# AOGD BULLETIN

Volume 20 I April 2021 I Monthly Issue 12

Price ₹30 Only

## CARING FOR WOMEN'S HEALTH : EVIDENCE, ATTITUDE & PRACTICE

***Dedicated Issue:***

**Part I- National Health Programmes pertaining to women's health**

**Part II- Reproductive Endocrinology**


**AOGD SECRETARIAT**

Institute of Obstetrics & Gynaecology,
Sir Ganga Ram Hospital
Sarhadi Gandhi Marg, Old Rajinder Nagar, New Delhi-110060
Tel.: 011-42251768, 1789
E-mail: secretaryaogdsgrh2020@gmail.com

**Website: www.aogd.org**

# AOGD Office-Bearers 2020-21

**Dr Mala Srivastava**
President

**Dr Kanika Jain**
Vice President

**Dr Mamta Dagar**
Hon. Secretary

**Dr Neeti Tiwari**

**Dr Sunita Kumar**

Joint Secretary

**Dr Shweta Mittal Gupta**
Treasurer

**Dr Tarun Das**
Co-Treasurer

**Dr Debasis Dutta**

**Dr Geeta Mediratta**

**Dr Chandra Mansukhani**

**Dr Punita Bhardwaj**

Scientific Advisors

## Editorial Board

**Dr Geeta Mediratta**

**Dr Chandra Mansukhani**

Editors

**Dr Ruma Satwik**

**Dr Sharmistha Garg**

**Dr Sakshi Nayar**

**Dr Ila Sharma**

Co-Editors

**Dr Debasis Dutta**

**Dr Gaurav Majumdar**

**Dr Ankta Srivastava**

Web Editors

# AOGD Bulletin

**Volume 20 • Monthly Issue 12 • April 2021**





**AOGD Secretariat**
Institute of Obstetrics and Gynecology, Sir Ganga Ram Hospital
Sarhadi Gandhi Marg, Old Rajinder Nagar, New Delhi-110060
Tel.: 011-42251768, 1789
E-mail: secretaryaogdsgrh2020@gmail.com | www.aogd.org


## Contents






**Publisher/Printer/Editor**
Dr Geeta Mediratta and Dr Chandra Mansukhani on behalf of Association of Obstetricians & Gynecologists of Delhi.

**Printed at**
Process & Spot C-112/3, Naraina Industrial Area, Phase-1, New Delhi 110 028

**Published from**
Institute of Obstetrics & Gynaecology
Sir Ganga Ram Hospital, Sarhadi Gandhi Marg, Old Rajinder Nagar, New Delhi-110 060

**Editors**
Dr Geeta Mediratta, Dr Chandra Mansukhani
Ph. No. 011-42251768, 1789; Email: secretaryaogdsgrh2020@gmail.com

# From the President's Pen

**Greeting to all the members of AOGD!!**

It's my privilege and pleasure to write this message of my tenure. We have officially handed over the secretariat of AOGD to Dr. Achla Batra our President of AOGD on 26/03/2021 at the virtual meet. We handed over physically to the team Safdarjung on 31/03/2021, with Dr. Achla Batra heading the team, together with Dr. Jyotsana Suri our Vice President AOGD and Dr. Monika Gupta Secretory AOGD, Dr. Upma Saxena our Treasurer AOGD. Dr. Rekha Bharti our chief Editor of AOGD and Dr. Anita Kumar joint Secretory of AOGD 2021-2022.

The Corona crisis continues and cases are rising as a second wave grips our city of Delhi. We should continue to take precautions in the form of mask & social distancing. If possible all of us should also take vaccine against this Corona virus. All our Corona warriors must keep healthy and happy, while they take care of patients during these difficult times. The condition are challenging and so is our new Team AOGD which is confident enough to face the rough situation. We all together will tide over the tough times and later on take forth our torch of learning and teaching from AOGD Secretariat.

Thanks giving is a very sacred task of acknowledging and yet balancing the contribution of various personalities. I pay homage to Dr. K. Gujral, Dr. H. Khullar and Dr. A. Majumdar who have really guided us throughout my tenure.

I am extremely grateful to Dr. Kanika Jain and Dr. Mamta Dagar for their untiring and innovative inputs and unconditional support. I am truly thankful to Dr. Geeta Mediratta, Dr. Chandra Mansukhani, Dr. Sharmistha Garg, Dr. Ruma Satwik and Dr. Ila Sharma for their tremendous editorial as well as scientific support. I have been very ably assisted by the very energetic and optimistic treasurer Dr. Shweta Gupta Mittal, and Dr. Tarun Das during these difficult corona times. Besides the help also came from Dr. Punita Bhardwaj, Dr. Debasis Dutta, Dr. Sunita Kumar, Dr. Neeti Tiwari, Dr. Gaurav Majumdar, Dr. Sakshi Nayyar, Dr. Ankita Srivastava for their valuable contribution at various stage of our tenure.

I am also thankful to all my residents as well as my postgraduate students for their efforts of running around and giving a buffer stability between patient care and organisational hurdles and very courteous to offer their services with a smile. During difficult decision making I was always guided by our Patrons, advisors as well as esteemed executive members and Chairpersons of the various sub-committees of AOGD, who give me direction and support.

I must thank the faculties of all the institution of Delhi who gave me unconditional support. I must confess that almost each and every member of AOGD whether they were seniors, contemporary or juniors stood by me and made my journey easy and achievable.

We tried to do the best of our ability to provide an environment of academics. We offered our services with all humility. We would rather confess to be wrong if anywhere, than arguing when we were wrong.

We all are looking forward for new horizons, newer advances and happening days for AOGD in future.

**Long live AOGD!**

**Dr Mala Srivastava**
President, AOGD

# From the Vice-President's & Secretary's Desk

**Dr Kanika Jain**
Vice President AOGD
(2020-21)

**Dr Mamta Dagar**
Secretary AOGD
(2020-21)

Greetings to all members of the association

With a sense of great honour and privilege, we address you for the last time as the AOGD Vice President and Secretary 2020-21. The year in which AOGD has confirmed and consolidated it's position as the leading body in women's health all over India. Thank you all for giving us the opportunity to lead this legendary organization.

The impact of the global pandemic has been devastating, resulting an emotional and physical toll on every human being.

In a year that presented so may challenges, we increased our activities; Conferences and academic sessions were conducted online. This was a paradigm shift from face-to-face to virtual meetings on E-platforms, achieved through the combined commitment and hard work of all the members. The number of sessions and registrations reached an all-time high in 2020.

We successfully demonstrated we are a family, bonded by a common purpose, to care for women and their health. To every AOGD member, our staff, sponsors and trainees; great work !!.

The topic of this ***April bulletin*** is '***National health programs pertaining to women's health***', which every treating doctor must be aware of in India. Our Editorial team has again chosen a very appropriate subject to be brought to light with the help of guest editors; Dr A. G. Radhika and Dr Richa Sharma. We're sure it'll be of immense use for our readers.

As we pass the torch of leadership to the next ***AOGD team from Safdarjung Hospital***, we also wish to pass on our lessons learned.

- Challenges like Covid-19 will come but we must face them head on.
- Team work is the spirit to success and growth
- Learn from the experience and guidance of seniors and Pass the torch of your experience and wisdom and mentor the next generation.

We are thankful to all our team members, advisors and all seniors for their continuous support, and our heartfelt wishes & good luck to the new team.

As is aptly said: "***If you want to leave your foot-prints, don't drag your feet***"

Regards,

**Dr Kanika Jain**
Vice President AOGD (2020-21)

**Dr Mamta Dagar**
Secretary AOGD (2020-21)

## Monthly Clinical Meeting

AOGD Monthly Virtual Clinical Meet will be organised by Apollo Hospital, New Delhi on 30th April, 2021 from 04:00pm to 05:00pm.

# From the Editor's Desk

**Dr A G Radhika**
Guest Editor

**Dr Richa Sharma**
Guest Co-Editor

**Dear Friends,**

It gives me immense pleasure to write the guest editorial message for this special issue of the Bulletin which focusses on National Health Programmes pertaining to women's health. Over the years there have been slow yet steady improvement Maternal & Child health indicators in India. The initial focus was on numbers (quantity) and mortality, today there is emphasis general quality of physical and mental health, financial assistance, IEC activities and logistic support.

Clinicians are understandably immersed in improving the academics and surgical skills. Learning & referencing the guidelines issued in developed countries is the norm today. However, it is equally important to be aware of the policies, facilities and benefits offered by our government through the National Health Programmes both to the client and the clinician. It is important to have a uniform standard of auditable treatment at all levels of healthcare. We have the innate desire to do "our bit" for the country. Active participation for the successful implementation these programmes is one such step in the direction of improvement of maternal health.

Some important highlights are the **"National Programme on Containment of Anti-Microbial Resistance"**,**"National Digital Health Mission for digitalisation of data management"**, **"Inclusion of cancer prevention in the broader ambit of programme for prevention of non- communicable diseases (NCDs) ie screening for DM & Hypertension"**, **"Anaemia Mukt Bharat and National TB Eradication Programme (NTEP)"** are modifications of established ongoing programmes with greater thrust to diagnose and treat iron deficiency anaemia and eradicate TB", respectively. There has been a revamp of the Revised National TB Programme which is now renamed as NTEP. It has been included here with the purpose to provide an update on whole new set of strategies for eradication of TB in India. We do hope that this compilation is found useful by our members.

I thank our hardworking and dedicated AOGD Editors Dr Geeta Mediratta and Dr Chandra Mansukhani for giving us this opportunity to bring forth this last issue of the bulletin under their tenure.

**With Best Regards !!**

**Dr A G Radhika**
Senior Consultant
UCMS & GTB Hospital

**Dr Richa Sharma**
Pro fessor
UCMS & GTB Hospital

**Editorial Team**

# Farewell Message from Outgoing Editorial Team

**Dr Geeta Mediratta**
Chief Editor

**Dr Chandra Mansukhani**
Co-Editor

We sincerely hope that all of you are trying to cope up with a positive attitude given the current resurgence of Covid 19 infection. We all have to learn to fight this & keep ourselves safe.

This April 2021 bulletin will be the last bulletin brought by the Team AOGD Sir Ganga Ram Hospital. We hope that we could provide the academically useful articles on various themes on recent & practical topics and we hope that these will be useful references in day to day practise & patient care.

Dr. Radhika has nicely discussed all National health programmes about women's health in detail as already written above.

We have an additional section on Reproductive Endocrinology featuring an interesting article on "**Approach to a newborn with ambiguious genitalia**" by Dr Archana Dayal Arya.

Dr Ruma Satwik has written a very crisp and informative article on "**Applications of AMH in reproductive medicine**".

Dr. Pallavi Sharma has elaborated on "**Endocrinology of normal menstrual cycle**" in a very simple and lucid manner.

Dr. Abha Majumdar has written a comprehensive article on "**Hirsutism**", which will be very useful for all the Post-graduates.

And finally Dr. Ratna Puri has described the "**Utility of Genetic Testing in assessing of risk of cancer in women's health**".

Editorial team of AOGD, Sir Ganga Ram Hospital bids you farewell and wishes Team AOGD, Safdarjung Hospital, all the best.

**Editorial Team**

# National Health Mission (NHM), National Digital Health Mission (NDHM)

**Sruthi Bhaskaran[1], Abha Sharma[2]**
[1]Associate Professor, [2]MS (MCH), Sr Specialist, Department of Obstetrics and Gynecology, UCMS/GTB Hospital

## National Health Mission (NHM)[1]

The Indian government launched the National Health Mission (NHM) in 2013. NHM encompasses two sub-missions, namely **National Rural Health Mission** (since 2005), **National Urban Health Mission**.

The basic aim is **Health System strengthening in rural and urban areas**. The NHM envisages achievement of universal access to equitable, affordable & quality health care services that are accountable and responsive to people's needs.

**GOALS**

1. Reduce MMR to 1/1000 live births
2. Reduce IMR to 25/1000 live births
3. Reduce TFR to 2.1
4. Prevention and reduction of anaemia in women aged 15–49 years
5. Prevent and reduce mortality & morbidity from communicable, noncommunicable; injuries and emerging diseases
6. Reduce household out-of-pocket expenditure on total health care expenditure
7. Reduce annual incidence and mortality from Tuberculosis by half
8. Reduce prevalence of Leprosy to< 1/10000 population & incidence to zero in all districts
9. Annual Malaria Incidence to be < 1/1000
10. Less than 1 per cent microfilaria prevalence in all districts
11. Kala-azar Elimination by 2015, <1/1000 population in all blocks.

## Health Systems Strengthening Components:[1]

1. **Reproductive, Maternal, Newborn, Child Health and Adolescent (RMNCH+A) Services-** The main strategies for RMNCH+A include services for mothers, newborns, children, adolescents and women and men in the reproductive age group.
   a. **Maternal Health:** Improved access to skilled obstetric care including abortion care. Important programmes**: Janani Suraksha Yojana (JSY)**, **Janani Shishu Suraksha Karyakram (JSSK)**
   b. Prevention and Management of Reproductive Tract Infections (RTI) and Sexually Transmitted Infections (STI)
   c. System wide response to Gender Based Violence
   d. Newborn and Child Health
   e. Universal Immunization
   f. Child Health Screening and Early Intervention Services: **Rashtriya Bal Swasthya Karyakram (RBSK)**
   g. Adolescent Health
   h. Family Planning services
   i. Addressing the Declining Sex Ratio
2. **Programmes for control of Communicable Diseases**
3. **Programmes for control of Non Communicable Diseases (NCD)**

**Major Initiative under NHM[1]**

1. Accredited Social Health Activist (ASHA)
2. Rogi Kalyan Samiti/Hospital Management Society
3. The Untied Grants to Sub-Centres (SCs)
4. Village Health Sanitation and Nutrition Committee (VHSNC)
5. **Janani Suraksha Yojana (JSY):** aims to reduce maternal mortality by encouraging them to deliver in government facilities. Under the scheme, cash assistance is provided to eligible pregnant women for giving birth in a government health facility
6. **Janani Shishu Suraksha Karyakram (JSSK):** It entitles all pregnant women delivering in public health facility to absolutely free delivery, including caesarean section, free drugs and consumables, free diagnostics, free diet, free provision of blood, free transport from home to health institution, between health institutions in case of referrals and drop back home.
7. Facility Based Newborn Care
8. National Mobile Medical Units (NMMUs)
9. My Hospital / MeraAspataal Initiative
10. 24 X 7 Services and First Referral facilities
11. KayakalpAwards
12. National Quality Assurance Programme
13. Health management information system (HMIS)

## National Digital Health Mission[2]

In his address to the nation on 74th Independence Day (2019), the PM launched the **National Digital Health Mission** to create a national digital health ecosystem that supports universal health coverage bycreating national health ID for every Indian. The implementation of NDHM will be done in 3 phases and the pilot phase has been rolled out in some of the Union Territories.

The National Digital Health Blueprint identifies building blocks that will be available as a collection of **cloud-based services.**

## Key Features

1. It comprises six key **building blocks**
   a. **Health Data-** Health Care provider facility will enrol in **NDHM Registry** to become **Health Information Providers (HIPs**); who will keep a digital copy of patients'personal health records, **HIUs (Health information users)** are the individuals/organizations who will get access to health data if consent is given by the individual.
   b. **Health ID - Single health ID** and **unique health ID based on Aadhaar can be created by** self from a mobile or a web application or by health care facility/organisation.
   c. **Health Registries- Health Workforce Registry** – will have information about doctors, nurses, paramedical staff, ASHAs etc. through Digi Doctor platform. **Healthcare Facility Registry-** will provide information abouthealthcare facility including hospitals, clinics, diagnostic centres, pharmacies etc.
   d. **Health Claims- Standard e-Claim form** can be used for any health insurance claim through a **Health Claims Platform (HCP)**
   e. **Health Data Analytics-** Every **HIP** is expected to generate aggregated data on the health information that is being managed by them.
   f. Open **Telemedicine and e-Pharmacy** Network
2. **The National Health Authority (NHA)** has been given the mandate to design, build, roll-out and implement the mission in the country.
3. **The core building block** of the mission is that **the health ID, DigiDoctor and Health Facility Registry** shall be owned, operated and maintained by the Government of India.
4. **Private stakeholders** will have an equal opportunity to integrate and create their own

**NDH Mimplementation in Nutshell:[2]**

| | Phase 1 | Phase 2 | Phase 3 |
|---|---|---|---|
| **Digi doctor** | - Unique ID for doctors - e-Prescription & e-Sign platforms ---Verification of doctors by National Health Authority (NHA) | - Verification with MCI/NMC/CCIM/ CCH<br>- Updating of qualification & employment<br>- Integrated state councils & Registers | - Real time feedback & rating of doctors |
| **Health care Facility Registry** | - Unique ID for hospitals & labs, e-Forms & e-Sign for facilities<br>- Validation through NHRR*/ PMJAY**<br>- Provisional verification by NHA | - Audit by statutory Health Facility Auditor<br>- Attestation & updating of data<br>- GIS*** based visualisation | - Automatic benefits enablement<br>- Unified application forms<br>- Converged audits |
| **Health ID** | - 'Health Account' for everyone<br>- Option of linking with AADHAR | - Linking of accounts- family & relationships<br>- Convergence of different schemes' IDs<br>- Automatic benefits enablement- PMJAY** etc. | - All health benefits & policies- private & public, linked to health ID |
| **Personal Health Records(PHR)** | - PDF & scanned Health records<br>- Power of consent with individual<br>- Prescription & reports in PHR | - Metadata & e-reports with analytics<br>- Integration with public & private HIPs | - Health biomarkers based preventive healthcare<br>- Personal health analytics for individual & family |

***Geographic information system, *National health resource repository, **Pradhan Mantri Jan Arogya Yojana, MCI-Medical council of India, NMC- National medical council, CCIM- Central council of Indian medicine

products for the market. The core activities and verifications, however, remain with the government.

5. The citizens will be able to give their doctors and health providers **one-time access to this data** during visits to the hospital for consultation

## References


1. NHM: National health mission, Ministry of health and family welfare Government of India:2018 https://nhm.gov.in/images/pdf/NHM/NHM_more_information.pdf
2. National Digital Health Mission, Ministry of health and family welfare Government of India & National health authority:2019 https://ndhm.gov.in/assets/uploads/NDHM_Strategy_Overview.pdf

# Pradhan Mantri Surakshit Matritva Abhiyan (PMSMA)

**Balkesh Rathi[1], Shailja Kundra[2]**
[1]Senior Specialist, [2]Medical Officer, Department of Obs. & Gynae, UCMS & GTB Hospital, Delhi

The Pradhan Mantri Surakshit Matritva Abhiyan has been launched by the Ministry of Health & Family Welfare (MoHFW), Government of India on 31st July 2016. The program aims to provide assured, free of costcomprehensive and quality antenatal care, universally to all pregnant women on a fixed date ie 9th of every monthat identified public health facilities (PHCs/ CHCs, DHs/ urban health facilities etc) in both urban and rural areas in addition to the routine ANC at the health facility/ outreach. PMSMA guarantees a minimum package of antenatal care services to women in their 2nd / 3rd trimesters of pregnancy at designated government health facilities.

## Aim of the PMSMA

Pradhan Mantri Surakshit Matritva Abhiyan envisages to improve the qualityand coverage of Antenatal Care (ANC) including diagnostics and counselingservices as part of the Reproductive Maternal Neonatal Child and Adolescent Health (RMNCH+A) Strategy. PMSMA is based on the premise that if every pregnant woman in India is examined by a physician and appropriately investigated at least once during the PMSMA and then appropriately followed up, the process can result in reduction in the number of maternal and neonatal deaths and morbidity in our country.

## Objectives of the Program

- Ensure at least one antenatal checkup for all pregnant women in their second or third trimester by a physician/specialist
- Improve the quality of care during ante-natal visits. This includes ensuring provision of the following services:
  - o All applicable diagnostic services
  - o Screening for the applicable clinical conditions
  - o Appropriate management of any existing clinical condition such as Anaemia, Pregnancy induced hypertension, Gestational Diabetes etc.
  - o Appropriate counselling services and proper


**Fig 1:** Pradhan Mantri Surakshit Matritva Abhiyan strategy[1]

documentation of services rendered

- o Additional service opportunity to pregnant women who have missed ante-natal visits

- Identification and line-listing of high risk pregnancies based on obstetric/ medical history and existing clinical conditions.
- Appropriate birth planning and complication readiness for each pregnant woman especially those identified with any risk factor or comorbid condition.
- Special emphasis on early diagnosis, adequate and appropriate management of women with malnutrition.
- Special focus on adolescent and early pregnancies as these pregnancies need extra and specialized care

## Provisions under PMSMA

Antenatal checkup services by specialists including Obstetrician, Radiologist/physician with support from private sector doctors to supplement the efforts of the government sector.

A minimum package of antenatal care services includes

1. Lab Investigations - Hb , Urine Albumin, RBS (Dip stick), Rapid Malaria test, Rapid VDRL test, Blood Grouping, CBC ESR
2. One ultrasound at 2nd trimester of pregnancy. When additional investigations are required, beneficiaries are to be advised to get those done and share the report during next PMSMA or during her routine ANC check - up visit.
3. Calcium& IFA supplements would be provided to all pregnant women attending the PMSMA clinics.
4. Identification and follow up of high risk pregnancies.

   Pregnant women would be given Mother and Child Protection Cards and safe motherhood booklets. A sticker indicating the condition and risk factor ofthe pregnant women would be added onto MCP card for each visit:

   - o Green Sticker- for women with no risk factor detected
   - o Red Sticker – for women with high risk pregnancy
5. Safe abortion care services after proper counselling.
6. Referral Transport Mechanism for High risk women: During PMSMA, 108 /102 /State owned ambulances/Private empanelled ambulances can also be used for referring those cases identified as high risk.

**Before leaving the facility every pregnant women to be counselled, may be individually or in groups, on the following topics:**

- Care during pregnancy.
- Danger signs during pregnancy.
- Birth preparedness & Complication readiness, contact details to be used in case of need
- Family Planning
- Importance of nutrition including iron - folic acid consumption and calcium supplementation.
- Rest
- Safe sex
- Institutional delivery.
- Identification of referral transport.
- Entitlements under Janani Suraksha Yojana (JSY)
- Entitlements and service guarantee under Janani Shishu Suraksha Karyakram (JSSK)
- Post - natal care.
- Breastfeeding and complementary feeding.

**A National Portal for PMSMA and a Mobile application have been developed to facilitate the engagement of private/ voluntary sector.**

## Reference

1. Pradhan Mantri Surakshit Matritva Abhiyan (PMSMA), National Health Portal (NHP), by the Ministry of Health and Family Welfare (MoHFW), Government of India.https://pmsma.nhp.gov.in/about-scheme/

# Janani Suraksha Yojana

**Balkesh Rathi[1], Shailja Kundra[2]**
[1]Senior Specialist, [2]Medical Officer, Department of Obs. & Gynae, UCMS & GTB Hospital, Delhi

Janani Suraksha Yojana (JSY) is a safe motherhood intervention under the National Rural Health Mission (NRHM), being implemented with the objective of reducing maternal and neonatal mortality by promoting institutional delivery among the poor pregnant women. The Yojana, launched on 12th April 2005, by the Hon'ble Prime Minister, is being implemented in all states and UTs with special focus on low performing state.

JSY is a 100% centrally sponsored scheme and it integrates cash assistance with delivery and post-delivery care. The Yojana has identified ASHA, the accredited social health activist as an effective link between the Government and the poor pregnant women in l0 low performing states, namely the 8 socioeconomically backward states of Bihar, Chhattisgarh, Jharkhand, Madhya Pradesh, Orissa, Rajasthan, Uttaranchal and Uttar Pradesh, referred to as the Empowered Action Group (EAG) states and Assam and J&K and the remaining NE States. In other eligible states and UTs, wherever, AWW and traditional birth attendant (TBAs) or ASHA like activist has been engaged in this purpose, she can be associated with this Yojana for providing the services.

## Role of ASHA

1. Identify pregnant woman as a beneficiary of the scheme and report facilitate registration for ANC.
2. Assist the pregnant woman to obtain necessary certifications wherever necessary, Provide and / or help the women in receiving at least three ANC checkups.
3. Provide and / or help the women in receiving at least three ANC checkups including TT injections, IFA tablets
4. Identify a functional Government health centre or an accredited private health institution for referral and delivery.
5. Counsel for institutional delivery.
6. Escort the beneficiary women to the pre-determined health center and stay with her till the woman is discharged.
7. Arrange to immunize the newborn till the age of 14 weeks.
8. Inform about the birth or death of the child or mother to the ANM/MO.
9. Post natal visit within 7 days of delivery to track mother's health afterdelivery and facilitate in obtaining care.
10. Counsel for initiation of breastfeeding to the newborn within one-hour of delivery and its continuance till 3-6 months and promote family planning

## Key Features of JSY

- The scheme focuses on the poor pregnant woman from states having low institutional delivery rates namely the states of Uttar Pradesh, Uttaranchal, Bihar, Jharkhand, Madhya Pradesh, Chhattisgarh, Assam, Rajasthan, Orissa and Jammu and Kashmir. While these states have been named as Low Performing States (LPS), the remaining states have been named as High performing States (HPS).
- Each beneficiary registered under this Yojana should have a JSY card along with a MCH card, for easy tracking of each pregnancy. ASHA/ AWW/ any other identified link worker under the overall supervision of the ANM and the MO, PHC should mandatorily prepare a micro-birth plan. Please see Annexure – I. This will effectively help in monitoring Antenatal Check-up, and the post delivery care.

### Eligibility for Cash Assistance

| | |
|---|---|
| LPS States | All pregnant women delivering in Government health centres like Sub-centre, PHC/CHC/ FRU / general wards of District and state Hospitals or accredited private institutions |
| HPS States | BPL pregnant women, aged 19 years and above |
| LPS & HPS | All SC and ST women delivering in a government health centre like Sub-centre, PHC/CHC/ FRU / general ward of District and state Hospitals or accredited private institutions |

**Note:** BPL Certification – is required in all HPS states,but places where BPL cards have not yet been issued or have not been updated, States/UTs can formulate a simple criterion for certification of poor and needy status of the expectant mother's family by empowering the gram pradhan or ward member.

**Scale of Cash Assistance for Institutional Delivery:**

| Category | Rural Area | | Total | Urban Area | | Total |
|---|---|---|---|---|---|---|
| | Mother's Package | ASHA's Package | | Mother's Package | ASHA's Package | |
| LPS | 1400 | 600<br>Rs. 300 for ANC & Rs. 300 for facilitating institutional delivery | 2000 | 1000 | 400<br>Rs. 200 for ANC & Rs. 200 for facilitating institutional delivery | 1400 |
| HPS | 700 | 200 | 900 | 600 | 200 | 800 |

**Limitations of Cash Assistance for Institutional Delivery**

| | |
|---|---|
| In LPS States | All births, delivered in a health centre (Government or Accredited Private health institutions ) |
| In HPS States | Upto 2 live births. |

Disbursement of money to expectant mother going to her mother's place for delivery should be done at the place she delivers. The entitlement of cash should be determined by her referral slip carried by her and her usual place of residence.

