism, accne, irregular periods.
- Combination of antiandrogen / OCPs for synergy.

Addressing metabolic problems

Need to decrease –insulin

- testosterone

Insulin Sensitizers



Pioglitazone

Anti- androgen

–Spironolcatone
--Cyproterone acetate
--Flutamide
--Finasteride

0021-972X/04/$15.00/0
Printed in U.S.A.

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Comparison of Efficacy of Spironolactone with Metformin in the Management of Polycystic Ovary Syndrome: An Open-Labeled Study

M. ASHRAF GANIE, M. L. KHURANA, M. EUNICE, M. GULATI, S. N. DWIVEDI, AND A. C. AMMINI

Departments of Endocrinology and Metabolism (M.A.G., M.L.K., M.E., A.C.A.), Radiology (M.G.), and Biostatistics (S.N.D.), All India Institute of Medical Sciences, New Delhi 110029, India

Drug Combinations

- OCP with Pioglitazone
- Metformin with OCP
- Metformin with Spironolcatone

Improved efficacy of low dose spironolactone and metformin combination than either drug alone in the management of women with polycystic ovary syndrome (PCOS): a six month, open label randomized study

Mohd Ashraf Ganie, M.D; D.M, Associate Professor, Madan Lal Khurana, PhD, Scient
Sobia Nisar**, MD, Senior Resident,
Parvaiz Ahmed Shah**, M.D, D.M, Professor,
Zaffar Amin Shah*, PhD, Additional Professor,
Bindu Kulshrestha****, MD; DM, Assistant Professor,
Nandita Gupta, PhD, Professor, Mohd Afzal Zargar #, PhD, Professor,
Tariq Ahmed Wani ***, M Sc, Biostatistician,
Syed Mudasir ®, PhD, Additional Professor,
Farooq Ahmed $, M.D, Senior Resident, Shenaz Taing ~, MD, Associate Professor

Departments of Obstetrics and Gynecology', Internal Medicine** Govt. Medical College, Clinical biochemistry University of Kashmir#, Clinical biochemistry®, Biostatistics ***, Radio diagnosis $, Immunology and Molecular Medicine*, Sheri-Kashmir Institute of Medical Sciences, Srinagar, J & K; Department of Endocrinology RML Hospital****, and, Endocrinology, Metabolism and Diabetes, All India Institute of Medical Sciences, Ansari Nagar, New Delhi–29, India.

Suggested Screening in PCOS

Assessment	Recommendation	Minimum frequency
Glucose tolerance	2-h oral GTT	•Every 2 years. •Annually if PCOS and additional risk factors
Cardiovascular risk	Body mass index	Annually
	Waist circumference	Annually
	Smoking status	At each visit
	Physical activity status (and advice)	Annually
	Blood pressure	Annually
	Lipid profile	Annually if abnormal or obese. Every two years if found normal.

British Journal of Diabetes and Vascular Disease. 2013;13(3):115-123

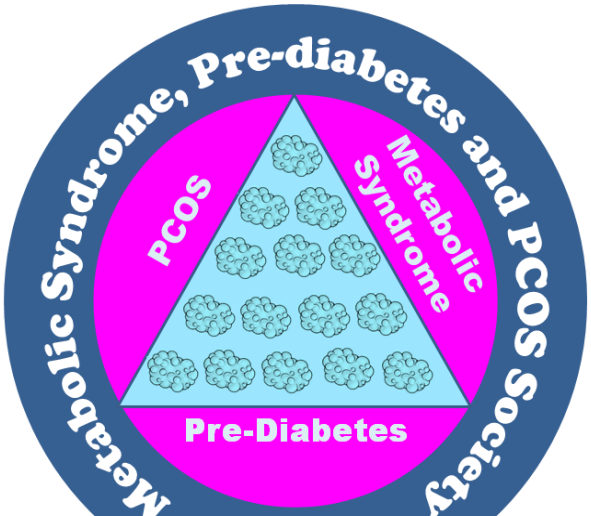
SUMMARY & CONCLUSION

PCOS is a common and on rise- tip of iceberg

Constellation of metabolic abnormalities

- **PCOS-METABOLIC SYNDROME -PRE DIABETES–DM**
- **Global approach** –both its current clinical issues and long-term metabolic consequences
- Life style modification to re-enforce the importance of weight loss
- Pending the understanding pathogenesis –IDS,AA
- Metformin –drug of choice –metabolic abnormalities
- Lipid,NASH,Obesity, Psychiatric disorders-need

