Research on PCOS at National Institute for Research in Reproductive Health (ICMR)

- Epidemiological and Health Systems Research
  - Community based studies on prevalence, risk factors and co-morbidities
  - Assessing current management practices and capacity building

- Clinical
  - Multidisciplinary management of PCOS
  - Cohort of infertile and adolescents reproductive and metabolic outcomes

- Basic
  - Genetic and epigenetic studies to understand the pathophysiology of PCOS using a multifaceted approach of genomics and proteomics
  - Development of animal model of PCOS to study cystogenesis

- Bioinformatics - mapping all the genes involved in the pathogenesis of PCOS
Community based studies on PCOS
Challenges and Opportunities

Dr. Beena Joshi, Scientist E
Department of Operational Research, NIRRH

Dr. Sanjay Chauhan, Scientist F and Head
Department of Clinical & Operational Research, NIRRH

Dr. Rama Vaidya, Director
Division of Endocrine and Metabolic Disorders, KHS, Mumbai
Community based study of PCOS prevalence among adolescents and young girls in Mumbai

- Systematic multistage random sampling method (Zone-Ward –Health post area- 80,000 population)
- Inclusion Criteria : Age 15- 24 yrs, 2 years post menarche and unmarried
- A sample size of 900 was calculated assuming a prevalence of 10% and precision of 2% at 95% confidence level
- Considering a non-response rate of 10%, the total was estimated to be about 1000 girls
- Eligible girls in selected study area - approx. 10,600 (census data)
- Household list obtained
- Every 10th household approached
- History at household after informed consent
- Medical examination at health post
- Blood collection on 3rd to 7th day of normal cycle
- USG abdominal -collective activity
- All enrolled cases screened - Probable cases – Diagnosis of exclusion - Controls –Reference

Joshi B et al., IJEM 2014
### Participant Enrollment and Retention

**Enrollment**
- Only 3% girls had heard about PCOS
- Consent of parents/husbands
- Difficult to access high income groups
- Door to door survey in crowded slum – sensitive nature of questions
- Number of repeat visits
- Timings of the clinic
- Coordination for USG
- Girls were more concerned with cosmetic problems than menstrual
- Enroll only one from each household

**Strengths**
- Involvement of local health post providers and CHVs
- Capacity building
- Provision of comprehensive adolescent services with supply of medicines
- Follow-up and counselling
- Proximity to investigation facilities

**Dropouts**
- Stigma
- Parents refusal
- Got married or shifted residence
- No clinical symptoms - Not willing for investigations
- Inconvenient timing due to work or academic related activities

**Caution**
- Over-diagnosis
- Create anxiety

**Continuum of care- Referral services**
Investigations required

**Basic for PCOS diagnosis**
- UPT
- **Total Testosterone**
- SHbg
- T4, TSH
- Prolactin
- 17 OHP

**Diagnosis of MS**
- FBS
- 2 hrs post 75 gms glucose
- Lipid profile

**BMI- Criteria**
Reference norms - ± 2SD

**Pitfalls Of Ultrasonic Criteria ?**
- Significant intra-observer and inter-observer variability
- Single sonologist
Determining Prevalence of PCOS among adolescents and young girls in Mumbai

Enrolled Participants (n=1000)

*Dropouts (N=222)

Completed all Investigations (n=600)

Completed investigations Partially (n=178)

Probable PCOS
Rotterdam = 149 (24.8%)
AES = 79 (13.2%)

Probable PCOS
Rotterdam = 20 (11.2%)

True PCOS
Rotterdam = 144 (22.5%)
AES = 76 (10.7%)

Counseling Management Followup-70%

Salient findings

- 19% hyperinsulinemic
- History of oligomenorrhea
  - Specificity - 93.9%
  - Sensitivity - 83.3%
- 72% were lean PCOS
- Metabolic syndrome - 0.8%
- Mean 2hrs post glucose and LDL values significantly higher among obese and overweight

Common Phenotypes –
Mild - 52.6%  Frank - 27.4%
Classic - 13.3%  **Ovulatory** - 6.7%
Community based study in Srilanka

Stage 1 – Community survey

Community survey in one district (n=3,030)

Respondents = 2,915 (96.2%)

Non respondents = 115

Probable controls = 220

*Probable cases = 220

Drop outs = 30

N = 163

*Only with symptoms

Stage 2 – Clinical and bld inv

N = 178

Drop outs = 27

N = 151

Bypassed stage 2

N = 12

N = 171

Stage 3 – USG

N = 163

N = 176

Drop outs = 36

1 girl with ovulatory PCOS

Prevalence - 6.3% mainly reproductive phenotype

Rotterdam criteria

Kumarapeli V et al., 2008
Community based study - China

Invited participant 20,000 women

- Initial rejecters 3114
- Initial participants 16886 women

Completed questionnaire 15924

- Normal 15030
  - Blood test Control 2732
  - PCOS 984
  - Blood Test 833

Prevalence - 5.6% Rotterdam criteria

High prevalence of Metabolic disorders

- 10 Provinces
- 3 Strata
- 1 Township
- Villages in each township - 3 strata of equal number of villages
- One village

Rong Li et al., Human Reproduction 2013
Proposed ICMR Task force study on PCOS prevalence – Multi-centric study

• Through NIRRH Field Units/Medical Colleges -9 sites
• Involvement of Depts. of Community Medicine, OBGYN and Endocrinologist, Dermatologist, Psychiatry, Laboratory services
• Sample size - 6300 – Both Urban and Rural
• Multilayer stratified random sampling
• Purposive selection of rural setting - Ultrasound facilities (Observer dependency - ??? – Follow NIH criteria – Miss ovulatory phenotypes?)
• Most reliable method for S. Testosterone levels - LCMS – centralized facility – cost of transport
• External team unknown to the community - need to involve local grass root level health providers
• Ensure basic management at PHCs with good referral linkages to tertiary facilities

➢ Health economics of PCOS
Birth cohort study in Australia

Prevalence - 12%
Rotterdam criteria

National PCOS Guidelines
PCOS Australian Alliance 2011

Flow chart of women involved in the study; from tracing through to the interview and clinical examination.