**LPS Entitlements under Janani Suraksha Yojana**

| Rural Area | Urban Area | Eligibility Criteria |
|---|---|---|
| Financial Assistance for Institutional delivery | | |
| Rs. 700 | Rs. 600 | Available only to BPL/ SC/ ST women regardless of age and number of children for delivery in government / private accredited health facilities |
| Financial Assistance for Home delivery | | |
| Rs. 500 | Rs. 500 | Available only to BPL women who prefer to deliver at home regardless of age and number of children |

## Certificates Required for Availing JSY Benefits

- BPL certificate.
- S.C. / S.T. Certificate.
- ANC Registration in a Govt. Health Institution. (MCP Card)
- Bank Account Number and AADHAR Card Number should be filled in MCP Card.
- If an expectant mother does not have a BPL certificate but the Pradhan of Gram Panchayat where she resides certifies that she belongs to an economically weak / poor family, it will be sufficient to give her JSY benefits.
- In all such cases, where the JSY beneficiaries produce a certificate / document required to make the payment to JSY beneficiary which is signed by the Pradhan of the Gram Panchayat the same shall be accepted without insisting that a Magistrate should issue the certificate.

## Guidelines for Health Functionaries under JSY

- It is mandatory that all the JSY beneficiaries be registered for ANC checkups at their respective health institution (either a Sub Centre or a PHC / CHC / CH / DH / State Hospital).
- The benefit should be given at the time of Delivery before discharge from the hospital.
- For Home Deliveries Health Workers will disburse the amount.
- MCTC seeding of all beneficiaries is essential for assured benefit.

**Mode of Payment:** Through DBT for which MCTC seeding is essential in which Aadhar Card Number and Bank account number is required.

**Micro-Birth Plan for JSY Beneficiaries – Normal delivery**

| Steps | Activity | To Be Undertaken By | Proposed Time Line |
|---|---|---|---|
| 1 | Identification and Registration of Beneficiary | ANM/ASHA/AWW or any link worker<br>Provide 1st ANC immediately on Registration.<br>ASHA to follow up at Anganwadi Centres / Subcenter (SC), ensure that beneficiary attends the ANC on the indicated dates<br>and also call beneficiary to Anganwadi / SC to participate in Monthly meeting - enhanced cash & Transport assistance benefits for Institutional delivery | Atleast 20-24 weeks before EDD |
| 2 | Filling up of Maternal & Child card<br>( In duplicate– one each for mother andASHA/Link worker)(This will form part of the JSY'S Registration Card). | | Immediately on registration |
| 3 | 4 I-s':<br>1. Inform dates of 3 ANC &TT Injection (s)<br>2. Identify the health center for all referral<br>3. Identify the Place ofDelivery<br>4. Inform EDD | | |
| 4 | Collecting BPL ornecessary proofs/ certificates<br>Wherever necessary fromPanchayat / local bodies / Municipalities | ANM/ASHA/AWW or anlink worker | Within 2-4 weeksfrom Registration |
| 5 | Submission of completed JSY card in Health center for verification by the authorized/Medical officer.<br>II. Take necessary steps toward arranging transport or makingavailable cash to the beneficiary to come to the Health Centre<br>III. Ensure availability of fund to ANM/ Health worker /ASHA etc. | MO, PHC | Atleast 2-4 weeks before EDD |
| 6 | Payment of cash benefit /incentive to the motherand ASHA | ANM/ MO, PHC | At the institution |

**Micro-Birth Plan for JSY Beneficiaries –For complicated cases or those requiring cesarean section etc**:

| | | |
|---|---|---|
| **Ac – 1** | Pre-determine a Referral health centerand intimate the pregnant women | By ANM/ASHA/ link worker |
| **Ac – 2** | Familiarize the woman with the referral centre, if necessary carry a letter ofreferral from MO PHC | |
| **Ac – 3** | Pre-organize the transport facility in consultation with family members community leader | ANM/ASHA/ Community |
| **Ac – 3** | Arrange for the medical experts if thesame is not available in the referred heath center | MO, PHC |

## References

1. National Health Mission. Government of India Ministry of Health and Family Welfare Maternal Health Division Nirman Bhavan New Delhi. https://nhm.gov.in/WriteReadData/l892s/97827133331523438951.pdf

# Janani-Shishu Suraksha Karyakram (JSSK)

**Archana Chaudhary**
Specialist, Department of Obstetrics & Gynecology UCMS & GTB Hospital, Delhi

Janani-Shishu Suraksha Karyakram(JSSK) waslaunched on 1st June 2011. It is an initiative by Ministry of Health and Family Welfare, Government of India **to assurefree and cashless services to pregnant women** (normal deliveries and caesarean operations) and also treatment of sicknew born(up to 30 days after birth) accessing public health institutions across the country. Janani Suraksha Yojana was the primary step to increase institutional deliveries. Though it was successful, out-of-pocket expenses incurred by the stakeholders continued to be quite high. JSSK was launched to remove this deficiency.

The guidelines lay down lists of key steps to be taken by the states for effective implementation of this initiative which will serve as a reference tool and facilitate the state in planning necessary interventions.

It invokes a new approach to healthcare, placing for the first time, **emphasis on entitlements and elimination of out-of-pocket expenses incurred for the care of both pregnant women and sick neonates.** It aims to have all expenses related to delivery in a public institution to be borne entirely by the government with no user charges.

The broader aim of JSK was to

i. Encourage pregnant women to deliver at public health facilities and fulfil the commitment of achieving 100% institutional delivery
ii. Empower service providers working at the health facilities in providing quality ante-natal,intra-natal and post-natal services
iii. Reduce both maternal and infant mortality and morbidity

***Entitlements for pregnant women***

i. Free and zero expensedelivery and caesarean section
ii. Free drugs and consumables required during ANC, INC, PNC up to 6 weeks.

    Regular procurement, uninterrupted supply and availability of drugs and consumables should be ensured at all public health institutions. The head of the district/health facility is empowered to procure drugs and consumables to prevent stock outs.
iii. Free essential and desirablediagnostics (Blood, Urine tests and Ultra-sonography, etc.) during ANC, INC, PNC up to 6 weeks.

    If in-house facility is not available, free diagnostics can be provided through PPP/ outsourcing.
iv. Free diet during stay in the health institutions (up to 3 days for normal delivery & 7 days for caesarean section).
v. Free provision of blood without any user charges.
vi. Free transport from home to health institutions.
vii. Free transport between facilities in case of referral.
viii. Drop back from institutions to home after 48 hrs stay.
ix. Exemption from all kinds of user charges levied for OPD, admissions, diagnostics and blood.

***Entitlements for sick newborns till 30 days after birth. This has now been expanded to cover sick infants:***

- Free and zero expense treatment.
- Free drugs and consumables.
- Free diagnostics.
- Free provision of blood.
- Free transport from home to health institutions.
- Free transport between facilities in case of referral.
- Drop back from institutions to home.
- Exemption from all kinds of user charges.

At state and district level, the state nodal officer and district nodal officers are nominatedto monitor and follow up the progress in implementation of the scheme.

At national level, the scheme is monitored by National Health Systems Resource Centre (NHSRC) under guidance and support from Maternal Health Division, Ministry of Health & Family Welfare, Government of India.

## Reference

1. Guidelines for Janani-Shishu Suraksha Karyakram (JSSK), NRHM, Maternal health division, Ministry of Health and Family welfare, Government of India. Nirman Bhavan, New Delhi. https://nhm.gov.in/images/pdf/programmes/guidelines-for-jssk.pdf

# Intensified National Iron Plus Initiative (I-NIPI)

**Nazia Parveen**
Assistant Professor, Department of Obstetrics & Gynecology, UCMS & GTBH, Delhi

The reduction of anemia is one of the important objectives of the POSHAN Abhiyaan launched in March 2018. Complying with the targets of POSHAN Abhiyaan and National Nutrition Strategy, intensified Iron-plus Initiative (I-NIPI)strategy of the Anemia Mukt Bharat Campaign has been designed to reduce prevalence of anemia by 3% per year among **six target beneficiary** groupsie. children, adolescent boys & girls, women in the reproductive groups (20 -24 years), through six interventions and six institutional mechanisms (fig.1)



Approximately 450 million beneficiaries - nearly 50% of the country's population - will be reached

**Fig 1:** Anemia Mukt Bharat 6X6X6 strategy[1]

## Prevalence of Anemia in India

According to the National Family Health Survey 4 (NFHS-4), 2015/16, anemia prevalence across all ages is extremely high in India (fig.2).

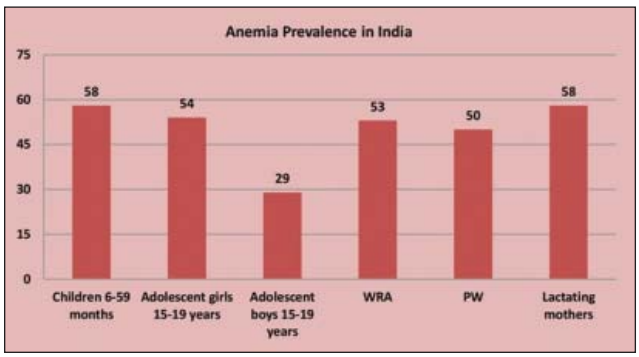



**Fig 2:** Prevalence of Anemia in India[2]

### WRA – Women in Reproductive age, PW- Pregnant women

| | |
|---|---|
| **1970** | **National Nutritional Anemia Prophylaxis Program (NNAPP)**<br>60 mg iron supplementation for PW and 20 mg for 1-5 yr x100 days |
| **1991** | **National Nutritional Anemia Control Program (NNACP)**<br>60 mg iron changed to 100 mg |
| **2007** | 5-10 yrs age group added |
| **2013** | **National Iron Plus Initiative (NIPI)**<br>Weekly and biweekly supplementation.<br>Test and treat, Life cycle approach |
| **2018** | **Anemia Mukt Bharat- I-NIPI Program Intensification**<br>PW 60 mg x180 days, IFS for WRA 6x6x6 strategy, Life Cycle Approach |

**Fig 3:** Evolution of Anemia Control Programs[3]

## Anemia Mukt Bharat Targets (Fig 4)

| Age group | Anemia prevalence (%) | |
|---|---|---|
| | Baseline (NFHS 4) | National Target 2022 |
| Children 6-59 months | 58 | 40 |
| Adolescent girls 15-19 years | 54 | 36 |
| Adolescent boys 15-19 years | 29 | 11 |
| Women of reproductive age | 53 | 35 |
| Pregnant women | 50 | 32 |
| Lactating women | 58 | 40 |

**Fig 4:** Beneficiary wise Anemia reduction targets[1]

A. **Interventions**

1. Prophylactic Iron and Folic Acid supplementation
2. Deworming
3. Intensified year-round Behaviour Change Communication Campaign (Solid Body, Smart Mind) focusing on four key behaviours
   - o Improving compliance to Iron Folic Acid supplementation and deworming
   - o Appropriate infant and young child feeding practices,
   - o Increase in intake of iron-rich food through diet diversity/quantity/frequency and/or

fortified foods with focus on harnessing locally available resources.

- Ensuring delayed cord clamping after delivery (by 3 minutes) in health facilities

4. Testing and treatment of anemia, using digital methods and point of care treatment, with special focus on pregnant women and school-going adolescents
5. Mandatory provision of Iron and Folic Acid fortified foods in government-funded public health programs
6. Intensifying awareness, screening and treatment of non-nutritional causes of anemia in endemic pockets, with special focus on malaria, haemoglobinopathiesandfluorosis

## Prophylactic Dose and Regime for Iron Folic Acid Supplementation

| Age Group | Dose and regime |
|---|---|
| School-going / Out-of-school adolescent girls, 10–19 years of age | **Weekly**, 1 Iron and Folic Acid tablet Each tablet containing 60 mg elemental iron + 500 mcg Folic Acid, sugar-coated, BLUE COLOUR |
| Women of reproductive age (non-pregnant, non-lactating) 20–49 years | **Weekly,** 1 Iron and Folic Acid tablet Each tablet containing 60 mg elemental Iron + 500 mcg Folic Acid, sugar-coated, RED COLOUR |
| Pregnant women and lactating mothers (of 0–6 months child) | **Daily**, 1 Iron and Folic Acid tablet starting from the fourth month of pregnancy ie. second trimester, continued throughout pregnancy (minimum 180 days during pregnancy) and to be continued for 180 days, post-partum Each tablet containing 60 mg elemental Iron + 500 mcg Folic Acid, sugar-coated, RED COLOUR |

***Note 1:*** *Prophylaxis with iron should be withheld in case of acute illness (fever, diarrhoea, pneumonia, etc.), and in a known case of thalassemia major/ history of repeated blood transfusion.*

***Note 2:*** All women in the reproductive age group in the pre-conception period and up to the first trimester of the pregnancy are advised to have 400 mcg of Folic Acid tablets, daily, to reduce the incidence of neural tube defects in the fetus.

1. **Dose and regime for deworming**

| Age Group | Dose and regime |
|---|---|
| School-going / out-of-schooladolescent girls 10–19 years of age | Biannual dose of 400 mg albendazole (1 tablet) |
| Women of reproductive age (non-pregnant, non-lactating) 20–49 years | Biannual dose of 400 mg albendazole (1 tablet) |
| Pregnant women | One dose of 400 mg albendazole (1 tablet), after the first trimester, preferably during the second trimester |

**Intensified 360-degreeInformation Education Communication (IEC) / Behaviour Change Communication (BCC)for Anemia Prevention & Behaviour Change**

**Focus on Social mobilization and behavior change: 4 keybehaviours**

1. Compliance to Iron Folic Acid supplements and deworming
2. Appropriate Infant and Young Child Feeding (IYCF)
3. Increase intake of iron-rich, protein-rich and vitamin C rich foods through diet diversification and consumption of fortified foods.
4. Practice of delayed cord clamping in all health facility deliveries followed by early initiation of breastfeeding within 1 hour of birth

3. **Test and Treat Strategy**

Testing:

1. Use of digital hemoglobinometers.
2. In two age groups-to begin with school-going Adolescent girls and boys 10-19 years, Weekly Iron Folic Acid Supplementation (WIFS) beneficiaries, using Rashtriya Bal SwasthyaKaryakram (RBSK) mobile teams.
3. Pregnant women at all ANC contact points.
4. At all high case load facilities at block level and above, hemoglobin level estimation will be done using Semi-Auto Analyzers.
5. This may be extended to all age groups, later

**Anemia treatment protocol for Adolescent Girls**

| |
|---|
| **All school-going adolescents 10–19 years in government/government-aided schools** |
| To be screened annually, in school premises by Rashtriya Bal SwasthyaKaryakram (RSBK) team |
| **Mild and Moderate Anemia** |
| 2 IFA tablets (each with 60 mg elemental iron and 500 mcg folic acid), once daily, for 3 months, orally after meals. |
| follow-up of adolescent after 45 days to 90 days, if Hb is normal then continue IFA prophylaxis |
| **If no improvement or severe anaemia** |
| Referrals |
| Management based on investigation and subsequent diagnosis |

**Anemia management protocol for Pregnant Women**

| |
|---|
| All pregnant women to be screened at each ANC visits |
| **If Hb: 10–10.9 g/dl (mild anemia)orHb 7–9.9 g/dl (moderate anemia)** |
| 2 tablets IFA (60 mg elemental Iron, 500 mcg Folic Acid) daily, orally |
| OR |
| IV Iron Sucrose or Ferric Carboxy Maltose (FCM) late in pregnancy or in case of non-compliance |
| Follow up after 2months- |
| If Normal Hb – continue IFA Prophylaxis |
| If Hb is not improved(< 1g/dl rise in one month) – Investigate / refer |
| **If Hb: 5.0–6.9 g/dl (severe anemia)** |
| Hospitalization, Evaluation, Blood transfusion |

5. **Mandatory provision of Iron and Folic Acid fortified foods in government-funded public health programs**
6. **Intensifying Awareness, Screening & Treatment of Non-nutritional causes of Anemia in Endemic Pockets, with special focus on Malaria, Haemoglobinopathies**

**Integrated Malaria and Anemia testing** in endemic regions, beneficiaries who report with recent fever and being screened for anemia, to be screened for malaria also and vice versa. Fixed days for screening for anemia at PMSMA sites and annually by RBSK teams in schools will provide screening for malaria under National Vector Borne Disease Control program (NVBDCP). Anemia Mukt Bharat plays a key role for utilization of long-lasting insecticides nets (LLINs) by all target groups especially pregnant mothers and under five children by promoting IEC/BCC. Indoor Residual Spray (IRS) before and after monsoon season to be carried out with appropriate insecticides in school premises and residential areas.

**Screening for hemoglobinopathies**, integrated with ANC services during 1st trimester in endemic regions. Women with severe anemia to be referred to higher centers, if found screening positive then their husbands should also be screened for the carrier status. If the couple is found positive then they should be referred to higher centers for prenatal diagnosis before 20 weeks of pregnancy.

To provide premarital and preconception screening and counseling for informing the community about the preventive options and management as per the national guidelines on prevention and control of hemoglobinopathies 2016.

**Coordinated action with National program for the prevention and control of fluorosis (NPPCF),** use of safe drinking water, focus on diet corrections (calcium, magnesium, vitamin C) by dietary diversity.

**Six Institutional Mechanism**

1. Intra-ministerial coordination
2. National Anemia Mukt Bharat Unit
3. National Centre of Excellence and Advanced Research on Anemia Control
4. Convergence with other ministries
5. Strengthening supply chain and logistics
6. Anemia Mukt Bharat dashboard and digital Portal-one-stop shop for anemia

## What's New?

- Coordinated management efforts – intra &inter ministerial
- Target based monitoring and KPI reviews and awards; Private schools; 60 mg instead of 100 mg prophylactic dose, sugar coated.
- Communication materials for extensive awareness, intensive 360 degree communication campaigns - Creating a Jan Andolan…
- Use of digital methods of hemoglobin estimation and point of care treatment, newer treatment strategies – IV Iron Sucrose and FCM
- Linkage with Malaria; mandating use of fortified

food in public health programs, specially double fortified salt (iron and iodine)

**ASHA incentive for Anemia Mukt Bharat**: ASHA will be provided a total of Rs. 150 per month per ASHA for covering at least 70 % of the beneficiaries for IFA supplementation in two age groups: children 6-59 months and WRA.

## References


1. OPERATIONAL GUIDELINES INTENSIFIED NATIONAL IRON PLUS INITIATIVE (I-NIPI). https://anemiamuktbharat.info/wp-content/uploads/2019/09/Anemia-Mukt-Bharat-Brochure_English.pdf
2. NFHS 4, 2015-16
3. Bhatia V, Sahoo DP, Parida SP. India steps ahead to curb anemia: Anemia Mukt Bharat. Indian J Community Health.2018;30(4):312 -6.
4. Ministry of Health and Family Welfare. Policy on control of nutritional anemia. New Delhi: MoHFW, Government of India; 1991.
5. Ministry of Health & Family Welfare. Vitamin A and IFA Supplementation. New Delhi: MoHFW, Government of India; 2006. Available from: http://www.motherchildnutrition.org/india/pdf/mcn-vitamin-a-ifa-supplementation.pdf, accessed on August 16, 2018.
6. Ministry of Women & Child Development. Review of the Policy regarding micronutrient – Iron, folic acid (IFA). New Delhi: MWCD, Government of India; 2010. Available from: http://www.wcd.nic.in/sites/default/files/1-SABLA scheme_0. pdf, accessed on August 16, 2018.

# National Iodine Deficiency Disorders Control Programme (NIDDCP) & National Guidelines for Screening of Hypothyroidism During Pregnancy

**Jagriti[1], Richa Sharma[2]**
[1]Postgraduate Student, [2]Professor, Department of Obstetrics & Gynecology, UCMS & GTB Hospital, Delhi

National Goitre Control Programme (NGCP) was launched by the Government of India in 1962. It was renamed as "National Iodine Deficiency Disorders Control Programme (NIDDCP)" in August, 1992 keeping in view the wide spectrum of Iodine Deficiency Disorders like mental and physical retardation, deaf mutism, cretinism, still births, abortions etc.The programme is being implemented in all the States/UTs. It is a 100% centrally assisted programme.

## NIDDCP Goals

- To bring the prevalence of IDD to below 5% in the country.
- To ensure 100% consumption of adequately iodated salt (15ppm) at the household level.

## NIDDCP Objectives

- Surveys to assess the magnitude of Iodine Deficiency Disorders in the districts.
- Supply of iodated salt in place of common salt.
- Resurveys to assess iodine deficiency disorders and the impact of iodated salt after every 5 years in the districts.
- Laboratory monitoring of iodated salt and urinary iodine excretion.
- Health Education and Publicity.

To ensure the use of iodated salt the Government of India has issued notification banning the sale of non-iodated salt for direct human consumption in the country with effect from May, 2006 under the Prevention of Food Adulteration Act 1954.

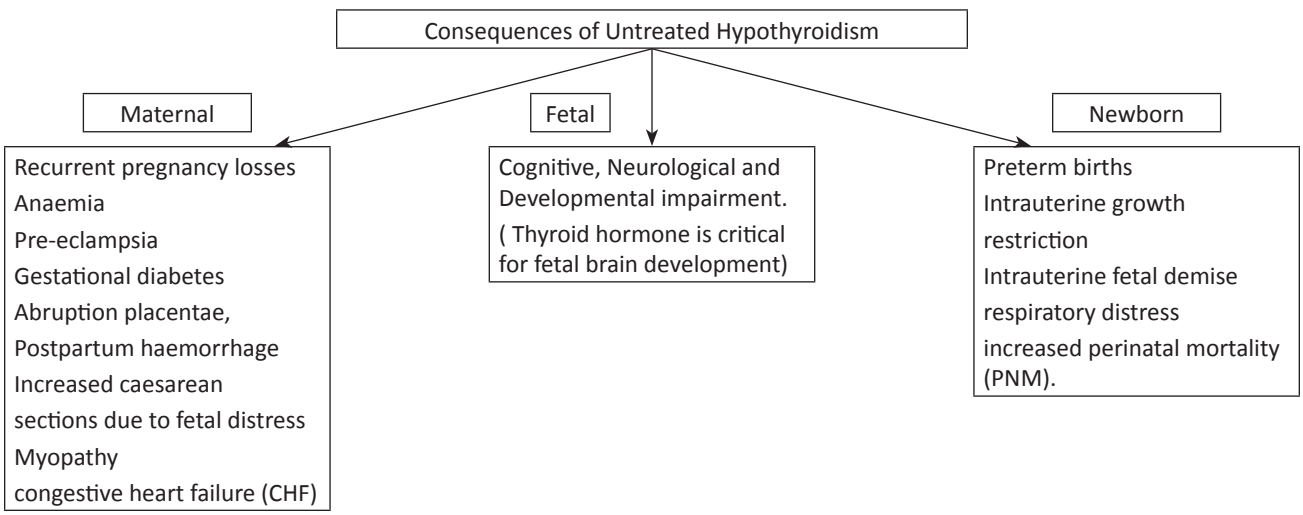
Ministry of Health & Family Welfare is the nodal Ministry for implementation of National Iodine Deficiency Disorders Control Programme (NIDDCP).

## National Guidelines for Screening and Treatment of Hypothyroidism during Pregnancy 2014

**Aim:** To reduce maternal morbidity and serious complications during pregnancy and childbirth

**Objectives:**

- To reduce maternal, fetal and neonatal complications associated with hypothyroidism by screening pregnant women at risk for hypothyroidism.
- To reduce the burden of complications due to hypothyroidism during pregnancy through early diagnosis and treatment.



## All High Risk Antenatal Women to be Screened for Hypothyroidism at The First Antenatal Visit

***High risk factors for hypothyroidism***

1. Residing in an area of known moderate to severe iodine insufficiency(according to area mapping)
2. Obesity (pre-pregnancy/first trimester Body Mass Index (BMI) ≥30 kg/m2)
3. History of prior thyroid dysfunction or prior thyroid surgery
4. Symptoms of thyroid dysfunction or the presence of goiter
5. History of thyroid dysfunction in first degree relative (parents/siblings/children)
6. History of diagnosed mental retardation in family/previous births
7. Known case of autoimmune diseases like Type I diabetes/Systemic Lupus
8. Erythematosus (SLE)/Rheumatoid Arthritis (RA)/Addison's disease/Coeliac disease, etc.
9. History of recurrent miscarriages, pre-term delivery, intrauterine demise,
10. pre-eclampsia/eclampsia, abruptio placentae
11. History of infertility (inability to conceive after one year of unprotected intercourse)
12. Use of amiodarone or lithium, or recent administration of iodinated radiologic contrast

**Overt Hypothyroidism** - serum TSH>2.5-3mIU/l with low FT4 levels or TSH>10mIU/l irrespective of FT4

**Subclinical hypothyroidism** - serum TSH between 2.5 and 10mIU/L with normal FT4

**Normal values:**

Ist trimester - 0.1-2.5mIU/ l

IInd trimester - 0.2-3mIU/l

IIIrd trimester- 0.3-3mIU/l.

## Protocol for Management of Hypothyroidism

***Drug of choice***: Levothyroxine - category A drug, to be taken orally, in the morningempty stomach and should not take anything orally for at least half an hour after intake of the medicine.

***Instructions***

If dose is missed on one day, the patient may take the same as soon as she remembers and should not eat anything for the next half hour, If she misses the tablet altogether, she should takedouble the dose on the next morning

TSH 2.5/3 to 10 start 25 µg levothyroxine / day

TSH >10, start 50 µg of levothyroxine / day

- If initial TSH <10, treatment is to be stopped afterdelivery but if it was >10, treatment will continue in same dose after delivery
- If TSH between 3-10mIU/l, treatment to be discontinued after delivery
- If woman is already taking treatment in pre-pregnancy, treatment will continue during pregnancy with same target range
- Once treatment has started, TSH levels should be repeated every 4- 6 weeks and doses to be adjusted (Table. 1, 2)
- Deliver uncomplicated cases at PHC/CHC under supervision of Medical Officer
- Refer cases with associated complications at a higher centre for delivery under the supervision of an obstetrician.