Metabolic Syndrome, Pre-diabetes and PCOS Society

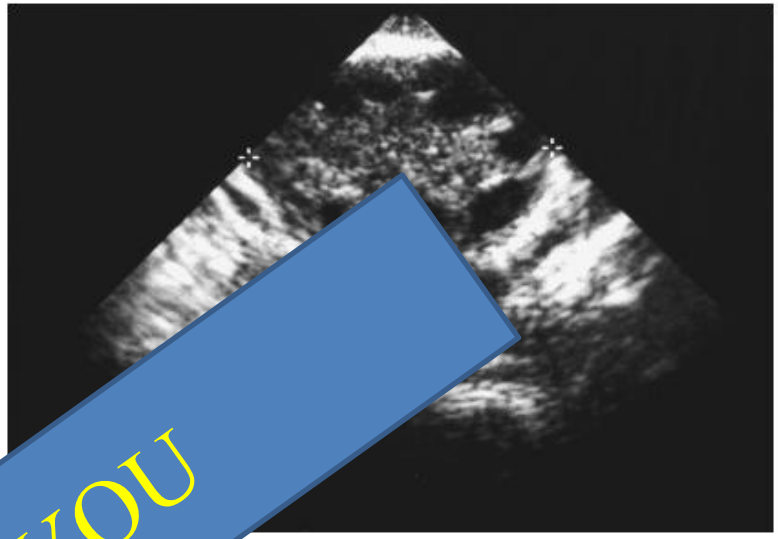


MP-PCOS

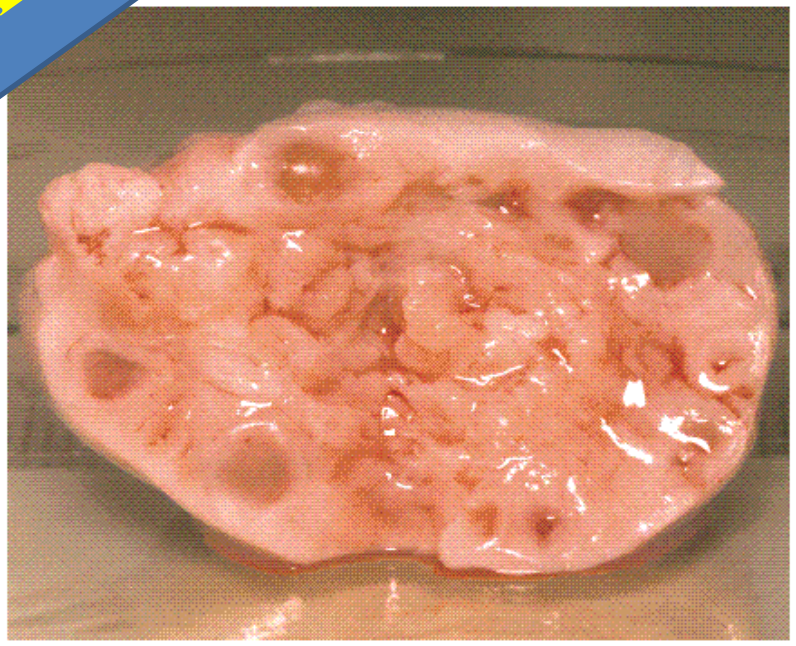
(M. P.PCOS)

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THANK YOU

Thanks