Wendy M et al., Human Reproduction 2010
**Cohort studies**

- A large-scale, population-based retrospective cohort study in Taiwan among 3,566 PCOS vs 14,264 matched non PCOS. The adjusted hazard ratio of uterine cancer and breast cancer in subjects with PCOS were higher (HR: 8.42 [95% confidence interval: 1.62–43.89] and HR: 1.99 [95% confidence interval: 1.05–3.77], respectively) than that of the controls during the follow-up.  
  
  Cheng-Che et al., The Oncologist. 2015

- A long cohort of children born in the KEM Hospital since 1993 in the city of Pune and whose weights at birth were recorded in the labour ward register were followed up to determine the relationship between birth-weight and cardiovascular disease (CVD) risk factors and PCOS. Lower birth-weight was associated with increased insulin resistance. The highest levels of CVD risk factors were in children of low birth weight but high fat mass at 8 years.  
  
  Pune Maternal Nutrition study Yajnik S et al., 2010
Acknowledgement

- Dr. Duru Shah and PCOS Society
- Co authors – Dr. Rama Vaidya and Dr. Sanjay Chauhan
- ICMR
- NIRRH – Director, Co- Scientists, Staff
- Study participants and gatekeepers
Economic burden to a woman affected with PCOS

**Cosmetologic therapies**
- Per session: ₹ 7000

**Metabolic & CVD**
- Per session: ₹ 4000 - 50000

**Initial evaluation**
- ₹ 4000 - 5000

**Menstrual disorders, infertility**
- Per month: ₹ 5000 – 1 L (IVF)

**Lifestyle MRx**
- ₹ 20-50000/yr

**Economic burden to a woman affected with PCOS**

42nd Foundation Day NIRRH

RAV 24th Feb. 2012
Mind mapping

Draft to be completed

Involvement of stakeholders

Parents/ Husbands

Local health providers

Tertiary referral centers

Healthy lifestyle promotion

Sensitisation

Capacity building

Educational activities

IEC material

Girls

Women

Local perceptions, practices

Create Awareness

Screening early
detection

Prevention

Support groups

Good cohort for FU

Community based

Studies on PCOS

Participatory research

Green – opportunities

Red will go on left side for challenges
Studies among defined population groups other than hospital settings

- Use of convenience samples eg.
  - recruiting women through publicity campaigns employee medical examinations
  - blood donors
  - school going girls etc.

- Non randomized
- Statistical evidence lacking to determine the representativeness of participants
Opportunities

• Influence policy and program - Australia National Health Program Awareness
• Participatory learning and involvement
• Local support group network
• Early screening
• Access to health services
• Health interventions
• Involvement of health system
• Capacity building
<table>
<thead>
<tr>
<th>Country</th>
<th>Methodology and Sample size</th>
<th>Prevalence %</th>
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<tbody>
<tr>
<td>Australia</td>
<td>Birth cohort 728 women predominately Caucasian women aged 27–34 years, born in Adelaide, South Australia</td>
<td>12</td>
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<tr>
<td>Rong Li et al., 2013</td>
<td>10 provinces and municipalities multi-layer, stratified sampling method Rural: Urban ratio of 1:1 Women from 152 cities and 112 villages 20,000 women aged 19-45 yrs</td>
<td>5.6</td>
</tr>
<tr>
<td>Srilanka</td>
<td>4 divisional secretariat areas of a district randomly selected Clustersampling proportionate to population size 3,030 women aged 15-39 yrs</td>
<td>6.3 (Rotterdam)</td>
</tr>
<tr>
<td>India</td>
<td>1200 adolescent and young girls (15-24 yrs) from a defined selected geographical area in Mumbai</td>
<td>10.5 (AES)</td>
</tr>
<tr>
<td></td>
<td>A long cohort of children born in the KEM Hospital in the city of Pune and whose weights at birth were recorded in the labour ward register were followed up to determine the relationship between birth-weight and cardiovascular disease</td>
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</table>
Community based study - China

October 2007 to September 2011, women 19–45 years
Top 10 provinces and municipalities
A multi-layer, stratified sampling
Rotterdam criteria

High prevalence of Metabolic disorders

- 10 Provinces
- 3 Strata
- 1 Township
- Villages in each township -3 starta of equal number of villages
- One village

Rong Li et al., Human Reproduction 2013
### PCOS Phenotypes* (n=600)

- **Mild (J)**: 52.6%
- **Classic(B, D, F)**: 13.3%
- **Frank(A, C, E)**: 27.4%
- **Ovulatory(G, H, I)**: 6.7%

<table>
<thead>
<tr>
<th>Signs/Symptoms</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
<th>H</th>
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<td>Biochemical Hyper Androgenemia (FAI)</td>
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<td>Oligomenorrhea</td>
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<td>Polycystic ovaries on USG</td>
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**PCOS (N=135)**

| PCOS (N=135) | 8.1 | -   | 8.9 | 5.2 | 10.4 | 1.5 | 1.5 | 8.1 | 3.7 | 52.6 |