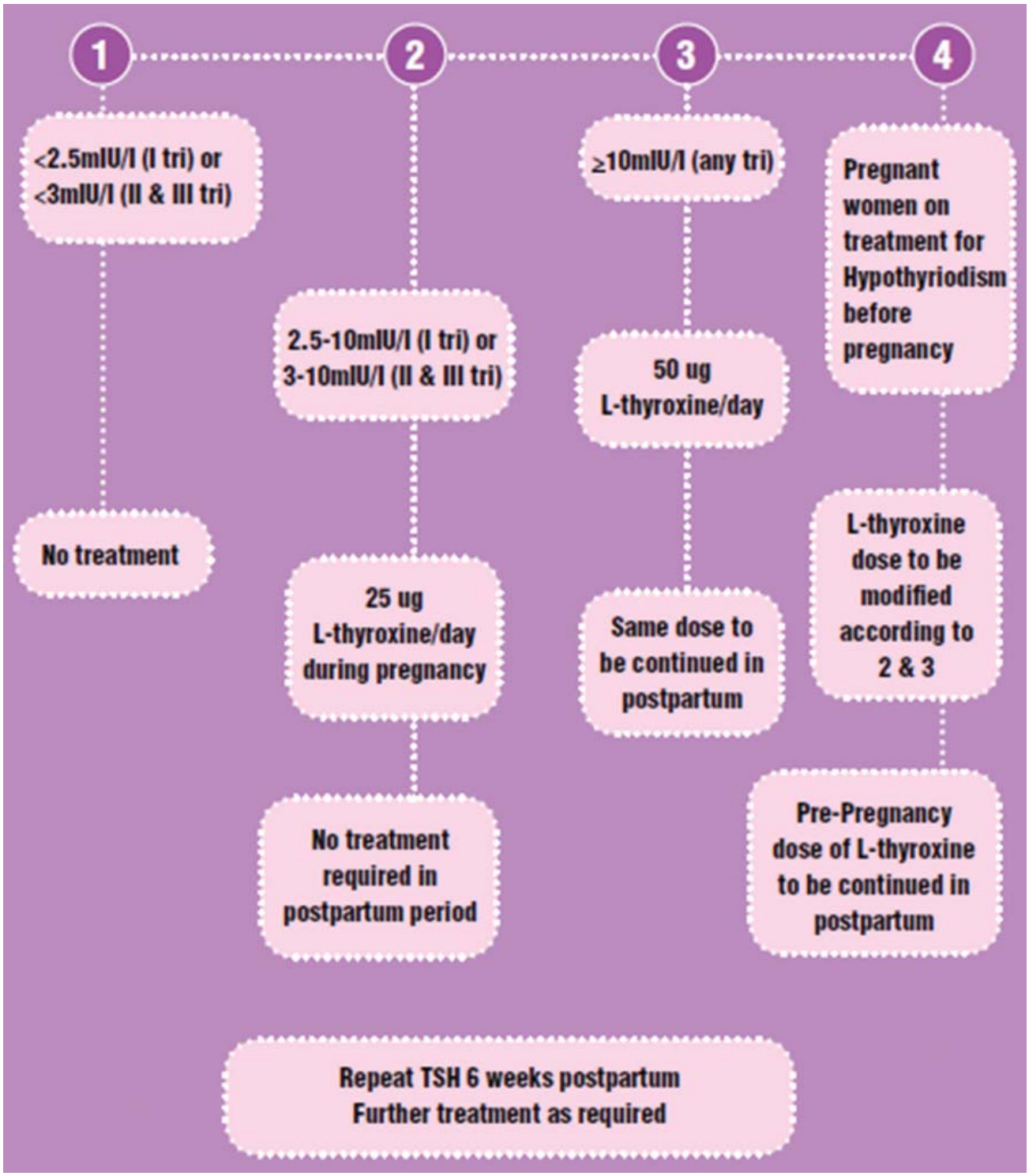
**Table 1:** Dose of thyroxine should be adjusted depending upon TSH levels[2]

| TSH level 1st trimester 2nd/ 3rd trimester | | Current dose | Increase to |
|---|---|---|---|
| >2.5 | > 3 | 25 | 50 |
| >2.5 | > 3 | 50 | 75 |
| >2.5 | > 3 | 75 | 100 |
| >2.5 | > 3 | 100 | 125 |
| >2.5 | > 3 | | |

**Table 2:** At all times, TSH <0.1 should be avoided by decreasing the dose[2]

| TSH level | Current dose | Change to |
|---|---|---|
| < 0.1 | 25 | 12.5 |
| < 0.1 | 50 | 25 |
| < 0.1 | 75 | 50 |
| < 0.1 | 100 | 75 |

**Flow Chart – Treatment of Hypothyroidism in Pregnancy[2]**




## References


1. National Iodine Deficiency Disorders Control Programme. Directorate General of Health Services, Ministry of Health & Family Welfare Government of India. https://dghs.gov.in/content/1348_3_NationalIodineDeficiency.aspx
2. National guidelines for Screening and treatment of Hypothyroidism during Pregnancy Maternal Health Division Ministry of Health & Family Welfare Government of India. December 2014 http://nhm.gov.in/images/pdf/programmes/maternal-health/guidelines/National_Guidelines_for_Screening_of_Hypothyroidism_during_Pregnancy.pdf

# Prevention and Control of Hemoglobinopathies in India Thalassemias, Sickle Cell Disease and Other Variant Haemoglobins

**Natasha Gupta**
Assistant Professor; Department of Obs Gynae, Guru Teg Bahadur Hospital

Hemoglobinopathies are the commonest genetic disorders worldwide and include Thalassemias and abnormal variants such as Hemoglobin S, D, E etc. In India, prevalence of ß Thalassemia carriersis estimated at 3-4% while that of HbSranges from 5- 48% (tribal communities). HbE is common in the North Eastern states, HbD is present in about 2% of people in Punjab.

Severity of these autosomal recessive disorders manifest in children born to "healthy" carrier couples, this makes prevention and "carrier" detection an important public health intervention.

**Prevention and Control of Hemoglobinopathies in India** was launched in 2016 by the National Health Mission with the **mission** to improve care of all Thalassemia and Sickle Cell Disease patients for their better futureand to lower the prevalence of hemoglobinopathies through screening and awareness strategies. Hemoglobinopathies like Thalassemia, Sickle Cell Anaemia and other haemoglobin variants like Hb D and Hb E are included in its ambit.

## Prevention and Control Strategies

1. Carrying out awareness, education and screening programmes in the community and schools (fig 1)
2. Establishing laboratories for carrier screening for hemoglobinopathiesand newborn screening for sickle cell disease at the district level (fig 2, 3)
3. Screening pregnant women and their husbands to prevent the birth of children affected with thalassemia major or sickle cell disease
4. Screening of newborns, young children, and adolescents for prevention and detection of hemoglobinopathies for early intervention and management is undertaken under Rashtriya Bal Suraksha Karyakram through coordination between District Early Intervention Centres (DEICs) and the Mobile Health Teams at Anganwadi Centres (AWCs) and schools from district to block level.

   **Intervention:** Screening ofall class VIII students ofgovernment and aided schoolsand non school going at AWCs backed with continued IEC for Class IX to XII students
5. Establishing Prenatal diagnostic centers in Medical Colleges in the States where required.
6. Management of patients with Thalassemia and Sickle Cell disease
7. IEC strategies and modules
8. Reporting and monitoring
9. Training
10. Human resource management and budget allocation

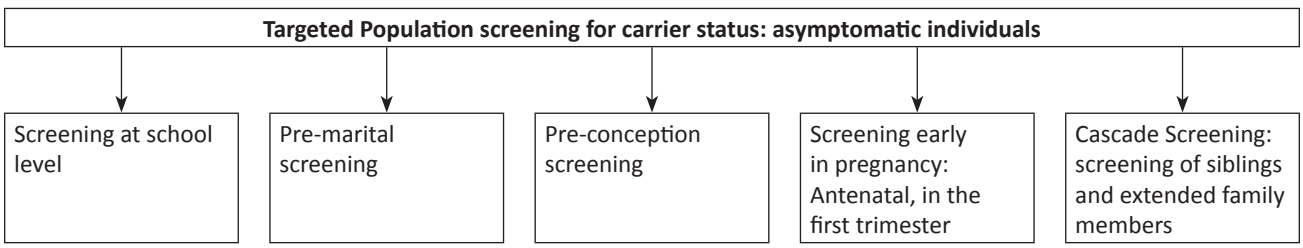



**Fig 1:**

| NESTROFT Test (Naked Eye Single Tube Red cell Osmotic Fragility Test) | DCIP test (Di-Chlorophenol-IndoPhenol) | Solubility Test |
|---|---|---|
| For Beta thalassemia trait<br>Sensitivity of 91-100% specificity of 85.47%<br>PPV 66%, NPV 97- 100% | For detection of hemoglobin E carriers, especially in eastern states like Assam and Bengal.<br>sensitivity 100%<br>specificity 98.7%<br>PPV 98.6% , NPV 100% | For Hb S, it is rapid (5 min), reliable with minimal observer variation.<br>Sensitivity 100% Specificity 91.66%<br>PPV 80% NPV 100% |

**Fig 2: Screening tests for"carriers" of hemoglobinopathies** (with Hemoglobin estimation)

| |
|---|
| **Initial screening** |
| 1. NESTROFT, Solubility test, DCIP test, Hemoglobin estimation |
| 2. Complete blood counts (CBC) *(Samples positive for tube tests in field are also subjected to CBC in lab)* |
| Based on RBC indices,Serum Iron and Ferritin studies to be done where required |
| **Diagnostic test** |
| High performance liquid chromatography (fig 3) |
| **Confirmatory test** |
| DNA Based tests |
| Reverse Dot Blot hybridization, ARMS, Gap PCR, DNA Sequencing -for unknown mutations |
| *(Specially to be used where HPLC is non contributory and for all prenatal diagnostic testing)* |

**Fig 3:** Screening protocols for Hemoglobinopathies in community settings and Public health facilities

| Tests | Findings in disease states | Normal values |
|---|---|---|
| Complete Blood Counts (CBC) | Severe anemia with microcytic hypochromic red cell indices (Hb<g/dl; MCV:50-70fi; MCH: 12-20pg;) | Hb: 12-17 gm/dl<br>MCV: 80-100 fi<br>MCH: 27-32 pg |
| Peripheral Blood Smears | RBCs showing anisopoikilocytosis (tear drop cells, target cells), microcytosis hypochromia, and nucleated red cells markedly increased in relation to degree of anemia | Normocytic Normochromic |
| Hemoglobin HPLC | HPLC pattern in β-thalassemia | |
| | HbA: 0-30%<br>HbF: 70-100%<br>HbA2: 2-5% | HbA: 96-98%<br>HbF: <2%<br>HbA2: 2.2-3.3% |
| | HPLC pattern in Sickle cell syndromes | |
| | HbA: 0-30%<br>HbS: >50%<br>HbF: <50%<br>HbA2: <3.6% (Only given here as typical finding of homozygous Hb SS. Details and differentiation in DEIC lab manual | |

**Fig 4:** Diagnostic criteria: Beta thalassemia Major & Intermedia and Sickle cell disease

| Genotype | HbA2 | HbF | Variant Hb | MCV and MCH |
|---|---|---|---|---|
| Normal | 2.3-3.5 | <2.0 | | 80-100fi and 27-32pg |
| βTT* | 4.0-8.0 | 0.5-4.0% | | Reduced |
| Hb Lepore Trait | <2% | | 5-15% | Reduced |
| β Thalassemia Trait | <3.0% | 5-20% | - | Reduced |
| HPFH Trait | Normal | 15-30% | - | Normal |
| Hb S Trait | 3-4% | | 35-40% | Normal |
| Hb D Trait | Normal | | 40-45% | Normal |
| Hb E Trait | Normal | | 25-30% | Normal |

**Fig 5:** Diagnostic criteria for Trait

| | |
|---|---|
| **Step 1** | Micro-planning for antenatal screening and referral for prenatal diagnosis. Screening of all pregnant women on first visit (1st trimester) to CHC/ PHC by tube tests (NESTROFT, DCIP test, Solubility test) along with routine Hb, Urine test for protein, Blood Group, HIV and Blood sugar. |
| **Step 2** | If Screening test positive, refer the patient along with husband by 104 / 108 service to District Hospital/ DEIC for further testing |
| **Step 3** | The pregnant woman to be admitted at District Women Hospital under JSSK for conduction of CBC and Hemoglobin HPLC test of both wife and husband |
| **Step 4** | If wife and husband both are detected to be hemoglobinopathy carriers on Hb- HPLC testing, an Ultrasound test (USG) of the wife (the pregnant woman) to be done to determine the oestational ace of the fetus and provision of counseling the couple |
| **Step 5** | One of the following steps to be followed depending on gestational age-<br>a. If gestational age 12 weeks or less, couple to be referred to nearest tertiary centre for prenatal diagnosis by CATS through coordination with the DH/DEIC<br>b. If gestational age >12 weeks but < 20 weeks, consultation for possible PND by amniocentesis at the tertiary centre<br>c. If gestational age > 20 weeks, counseling for possible outcomes of pregnancy and follow up of pregnancy. If the baby born is an affected child determined by DNA based tests, then after family counselling, early intervention by registration in DH/DEIC for management and care is required. |

**Universal antenatal screening and prenatal diagnosis of**

Under this provision all pregnant women attending public healthcare facilities at all the levels are to be screened for carrier status as per screening guidelines and are to be followed up with prenatal diagnosis where required.

## Screening for Beta Thalassemia

**Prenatal diagnosis-preventing the birth of an affected child of "at risk couple"**

Hospitals with facility for obstetrical care, NICU and a genetic lab can serve as centres for prenatal diagnosis

**Pre-requisites of prenatal sampling include:**

- Thalassemia carrier status of the couple under investigation
- Blood group of the mother to prevent Rh incompatibility, if present
- Pre test counseling, written informed consent of couple

***Fetal sampling methods available for prenatal diagnosis ( USG guided )***

1. **CVS-** between 10-12 weeks of gestation. (trans-abdominal route or trans-cervical
2. **Amniocentesis** - after 16 weeks of gestation or if fetal position prevents CVS
3. **Fetal blood sampling - (Cordocentesis):** at 18-20 weeks of gestation. sampling is done by cardiac puncture or from the hepatic vein

Fetal blood analysis by Complete Blood, Hb fraction analysis by cation-exchange, HPLC and DNA based tests identify the defect at the gene level and provide final confirmation of the defect

**Choices available to an 'at risk' couple:**

- Termination of the affected child
- Not to have children
- To adopt children
- To proceed to in-vitro fertilization (e.g. PGD)

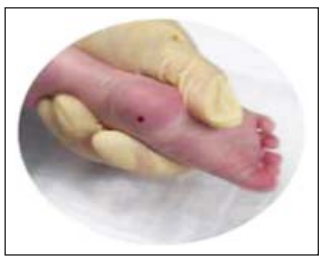
## Diagnosis of Hemoglobinopathies at Birth (fig. 5)

4 good quality dried blood spot card should be taken and *dispatched to the laboratory within 24 hours of collection*

**Techniques used for analysis of newborn samples:**

3 techniques for Newborn dried blood spot sample as primary screen.

- High performance liquid chromatography (HPLC)
- Isoelectric focusing (IEF)
- Capillary Electrophoresis (CE)



## References

1. Prevention and control of hemoglobinopathies in india, Thalassemia, sickle cell disease and other haemoglobin varients: NHM guidelines 2016

# National AIDS Control Programme

**Astha Srivastava, A G Radhika**
Assistant Professor; Department of Obs Gynae, Guru Teg Bahadur Hospital

The Government of India established the National AIDS Committee in 1986, which set the foundation for the establishment of National AIDS Control Organization (NACO) in 1992 to oversee the policies for prevention and control of the infection.

The first phase of the National AIDS Control Programme (NACP) started in 1992 and lasted until 1999. This was followed by NACP-II (2000-2005), NACP-III (2006-2011) and NACP-IV (2012-2017).

**Component 1:** Intensifying and Consolidating Prevention services with a focus on HRG and vulnerable populations

**Component 2:** Expanding IEC services for (a) general population and (b) high risk groups with a focus on behavior change and demand generation

**Component 3:** Comprehensive Care, Support and Treatment

**Component 4:** Strengthening institutional capacities

**Component 5:** Strategic Information Management Systems (SIMS)

Since **prevention** is an important aspect of the programme, special focus is placed on the following

i. Awareness-raising
ii. Management STI /RTI
iii. Integrated Counselling and Testing Centre (ICTC)
iv. Prevention of Parent to Child Transmission of HIV/AIDS (PPTCT)
v. Post Exposure Prophylaxis (PEP)
vi. Condom Promotion Programme
vii. Access to Safe blood

## PPTCT Services under NACP IV

Transmission of HIV/AIDS (PPTCT) programme was launched in the country in the year 2002.

With effect from 1st January 2014, pregnant women who are found to be HIV positive are initiated on lifelong ART irrespective of CD4 count and WHO clinical Staging.

All pregnant women living with HIV receive a "single-pill" triple-drug ART regimen ie **Tenofovir Disoproxil Fumarate (TDF) + Lamivudine (3TC) + Efavirenz (EFV)** regardless of CD4 count or clinical stage, both for their own health and to prevent vertical HIV transmission and for additional HIV prevention benefits. All pregnant women are **tested for Syphilis and are also referred to DOTS centre rule out HIV-TB coinfection** under the new strategy.

**HIV Exposed Infant WED**

- Exclusive breastfeeds up to 6 months (preferred Option-I WHO/NACO Guidelines 2010-11) and continued breastfeeds in addition to complementary feeds after 6 months up to 1 year for EID negative babies and up to 2 years for EID positive babies who receive Paediatric ART.
- Postpartum ARV prophylaxis for infant for minimum 6 weeks.
- Early infant diagnosis (EID) at 6 weeks of age; repeat testing at 6 months, 12 months & 6 weeks after cessation of breastfeeds.
- Co-trimoxazole prophylaxis from 6 weeks of age.
- HIV care and Pediatric ART for infants and children diagnosed as HIV positive through Hi.
- Growth and nutrition monitoring.
- Immunizations and routine infant care.
- Gradual weaning after 6 months and introduction of complementary feeds from 6 months onwards along with continuation of BF for at least 1 year for adequate growth & development of the child.
- Confirmation of HIV status of all babies at 18 months using all 3 Antibody (Rapid) Test.

## Goal and Objectives of PPTCT Services in India

**Goal:** To work towards elimination of pediatric HIV and improve maternal, newborn and child health and survival in the context of HIV infection

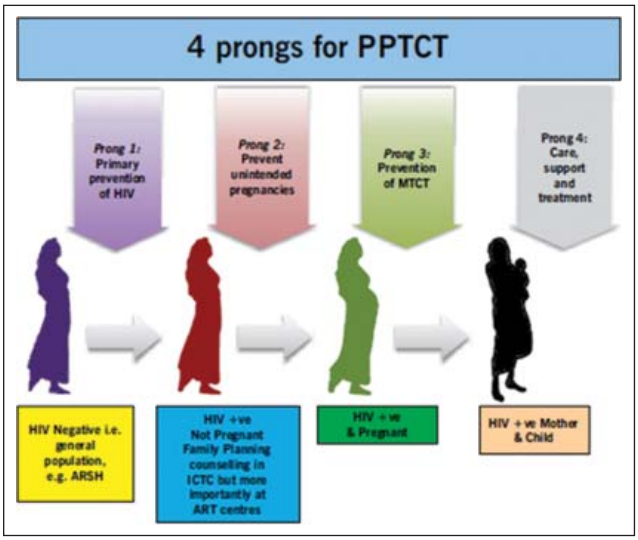
**Objectives:**

1. To detect more than 90 % HIV infected pregnant women in India
2. To provide access to comprehensive PPTCT services to more than 90 % of the detected pregnant women
3. To provide access to early infant diagnosis to more than 90 % HIV exposed infants
4. To ensure access to anti-retroviral drug (ARVs)

prophylaxis or Anti-Retroviral Therapy (ART) to 100 % HIV exposed infants

5. To ensure more than 95 % adherence with ART in HIV infected pregnant women and ARV/ ART in exposed children

The PPTCT services provide access to all pregnant women for HIV diagnostic, prevention, care and treatment services.




## The Essential Package of Services under the PPTCT Programme

1. Routine offer of HIV counselling (Group/ Individual counselling) and testing to all pregnant womenattending ante-natal care, with 'opt out' option.
2. Ensure involvement of spouse & other family members and move from an "ANC centric" to a"Family centric" approach.
3. Provide ART to all HIV infected pregnant women regardless of WHO staging and CD4 countresults. Preferred regimen is TDF+3TC+ EFV.
4. Promote institutional delivery for all HIV infected pregnant women (ANMs/ ASHAs, Communityworkers to accompany to institutions; reduction of stigma and discrimination amongst healthcare providers through sensitisation and capacity building).
5. Provision of care for associated conditions (STI/ RTI, TB & other Opportunistic Infections (OIs).
6. Provide nutrition counselling and psychosocial support for HIV infected pregnant women- Linkages with ANM, ASHAs, Community outreach workers, DLNs to advise them on the rightfoods to take and to go to Anganwadi Centres for nutritional support and to the district levelnetwork of Positive People for peer counselling and psycho-social support.
7. Provide counselling and support for initiation of exclusive breastfeeds within an hour of deliveryas the preferred Option and continue for 6 months. After 6 months, complementary feedingshould be given along with breastfeeds. A small number of babies born to HIV infected motherswho have serious illness or have died and a few reluctant mothers (who at their own risk despitecounselling) may decide not to breastfeed but adopt exclusive replacement feeding (ERF).
8. Provide antiretroviral prophylaxis to infants from birth up to a minimum period of 6 weeks.
9. Integrate follow-up of HIV-exposed infants (HEIs) into routine healthcare services includingimmunization.
10. Ensure initiation of Co-trimoxazole Prophylactic Therapy (CPT) and Early Infant Diagnosis (EID) using HIV DNA PCR at 6 weeks of age onwards as per the EID guidelines.
11. Strengthen follow-up and outreach through ANMs, ASHAs and District level networks and otheroutreach workers to support HIV infected pregnant women and their family.

## Management of STI/RTI: Integrated Counselling and Testing

At theIntegrated Counselling and Testing Centre (ICTC) the client is counselled and tested for HIV, on his/her own free will or as advised by a medical provider.

This approach classifies STIs/RTIs intosyndromesand provides treatment for themost common organisms causing the syndrome (Syndromic Case Management, SCM). The SCM achieves high cure rates because it provides immediatetreatment on the first visit and at little or no laboratory cost.

The following seven pre-packed STI/RTI kits are available for syndromicmanagement of STIs/RTIs. These kits are developedbased on the National Guidelines on Prevention, Management and Control of Reproductive TractInfections including Sexually Transmitted Infections, Ministry of Health and Family Welfare, August 2007.

| Kit No. | Syndrome | Colour | Drugs |
|---|---|---|---|
| Kit 1 | Urethral discharge, Ano rectal discharge, Cervicitis | Grey | Tab. Azithromycin 1 g (1) and Tab. Cefixime 400 mg (1) |
| Kit 2 | Vaginitis | Green | Tab. Secnidazole 2 g (1) and Tab. Fluconazole 150 mg (1) |
| Kit 3 | Genital Ulcer Disease | White | Inj. Benzathine penicillin 2.4 MU (1) and Tab. Azithromycin 1 g (1) and Disposable syringe 10 ml with 21 gauge needle (1) and Sterile water 10 ml(1) |
| Kit 4 | Genital Ulcer Disease | Blue | Tab. Doxycycline 100 mg (30) and Tab. Azithromycin 1 g (1) |
| Kit 5 | Genital Ulcer Disease | Red | Tab. Acyclovir 400 mg (21) |
| Kit 6 | Lower Abdominal Pain | Yellow | Tab. Cefixime 400 mg (1) and tab. Metronidazole 400 mg (28) and Cap. Doxycycline 100 mg (28) |
| Kit 7 | Inguinal bubo | Black | Tab. Doxycycline 100mg (42) and Tab. Azithromycin 1 g (1) |

*NACO Operational Guidelines for Strengthening STI/RTI Services 2007*

The Union Ministry of Health and Family Welfare launched the National Strategic Plan 2017-24 aimed at eradicating HIV/AIDS by 2030.Mission SAMPARK was also launched to trace those who are Left to Follow Up and are to be brought under Antiretroviral therapy (ART)

## Key Facts

The National Strategic Plan 2017-24 will pave a roadmap not only for achieving the target of **90:90:90 Strategy** but also strive along with partners towards fast-track strategy of ending the AIDS epidemic by 2030. Mission SAMPARK will further aid to will help in fast-tracking the identification of all who were HIV positive and subsequently linking to ART programme.

## 90:90:90 Strategy

From:https://www.avert.org/infographics/unaids-90-90-90-target


## References

1. National AIDS control programme,strategy document, Department of AIDS control, MOHFW – GOI 2012 – 2017 http://naco.gov.in/sites/default/files/National_Guidelines_for_PPTCT_0.pdf

# National Tuberculosis Elimination Program (NTEP)

**Kusum Dogra[1], A G Radhika[2]**
[1]Assistant Professor, [2]Senior Consultant, UCMS & GTB Hospital, Delhi

Revised National Tuberculosis Control Program (RNTCP) was launched in 1997. It wasrenamed as **National Tuberculosis Elimination Program (NTEP)** in 2019.

**The National Strategic Plan (NSP) 2** for TB elimination 2017 -2025 in India has been devised with a vision and goal

**Vision:** TB-Free India with zero deaths, disease and poverty due to tuberculosis

**Goal:** To achieve a rapid decline in burden of TB, morbidity and mortality while working towards **elimination of TB in India by 2025**.It is driven by the **DETECT-TREAT-PREVENT-BUILD** approach.

**Key Services** are

1. Free diagnosis and treatment for TB patient
2. Provision of rapid diagnostics
3. Testing of all TB patients for drug resistance and HIV
4. Management of associated diseases
5. Prompt treatment with the right drugs and regimens along with suitable patient support systems including financial ( through direct benefit transfer) and nutrition support.
6. This is supplemented by prevention strategies including active case finding, contact tracing and airborne infection control.
7. Treatment adherence support
8. At present TB drugs are free at government centres. The NSP plan is that eventually TB drugs will be available free from private centre pharmacies as well.

## Newer Initiative of NTEP

- Introduction of CB-NAAT (Cartridge Based Nucleic Acid Amplification tests such as GeneXpert and TruNat) for diagnosis of TB
- Intensified TB case finding by door to door visit in communities or vulnerable populations. Suitable incentive for private doctors and patients on successful completion of treatment in hilly/tribal area.
- Screen all TB patients for **rifampicin resistance and provide additional drugs**.
- **Important Treatment strategies**
  - Patients are classified based on drug susceptibility results; the categories are drug-sensitive, and mono, poly, multi and extensively drug resistant.
  - The thrice weekly intermittent TB regimen(used since programme inception) has now been **switched to daily Fixed Dose Combination regimen for treatment of all TB patients.**
  - **Directly Observed Drug Treatment (DOT) to continue**
  - **Case Definitions are classified as**
    i. Microbiologically confirmed TB
    ii. Clinically diagnosed TB
    iii. According to anatomical site of disease, history of previous treatment, drug resistance
  - For drug sensitive TB, administer daily fixed dose combinations of first-line anti-TB drugs in appropriate weight bands (5 weight bands for adults and 6 weight bands for pediatrics) for all forms of TB and in all ages, including four drug FDC in the intensive phase and three drug FDCs in the continuation phaseie2HRZE/4HRE.
    **i. Intensive phase** (IP) consists of 8 weeks-Isoniazid (H), rifampicin (R), pyrazinamide (Z) and ethambutol (E) given under direct observation in daily dosages as per weight band categories
    **ii. Continuation phase** (CP) consists of 16 weeks of isoniazid, rifampicin and ethambutol in daily dosages. The CP may be extended by 12-24 weeks in certain forms of TB like CNS TB, Skeletal TB, Disseminated TB etc.

**This injection free treatment is followed for new and previously treated cases (H & R sensitive/unknown)**

- **All Rifampicin Resistant (RR) /Multi Drug Resistant TB patients** are subjected to baseline Kanamycin and Levofloxacin drug sensitivity testing. Extended Drug Sensitivity Testingis being introduced to all second line drugs in a phased manner.
- **RR/MDR-TB patients without additional drug resistance** are treated with standard shorter course treatment regimen for MDR TB. And

in those with mixed patterns of resistance, standard MDR TB regimens were modified as per revised guidelines.

a. **Management of INH Mono and Poly drug resistance**: INH mono-poly resistance is known to be around thrice as prevalent as RR-TB. A specific 9-12 month treatment regimen has been initiated to manage H mono-poly resistance with available first line drugs strengthened with a fluoroquinolone and a second line injectable.

b. **Shorter MDR-TB regimen:** The shorter MDR-TB regimen will be scaled up for all RR-TB patients that meet criteria for this regimen.

c. **Regimens containing newer drugs**: In 2016, RNTCP introduced **Bedaquiline** for management of Rifampicin Resistant -TB patients with additional resistance to fluoroquinolones and/or second line injectables. RNTCP also introduced another new drug **Delamanid**to evaluate the use of these newer drugs in combination therapy to reduce the duration of DR TB regimens to 4-6 months.

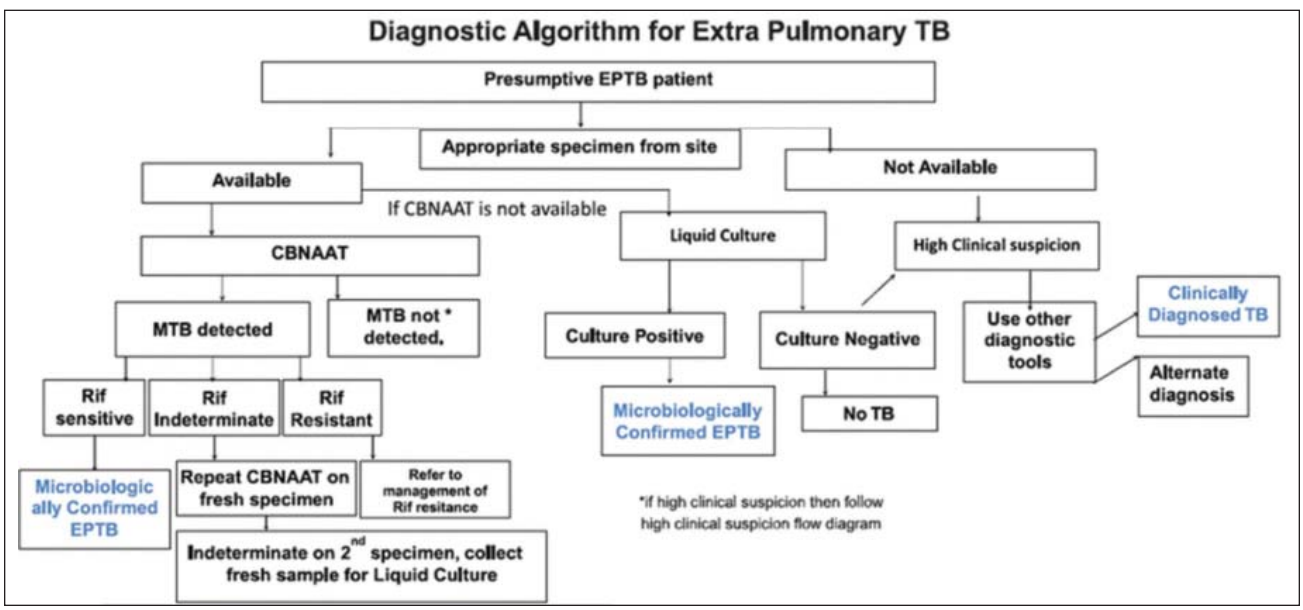
d. **Drug sensitivity Testing Guided DR-TB Regimen:** Extensive Drug Resistance (XDR) TB patients with or without resistance to any other first or second line drugs, who do not consent or are not eligible for newer drugs will be managed by an appropriate regimen designed based on their DST results.

e. **Non-tuberculous Mycobacteria (NTM) treatment:** NTM are environmental opportunistic microorganisms that can cause human disease with signs and symptoms similar to MTB, can affect the lungs or any other extra-pulmonary site. RNTCP will initiate NTM diagnosis (via smear microscopy, rapid molecular tests, conventional culture and species identification) and the treatment depending on the species of NTM identified

- **NIKSHAY** is a case based, web based TB notification system to support TB notification &strengthen TB surveliance. Non declaration of TB is now punishable offence under IPC 269, 270 in which there is imprisonment from 6months to 2 years
- After completion of the treatment, **followup of patients** should be done on 6,12,18 and 24 months by clinical and sputum examination.
- **NikshayPoshanYojna (NPY**) in which patient gets Rs 500 /-month for nutritional support throughout the duration of treatment of TB
- Introduction of **RT-MERM (Real Time Medication Event Reminder-Monitor)** device which provide programmable visual and audible reminders of daily dosing and of monthly refill for compliance.

## References

1. National Strategic Plan for Tuberculosis 2017-2025. Elimination by 2025; RNTCP https://tbcindia.gov.in/WriteReadData/National%20Strategic%20Plan%202017-25.pdf accessed on 5th Feb 2021



# Pradhan Mantri Swasthya Suraksha Yojana(PMSSY)

**Shilpa Singh**
Assistant Professor, Department of Obs & Gynae, UCMS & GTBH, Delhi

Pradhan Mantri Swasthya Suraksha Yojana[1] (PMSSY) was announced in 2003 with theobjective of correcting regional imbalance in availability of affordable/reliable tertiary healthcare services and to augment facility for quality medical education in India.

PMSSY has two components-

1. Setting up AIIMS like institution
2. Upgradation of government medical college (GMC)/institution

## Detailed Objectives

1. Each new AIIMS to add
   - State of art modular OT and diagnostic facility
   - 15-20 superspeciality department
   - 750beds
   - 100 UG(MBBS) seats
   - 60 BSc(Nursing) seats
   - Focus on PG education and research
2. Each upgradation of GMC/Institution will add
   - 8-10 superspeciality department
   - 150-250 beds
   - Around 15 new PG seats

### Implementation Guidelines

| 1. Setting up AIIMS like institution | 2. Upgradation of Medical colleges |
|---|---|
| • Site selection to be done by challenge method<br>• Medical equipment procurement<br>• Standard staffing pattern<br>• Phased operalisation | • Selection of medical colleges for upgradation<br>• Nomination of mentor institute<br>• Gap analysis committee constitution to decide requirement |

## Achievements in Last 5 Years

A.

1. Six functional AIIMS under phase I

   In six functional AIIMS (AIIMS-Patna, AIIMS-Rishikesh, AIIMS-Jodhpur, AIIMS-Bhopal, AIIMS-Bhubaneshwar and AIIMS-Raipur) the derailed construction work is put back on track and expedited:
   - 3613 hospital beds added
   - Daily OPD patients increased to 7 times(from1700 to more than 12000)
   - Basket of services expanded and presently on an average 2600 major surgeries/month
   - 750PG seats added
2. New AIIMS under phase II, IV, V, VI, VII

   14 new AIIMS sanctioned since May 2014 taking tally of AIIMS to 22
   - OPD began in AIIMS Raebareilli, Mangalagiri, Gorakhpur in year 2018-19
   - MBBS courses started at AIIMS-Mangalagiri and Nagpur from 2018-19 session

**Status of 22 AIIMS**

| Fully functional AIIMS (6) | AIIMS where MBBS classes, partial IPD and OPD Started (6) | AIIMS where only MBBS classes (2) | Activities in progress (8) |
|---|---|---|---|
| Bhopal<br>Bhubaneswar<br>Jodhpur<br>Raipur<br>Rishikesh | Raebareilly*#<br>Gorakhpur*#<br>Magalagiri*<br>Nagpur*<br>Bathinda*<br>Bibinagar | Kalyani*<br>Deoghar* | Bilaspur*<br>Guwahati*<br>Rajkot<br>Samba (Jammu)<br>Awantipor (Kashmir)<br>Manethi**<br>Madurai<br>Darbhanga (Bihar) |

*Construction for main building in progress/started
**Alternative site being selected
#IPD for COVID-19 treated started shortly

B. Upgradation of existing GMC
   - Construction of trauma centres in 23 out of 58 approved projects(excluding 8 done before 2014)
   - 17 new projects approved for upgradation under phase IV and V(civil work in 13 of these)
   - More than 4000 superspeciality beds added in GMC upgradation project.

The completion timeline of all 75 GMC up-gradation projects is given below:

| Year | No. of GMC up-gradation projects |
|---|---|
| Completed by March 2018 | 15 |
| Completed in 2018-19 | 16 |
| To be completed in 2019-20 | 17 (12 already completed) |
| To be completed in 2020-21 | 23 |
| To be completed in 2021-22 | 4 (Delhi, Surat, Cuttack, Patna) |
| Total | 75 |

## References

1. Ministry of Health & Family Welfare. Pradhan Mantri Swasthya Suraksha Yojana (PMSSY). Available from: http://pmssy-mohfw.nic.in/. Accessed on 25th December 2020.

# LaQshya Programme

**Seema Prakash[1], Sanjeeta Behera[2]**
[1]Senior Specialist, [2]Senior Medical Officer, UCMS & GTB Hospital, Delhi

## National Labour Room Quality Improvement Initiative

The institutional births in India have doubled from 38.7% to 78.9% in the decade 2015-16 (NFHS-4) but the commensurate reduction in maternal and newborn mortality and stillbirths has not taken place. One of the major factors being inadequacies in the quality of care provided in health facilities.

Hence, an initiative by the National Health Mission, Ministry of Health & Family welfare, Government of India started on 11th December 2017. LaQshya program is expected to benefit every pregnant woman and newborn delivering in public health institution. The concept of Care Around birth (CAB) in Labour room and Maternity Operation Theatres and Respectful Maternity Care (RMC) have been emphasized.

It aims to adopt a holistic and comprehensive approach at all levels of care to improve and strengthen Quality of Care (QoC) during intrapartum and immediate post partum period.

## Sustainable Development Goals of LaQshya

**Targets by 2030**

- Reduce the global maternal mortality ratio to less than 70 per 100,000 live births
- Reduce neonatal mortality to at least as low as 12 per 1,000 live births
- To reduce under-5 mortalityto at least as low as 25 per 1,000 live births.

**Objectives**

1. To reduce Maternal and newborn morbidity and mortality due to APH, PPH, Retained placenta, Preterm labour, Pre-Eclampsia, Eclampsia, Obstructed labour, Puerperal sepsis, newborn asphyxia and Sepsis.
2. Improve Quality Of Care(QOC) during delivery and immediate post-partum periodat all Government Medical College hospitals, all District Hospitals & equivalent healthy facilities, all designated FRUs and high case load CHCs with over 100 deliveries/60 (per month) in hills and desert areas.
3. Management of complications and to ensure timely referrals and having an effective follow-up system.
4. To provide Respectful Maternity Care (RMC) to all pregnant women attending the Healthfacility and enhance satisfaction of beneficiary.

## Key Features

o LaQshya program envisagesto improve quality of care in labour room and maternity OT.

o Under the initiative, multi-pronged strategy has been adopted such as improving Infrastructure upgradation, ensuring availability of essential equipment, providing adequate Human Resources, capacity building of health care workers and improving quality processes in labour room.

o Implementation of 'fast-track' interventions (NQAS assessment, Trainings, Mentoring, Reviews etc.)

o Capacity-building of healthcare workers by skill-based training like Dakshta& improving quality processes in the labour room.

o To strengthen critical care in Obstetrics, dedicated Obstetric ICUs at Medical College Hospital level and Obstetric HDUs at District Hospital are operationalized under LaQshya program.

**LaQshya includes harmonizing efforts** to bring together all existing efforts

- Coalesces Quality Assurance (QA) & Quality Improvement (QI)
- Coordinated efforts – National Health Mission, State Health Departments and Medicalcolleges
- DAKSHATA (National Quality Assurance Standards)
- DAKSH (Skill Lab Training)
- CAB (Care Around Birth ) Learning from USAID-ASSIST

## Institutional Arrangements Under National Quality Assurance Programme (NQAP) & LaQshya

Under the National Health Mission, the States have been supported in creating Institutional framework for the Quality Assurance – State Quality Assurance Committee (SQAC), District Quality Assurance Committee (DQAC), Quality Team at the facility level and Central Quality Supervisory Committee at National level (CQSC). These committees will also support implementation of LaQshya interventions.

The initiative prioritizes local problem solving thereby ensuring ownership and accountability of facility level through formation of Quality circles and quality teams at the intervention facilities. QI methodologies (Plan-Do-Check-Act PDCA cycle) will be used to drive and sustain change **under CAB Program (Care Around Birth) through 6 defined QI Cycles**

1. Real time Partograph generation, Usage of Safe birth and surgical safety check-list and strengthening documentation practices for generating robust data for driving improvement.
2. Presence of birth companion during delivery, Respectful Maternal Care (RMC) andenhancement of patients' satisfaction.
3. Assessment, Triage and timely management of complications including strengthening referral protocols.
4. Management of Labour as per protocols including Active Management of Third Stage of Labour (AMTSL) & rationale use of Oxytocin.
5. Essential and Emergency Care of newborn and Pre-term babies including management of Birth asphyxia, timely initiation of Breast feeding as well as Kangaroo Mother Care (KMC) for pre-term newborn.
6. Infection prevention including Bio-medical waste management.

## Targets

***Following facilities are being taken under LaQshya initiative on priority:***

- o All Government Medical College hospitals.
- o All District Hospitals & equivalent healthy facilities.
- o All designated FRUs and high case load CHCs with over 100 deliveries/60 (per month) in hills and desert areas.

**LaQshya Interventions:** To be undertaken in a phased manner

**Structural Improvement**

- Upgrading the infrastructure as per norm & realistic case-load.
- Human Resource augmentation and skill upgradation.
- Ensuring availability of adequate functional & calibrated equipment, as per need.
- Strengthening the supply chain system of drugs & consumables for ensuring their availability in the labour room and OT as per need.

**Process Improvement**

- Assessment and Triage
- Management of Labour including Active Management of Third stage of labour.
- Management of complications and High-Risk Pregnancies.
- Management of referral services.
- Perioperative processes for C-Section.
- Newborn care and resuscitation.
- Management of required support services for the Labour room, Maternity OT & HDU.
- Sensitization of the Staff on RMC and its monitoring.

## Certification, Incentives & Branding

**Quality Certification**

- The external assessment and certification by external assessors empanelled with NHSRC.
- Certification valid for 3 years subject to annual verification of the scores by the State Quality Assurance Committee.

## Incentives

- Government Medical Colleges &Hospitals- Rs. 6 Lakhs
- District Hospitals & equivalent health facilities- Rs. 3 lakhs
- All designated FRUs(First Referral Units) and high case load CHCs(community Health Centres) with over 100 deliveries/ 60 (per month) in hills and desert areas- Rs.2 Lakhs.

**Incentives given on achievement of following criteria**

- Quality Certification of Labour Room and/or OT
- 75% achievement of facility level targets
- At least 80% satisfaction of beneficiaries.

## Branding

The departments may be provided badges (LaQshya Medal) based on the quality score, achieved in the state level assessment.

**Platinum Badge**: Achieving more than 90% core.

**Gold Badge**: Achieving More than 80% Score.

**Silver Badge**: Achieving more than 70% Score.

1. **Digital Innovation**
   - LaQshya Web portal- All LaQshya related data to be uploaded on the portal for prompt report generation as well as visualization of dashboard to monitor progress in key maternal new born indicators at various levels (facility, District, State & National)
   - Safe delivery App- Job aid as well as training tool for health workers.

## References

1. LaQshya, Labour Room Quality Improvement Initiative, NHM, Ministry of Health & Family welfare 2017. Available at https://nhm.gov.in/New_Updates_2018/NHM_Components/RMNCH_MH_Guidelines/LaQshya-Guidelines.pdf

# Mothers Absolute Affection Programme (MAA) for Infant and Young Child Feeding

**Bhanupriya**
Associate Professor, Department of Obs & Gynae, UCMS & GTBH, Delhi

"Mother's Absolute Affection" is a nationwide programme of the Ministry of Health and Family Welfare, launched on 5th August 2016 to bring undiluted focus on promotion of breastfeeding and provision of counseling services for supporting breastfeeding through health systems. The programme has been named 'MAA' to signify the support a lactating mother requires from family members and at health facilities to breastfeed successfully.

**MAA is a country wide intensified breastfeeding promotion campaign targeting,**

- All States & Union Territories (UTs)
- Around 3.9 crore pregnant & lactating mothers
- 8.8 lakh ASHAs
- 1.5 lakhs Sub-centres
- 17,000 Birthing Facilities/Delivery Points

## Goals

The goal of the 'MAA' Programme is to revitalize efforts towards promotion, protection and support of breastfeeding practices through health systems to achieve higher breastfeeding rates.

## Objectives of the Programme to Achieve The Above Mentioned Goal are

- Build an enabling environment for breastfeeding through awareness generation activities, targeting pregnant and lactating mothers, family members and society in order to promote optimal breastfeeding practices. Breastfeeding to be positioned as an important intervention for child survival and development.
- Reinforce lactation support services at public health facilities through trained healthcare providers and through skilled community health workers.
- To incentivize and recognize those health facilities that show high rates of breastfeeding along with processes in place for lactation management.

## Components of MAA

1. Enabling Environment and demand generation through mass media, mid media and community.
2. Community level activities
   - o Orientation of ASHAs/AWWs and interpersonal communication and community dialogue through mothers' meeting conducted by ASHA.

   ASHA incentive: Rs 100 for conducting quarterly mother's meeting ie. Rs 300 for three quarters
   - o Trained ANMs at sub-centres for providing skilled care in the communities.
3. Capacity building of healthcare providers
   - o Capacity building of ANMs/nurses/doctors – at all delivery points.
   - o Role re-enforcement regarding lactation support services.
4. Awards - Recognition for best performing baby friendly facilities. Award for delivery points demonstrating breastfeeding process is the cash prize of Rs10,000/- for facility per district. Criterion for the awards includes 10 steps of baby friendly health initiative for at least 6 months.

## Key Message to be Delivered to the Mothers

1. Early initiation of breastfeeding; immediately after birth, preferably within one hour.
2. Breast-milk alone is the best food and drink for an infant for the first six months of life. No other food or drink, not even water
3. After 6 months of age, babies should be introduced to semi-solid, soft food (complementary feeding) but breastfeeding should continue for up to two years.
4. From the age of 6–8 months a child needs to eat two to three times per day and thereafter, three to four times per day starting at 9 months – in addition to breastfeeding.

5. During illness, children need additional fluids and encouragement to eat regular meals, and breastfeeding infants need to breastfeed more often. After illness, children need to be offered more food than usual, to replenish the energy and nourishment lost due to the illness.
6. Benefits of Breastfeeding to the baby and mother as below:
   - **a. Benefits for the baby**
     - **i.** Early skin-to-skin contact keeps the baby warm.
     - **ii.** It helps in early secretion of breast milk.
     - **iii.** Feeding first milk (colostrum) protects the baby from diseases.
     - **iv.** Helps mother and baby to develop a close and loving relationship.
     - **v.** Decreased risk of illness such as diarrhea, pneumonia, ear, and throat infections.
     - **vi.** Improved intelligence.
     - **vii.** Ensures development and growth.
   - **b. Benefits for the mother**
     - **i.** Helps womb to contract and the placenta is expelled easily.
     - **ii.** Reduce the risk of excessive bleeding after delivery
     - **iii.** Reduces the risk of breast cancer, uterine cancer and ovarian cancer
     - **iv.** Lessens osteoporosis
     - **v.** Benefits child spacing
     - **vi.** Promotes post-partum weight loss
     - **vii.** Financially viable

## Reference

1. http://unicef.in/AddNewPage/PreView/19
2. http://vikaspedia.in/health/health-campaigns/mothers-absolute-affection
3. http://nhm.gov.in/MAA/Operational_Guidelines.pdf

# National Family Planning

**Rashmi Gupta**
Senior Medical Officer, Incharge of Family Planning Unit, Guru Teg Bahadur Hospital, Delhi

India was the first country in the world to launch Family Planning Programme in 1952. The programme has evolved from a targeted to target free approach and has now been anointed as a critical intervention to reduce maternal and child mortality & morbidity beyond simple strategy for achieving population stabilization.

The government has drawn out comprehensive National & State roadmaps & also district action plans adopting a decentralized planning approach focusing on operationalization of facilities & delivery of services.

The RMNCH+ A strategy has provided a platform for addressing the reproductive rights while integrating the current Family Planning services with maternal, child as well as adolescent health.

Recent strategies include Institutionalization of fixed day services with aggressive focus on quality in Family Planning, revitalizing Post-Partum and Post-Abortion Family Planning services, enhanced focus on male participation and community based scheme through ASHAs, streamlining and strengthening commodity security, public private partnership etc. The government is also harnessing the expertise of various partners in the field of advocacy, capacity building, IEC and Behaviour Change Component (BCC) through a new focused communication campaign, programme management, quality improvement, evaluation & assessment, feasibility studies, development of resource material & E-learning modules, software development, social marketing, social franchising & provision of skilled human resources for successful implementation of the programme.

## Key Highlights of the Programme

A. **India's Strategy**

1. Increased focus on spacing services without disturbing the sterilization pie.
2. Voluntary adoption of Family Planning based on felt need of the community.
3. Focus on male participation.
4. Right based approach to Family Planning.
5. Expanding contraceptive choices.

B. **CONTRACEPTIVE BASKET OF CHOICE UNDER NATIONAL FAMILY PLANNING PROGRAMME**

1. Temporary Methods
   a. Condoms (Nirodh)
   b. Oral contraceptive pill
      i. COC's (Mala-N)
      ii. Centchroman (Chhaya)
      iii. Emergency Contraceptive Pills (Ezy Pill)
      iv. Progesterone only Pills-under pilot
   c. IUCD – CuT 380A, Cu T 375
   d. Injectable Medroxy Progesterone Acetate (ANTARA)
2. Permanent Methods
   a. Male sterilization (Conventional, Vasectomy/NSV)
   b. Female Sterilization (Minilap/Laparoscopy)

| States | | Acceptor | ASHA/ Health Worker | Others | Total |
|---|---|---|---|---|---|
| **11 High focus states (UP, BH, MP, RJ, CG, JH, OD, UK, AS, HR, GJ)** | VAS. | 2000 | 300 | 400 | 2700 |
| | TUB. | 1400 | 200 | 400 | 2000 |
| | TUB. (PPS) | 2200 | 300 | 500 | 3000 |
| **Mission Parivar Vikas Districts** | VAS. | 3000 | 400 | 600 | 4000 |
| | TUB. | 2000 | 300 | 500 | 2800 |
| | TUB. (PPS) | 3000 | 400 | 600 | 4000 |
| **Other High focus states (NE states, J & K, HP)** | VAS. | 1100 | 200 | 200 | 1500 |
| | TUB. | 600 | 150 | 250 | 1000 |
| **Non High focus states** | VAS. | 1100 | 200 | 200 | 1500 |
| | TUB. (BPL + SC/ ST only) | 600 | 150 | 250 | 1000 |
| | TUB. (APL) | 250 | 150 | 250 | 650 |

**C. Augmenting the demand through ASHA schemes for Family Planning:-**

i. Home delivery of contraceptive

ii. Ensuring spacing at birth.

iii. Pregnancy test kits –for early management of pregnancy.

**D. Promoting Quality Sterilization Services**

**Sterilization Compensation Scheme:-**

The compensation package has been enhanced in 2014 for 11 high focus high TFR states.

i. Higher package for Post-Partum sterilization & Male sterilization

ii. Higher package for (Mission Parivar Vikas) districts.

**Mobile Teams Dedicated Family Planning Services**

The scheme has been introduced in high focus states in 2014-2015 to provide sterilization services in areas where there is the dearth of service providers.

**Scheme for Ensuring Drop Back Services to Sterilization Clients**

It was launched in 2015 and can be availed as per demand from the beneficiaries.

**National Family Planning Indemnity Scheme**

The scheme was revised in 2013 & is now being operated by the state governments directly with NHM funding.

1. The clients are indemnified in the unlikely events of death, complications and failures following sterilization.
2. The providers/accredited intuitions are indemnified against ltiigations.

**E. Promoting Quality IUCD Services**

i. Interval IUCD – Can be provided in all public health facilities by a trained provider in OPD

ii. PPIUCD – Inserted within 48 hours after delivery.

iii. PAIUCD – Inserted within 12 days of abortion in PHC & other health facilities.

**Extended PLPPSA Scheme – Programme Linked Payment PLAN to Service Providers, Acceptors & ASHA's**

a. Trained/skilled empanelled providers inserting PPIUCD / PAIUCD is given Rs.150 per insertion.

b. ASHA accompanying the client is given Rs.150/-

c. Beneficiary is given Rs.300/- per insertion.

Provider's base for IUCD services is being increased by utilizing the army of doctors qualified in ISM ( Unani , Siddha and Homeopathy) after giving them structured training for provision for IUCD.

**F. Generating demand & awareness for Family Planning services.**

I. Improved counseling through RMNCH counselors.

II. Celebrating of World Population Day & fortnight (11th July – 24th July)

III. Celebrating of Vasectomy fortnight (21th November to 4th December)

**G. FP- LMIS**

Family Planning Logistic management information system has been incorporated in National Family Planning Programme to ensure the right commodities, in the right quantities reach right place at the right time.

**H. Public Private Partnership**

It is assumed that effective collaboration with the private sector in the from of public private partnership would address the unmet need in the Family Planning significantly.

| Claims arising out of Sterilization Operation | | Amount (Rs.) | Additional as per Hon'ble SC Directives |
|---|---|---|---|
| A | Death at hospital/ within seven days of discharge | 2,00,000 | 2,00,000 |
| B | Death following Sterilization (8th – 30th day from discharge) | 50,000 | 50,000 |
| C | Expenses for treatment of Medical Complications | 25,000 | 25,000 |
| D | Failure of Sterilization | 30,000 | 30,000 |
| E | Doctors/facilities covered for litigations up to 4 cases per year including defense cost | 2,00,000 (per case) | |

# National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS)

**Sruthi Bhaskaran[1], Abha Sharma[2]**
[1]Associate Professor, [2]MS (MCH), Sr Specialist, Department of Obstetrics and Gynecology, UCMS/GTB Hospital

The three most commonly occurring cancers in India are those of the breast, uterine cervix and lip/oral cavity. The cancer control program in India was started in 1975. It was renamed as the National Cancer Control Program (NCCP) in 1985 and revised in 2005, with the aim of **primary cancer prevention** by health education, **secondary cancer prevention** by early detection through opportunistic screening & education on self examination, **strengthening of existing cancer treatment** facilities & palliative care.[1] Since cancer, diabetes, cardiovascular diseases and stroke are largely preventable by modifying risk factors, in **2011** National cancer control Program was integrated withNational program for prevention of and control of diabetes, cardiovascular diseases and stroke **(NPDCS).** Thus, **National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS)[2]** was formulated.

**Objectives** of NPCDCS are as follows:

1. Health promotion through behavior change with involvement of community, civil Society, community- based organizations, media etc.
2. Opportunistic screening at all levels in the health care delivery system from subcentre and above for early detection of diabetes, hypertension and common Cancers.
3. To prevent and control chronic Non-Communicable diseases, especially Cancer, Diabetes, CVDs and Stroke.
4. To build capacity at various levels of health care for prevention, early diagnosis, treatment, IEC/ BCC, operational research, and rehabilitation.
5. To support for diagnosis and cost- effective treatment at primary, secondary and tertiary levels of health care.
6. To support for development of database of

| Health Facility | Packages of Services |
|---|---|
| **Sub centre** | Health promotion for behavior change and counselling 'Opportunistic' Screening of Diabetes using glucometer kits and Blood Pressure measurement. Awareness generation of early warning signals of common cancer. Referral of suspected cases to CHC/ nearby health facility. |
| **PHC** | Health promotion for behavior change and counseling 'Opportunistic' Screening of Diabetes using glucometer kits and Blood Pressure measurement. Clinical diagnosis and treatment of common CVDs including Hypertension and Diabetes. Identification of early warning signals of common cancer Referral of suspected cases to CHC |
| **CHC/FRU** | Prevention and health promotion including counseling. Early diagnosis through clinical and laboratory investigations. Management of common CVDs, diabetes and stroke cases. Lab. investigations and Diagnostics: Blood sugar, Total Cholesterol, Lipid Profile, Blood Urea, XR, ECG.USG (To be outsourced. If not available). 'Opportunistic' Screening of common cancers (Oral. Breast and Cervix). Referral of complicated cases to District Hospital/higher health care facility |
| **District Hospital** | Diagnoses and management of cases of CVDs, Diabetes. Stroke and i.ancer (outpatient, inpatient and intensive Care) including emergency services particularly for Myocardial Infarction & Stroke. Lab. investigations and Diagnostics: Blood sugar, Lipid Profile, KFT, XR, ECG,USG ECHO, CT Scan, MRI etc (To be outsourced, if not available). Referral of complicated cases to higher health care facility. Health promotion for behavior change and counseling. 'Opportunistic' Screening of NCDs including common cancers (Oral. Breast and Cervix). Follow up chemotherapy in cancer cases. Rehabilitation and physiotherapy services. |
| **Medical College** | Mentonng of District Hospitals. Early diagnosis and management of Cancer, Diabetes, CVDs and other associated illnesses. Training of health personnel. Operational Research |
| **Tertiary Cancer Centre** | Mentoring of District Hospital and outreach activities. Comprehensive cancer care including prevention, early detection, diagnosis, treatment, palliative care and rehabilitation. Training of health personnel. Operational Research |

NCDSthrough Surveillance System and to monitor NCD morbidity and mortality and risk factors.

7. **The programme offers opportunistic screening for diabetes and hypertension to all pregnant women in the antenatal clinic**

**Strategies for cancer prevention and control are[2]**

1. **Health promotion:** Various approaches such as mass media, community education and interpersonal communication are used for behaviour change focusing on avoidance of tobacco and alcohol, awareness about warning signs of cancer. Interpersonal communication is to be carried out through ASHA/AWW/SHGs/ youth clubs, panchayat members etc. for which IEC material is developed.
2. **Early diagnosis:** Opportunistic screening of common cancers (breast, cervical, oral) among the population 30 years and above will be carried out at different levels of health facilities. Screening for prostate cancer at CHC and District hospitals in 60 years+ male can also be considered.
3. **Treatment:**

   **Community health centres (CHC**)- NCD clinics are being established at CHC's to manage cancers. Screening, diagnosis and early management are the key functions of the clinic.

   **District Hospital-** Selected districts have been strengthened to provide comprehensive, supportive and curative services for cancer. Program district hospital has been provided the financial support for day care chemotherapy facility, chemotherapy drugs, hiring of manpower and investigations (mammography) etc.

   **Tertiary cancer centre (TCC)-** Strengthening of comprehensive cancer care at medical colleges/institute/district hospitals as TCC. The comprehensive care included provision of radiotherapy, chemotherapy, surgical oncology and diagnostic facilities.
4. **Supervision, monitoring and evaluation-** NCD cell at different levels to supervise and monitor the program.
5. **Research and Surveillance:** Cancer registry program of ICMR would be supported by having a data base for cancer cases in the country including rural areas.

**Activities under the program:**

1. **Membership of IARC: International agency for research on cancer** (IARC) is a specialised agency of WHO to coordinate international cooperation in cancer research. India became a member in May 2006. IARC has extended technical and financial support for several cancer research and preventive projects in India.
2. **National cancer awareness day:** November 7 is being observed as National cancer awareness day since 2001, to create more awareness about cancer.

**The "Health Minister's Cancer Patient Fund (HMCPF) within the Rashtriya Arogya Nidhi (RAN)"** [3] set up in 2009. In order to utilize the Health Minister's Cancer Patient Fund, the Revolving Fund as under RAN, has been established in 27 Regional Cancer Centres (RCCs). The financial assistance to a Cancer Patient up to Rs. 2,00,000/- (Rs. Two lakh only) [Rs. 5,00,000/- in emergency cases], would be processed by the RCC concerned, on whose disposal the Revolving Fund has been placed. Individual cases, which require assistance of more than Rs. 2.00 lakh is to be sent to the Ministry for processing. Revolving Funds have been created in all the 27 Regional Cancer Centres (RCCs) and funds upto Rs. 50 lakhs will be placed at their disposal

## Eligibility for Health Minister's Cancer Patient Fund (HMCPF) within RAN :

1. The Beneficiaries are the patients, living below poverty line.
2. Assistance is admissible for treatment in 27 Regional Cancer Centre(s) (RCC) only.
3. Central Govt./State Govt. /PSU employees are not eligible for financial assistance from HMCPF.
4. Grant from HMCPF would not be used where treatment /facilities for cancer treatment are available free of cost.

## National Cancer Registry Programme (NCRP)[4]

For data base of cancer cases, National Cancer Registry Programme (NCRP) was initiated in 1982 by ICMR, which gives a picture of the magnitude and patterns of cancer. There are two types of registries; Population Based Cancer Registry and

Hospital Based Cancer Registries, which was started in January 1982. The Population-based registries take the sample population in a geographically defined area while the Hospital-based registries take the data from patients coming to a particular health institution. At present there are about 21 Population-based registries and 6 Hospital-based registries all over the country. In 2001, data from all cancer registries and all medical colleges were collated for the "Development of an Atlas of Cancer in India" (www.canceratlas.india.org) to have an idea of patterns of cancers in several other parts of the country, including those not covered under the NCRP.Based on the NCRP, it is estimated that there are about 28 lakh cases of different type of Cancers in the country with occurrence of about 11 lakh new cases and about 5 lakh deaths annually. The common cancers are breast, cervical and oral cancer.

## References


1. National cancer control programme, Guidelines, Ministry of Health and family welfare:2005 https://main.mohfw.gov.in/Organisation/Departments-of-Health-and-Family-Welfare/national-cancer-control-programme
2. National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke: Training Module for Medical Officers for Prevention, Control and Population Level Screening of Hypertension, Diabetes and Common Cancer (Oral, Breast & Cervical); National Centre for Disease Control Directorate General of Health Services Ministry of Health and Family Welfare, GOI, 2017 National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular diseases and Stroke (NPCDCS) | Ministry of Health and Family Welfare | GOI (mohfw.gov.in)
3. Guidelines of Health Minister's Cancer patient fund (HMCPF) under Rashtriya Arogya Nidhi (RAN)
4. https://main.mohfw.gov.in/sites/default files/ 1493693747note_0.pdf

# National Programme on Containment of Anti Microbial Resistance

**Monal Garg[1], Richa Sharma[2]**
[1]Postgraduate Student, [2]Professor, Department of Obstetrics & Gynecology, UCMS & GTB Hospital, Delhi

Antimicrobial resistance in pathogens causing has become a matter of great public health concern. The rapid spread of multi-resistant bacteria and the dearth of newer pose an increasing threat. It is observed that resistance has emerged even to newer & more potent antimicrobial agents.

The Government of India has launched a "***National Programme on Containment of Antimicrobial Resistance***" under the 12th five year plan (2012-2017) which is being coordinated by National Centre for Disease Control.

## Objectives

1. To establish a **laboratory-based AMR surveillance system of 30 network labs** in the country and to generate quality data on antimicrobial resistance for pathogens of public health importance.
2. To **strengthen infection control guidelines** and practices and promote rationale use of antibiotics.
3. To **generate awareness** among healthcare providers and in the community about rationale use of antibiotics.

## Proposed Activities

a. **Surveillance for Containment of Antimicrobial Resistance in various geographical regions** - National Antimicrobial Surveillance network (NARS-Net) has been established to determine the magnitude and trends of AMR in different geographical regions of the country. NARS-Net are required to submit AMR surveillance data of seven priority bacterial pathogens of public health importance: **Klebsiella** spp**., Escherichia coli, Staphylococcus aureus, and Enterococcus** spp.**, Pseudomonas** spp**, Acinetobacter** spp**., Salmonella enterica** serotypes Typhi and Paratyphi.

b. **Rational use of antibiotics**. A common unified National Treatment Guidelines for antimicrobial use in infectious diseases 2019 has been released and uploaded

c. **National Guidelines for Infection Prevention and Control in Healthcare facilities**" developed with support from WHO and have been disseminated to various stakeholders and also available on NCDC website

d. **Training and capacity building of professionals in relevant sectors.**

**e. IEC for dissemination of information about rational use of antibiotics.**

**Table 1:** Network of medical colleges/labs under AMR program

| | |
|---|---|
| 1. | BJMC Pune, Maharashtra |
| 2. | BJMC Ahmedabad, Gujarat |
| 3. | GSVM Medical college Kanpur, UP |
| 4. | GMCH Chandigarh |
| 5. | SMS Medical College Jaipur, Rajasthan |
| 6. | LHMC, Delhi |
| 7. | VMMC and Safdarjung Hospital, Delhi |
| 8. | MMC & RI Mysore, Karnataka |
| 9. | KAPV Government Medical College, Trichy, Tamil Nadu |
| 10. | Government Medical College, Thiruvanathapuram, Kerala |
| 11. | Guwahati Medical college, Guwahati, Assam |
| 12. | Mahatma Gandhi Memorial Medical college, Indore, MP |
| 13. | NEIGRIHMs, Shillong, Meghalaya |
| 14. | IGMC, Shimla, HP |
| 15. | Medical College, Jammu |
| 16. | Medical College, Aurangabad, Maharashtra |
| 17. | Osmania General Hospital & Osmania Medical College, Hyderabad, Telangana |
| 18. | SCB Medical College Hospital, Cuttack, Odisha |
| 19. | Agartala Govt. Medical College & GBP Hospital |
| 20. | Guntur Medical College & Govt. General Hospital, Andhra Pradesh |
| 21. | Jawaharlal Nehru Memorial Medical College, Raipur, Chattisgarh |
| 22. | Rajendra Institute of Medical Sciences, Ranchi, Jharkhand |
| 23. | B D Sharma PGIMS Rohtak, Haryana |
| 24. | Indira Gandhi Institute of Medical Sciences, Sheikhpura, Patna, Bihar |
| 25. | Medical College, Haldwani, Uttarakhand |
| 26. | Gandhi Medical College, Bhopal, Madhya Pradesh |
| 27. | Calcutta School of Tropical Medicine, Kolkata, West Bengal |
| 28. | LLRM Govt. Medical College, Merrut, Uttar Pradesh |
| 29. | GMERS Medical College, Valsad, Gujarat |

f. **Development of National Repository of Bacterial strains / cultures**- onsite visits to be undertaken to assess the lab capacity and hand holding for strengthening Internal Quality Control and Proficiency testing in these labs. 1% resistant strains are required to be submitted every quarter by the sites for confirmation to NCDC

- Starting with a network of 10 State medical colleges which were initially included under the programme as of March 2017, it has been expanded in a phased manner and currently includes 29 state medical college labs in 24 states/UTs (Table 1)

## National Action Plan on Antimicrobial Resistance (2017-2021):

The Prime Minister, Shri Narendra Modi, highlighted India's role in tackling AMR during his Mann ki Baat address in July 2016. The following AMR committee/groups were notified on 27 September 2016 (fig.1):

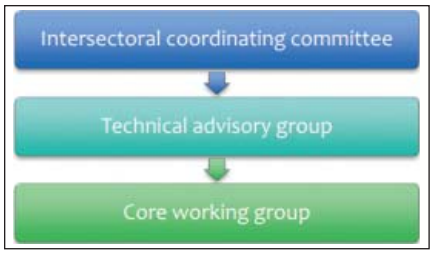



**Fig 1:** key governance mechanism for AMR[2]

**Strategies** (fig.2)

- The first 5 strategic priorities are aligned with the Global Action Plan on AMR.
- Sixth strategic priority: India's role in containment of AMR at the **international level**.


**Fig 2:** NAP-AMR Strategies 2017-2021[2]

The focus areas of the six strategic priorities of NAP-AMR( fig 3)

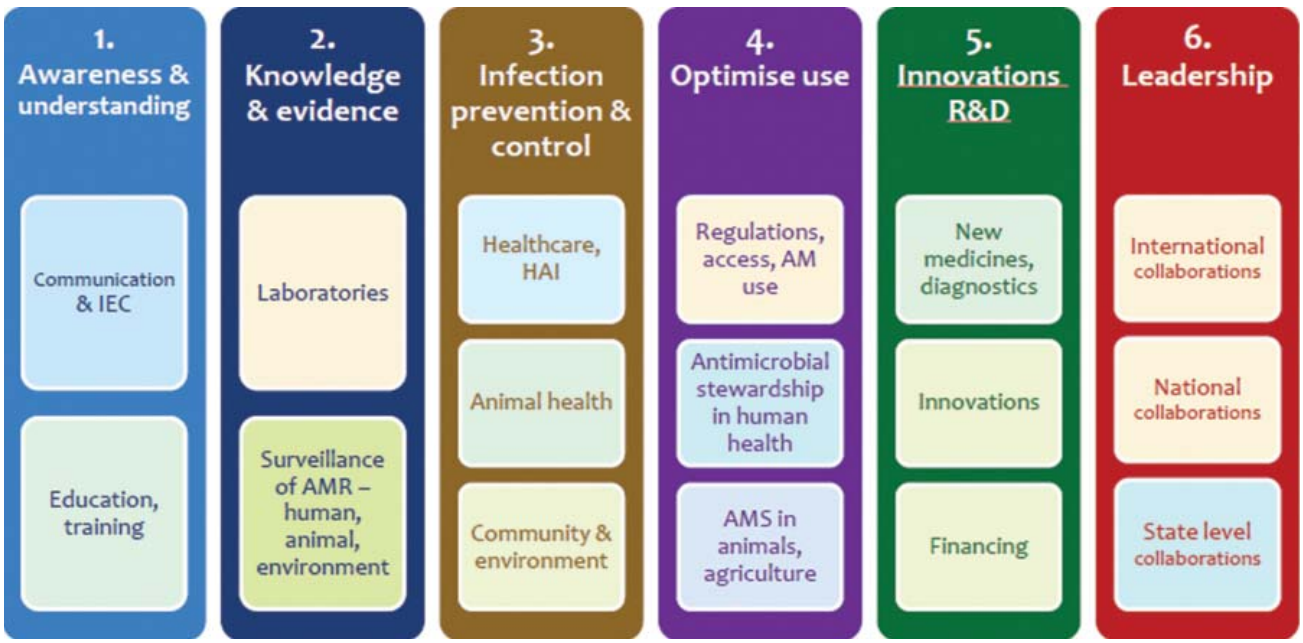



**Fig 3:** Focus areas NAP-AMR[2]

## References

1. National Programme on Containment of Anti-Microbial Resistance (AMR). DGHS, MOHFW
2. National Action Plan on Antimicrobial Resistance (NAP-AMR) 2017 – 2021, april 2017

# Approach to a Newborn with Atypical Genitalia

**Archana Dayal Arya**
Senior Consultant Pediatric & Adolescent Endocrinologist, Institute of Child Health, Sir Ganga Ram Hospital, New Delhi

## Definition

Ambiguous or Atypical Genitalia is a discrepancy between the external genitalia, gonads and the chromosomal sex of a baby.

The terms hermaphrodite, peseudohermaphrodite and intersex were replaced by a broader term "Disorders of Sexual Differentiation" (DSD) in a consensus in 2006. Recently the term "Differences in Sexual Differentiation" has also been used to describe patients with atypical genitalia.

## Normal Sexual Development

The bipotential gonad differentiates into male or female gonads based on the chromosomes.

The presence of a Y chromosome containing the SRY gene results in the development of Testes.

The Sertoli cells in the Testes secrete the Anti Mullerian Hormone (AMH) also known as Mullerian Inhibiting Substance (MIS) that prevents the Mullerian Structures (Uterus, Fallopian tubes) from developing.

The Leydig cell of the Testes produce Testosterone. Testosterone is further converted to its active form, Dihydrotestosterone(DHT) in the presence of 5α reductase. DHT acts on the androgen receptors to produce masculinization of the external genitalia.

Gonadotropin-releasing hormone (GnRH) and testosterone along with insulin-like 3 (INSL3) are secreted by the Leydig cells result in descent of the testes. INSL3 is produced by the testes only; hence a gonad palpable below the inguinal ligament is likely to have testicular tissue (Testes or ovotestes)

Absence of the Y chromosome and SRY gene in Females (XX) results in the development of ovaries.

## Types of DSD

### 46XY DSD (Undervirilized Male)

This can occur due to

1. Global defect in testicular function (dysgentic or ovotestes) result in absence of
   - Testosterone: leading to incomplete virilization
   - AMH: results in presence of Mullerian structures
2. Insufficient Androgen Synthesis from the Gonads or Adrenal glands (5<reductase Type 2 deficiency, 17®HSD type 3 deficiency)
3. Partial Androgen Insensitivity
4. Ovotesticular DSD; Presence of both testicular and ovarian tissue in the same individual

### XX DSD (Virilized female)

The commonest cause of XX DSD is Congenital Adrenal Hyperplasia due to 21-hydroxylase deficiency. These babies have clitoromegaly or male appearing genitalia at birth with no palpable gonads. The uterus and ovaries appear normal, and they may have hyperpigmentation. CAH could be associated with salt losing.

Other rare types of CAH, 11β(OH) and 3βHSD deficiency also result in overproduction of androgens by the adrenal glands.

Overproduction of testosterone by the gonads (XX testicular or ovotesticular DSD) due to mutations in ovarian development may rarely cause virilization of an XX baby.

Exposure of developing fetus to excess androgen either exogenous or placental insufficiency or placental aromatase deficiency can lead to virilization of an XX baby.

### 45X/46XY Mosaicism

This is the second most common DSD. Babies may present with severe hypospadias, small testes usually on the right side and a streak gonad with mullerian remnants on the left side

## Approach to a Baby with Atypical Genitalia

Suspicion of a genital abnormality should be there if the baby has;

- Small penile size
- Non palpable testes with male appearing genitalia
- Unilateral cryptorchidism with hypospadias

- Severe Hypospadias
- Asymmetry of the scrotal sac/labia
- Suspected Clitoromegaly especially with hyperpigmentation and single urogenital opening
- Genitalia don't match the prenatal sex (if determined as in other countries)

The two important problems that are faced by the obstetrician immediately after delivering the baby are;

1. Is there any immediate risk to the baby since abnormal genitalia could be a part of a generalised disorder
2. Sex Assignment

Parents are usually very anxious to know the sex of the baby immediately, but if an abnormality is observed, the doctor should not feel pressured to assign the sex.

A guarded reply should be given, such as seems to be a male/female but the appearance is not clear so we should evaluate the baby. Ask the parents not to announce the birth of the baby till the problem is better defined.

Allay their anxiety by explaining to them that these problems do occur in a lot of babies and can be identified and rectified.

A rapid diagnosis can be made in cases of CAH but diagnosing other conditions could take longer. The parents should be explained the importance of making an accurate diagnosis before sex assignment.

## History

A detailed history should be obtained regarding;

- **Maternal Hirsutism:** due to ovarian/adrenal tumors or placental aromatase deficiency
- **Maternal Drug exposure:** exogenous androgens or drugs that interfere with testosterone synthesis eg. Spironolactone or estrogens
- **Placental insufficiency:** Testosterone is secreted by the placenta in first trimester, hence insufficiency can result in inadequate virilization
- **Family history** :ambiguous Genitalia, CAH, unexplained death of an infant (CAH), undervirilized males (partial androgen Insensitivity (AIS) and women with amenorrhea or infertility (complete AIS). Consanguinity suggests the possibility of an autosomal recessive disorder. Positive family history may not be obtained in these cases.

## Physical Examination

A thorough physical exam of the baby should be done by the attending physician and referred immediately to a Pediatric Endocrinologist for detailed evaluation of the infant.

**Examination** should include a general physical examination including the vital signs and a complete systemic examination

- Dysmorphic Facies, hypotonia and associated congenital malformations are likely to be associated with a genetic syndrome
- Midline facial anomalies and micropenis with small testes especially with associated hypoglycemia suggest an abnormality of the pituitary gland.
- Hyperpigmentation: due to raised ACTH secondary to abnormalities of the adrenal gland eg.CAH
- Respiratory/Cardiovascular abnormality
- Abdominal Mass/ Hernia

## Genital Examination

**1. Measure the Penis/Clitoris**

- Measurement of the Stretched Penile Length(SPL). In a full term male baby the average SPL is 3.5 cms and should be at least 2.5cms with a width of 1 cms for male sex assignment.

Do not assign male sex to babies with SPL<1.9cms without evaluation of cause and response to therapy

2. **Inspect the location of the urethral opening**

- Look for Separate vaginal and urethral opening
- Urethral opening at the base of the phallus could be a part of hypospadias or a urogenital sinus

3. **Presence/ Absence/Location of Testes:**

- Non palpable testes with a small penis should raise the suspicion of CAH
- Gonads beneath the inguinal ligament usually have testicular tissue
- Asymmetry of the gonads
- Hernias/ mass in the inguinal region

- Labioscrotal Fusion and Anogenital ratio; >0.5 suggests posterior labial fusion due to androgen exposure.

## Immediate Investigations

- **Karyotyping (urgent**); for chromosomal sex or FISH for SRY (whichever result is faster)
- **17(OH)Progesterone, DHEAS, Androstenedione:** for CAH

  Tests for other rare causes of CAH can be done if there is a clinical suspicion eg.11 Deoxycortisol, 17 hydroxypregnenolone, ACTH,Cortisol
- **S.Electrolytes:** Salt wasting CAH
- **AMH and Inhibin B** to determine the presence and function of the testes
- **LH, FSH, Testosterone, Dihydrotestosterone, Estradiol**

  Testosterone levels should be checked preferably after a week and not before 48 hours since the levels are usually suppressed

  Stimulated Testosterone; DHT ratios may be needed for some babies to confirm the diagnosis
- **USG** of the Inguinoscrotal region for tetes and pelvic region for Mullerian Structures
- **Genitogram** should be done depending on the disease suspected.
- **Genetic Testing:** should be done once a clinical diagnosis is made, but it should not delay the sex assignment.

## Sex Assignment

The Gender assignment is based on the diagnosis and how well the child would be able to function as an adult in terms of gender identity, sexual functioning and fertility.

This will depend on the degree of development and functioning of reproductive organs as well as the response to hormonal therapy

The final decision regarding sex assignment should be made after detailed discussion of a multispeciality team comprising of a Pediatric Endocrinologist and Surgeon, Geneticist and the parents. The family's social and cultural beliefs may play a role in the decision making.

The Gender identity is known for some types of DSD but in others the decision making could be difficult.

## Clinical Clues to Diagnosis

| Clinical Clue | Disease |
|---|---|
| History of Consanguinity | Autosomal Recessive Disorder |
| Amenorrhea/Infertility in maternal aunts | Androgen insensitivity |
| Maternal Hirsutism | Virilizing adrenal or ovarianTumor or placental aromatase deficiency |
| Dysmorphic Appearance | Syndromic Disorder |
| Midline Anomalies micropenis with small sized testes and hypoglycemia | Abnormality of Pituitary gland |
| Hyperpigmentation especially of genitalia | Congenital Adrenal Hyperplasia |

## Key Points

- Immediate evaluation for babies with DSD is very important for sex assignment as well as any associated anomalies
- Do not assign the sex of the baby before making a diagnosis and discussing with the multispeciality team and parents

# Mistakes Made in Interpreting Anti-Mullerian Hormone

**Ruma Satwik**
Consultant, Centre of IVF and Human Reproduction, Sir Gangaram Hospital, New Delhi

The one hormone that has eased its way into most subspecialities of gynaecology is Antimullerian hormone. From a specialist in reproductive medicine seeking to tailor-make ovarian response prior to controlled ovarian stimulation to a gynae-endoscopic surgeon wishing to determine ovarian reserve before and after ovarian cystectomy; from a gynae-oncologist wanting to establish the etiology of an ovarian tumour to a gynae-endocrinologist wishing to discriminate between ovarian or pituitary causes of amenorrhoea; anti-mullerian hormone is ordered and utilized universally. Despite its widespread usage, there are some common but easily avoidable mistakes that we tend to make in its interpretation affecting decision-making in clinical practice. This could have far-reaching implications in patient management. This article talks about ten such mistakes and the measures taken, largely incumbent on updating ourselves, to avoid them.

1. **Being unaware of the units of reporting**

   Anti-mullerian hormone in most laboratories is reported in ng/mL. The mean normal range in women between 25-35 years varies from 1.2-3.5ng/ml[1].

   A few laboratories would report this in picomoles/L, a conversion obtained by using a factor of 7.18, such that 1ng/ml =7.18pmol/L. So, the normal range of AMH in women reported in pmol/L for ages between 25-35 years is 8.6-25 pmol/L

2. **Being unaware of laboratory variation**

   The same blood sample divided into three aliquots and sent to three different laboratories simultaneously could return different results. This could be due to, the method of testing: whether manual or automated, the technology used: whether immunoassay with monoclonal/ polyclonal antibodies or chemiluminescence assay or due to different storage times and temperature that the sample is subjected to prior to testing.

   – Manual testing is subject to errors due to manual mixing of reagents and serum in a multi-step process lending itself to greater errors than the automated method.

   – *DSL* assay and the *IOT* assays, the first AMH assays, were manual assays and were replaced by *Gen II Beckman Coulter assay*, a semi-automated assay using two monoclonal antibodies.

   – *Gen II Beckman Coulter* AMH values are approximately 20% lower than the newer automated Elecys assay.[2] It is considered less precise than the newer assays: automated *Access* or *Elecys* assay both of which use immunofluorescence to detect the attachment of two monoclonal antibodies to epitopes on AMH molecule. The differences in current assays arise due to antibody specificity and differences in calibrating results.

   – In perimenopausal women, more than 95% of the AMH in the circulation can be detected by *PicoAMH ELISA* assays while only 36% can be detected by Beckman Coulter gen II assay[3]

   – AMH values are increased by 23% compared with fresh samples when stored at -20°C for 5 days and by 58% when stored at room temperature.[4]

   Having one standard laboratory to test AMH that uses updated systems to perform tests daily, runs regular controls, is open to questions on sample storage, test performance, errors etc. and is approved by a standard authority should be the way to minimize laboratory variations.

3. **Being unaware of the effect of sex steroids on Anti-Mullerian hormone**

   Often, women on contraceptive pills wish to be counseled on fertility options. If AMH is ordered during its use or shortly after stoppage, it is likely to be lower by an average of 19% since OCPs tend to suppress ovarian function.[5] Infact with the use of hormonal contraception, irrespective of its route of administration, AMH

in users begins to decline significantly from week five onwards and is reduced by upto 50% by week 9[6] Hence it is best to elicit a history of contraceptive usage prior to ordering AMH and to order it at least three months after discontinuing hormonal contraception.

4. **Making the patient wait till day 2/3 for AMH testing**

   A highly debated issue relates to whether AMH significantly varies or not throughout the menstrual cycle. Several studies have suggested that serum AMH levels fluctuate only little during the menstrual cycle, as would be expected from the evidence that AMH is not secreted by the dominant follicle or corpus luteum.

   A study on 257 regularly menstruating women found that serum AMH levels in the follicular phase were higher than those in the luteal phase in all categories of ovarian responders. This difference amounts to approximately 16-20% of the follicular phase value. However, in current practice, these fluctuations in serum AMH concentrations are not large enough to alter decision making, hence the authors suggested that the timing of AMH measurements during the menstrual cycle could be random[7]. Also, in an earlier pioneering study, La marca et al had shown that the intra-cycle variability is lowest for this hormone[8] when compared to other reproductive hormones and that it may be ordered at any time in a natural menstrual cycle for the sake of convenience.

   However, in a gonadotropin stimulated cycle, the value might be significantly lower at and after ovulation than in an unstimulated cycle.[9] This is probably secondary to the gonadotrophin effect on the process of follicular development. So, the recommendation is to avoid testing immediately after an unexpectedly poor oocyte recovery in an IVF cycle.

5. **Taking low values to mean low natural fertility**

   AMH represents ovarian reserve or the pool of follicles kept away from entering into the cycle of growth and certain death. It is secreted by small-antral and pre-antral follicles. Low AMH means lower pool of such follicles. A lower pool also means lower recruitable follicles in the phase of luteo-follicular transition translating as lower retrieved oocytes during in-vitro fertilization cycle. Thus, AMH has been found to have a strong correlation with retrieved oocyte numbers.[10]

   It however **does not denote low natural fertility**. Low AMH in healthy women in their mid-20s did not predict reduced fecundability in a study involving 430 women wanting to plan conception. The study revealed equal cumulative probability of conception in six months for women with AMH < 14 pmol/L versus women with AMH between 14 and 39 pmol/L.[11] Similarly, in another study of women between 25 to 42 years, the time to natural conception remained the same for women with low AMH (<9.5 pmol/L) versus women with normal AMH (9.6-33pmol/L). Women with AMH as low as 1.2 pmol/L could have live-births. The cumulative pregnancy rate was higher for high AMH range but equally respectable figures were obtained for the low AMH range too at two years. (60, 70 and 78% for low, intermediate and high AMH ranges).[12]

   *Period of trying and age are important factors in determining average monthly fecundability*. AMH alone should not be taken as a marker of low natural fertility especially in women under 35 years with a period of trying that is less than one year.

   Low AMH coupled with increased age (>37) and a period of trying exceeding one year could mean low fecundability.

6. **A very high AMH, yet no response to usual stimulation.**

   While AMH strongly correlates with ovarian response to gonadotropins, it is not the only factor to do so. Body mass index and responsiveness of follicles to gonadotropins matter as well. The diagnosis of poor responsiveness of follicles to exogenous gonadotropins is rare and often reached when one or more previous COS cycles have shown unexpectedly poor ovarian response in women with good ovarian reserve markers. In some such instances one might find an FSH receptor polymorphism on genetic analysis. FSH dosage is either increased substantially or LH is added in order to elicit appropriate ovarian response. This is however rare and out of the scope of what we are discussing.

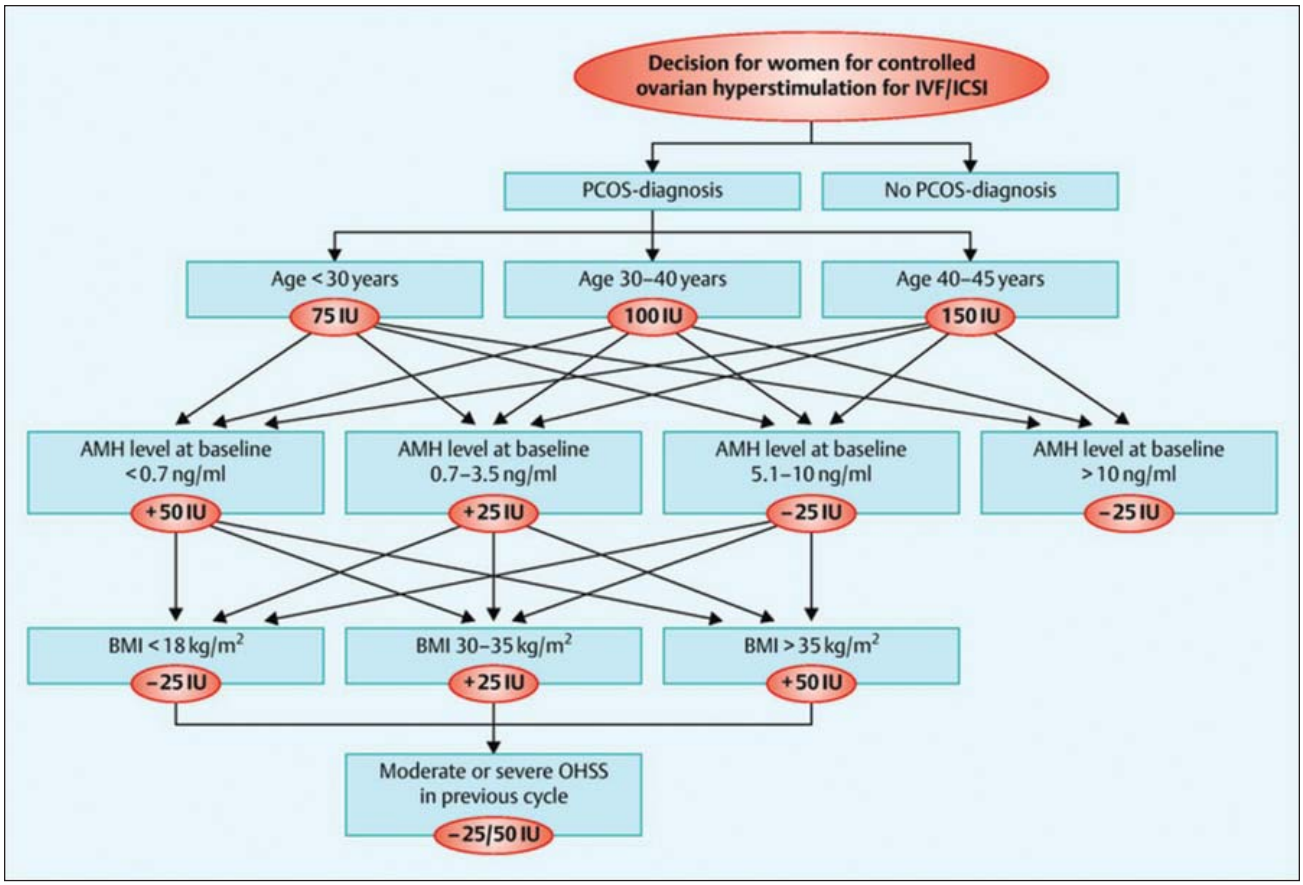



**Fig 1:** Titrating Gn dose in PCOS women. There are four levels at which decision is made. Age, AMH, BMI, and previous h/o moderate or severe OHSS. Notice that a BMI above 30kg/m2 practically cancels the effect of high AMH and more than 35Kg// m2 leads to an increase in dosing from baseline by 25 units even in women with an AMH of 10ng/ml.

Figure courtesy: Fischer et al, 2016.

But one other mistake that is more likely made while titrating gonadotropin dosage is not accounting for the body mass index of the individual while deciding on appropriate gonadotropin dosage. So, two women with AMH of 7ng/ml each with BMIs of 21Kg/m2 and 30Kg/m2 will respond very differently to a daily dose of 75 IU of gonadotropins. While the first one may most likely require a titrating down of dosage midway of stimulation, the second may not respond even after 10-14 days of this dosing. While we know through our clinical experience and several studies that obese PCOS women require higher starting dose than non-obese PCOS in order to produce the same response, we don't often appreciate the quantum of influence that BMI could have in choosing an appropriate dosage.

A recommendation on dose titration by Fisher et al is given in figure 1[13]

7. **The paradoxical effect of very high AMH on follicular sensitivity**

   Apart from BMI playing a significant role in mitigating the effect of high AMH on ovarian response, it is also worthwhile to know that a very high AMH might actually cause follicular resistance to FSH stimulus[14]. One action of AMH is to REDUCE follicular sensitivity to FSH at the small antral follicle stage. (Figure 2) This translates into the clinical knowledge that at the luteo-follicular transition when small rise in pituitary FSH picks up a cohort of follicles to start growing, a very high AMH causes the follicles to offer greater resistance to FSH. A very high AMH might mean that one may have to start gonadotropins at a much higher dose than was considered BMI-appropriate to overcome this resistance.

8. **Offering donor eggs to women based on low AMH alone**

   Consider this situation. A 37-year old lady

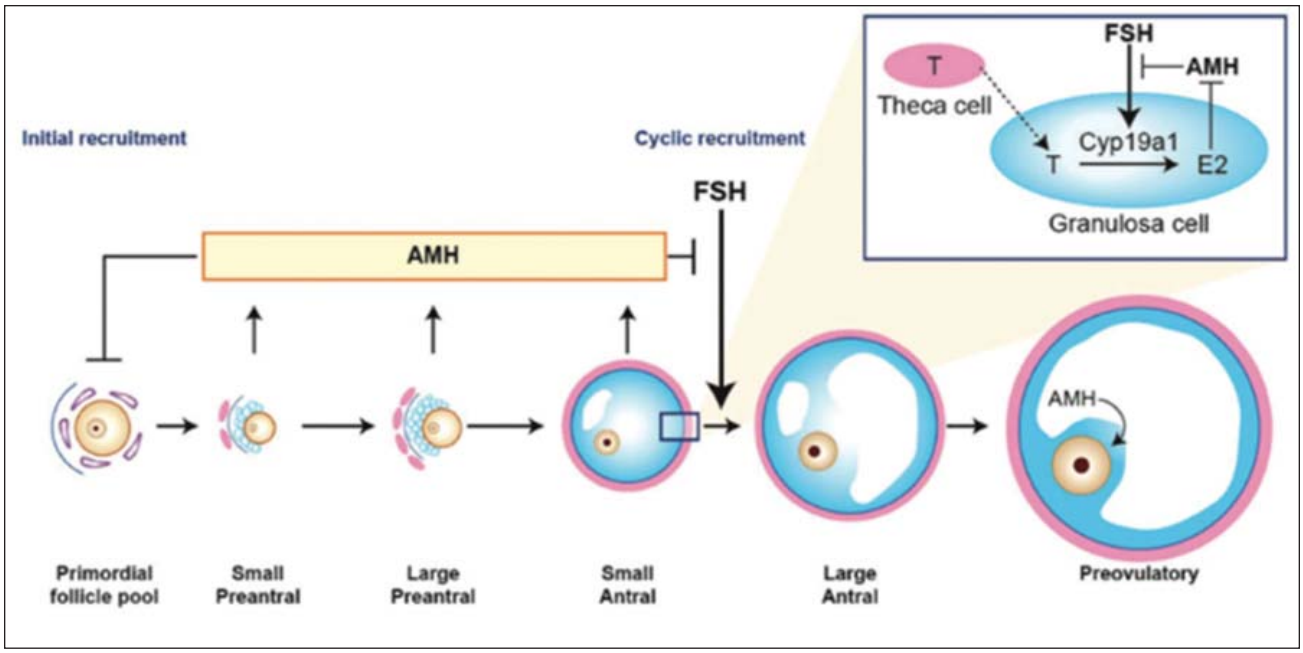



**Fig 2:** Follicular development from primordial to preovulatory follicular stage and sites of action of AMH and FSH. From Didier et al 2014[15]

married for 3 months with regular menstrual cycles visits a clinic to seek fertility counseling. She is otherwise healthy and reports no significant past illnesses or surgeries. An AMH is ordered and the results show a value of 0.3ng/mL. What would your advise be to such a woman? That you have low natural fertility, that you need to go into IVF soon or that you need to go into IVF with donor eggs.

**Approach:** Get a baseline semen and ultrasound done along with general blood tests and if normal, counsel her on fertile period, improving general health, importance of an ideal weight and ask her to return after six months of active trying if still not pregnant. Thereafter, the approach could be to test tubal patency by the least invasive method like HSG and basing management on results. Offer IVF with self-eggs if unable to get pregnant despite one year of active trying.

**Rationale:** Firstly, to put her in the category of subfertile based on AMH alone, before at least six months (age>35 yrs.) of trying have elapsed, is going against the established definitions of infertility given by ASRM and RCOG. Secondly, while AMH level is known to drop with ageing, it is incorrect to presume that ovarian reserve would drop precipitously over a short period. In women between 18-40 years of age a secondary analysis of 1326 women undergoing 1-3 cycles of IVF and repeated AMH testing at screening visit and at the start of each IVF cycle, has shown that AMH values remain stable for a period of upto one year between consecutive or non-consecutive menstrual cycles.(Figure 3) [16] Hence there is no real panic in rushing women into IVF within the next 2-6 months. Waiting till at-least six months of active trying are over will bear its dividends.

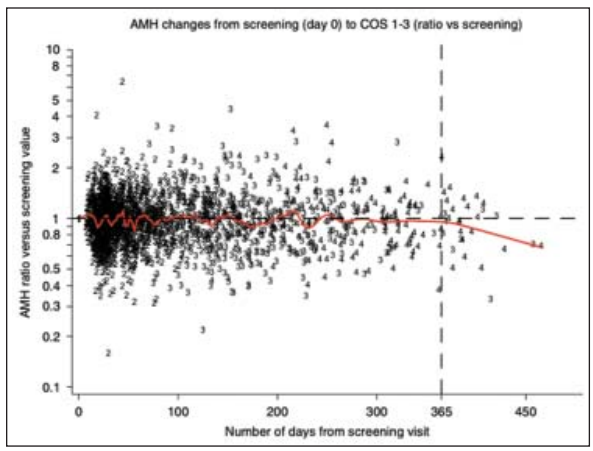



**Fig 3:** AMH changes expressed as a ratio of the AMH at screening visit plotted against time. Not that the mean ratio remains at 1 till 365 days before beginning to decline. From Nelson Scott et al 2019.

Lastly, it is agreed that AMH, independently of age, has some association with predicting live birth after assisted conception and may

be helpful when counselling couples before undergoing fertility treatment. However, its predictive accuracy is poor.[17] Prognosis for live birth in women over 35 with AMH < 0.5ng/ml is considered to be between 15-25% per started cycle in the current practice.[18,19] Age, AMH, period of trying, past live births and infertility etiology have a role in determining a couple's chance for live births in IVF and should be considered while prognosticating couples. The decision could only be informed once the couple has full information on this. Hence offering donor eggs in the above case as a first measure appears uninformed.

9. **Being unaware of Anti-mullerian hormone levels in men**

   Anti-mullerian Hormone derives its name by virtue of its action in male fetuses. AMH is secreted from Sertoli cells of testes from the seventh week of gestation It is meant to cause regression of mullerian ducts. Its absence would lead to the presence of both male and female internal genital organs causing hermaphroditism. AMH levels in male fetuses rise steadily reaching a peak at birth, then remain stable till 12 years of age, thereafter, beginning to decline with rising testosterone levels of puberty. (Figure 4). A common notion is that levels in men would be undetectable. But as figure 4 shows, not only AMH remains detectable throughout adulthood, but also its levels remain 5-20 times higher than females. [20] On the contrary, female fetuses do not secrete AMH and its secretion only begins at birth, peaking at 20 years, thereafter, declining with age.

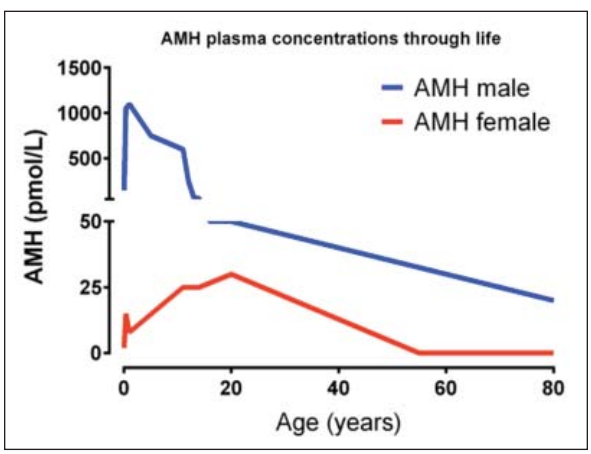



**Fig 4:** AMH levels throughout life in men and women.

10. **Being unaware of its other diagnostic potential.**

    AMH in females is secreted from granulosa cells and it can be a marker of granulosa cell tumours. The mean AMH level of 190.3 ng/ml (range: 2-1124ng/ml) have been described in such tumours[21]. Cut-offs of upto 13ng/ml have yielded better sensitivity and specificity. Its sensitivity in detecting granulosa cell tumours is similar to that of Inhibin B[22]. It has also been used for diagnosing neonatal sex in cases of ambiguous genitalia. The etiology of delayed puberty, whether central or peripheral, could be ascertained by checking AMH levels. In central causes of delayed puberty, AMH remains low or undetectable in girls and very high in boys. AMH has also been used as a predictor of menopause with there being a 60% chance of menopause in the next five years with undetectable AMH levels.[23]

    In conclusion, it becomes imperative for clinicians to update themselves with the new knowledge areas pertaining to Anti-mullerian hormone physiology, its actions and its applications. Future applications of AMH could be in preventing oocyte loss due to chemo- or radiotherapy.

## References

1. Cui, L., Qin, Y., Gao, X., Lu, J., Geng, L., Ding, L., … Chen, Z.-J. (2016). *Antimüllerian hormone: correlation with age and androgenic and metabolic factors in women from birth to postmenopause. Fertility and Sterility, 105(2), 481–485. e1.*doi:10.1016/j.fertnstert.2015.10.017
2. Bungum L, Tagevi J, Jokubkiene L, et al. The Impact of the Biological Variability or Assay Performance on AMH Measurements: A Prospective Cohort Study With AMH Tested on Three Analytical Assay-Platforms. *Front Endocrinol (Lausanne)*. 2018;9:603. Published 2018 Oct 16. doi:10.3389/fendo.2018.00603
3. Robertson DM, Kumar A, Kalra B, Shah S, Pruysers E, Vanden Brink H, et al. Detection of serum antimüllerian hormonein women approaching menopause using sensitive antimüllerian hormone enzyme-linked immunosorbent assays. Menopause (2014) 21:1277–86. 10.1097/
4. **Rustamov O**, Smith A, Roberts SA, Yates AP, Fitzgerald C, Krishnan M, Nardo LG, Pemberton PW.Anti-Mullerian hormone: poor assay reproducibility in a large cohort of subjects suggests sample instability. Hum Reprod. 2012 Oct;27(10):3085-91
5. Birch Petersen K, Hvidman HW, Forman JL, Pinborg A,

Larsen EC, Macklon KT, Sylvest R, Andersen AN. Ovarian reserve assessment in users of oral contraception seeking fertility advice on their reproductive lifespan. Hum Reprod. 2015 Oct;30(10):2364-75.

6. Kallio S, Puurunen J, Ruokonen A, Vaskivuo T, Piltonen T, Tapanainen JS. Antimüllerian hormone levels decrease in women using combined contraception independently of administration route. Fertil Steril. 2013 Apr;99(5):1305-10.
7. Gorkem U, Togrul C. Is There a Need to Alter the Timing of Anti-Müllerian Hormone Measurement During the Menstrual Cycle?. *Geburtshilfe Frauenheilkd*. 2019;79(7):731-737. doi:10.1055/a-0840-3817
8. La Marca A, Stabile G, Artenisio AC, Volpe A. Serum anti-Mullerian hormone throughout the human menstrual cycle. Hum Reprod. 2006 Dec;21(12):3103-7
9. La Marca A, Malmusi S, Giulini S, Tamaro LF, Orvieto R, Levratti P, Volpe A. Anti-Müllerian hormone plasma levels in spontaneous menstrual cycle and during treatment with FSH to induce ovulation. Hum Reprod. 2004 Dec;19(12):2738-41.
10. Satwik R, Kochhar M, Gupta SM, Majumdar A. Anti-mullerian hormone cut-off values for predicting poor ovarian response to exogenous ovarian stimulation in in-vitro fertilization. J Hum Reprod Sci. 2012 May;5(2):206-12. d
11. Hagen CP, Vestergaard S, Juul A, Skakkebæk NE, Andersson AM, Main KM, Hjøllund NH, Ernst E, Bonde JP, Anderson RA, Jensen TK. Low concentration of circulating antimüllerian hormone is not predictive of reduced fecundability in young healthy women: a prospective cohort study. Fertil Steril. 2012 Dec;98(6):1602-8.e2.
12. Korsholm AS, Petersen KB, Bentzen JG, Hilsted LM, Andersen AN, Hvidman HW. Investigation of anti-Müllerian hormone concentrations in relation to natural conception rate and time to pregnancy. Reprod Biomed Online. 2018 May;36(5):568-575.
13. Fischer D, Reisenbüchler C, Rösner S, Haussmann J, Wimberger P, Goeckenjan M. Avoiding OHSS: Controlled Ovarian Low-Dose Stimulation in Women with PCOS. *Geburtshilfe Frauenheilkd*. 2016;76(6):718-726
14. Pellatt L, Rice S, Dilaver N, Heshri A, Galea R, Brincat M, Brown K, Simpson ER, Mason HD. Anti-Müllerian hormone reduces follicle sensitivity to follicle-stimulating hormone in human granulosa cells. Fertil Steril. 2011 Nov;96(5):1246-51.e1.
15. Didier Dewailly, Claus Yding Andersen, Adam Balen, Frank Broekmans, Nafi Dilaver, Renato Fanchin, Georg Griesinger, Tom W. Kelsey, Antonio La Marca, Cornelius Lambalk, Helen Mason, Scott M. Nelson, Jenny A. Visser, W. Hamish Wallace, Richard A. Anderson, The physiology and clinical utility of anti-Müllerian hormone in women, *Human Reproduction Update*, Volume 20, Issue 3, May/June 2014, Pages 370–385
16. Nelson SM, Larsson P, Mannaerts BMJL, Nyboe Andersen A, Fauser BCJM. Anti-Müllerian hormone variability and its implications for the number of oocytes retrieved following individualized dosing with follitropin delta. Clin Endocrinol (Oxf). 2019 May;90(5):719-726
17. Iliodromiti S, Kelsey TW, Wu O, Anderson RA, Nelson SM. The predictive accuracy of anti-Müllerian hormone for live birth after assisted conception: a systematic review and meta-analysis of the literature. Hum Reprod Update. 2014 Jul-Aug;20(4):560-70.
18. Peuranpää P, Hautamäki H, Halttunen-Nieminen M, Hydén-Granskog C, Tiitinen A. Low anti-Müllerian hormone level is not a risk factor for early pregnancy loss in IVF/ICSI treatment. Hum Reprod. 2020 Mar 27;35(3):504-515.
19. Reijnders IF, Nelen WL, IntHout J, van Herwaarden AE, Braat DD, Fleischer K. The value of Anti-Müllerian hormone in low and extremely low ovarian reserve in relation to live birth after in vitro fertilization. Eur J Obstet Gynecol Reprod Biol. 2016 May;200:45-50.
20. Jeffery, A., Streeter, A., Hosking, J., et al. (2015). Anti-Müllerian hormone in children: a ten-year prospective longitudinal study (EarlyBird 39). *Journal of Pediatric Endocrinology and Metabolism*, 28(9-10), pp. 1153-1162.
21. Andrew H. Lane, Mary M. Lee, Arlan F. Fuller, David J. Kehas, Patricia K. Donahoe, David T. MacLaughlin, Diagnostic Utility of Müllerian Inhibiting Substance Determination in Patients with Primary and Recurrent Granulosa Cell Tumors, Gynecologic Oncology, Volume 73, Issue 1,1999, Pages 51-55,
22. Chen S, Yang B, Fan J. Diagnostic value of Anti-Mullerian hormone in ovarian granulosa cell tumor: A meta-analysis. Eur J Obstet Gynecol Reprod Biol. 2020 Oct;253:266-272
23. Kim C, Slaughter JC, Wang ET, Appiah D, Schreiner P, Leader B, Calderon-Margalit R, Sternfeld B, Siscovick D, Wellons M. Anti-Müllerian hormone, follicle stimulating hormone, antral follicle count, and risk of menopause within 5 years. Maturitas. 2017 Aug;102:18-25

# Endocrinology of Normal Menstrual Cycle

**Manjula Salgotra[1], Pallavi Sharma[2], Chandra Mansukhani[3]**
[1]Senior resident –Department of OBGY –GMC Kathua, [2]Assistant Professor, Department of OBGY -GMC Kathua
[3]Senior Consultant, Department of OBGY- SGRH

## Introduction

The normal menstrual cycle in females is a complex series of physiological changes starting from the puberty. It is regulated by the complex interactions of the hypothalamus, pituitary and gonads (hypothalamic-pituitary-gonadal axis).

The initiation of ovulation—the release of an oocyte from the ovary—marks the transition from puberty into reproductive age in females. The ovarian reserve is comprised of ovarian follicles and their supporting cells. These follicles grow and develop in a process called folliculogenesis, which involves release of one follicle and atresia of the remaining follicles approximately every 28 days. Folliculogenesis begins with follicles in a resting state. These small primordial follicles are present in newborn females and are the prevailing follicle type in the adult ovary. After puberty, a few primordial follicles will respond to a recruitment signal each day, and will join a pool of immature growing follicles called primary follicles.

Primary follicles start with a single layer of granulosa cells, but the granulosa cells then become active and change from a flat or squamous shape to a rounded, cuboidal shape as they increase in size and proliferate. As the granulosa cells divide, the follicles—now called secondary follicles increase in diameter, adding a new outer layer of connective tissue, blood vessels, and **theca cells**. Within the growing secondary follicle, the primary oocyte now secretes a thin acellular membrane called the zona pellucida which plays a crutial role in fertilization. A thick fluid, called follicular fluid, that has formed between the granulosa cells also begins to collect into one large pool, or antrum. Follicles in which the antrum has become large and fully formed are considered tertiary follicles (or antral follicles). Several follicles reach the tertiary stage at the same time, and most of these will undergo atresia. The one that does not die will continue to grow and develop until ovulation, when it will expel its secondary oocyte surrounded by several layers of granulosa cells from the ovary. Approximately 99 percent of the follicles in the ovary will undergo atresia, which can occur at any stage of folliculogenesis. The final stages of development of a small cohort of tertiary follicles, ending with ovulation of a secondary oocyte, occur over a course of approximately 28 days. These changes are regulated by GnRH, LH, and FSH.

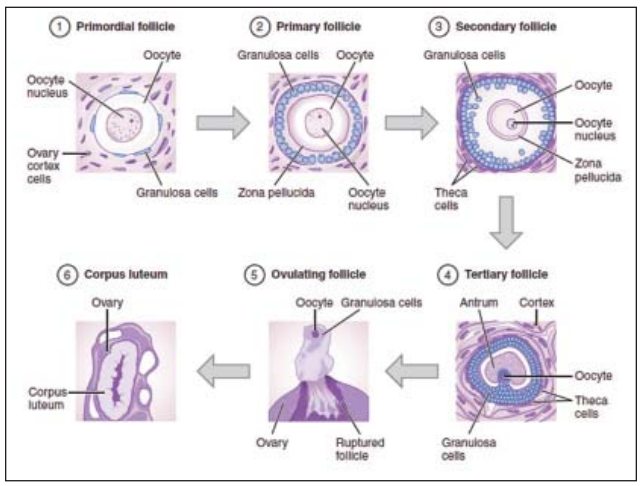



**Fig 1:** Folliculogenesis -The maturation of a follicle is shown in a clockwise direction proceeding from the primordial follicles.

Normal menstrual cycle is a coordinated event occurring at regular intervals. It is a complex interplay between the hypothalamus which contributes to the secretion of GnRH, After being transported to the anterior pituitary, GnRH activates its 7-transmembrane G-protein receptor. This further signals the anterior pituitary to secrete stimulating follicle hormone (FSH) and luteinizing hormone (LH) which provide input to the ovaries. The ovary in response to these hormones recruits a dominant follicle and secrets estradiol and inhibin A. A peak of estradiol triggers discharge of LH, responsible for ovulation and posterior secretion of progesterone by the corpus luteum, which in turn involutes 14 days later if does not receive stimulation of hCG. It has been established that during the menstrual cycle ovarian steroids are the principal mediators of feedback mechanisms. The menstrual cycle can be broadly divided into two phases.

1. Folliclular phase

2. Luteal phase

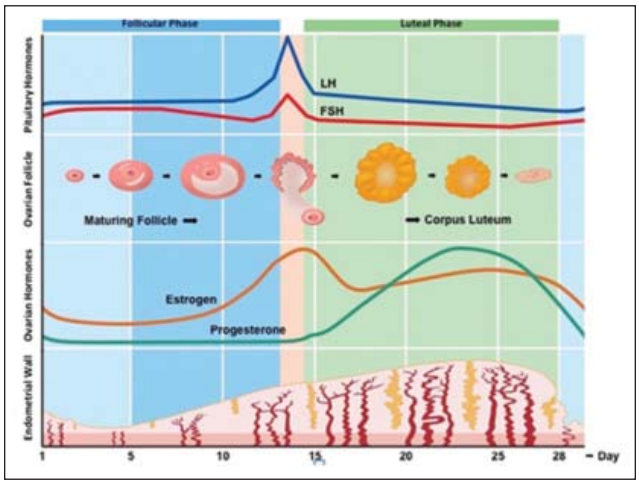



**Fig 2 :** Phases of menstrual cycle

## Follicular Phase

The follicular phase involves events related to the selection of a solitary follicle (dominant follicle) from within a group of immature follicles. The variability in length of the menstrual cycle occurs due to variations in the length of the follicular phase. This process occurs over the period of 10–14 days and comprises of a series of sequential actions of hormones and autocrine-paracrine peptides on the follicle. The follicle destined to ovulate through a period of initial growth from a primordial follicle grows into preantral, antral, and preovulatory follicle. The majority of this period (until a late stage) involves responses that are independent of hormonal regulation[1]. The rise in FSH is the critical feature in rescuing a cohort of follicles from atresia, the usual fate of most follicles, eventually allowing a dominant follicle to emerge and pursue a path to ovulation.

Various factors are involved in the molecular events that regulate primordial follicle formation. These include members of the transforming growth factor beta (TGF-β) super family of proteins and a different family of trophic factors called neurotrophins. Activins, inhibins, antimullerian hormone (AMH), and bone morphogenetic proteins (BMPs) are members of the TGF-**β family of proteins. AMH is a vital** inhibitor of primordial follicle growth, and BMPs exert the opposite effect[2]. Once growth is accelerated, the follicle progresses to the preantral stage, the granulosa cells of the preantral follicle have the capacity to synthesize all three classes of steroids; though, significantly more estrogens than either androgens or progestins.

An aromatase enzyme system acts to convert androgens to estrogens and is a factor limiting ovarian estrogen production. Aromatization is induced or activated through the action of FSH. In the presence of FSH, estrogen becomes the dominant substance within the follicular fluid. Specific receptors for FSH are not detected on granulosa cells until the preantral stage[3], and the preantral follicle requires the presence of FSH to aromatize androgens and generate its own estrogenic microenvironment[4]. Cellular estrogen production is, therefore, limited by its FSH receptor content.

Androgens have a complex role in early follicular development. Specific androgen receptors are present in the granulosa cells[5]. The androgens serve not only as a substrate for FSH-induced aromatisation but, in low concentrations, can further enhance aromatase activity. When exposed to an androgen rich environment, preantral granulose cells favour the conversion of androgens to more potent 5 alpha reduced androgens rather than to estrogens[6]. These androgens cannot be converted to estrogen and, infact, inhibit aromatase activity[7].

In human preantral and antral follicles, LH receptors are present only on the theca cells and FSH receptors only on the granulosa cells[8,9]. Theca interstitial cells, located within the theca interna, have approximately 20,000 LH receptors in their cell membranes. In response to LH, theca tissue is stimulated to supply androgens which be converted, through FSH-induced aromatization, to estrogens within the granulosa cells. By altering gonadotropin secretion through feedback mechanisms, it optimizes its own environment to the detriment of the lesser follicles. GnRH plays an essential role in the control of gonadotropin secretion and the pattern of gonadotropin secretion seen in the menstrual cycle is due to the feedback modulation of steroids and peptides originating in the dominant follicle, acting directly on the hypothalamus and anterior pituitary[10].

The secretion of FSH is extremely sensitive to the negative inhibitory effects of estrogen even at low levels. At higher levels, estrogen combines

with inhibin for a suppression of FSH which is profound and sustained. In contrast, the influence of estrogen on LH release varies with concentration and duration of exposure. At low levels, estrogen imposes a negative feedback relationship with LH. At higher levels, however, estrogen is capable of exerting a positive stimulatory feedback effect on LH release. There are two critical features in this mechanism: the concentration of estradiol and the length of time during which the estradiol elevation is sustained. In women, the estradiol concentration necessary to achieve a positive feedback effect on LH release is more than 200pg/ml, and this concentration must be sustained for approximately 50 hours[11]. In a well-established monthly pattern, the gonadotropins are secreted in a pulsatile fashion with a frequency and magnitude that vary with the phase of the cycle. While the pulsatile pattern of gonadotropins is directly due to a similar pulsatile secretion of GnRH, the amplitude and frequency modulations are the consequence of steroid feedback on both the hypothalamus and the anterior pituitary[12].

## Role of Inhibin, Activin and Follistatin

This family of peptides is synthesized by the granulosa cells in response to FSH and secreted into the follicular fluid[13]. Inhibin is an important inhibitor of FSH secretion. Activin stimulates FSH release in the pituitary and augments FSH action in the ovary. Follistatin suppresses FSH activity, by binding activin.

The Two Forms of Inhibin are:

Inhibin A: Alpha-Beta A

Inhibin B: Alpha-Beta B

FSH and Inhibin share a reciprocal relationship[14]. FSH stimulates the secretion of inhibin from granulosa cells and, in turn, is suppressed by inhibin. Assay techniques have revealed that inhibin B is the form of inhibin predominantly secreted by granulosa cells in the follicular phase of the cycle[15]. The secretion of inhibin B into the circulation amplifies the withdrawal FSH from other follicles so that the emerging follicle secures dominance. With the appearance of LH receptors on the granulosa cells of the dominant follicle and the subsequent development of the follicle into a corpus luteum, inhibin expression comes under the control of LH, and expression changes from inhibin B to inhibin A. Inhibin A, therefore, contributes to the suppression of FSH to nadir levels during the luteal phase and to the changes at the luteal-follicular transition.

Activin is derived from granulosa cells and it augments the secretion of FSH and inhibits prolactin, ACTH, and growth hormone responses. It increases pituitary response to GnRH by enhancing GnRH receptor formation[17]. Inhibin and follistatin block the effects of activin. Therefore, the pituitary secretion of FSH is considerably regulated by the equilibrium of activin and inhibin, with follistatin playing a role by inhibiting activin and enhancing inhibin activity. Inside the ovarian follicle, activin and inhibin influence growth and development by modulating theca and granulosa responses to the gonadotropins.

As the preovulatory follicle matures, it produces increasing amounts of estrogen. During the late follicular phase, estrogens rise slowly at first, then rapidly, reaching a peak approximately 24–36 hours prior to ovulation[18]. The onset of the LH surge occurs when the peak levels of estradiol are achieved[19]. LH promotes luteinization of the granulosa in the dominant follicle, resulting in the production of progesterone. Progesterone affects the positive feedback response to estrogen in both a time- and dose-dependent manner. When introduced after adequate estrogen priming, progesterone facilitates the positive feedback response of estrogen by direct action at the level of the pituitary, and in the presence of subthreshold levels of estradiol, it can induce a characteristic LH surge[20]. Hence, appropriately low levels of progesterone derived from the maturing follicle contribute to the precise synchronization of the midcycle surge. In addition to its facilitator action on LH, progesterone at midcycle is also responsible for the FSH surge[21].

With the LH surge, the meiosis in the oocyte resumes, there is luteinization of granulosa cells and progesterone production, expansion of the cumulus, and the synthesis of prostaglandins and other eicosanoids essential for follicle rupture. Estradiol levels fall dramatically immediately prior to the LH peak. This may be due to LH down regulation of its own receptor or because of direct inhibition of estradiol synthesis by progesterone. Progesterone is also responsible for stimulating the

midcycle FSH which serves to free the oocyte from follicular attachments, to convert plasminogen to the proteolytic enzyme, plasmin, and to ensure that sufficient LH receptors are present to allow an adequate normal luteal phase.

## Luteal Phase

The early luteal phase begins with active angiogenesis mediated by VEGF. New vessel growth is held in check by angiopoietin-1 working through its receptor Tie-2 on endothelial cells. The corpus luteum, being a transient endocrine organ that predominantly secretes progesterone, and its primary function is to prepare the estrogen primed endometrium for implantation of the fertilized ovum. Peak vascularisation is achieved eight to nine days after ovulation which approximates around the time of expected implantation. **This time also corresponds to peak serum levels of progesterone and estradiol. Estrogen levels rise and fall** two times during the menstrual cycle. Estrogen levels rise during the mid-follicular phase and then drop abruptly after ovulation. This is followed by a secondary rise in estrogen levels during the mid-luteal phase with a decrease at the end of the menstrual cycle. The secondary rise in estradiol parallels the increase in serum progesterone and 17α-hydroxyprogesterone levels.

The means by which the corpus luteum regulates steroid secretion is not completely understood. Regulation may be determined in part by LH secretory pattern and LH receptors or variations in the levels of the enzymes regulating steroid hormone production, such as 3β-HSD, CYP17, CYP19, or side chain cleavage enzyme. The secretion of progesterone and estradiol during the luteal phase is episodic, and correlates closely with pulses of LH secretion[22]. LH has a regulatory role in luteal phase. The frequency and amplitude of LH secretion in follicular phase subsequently regulates the luteal phase function[23]. Moreover, the life span of the corpus luteum can be reduced by continuous LH administration during the follicular or luteal phase, reduced LH concentration, decreased LH pulse frequency, or decreased LH pulse amplitude[24]. The role of other luteotropic factors such as prolactin, oxytocin, inhibin and relaxin is still uncertain[25]. The corpus luteum function begins to fall 9-11 days after ovulation. The demise of corpus luteum results in nadir of circulating levels of estradiol, progesterone and inhibin. The decrease in inhibin A, removes a suppressing influence on FSH secretion in the pituitary. The decrease in estradiol and progesterone allows a progressive and rapid increase in the frequency of GnRH pulsatile secretion and removal of the pituitary from negative feedback suppression. The removal of inhibin A and estradiol and increasing GnRH pulses combine to allow greater secretion of FSH compared with LH, with an increase in the frequency of the episodic secretion.

## Normal Menstruation

With the cessation of hormones the endometrium is not able to sustain itself leading to its shedding, labelled as menstruation. This is considered day 0 to day 5 of the next menstrual cycle. The duration of menses can vary. The usual duration of the menstrual flow is 3-5 days, but flows as shorts as 1 day and as long as 8 days can occur in a normal female. The amount of blood loss can range from slight spotting to 80 mL and the average being 30 mL. Loss of more than 80 mL of the blood is considered abnormal.

Menstrual blood is chiefly arterial, with only 25% of the blood being the venous. It contains prostaglandins, tissue debris, and relatively large amounts of fibrinolysis from endometrial tissue. The fibrinolysis lyses clot so that menstrual blood does not contain clots typically unless the flow is heavy. Various factors can affect the amount of blood flow, including medications, the thickness of the endometrium, blood disorders, and disorders of blood clotting, etc.

## References


1. Oktay K, Newton H, Mullan J, Gosden RG, Development of human primordial follicles to antral stages in SCID/hpg mice stimulated with follicle stimulating hormone, Hum Reprod 13:1133, 1998.
2. Trombly DJ, Woodruff TK, Mayo KE, Roles for transforming growth factor beta superfamily proteins in early folliculogenesis, Semin Reprod Med 27:14, 2009.
3. Okay K, Briggs DA, Gosden RG, Ontogeny of follicle-stimulating hormone receptor gene expression in isolated human ovarian follicles, J Clin Endocrinol Metab 82:3748, 1997.
4. McNatty KP, Makris A, DeGrazia C, Osathanondh R, Ryan KJ, The production of progesterone, androgens, and estrogens by granulosa cells, thecal tissue, and stromal tissue from

human ovaries in vitro, J Clan Endocrinol Metab 49:687, 1979.

5. Hild-Petito S, West NB, Brenner RM, Stouffer RL, Localization of androgen receptor in the follicle and corpus luteum of the primate ovary during the menstrual cycle, Biol Reprod 44:561, 1991.
6. McNatty KP, Makris A, Reinhold VN, DeGrazia C, Osathanondh R, Ryan KJ, Metabolism of androstenedione by human ovarian tissues in vitro with particular reference to reductase and aromatase activity, Steroids 34:429, 1979.
7. Hillier SG, Van Den Boogard AMJ, Reichert LE, Van Hall EV, Intraovarian sex steroid hormone interactions and the regulation of follicular maturation: aromatization of androgens by human granulosa cells in vitro, J Clin Endocrinol Metab 50:640, 1980.
8. Kobayashi M, Nakano R, Ooshima A, Immunohistochemical localization of pituitary gonadotropins and gonadal steroids confirms the two cells two gonadotropins hypothesis of steroidogenesis in the human ovary, J Endocrinol 126:483, 1990.
9. Yamoto M, Shima K, Nakano R, Gonadotropin receptors in human ovarian follicles and corpora lutea throughout the menstrual cycle, Horm Res 37(Suppl 1): 5, 1992.
10. Mais V, Kazer RR, Cetel NS, Rivier J, Vale W, Yen SS, The dependency of folliculogenesis and corpus luteum function on pulsatile gonadotropin secretion in cycling women using a gonadotropin-releasing hormone antagonist as a probe, J Clin Endocrinol Metab 62:1250, 1986.
11. Young JR, Jaffe RB, Strength-duration characteristics of estrogen effects on gonadotropin response to gonadotropin-releasing hormone in women. II. Effects of varying concentrations of estradiol, J Clin Endocrinol Metab 42:432, 1976.
12. Filicori M, Santoro N, Merriam GR, Crowley WF Jr, Characterization of the physiological pattern of episodic gonadotropin secretion throughout the human menstrual cycle, J Clin Endocrinol Metab 62:1136, 1986.
13. Rivier C, Rivier J, Vale W, Inhibin-mediated feedback control of follicle-stimulating hormone secretion in the female rat, Science 234:205, 1986.
14. McLachlan RI, Robertson DM, Healy DL, Burger HG, De Kretser DM, Circulating immunoreactive inhibin levels during the normal human menstrual cycle, J Clin Endocrinol Metab 65:954, 1987.
15. Groome NP, Illingworth PG, O'Brien M, Pai R, Rodger FE, Mather JP, McNeilly AS, Measurement of dimeric inhibin B throughout the human menstrual cycle, J Clin Endocrinol Metab 81:1401, 1996.
16. Kitaoka M, Kojima I, Ogata E, Activin-A: a modulator of multiple types of anterior pituitary cells, Biochem Biophys Res Commun 157:48, 1988.
17. Kaiser UB, Conn PM, Chin WW, Studies of gonadotropin-releasing hormone (GnRH) action using GnRH receptor-expressing pituitary cell lines, Endocr Rev 18:46, 1997.
18. Pauerstein CJ, Eddy CA, Croxatto HD, Hess R, Siler-Khodr TM, Croxatto HB, Temporal relationships of estrogen, progesterone, and luteinizing hormone levels to ovulation in women and infrahuman primates, Am J Obstet Gynecol 130:876, 1978.
19. Fritz MA, McLachlan RI, Cohen NL, Dahl KD, Bremmer WJ, Soules MR, Onset and characteristics of the midcycle surge in bioactive and immunoactive luteinizing hormone secretion in normal women: influence of physiological variations in periovulatory ovarian steroid hormone secretion, J Clin Endocrinol Metab 75:489, 1992.
20. Collins RL, Hodgen GD, Blockade of the spontaneous midcycle gonadotropin surge in monkeys by RU 486: a progesterone antagonist or agonist? J Clin Endocrinol Metab 63:1270, 1986.
21. Couzinet B, Brailly S, Bouchard P, Schaison G, Progesterone stimulates luteinizing hormone secretion by acting directly on the pituitary, J Clin Endocrinol Metab 74:374, 1992.
22. Filicori M., Butler J.P., Crowley W.F. Jr. Neuroendocrine regulation of the corpus luteum in the human. Evidence for pulsatile progesterone secretion. J Clin Invest. 1984;73(6):1638–1647.
23. McNeely M.J., Soules M.R. The diagnosis of luteal phase deficiency: a critical review. Fertil Steril. 1988;50(1):1–15.
24. Sheehan K.L., Casper R.F., Yen S.S. Luteal phase defects induced by an agonist of luteinizing hormone-releasing factor: a model for fertility control. Science. 1982; 215 (4529):170–172.
25. Auletta F.J., Flint A.P. Mechanisms controlling corpus luteum function in sheep, cows, nonhuman primates, and women especially in relation to the time of luteolysis. Endocr. Rev. 1988;9(1):88–105.

# Hirsutism

**Abha Majumdar**
Director, Centre of IVF and Human Reproduction, Sir Ganga Ram Hospital, New Delhi

## Introduction

Hirsutism is defined as the presence of terminal coarse dark hair in females in androgen dependent areas where women typically grow fine hair or no hair at all. These areas generally are at the upper lip, chin, chest, abdomen, and back. Hirsutism is different from hypertrichosis, which is generalized excessive hair growth at androgen independent areas and may be related to the use of certain androgenic medications, familial factors, or metabolic disorders[1].

Hirsutism is a common clinical condition seen in female patients of all ages affecting around 5-10% of the women[2]. The cause is mainly increase in androgen levels, which may be ovarian or adrenal in origin or it could be just increased sensitivity of hair follicles to normally circulating androgens. Consequently, only one-half of women with hirsutism have elevated levels of circulating androgens and the severity of hirsutism is not necessarily proportionate to the circulating androgen level.

Hirsutism has a massive psychosocial impact, especially in the young females and may turn out to be an emotional burden that can harm one's self-esteem and body image. Nevertheless, significant variability exists in how women view their hirsutism, ranging from not bothersome to humiliation.

## Causes

**Ovarian causes:** Polycystic ovarian syndrome (PCOS) and ovarian tumors.

**Adrenal causes:** Congenital adrenal hyperplasia (CAH) (most commonly due to 21-hydroxylase deficiency), Cushing's syndrome, and androgen-producing tumors.

**Androgenic drugs:** This group of drugs also constitute an important cause of hirsutism[3] such as danazol, testosterone, metoclopramide, reserpine, phenothiazines, anabolic steroids, and methyl dopa.

**Idiopathic hirsutism (IH):** This cause accounts for about 20% of women with hirsutism where androgen levels and ovarian function is found to be normal. The cause of increased hair in these women is thought to be related to disorders in peripheral androgen metabolism and activity. Onset of IH occurs shortly after puberty and has a slow progression. PCOS and idiopathic hirsutism accounts for almost 90% of hirsutism in women.

**Less common causes:** Hyper-androgenic-insulin resistant acanthosis nigricans (HAIRAN) syndrome is another cause encountered in women with insulin resistance and metabolic syndrome. Hyperprolactinemia and thyroid disorders are hormonal disorders which may increase adrenal DHEA-S production thus cause hirsutism. Perimenopausal women for a few years after menopause may manifest hirsutism due to decrease in ovarian estrogen secretion with continuous androgen production[4].

## Pathophysiology

80% of circulating testosterone (T4) is secreted either by the ovaries or adrenals, one half from each one of them. A small amount of circulating T4 is derived from the conversion of androgenic precursors, mainly androstenedione which is mostly derived from the ovaries and a small part from the adrenals as well. Dihydro-epiandrosterone (DHEA) and its sulphate (DHEA-S) is mainly derived from the adrenals thus considered adrenal androgens.

However, only 1-2% of T4 is in free form and is the active androgen. About 98-99% is bound to steroid hormone binding globulin (SHBG), albumin and other proteins and is biologically inactive. Only free T4 is converted to dihydrotestosterone (DHT), by the enzyme 5-alpha reductase type 2 isoenzyme present in the outer root sheath of the hair follicles or the pilosebaceous unit[5]. This isoenzyme predominates in the testes, prostate, and the hair follicles of beard and genital hair. DHT causes terminalization of the vellus hair and prolongs the anagen phase resulting in longer thicker hair

Idiopathic hirsutism with normal androgen levels is postulated to result from exaggerated peripheral

5-alpha reductase activity, androgen receptor polymorphisms, or altered androgen metabolism[6]. The relative activity of the 5-reductase enzyme can be determined by measuring 5-androstanediol glucuronide in either urine or blood. 5-alpha reductase enzyme is of two types. Type 2 is located primarily in the genital region, and type 1 is located mainly in the skin.

## The Pilosebaceous Unit

Two types of hair exist. The fine hair of the fetus are lanugo, and the peach fuzz hair of adults is vellus hair. These hairs are fine, short, and nonpigmented. Thick and pigmented hair is referred to as terminal hair. The hair of pubic, axillary, sternal, and facial areas are responsive to androgens, and those in other parts of the body are androgen independent. As androgen levels rise, more vellus hairs in the androgen-sensitive areas are converted into terminal hairs, resulting in hirsutism. Diagnosis involves a detailed history, ascertaining the degree of hirsutism and investigations to find the underlying cause to be able to treat it.

## Diagnosis

### History

**Family history and cultural background:** These are extremely important in diagnosing hirsutism. A patient is not hirsute if she does not think that she is different from her relatives and other women around her. A family history is especially important as CAH, PCOS and type 2 diabetes are inherited conditions associated with hirsutism.

**Rapid onset:** Rapid onset of hirsutism is characteristic of tumors of the adrenal or the ovary, whereas slow onset is more likely to be an endocrine disorder of the adrenal, ovary, or pilosebaceous unit.

**Time of onset:** Puberty onset is characteristic of PCOS and CAH whereas other endocrine diseases or tumor conditions may start at any age.

## External Physical Characteristics

### Hirsutism

Hirsutism is excessive recognizable hair growth due to increase in the number and length of terminal hairs. However, an increase in the number of hair follicles does not occur. Hirsutism also is difficult to quantify. The entire body needs to be inspected and the findings must be documented carefully. Particular attention should be directed to the upper lip, chin, sideburns, breasts, sternum, the midline between the umbilicus and the pubis, and the thigh.

**Ferriman and Gallwey** published a rating scale that is illustrated in Table 1. This scale allows the physician to measure a response to therapy objectively. This system is the most widely used and evaluates body areas for absent-to-severe hirsutism with scores of 0-4, respectively. Scores of 8 and higher are consistent with a diagnosis of hirsutism. This scale does not measure the thickness of the hair, which is another way of objectively assessing excess hair.

Although these scoring systems can be a useful aid in quantifying hirsutism and in evaluating treatment response, the scores remain somewhat subjective, and the diagnosis of hirsutism can be accomplished by the physician's clinical assessment of the sexual hair. Photographs are helpful for documentation and for following the progress of therapy.

**Table 1:** Ferriman-Gallwey Scoring System (1961)

| Body Area Evaluated | Score (Graded from 0-4*) |
|---|---|
| Upper lip | |
| Chin | |
| Upper abdomen | |
| Lower abdomen | |
| Upper arm | |
| Thighs | |
| Upper back | |
| Lower back/buttocks | |

*0 = No hirsutism, 4 = severe hirsutism

**Digital imaging of hair development:** A technique has been developed to assess hirsutism with video equipment and computer software. Digital imaging of hair development is recorded, which demonstrates a significant difference in hair form and growth rate between hirsute and non-hirsute women[7].

**Virilism:** Virilism is extreme hyperandrogenism and is characterized by temporal balding, breast atrophy, clitoral enlargement, deepening of the voice, and extreme hirsutism. A tumor must be suspected in the presence of virilism. The width and length of the clitoris must be examined. No consistent standard exists for clitoromegaly; however, a clitoris that

is 1 cm or more is considered abnormal, and an androgenic tumor should be suspected.

**Acne:** Acne lesions need to be documented in women presenting with hirsutism, including the number of whiteheads, blackheads, papules, pustules, and nodules. Several areas of the body need to be examined, including the face, chest, and back. Photographic documentation is helpful.

**Acanthosis nigricans:** Acanthosis nigricans in the presence of hirsutism raises the suspicion of insulin resistance and hyperandrogenism insulin resistance-acanthosis nigricans (HAIR-AN) syndrome.

## Investigations

**Laboratory Studies:** With hirsutism and, particularly virilism, the most important diagnosis to be made out or ruled out is of a tumor of the adrenal or the ovary.

**Serum testosterone and DHEAS levels are only useful in severe cases of hirsutism:** A tumor should be suspected with extremely elevated androgen levels.

1. Testosterone >2ng/ml (normal 0.08 to 0.6ng/ml),
2. DHEAS >7000ng/mL or 7mg/ml (Ages 20 to 29: 65 to 380 µg/dL or 1.75 to 10.26 µmol/L or 650 to 3800 ng/ml) (1 ug/dL = 10 ng/ml).
3. Suspect an ovarian etiology with elevated testosterone and an adrenal source with elevated DHEAS. 4 situations will be encountered with these 2 tests and accordingly the diagnosis is made.

1. **Testosterone level greater than 2 ng/ml and DHEAS level normal**: Possibly ovarian neoplasm: - pelvic ultrasound, CT scan of ovaries and ovarian and adrenal venous sampling
2. **Testosterone level variable and DHEAS greater than 7mg/ml:** Possible adrenal tumor or Cushing syndrome: - Adrenal CT scan to rule out tumor and 24-hour urinary free cortisol level or an overnight dexamethasone suppression test should diagnose Cushing's.
3. **Testosterone level > 0.7 ng/ml and DHEAS level elevated but < 7mg/ml:** The most probable diagnosis is PCOS, maybe adrenal hyperplasia and rarely Cushing syndrome. Rule out Cushing syndrome and diagnose CAH by confirming elevated 17hydroxy progesterone levels in follicular phase.
4. **Testosterone and DHEAS both are normal**. Possible diagnoses is end-organ hyper sensitivity which could be due to decreased SHBG causing increase free testosterone or increase levels of 5-Alpha-androstanediol-glucuronide in blood indicating hypersensitivity of hair follicles.

**17-OH-progesterone:** This test is used for confirming the diagnosis of CAH caused by absence of 21-hydroxylase in the pathway of steroid production. 17-OH-progesterone accumulates in blood and is elevated. This hormone is estimated in the follicular phase because 17-OH-progesterone and progesterone may be found elevated in the luteal phase of normal women too. All measurements should be obtained in the morning before 8 am because of the diurnal rhythm of adrenal steroids. Tests revealing levels above 2 ng/mL (6.05 nmol/L) need to be repeated and, if elevated, an ACTH stimulation test is performed. Following collection of a blood sample to measure baseline hormone concentrations, synthetic ACTH (Cortrosyn, 0.25 mg) is administered. A second blood sample is collected 60 minutes later. Levels above 10 ng/mL (1000ng/dl or 30.02 nmol/L) at 1 hour are diagnostic of CAH.

**Fasting glucose and insulin:** An elevated insulin level or, even better, a glucose-to-insulin ratio less than 4.5 indicates insulin resistance and may be done in cases of suspicion of HAIR-AN syndrome in absence of PCOS or CAH.

**Prolactin:** Prolactin occasionally is elevated in hirsutism. Obtaining findings about this hormone is recommended when other test results are normal.

**Serum TSH:** Hypophyseal hypothyroidism can act as a cofactor in hirsutism causing raised TSH[8].

**Androstanediol glucuronide:** This test is useful when testosterone and DHEAS levels are in the reference range in patients with hirsutism indicating increased peripheral conversion of testosterone to dihydrotestosterone. Finasteride like drug is recommended in these cases as they reduce local conversion of testosterone to DHT.

### Imaging Studies

**Ultrasound:** Ovarian ultrasound is used mainly

to determine if the patient has an ovarian tumor. Ovarian ultrasound can locate most ovarian tumors, but small hilar cell tumors are not located. The ovaries of 22-23% of healthy patients can have ultrasound evidence of PCOS, and patients with PCOS can have healthy ovaries. Ultrasound with color-flow Doppler is a helpful adjunct for tumor detection and localization.

**CT scan:** Adrenal androgen-secreting tumors usually can be detected with CT scans, particularly with newer machines and 1- to 2-mm cuts. CT scans are not useful for ovarian tumors.

**MRI:** Adrenal and some ovarian tumors can be detected with MRI; however, it is more useful for adrenal lesions.

**Radionuclide studies:** Iodomethyl-norcholesterol (NP-59) can light up steroid-secreting areas of the adrenal gland or ovary and, if available, is helpful to differentiate and locate a tumor when other radiographic studies fail to show a tumor.

## Procedures

**Ovarian and adrenal vein sampling:** In cases where the laboratory values indicate a tumor, but none can be determined by imaging studies, sampling of the ovarian and adrenal veins should determine the source of elevated androgens.

**Medical treatment:** Before starting medicine, diet and exercise should be advised to all women with PCOS which is the commonest cause of hirsutism, especially if obese. Upper body obesity has been shown to be associated with a reduced sex hormone-binding globulin level and increased free testosterone levels which can contribute to hirsutism.

## Drugs to Treat Hirsutism

1. Combined Oral contraceptives (OCPs) are first-line treatment for hirsutism, particularly in those women desiring contraception. Estrogen/progesterone combinations act by-
   a. Reduce gonadotropin secretion thus reduce ovarian androgen production.[9]
   b. Increase SHBG levels thus lower levels of free testosterone.
   c. Inhibits adrenal androgen production.[10]
2. Androgen receptor blockers
   a. Spironolactone is an androgen blocker and competes with DHT for binding to the androgen receptor. It also has variable pregestational activity thus decreases production of ovarian androgens along with an inhibitory effect on 5 alpha-reductase activity and competes with androgens for binding to SHBG. The starting dose is 50 mg twice daily and may be increased to a total daily dose of 200 mg. It takes at least six months to have any beneficial effect. OCPs should be combined to provide adequate contraception and also to minimize dysfunctional uterine bleeding which can occur with spironolactone. Side effects include polyuria, and hypotension with associated headaches, fatigue, or even syncope. Absolute contraindications include renal insufficiency, chronic renal impairment, hyperkalemia, pregnancy, and abnormal uterine bleeding.
   b. Cyproterone Acetate (CPA) and Drospirenone have strong progestogenic and antiandrogen properties even though the latter is a weaker anti androgenic agent compared to CPA. They decrease circulating testosterone and androstenedione levels through a reduction in circulating LH and have been used effectively in treatment for hirsutism[11]. CPA is available in combination with ethinyl estradiol (EE) (2 mg CPA and 35 µg EE/tablet) as oral contraceptive therapy such as in Diane 35 or as Yasmin which is a combination of Drospirenone and EE
   c. 5-alpha reductase (5AR) inhibitor is available by the name of Finasteride, effective in the treatment of IH[12]. Finasteride primarily inhibits type 2 5AR receptor activity. Another similar drug still in clinical testing is dutasteride, a "dual" type 1 and type 2 receptor inhibitor. It is predicted that this drug will be more potent than finasteride. All these 5-RA agents have the potential of feminizing a male fetus. Hence, effective contraception must be used by patients on these drugs.
   d. Gonadotrophin-releasing hormone (GnRH agonists) is reserved for women with severe hirsutism who do not respond to the OC and antiandrogens[13]. Long-acting GnRH analogs decrease gonadotrophin secretion

and therefore reduce ovarian stimulation and hence testosterone. It may be pertinent to add back hormone replacement therapy (HRT) in sequential or combined regimes to reduce symptoms of estrogen deprivation. HRT also increases SHBG thus further decreases peripherally available free testosterone. For the initial few months, the addition of 100-200 mg of spironolactone per day may help to further reduce the ovarian androgen production. After reduction of both the serum testosterone values and hirsutism, these patients can be switched to an oral contraceptive with or without spironolactone.

e. Glucocorticoids to suppress adrenals has mainly been used to treat hirsutism associated with congenital adrenal hyperplasia (CAH)[14]. They are used in a low bedtime dose of dexamethasone.

3. Biological modifiers of hair follicular growth

a. Eflornithine hydrochloride is a new agent, which is used as a topical cream (13.9%) for decreasing or facial hair growth in women. It is thought to inhibit hair growth by inhibiting an enzyme involved in keratin synthesis. The cream is applied to the face twice a day. Gradual improvement is seen in six to eight weeks. It can also be used in combination with laser treatments for better effects[15].

b. A new topical antiandrogen 2% fluridil gel is a safe and effective treatment method of hirsutism. However, this preparation is not available yet. Compared to systemic administration of antiandrogens, topical fluridil does not affect general health and sexual functions and, more importantly, does not decrease libido[16].

**Surgical Care:** Ovarian and adrenal tumors must be removed surgically

## Local Measures for Immediate Correction of Hirsutism

- Hair removal:
  - o Depilation: Removal of hair at the skin line is called depilation. Examples include shaving and using chemical depilatories.
  - o Epilation: Removal of unwanted hairs from below the surface of the skin is known as epilation. Examples include waxing, tweezing, or plucking by the patient and electrolysis or laser treatment by a professional.
  - o Electrolysis: This procedure is performed by a cosmetologist. Electrolysis uses a process called thermolysis, where a thin needle is inserted into the hair follicle parallel to the hair shaft. A small quantity of a high-frequency electrical current then is applied to the hair, heat is generated, and hair is destroyed. The dead hair is removed with forceps. As much as 25% of hair grows back, and the hairs that grow back frequently are smaller and less noticeable.
  - o Laser: The Soft Light laser is a low-energy Nd: YAG laser designed to remove hair with a specially formulated cream.
- Bleaching the hair in fair skinned people to make it less noticeable.

## Conclusion

It is important to establish the cause of hirsutism as far as possible. Mostly a detailed history with few investigations and ultrasound examination is enough to establish the cause in most cases. However, a small subgroup may require advanced investigations. Medical care for hirsutism is limited basically to drug therapy with agents that suppress ovarian or adrenal androgen production, inhibit the binding of androgens to their receptors, inhibit 5-reductase, or increase SHBG. Medications such as spironolactone, finasteride, flutamide, and cyproterone acetate has been demonstrated to be effective. Because each drug is categorized as class D or X in pregnancy, an effective form of contraception is required when using these compounds. Newer compounds are now made available as well as being investigated as topical creams with minimal side effects, which might make the treatment of hirsutism simpler without complications.

## References

1. Witchel, Selma Feldman, and Ricardo Azziz. “Nonclassic Congenital Adrenal Hyperplasia.” International Journal of Pediatric Endocrinology, vol. 2010, no. 625105, 2010. Accessed 16 Aug. 2020.
2. Ferriman D, Gallwey JD. Clinical assessment of body hair growth in women. J Clin Endocrinol Metab. 1961;21:1440–7. [PubMed: 13892577]

3. Leung AK, Robson WL. Hirsutism. Int J Dermatol. 1993;32:773–7. [PubMed: 8270330]
4. Martin KA, Chang RJ, Ehrmann DA, Ibanez L, Lobo RA, Rosenfield RL, et al. Evaluation and treatment of hirsutism in premenopausal women: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2008;93:1105–20. [PubMed: 18252793]
5. Rosenfield RL. Clinical practice. Hirsutism. N Engl J Med. 2005;353:2578–88. [PubMed: 16354894]
6. Azziz R, Carmina E, Sawaya ME. Idiopathic hirsutism. Endocr Rev. 2000;21:347–62. [PubMed: 10950156]
7. Gruber DM, Berger UE, Sator MO, Horak F, Huber JC. Computerized assessment of facial hair growth. Fertil Steril. 1999;72:737–9. [PubMed: 10521121]
8. Schmidt JB, Lindmaier A, Spona J. Hyperprolactinemia and hypophyseal hypothyroidism as cofactors in hirsutism and androgen-induced alopecia in women. Hautarzt. 1991;42:168–72. [PubMed: 1905280]
9. Burkman RT., Jr The role of oral contraceptives in the treatment of hyperandrogenic disorders. Am J Med. 1995;98:130–6. [PubMed: 7825633]
10. Shaw JC. Spironolactone in dermatological therapy. J Am Acad Dermatol. 1991;24:236–43. [PubMed: 1826112]
11. Van der Spuy ZM, le Roux PA. Cyproterone acetate for hirsutism. Cochrane Database Syst Rev. 2003. CD001125. [PubMed: 14583927]
12. Faloia E, Filipponi S, Mancini V, Di Marco S, Mantero F. Effect of finasteride in idiopathic hirsutism. J Endocrinol Invest. 1998;21:694–8. [PubMed: 9854686]
13. De Leo V, Fulghesu AM, la Marca A, Morgante G, Pasqui L, Talluri B, et al. Hormonal and clinical effects of GnRH agonist alone, or in combination with a combined oral contraceptive or flutamide in women with severe hirsutism. Gynecol Endocrinol. 2000;14:411–6. [PubMed: 11228061]
14. Emans SJ, Grace E, Woods ER, Mansfield J, Crigler JF., Jr Treatment with dexamethasone of androgen excess in adolescent patients. J Pediatr. 1988;112:821–6. [PubMed: 3361397]
15. Smith SR, Piacquadio DJ, Beger B, Littler C. Eflornithine cream combined with laser therapy in the management of unwanted facial hair growth in women: A randomized trial. Dermatol Surg. 2006;32:1237–43. [PubMed: 17034372]
16. Sovak M, Seligson AL, Kucerova R, Bienova M, Hajduch M, Bucek M. Fluridil, a rationally designed topical agent for androgenetic alopecia: First clinical experience. Dermatol Surg. 2003;28:678–85. [PubMed: 12174057]

# Utility of Genetic Testing in Assessing The Risk of Cancer in Women's Health

**Ratna Dua Puri, Deepti Gupta, Renu Saxena, Ishwar Verma**
Institute of Medical Genetics and Genomics, Sir Ganga Ram Hospital

## Introduction

According to the Cancer Atlas of India (ICMR) cancer of the breast is the commonest cancer in women in urban areas. In 2018, 1,62,468 new cases and 87,090 deaths were reported for breast cancer in India. Based on world estimates about 10% of these are due to hereditary cancer syndromes. These are malignancies that have a *genetic predisposition and occur due to inherited pathogenic variant in various genes.* Cancers encountered commonly by a gynaecologist in her practice are those of breast, ovaries, endometrium and colon.

In this short communication we highlight the steps for evaluation and management of women at risk of hereditary cancer syndromes through a series of case examples. We will only discuss hereditary breast and ovarian cancer syndrome [HBOC] as a prototype.

A. **Who are candidates for genetic counselling and genetic testing for hereditary cancer syndromes?**

**Case 1**

Let us take the case of Mrs. SM (one who seeks genetic counselling is called *consultand,* Fig 1; III.1). She is an asymptomatic 35-year-old lady who wants to know her risk of developing breast cancer. Her mother, (Fig. 1; II.1) was diagnosed to have ovarian cancer at age of 50 years. SM's maternal grandmother (Fig. 1; I.1) died of breast cancer at 55 years, and one maternal aunt (Fig. 1; II.5) had ovarian cancer at the age 45 years. Mrs. SM was worried that she might develop cancer of the breast/ovary and therefore sought genetic counselling to determine the risk of cancer in her lifetime. Because of the presence of three family members being affected with breast / ovarian cancer, genetic testing for BRCA1/2 was recommended. As she was asymptomatic at the time of testing, *the molecular test was performed in her symptomatic mother.*

Genomic DNA was extracted from SM's mother's blood sample, amplified, and sequenced for BRCA1/2 gene. A pathogenic nonsense mutation c.2494C>T (p.Arg2494Ter) in exon 15 of BRCA2 gene was identified. This mutation had not previously been reported in Indian population, although it was reported in Korean population[1]. Once the mutation was identified in Mrs. SM's mother, SM herself was tested for this family-specific germline mutation. Genetic testing showed her to be positive for the mutation. Mrs SM was explained about her risk of developing cancer and counselled for increased cancer

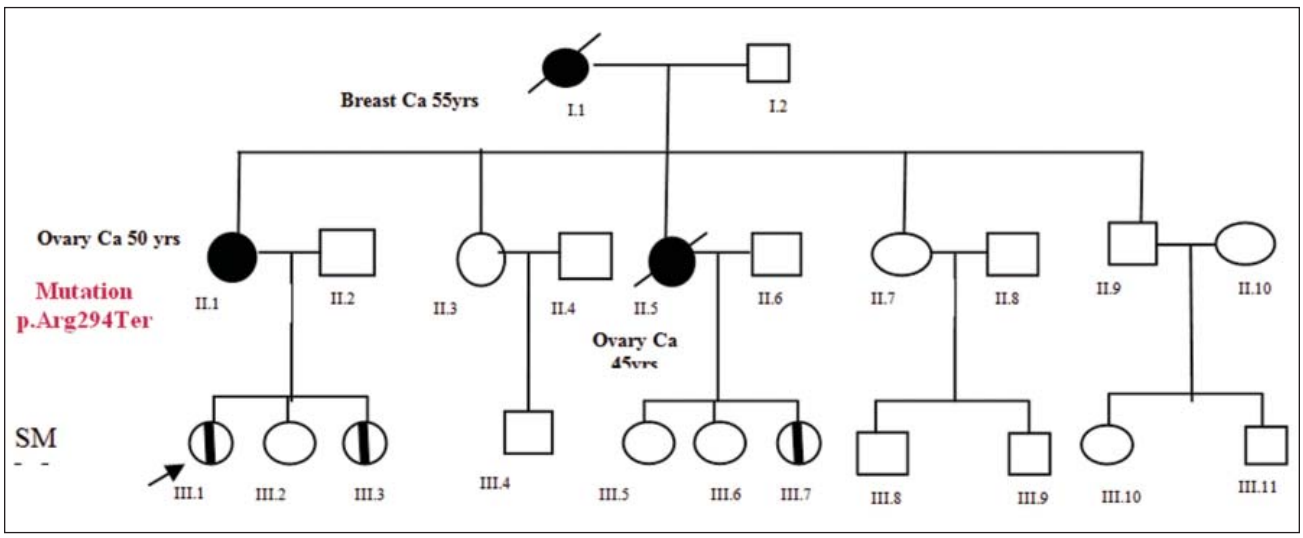



**Fig 1:** Detailed pedigree for Case 1

surveillance as per recommended guidelines. She was also advised to have her siblings, cousins and other family members tested for this particular mutation, so that they could also determine their risk of developing cancer.

Genetic testing was performed for her siblings (Fig. 1; III.2 and III.3), cousins (Fig. 1; III.5, III.6, III.7) and a maternal aunt (Fig. 1; II.7). Testing for family specific mutation revealed that *the SM's sibling (III.3) and cousin (III.7) were positive for the mutation* while the rest were negative for the mutation. Mutation screen negative family members now just had the general population risk for HBOC not requiring rigorous screening protocols. *Screen positive family members were counselled of the risk of developing cancer and managed as per guidelines.*

(*Following persons (II.7, III.1, III.2, III.3, III.5, III.6, III.7) underwent carrier screening for family specific p.Arg294Ter mutation, of which III.1, III.3 and III.7 were positive for the mutation (circle with black line) while II.7, III.2, III.5 and III.6 (empty circles) found to be negative for the same)

***Points Highlighted for Case 1***

a. First always test an affected woman.

b. *Hereditary Cancer risk assessment:* Three generation and beyond family history is indicated: information on affected members in the family, details of the pathology, imaging and reports. Testing the affected individual to identify the gene mutation and then the members at risk for the familial mutation[2]

c. Identify other women at an increased risk for hereditary cancer – all first degree relatives.

d. For each cancer case, *record the age at diagnosis and the type of cancer and if any blood DNA is available*

e. *Every woman with cancer does not require genetic testing as only 5-10% of breast cancer cases are hereditary*.

f. **Red flags in the history** to suggest a Hereditary Cancer Syndrome[3]

   i. Cancer diagnosed at a young age or less than 50 years for breast, ovarian, or colon cancer

   ii. Several different types of cancer in the same person

   iii. Multiple primary tumors, especially in the same organ in a single individual

   iv. Multiple close blood relatives that have the same type of cancer especially on the same side of the family

   v. Unusual presentation of a specific type of cancer (e.g., breast cancer in a man)

   vi. Occurrence of certain types of adult cancer in which the probability of harbouring a hereditary cancer syndrome is high like triple-negative breast cancer, epithelial ovarian cancer, fallopian tube cancer, or peritoneal cancer, especially serous histology (suggesting hereditary breast and ovarian cancer syndrome [10–15%]), colorectal cancer with DNA mismatch repair deficiency (suggesting Lynch syndrome [24%]), endometrial cancer with DNA mismatch repair deficiency (suggesting Lynch syndrome [12%])

g. **Who should undergo cancer genetic testing** (www.nccn.org [NCCN guidelines Version 1.2020][4]):

   1. The presence of a known pathogenic / likely pathogenic mutation in a blood relative in a cancer susceptible gene.
   2. Personal history of cancer at ≤ 45 years
   3. Personal history of cancer ≤ 50 years and a second primary breast cancer, ≥ 1 close blood relative with breast, ovarian, pancreatic, high grade or intraductal prostate cancer at any age or limited / unknown family history
   4. Personal history of male breast cancer
   5. Personal history of triple negative breast cancer at ≤ 60 years age
   6. Personal history of two or more types of cancer
   7. Personal history of epithelial ovarian cancer, fallopian tube, peritoneal cancer at any age
   8. A personal history of breast cancer and one or more relatives with breast cancer diagnosed before age 50, two or more relatives diagnosed with breast cancer at any age, one or more relatives with ovarian cancer, one or more relatives with male breast

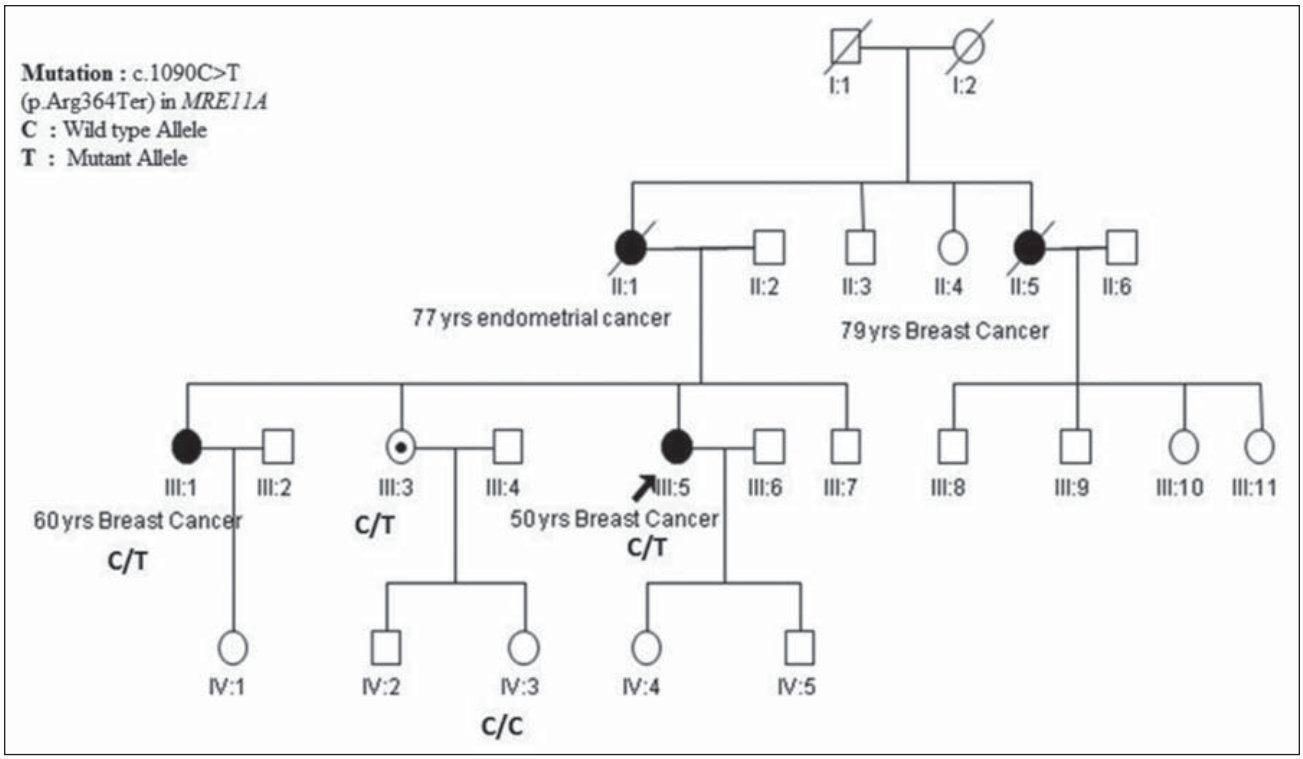



**Fig 2:** Detailed pedigree for case 2

cancer, or two or more relatives with prostate cancer or pancreatic cancer

9. A personal history of prostate cancer or pancreatic cancer with two or more relatives with BRCA-associated cancers
10. A history of breast cancer at a young age in two or more blood relatives, such as your parents, siblings or children
11. Any family history of cancer in a relative that meet one of the above criteria.

**What is the need for the above criteria for testing ?** – It has been reported that in patients not meeting the above there is a <1% possibility of identifying a mutation in a highly penetrant breast cancer gene and hence the clinical utility is limited[5,6].

**B. What test to perform?**

***Case 2***

Mrs RS was diagnosed with breast cancer at 50 years of age(Fig 2; III-5). Her elder sister (III-1) was diagnosed with breast cancer at 60 years. RS's mother (Fig 2; II-1) had endometrial cancer and maternal aunt (Fig 2; II-5) had breast cancer at the age of 77 and 79 years, respectively (Fig 2). With this family history genetic testing was advised.

Testing the BRCA1/2 for point changes and large deletions and duplications in *BRCA1/2* genes in RS did not identify a mutation. Further, *next generation sequencing (NGS) was performed* to test a panel of *30 known breast cancer susceptibility genes* in RS. A deleterious nonsense mutation c.1090C>T (p.Arg364Ter) in the *MRE11A* gene was identified. This mutation is previously reported in HBOC families (7, 8). Sanger confirmation was done for this mutation in RS.

After the identification of mutation in one affected person in the family (RS), the other affected and unaffected family members were advised to be tested for the family-specific germline mutation c.1090C>T (p.Arg364Ter). RS's sisters (Fig 2; III-1 who was affected and III-3 who was not affected) was found to be positive for the mutation. Her niece, 30 years old (Fig 2; IV-3) wanted to know her risk of developing cancer was tested for the familial mutation. She was negative for the mutation and not at an increased risk for breast and ovarian cancer[9].

(*Following individuals (III.1, III.3 and IV.3) underwent carrier screening for family specific

p.Arg364Ter mutation, of which III.1 and III.3 found to be heterozygous for the mutation, mentioned as C/T in pedigree while IV.3 was negative for the mutation and labelled as C/C in pedigree)

***Points highlighted from Case 2 :***

The genetic testing approach – There are **two main genetic testing options** for HBOC include

*a. BRCA 1 and 2 mutation testing*

*b. Multigene panel testing*

***Genetic testing should begin with an affected patient in the family***. The choice of testing will depend on two factors: 1. Mutation not known in the family 2. Mutation identified in one member of the family.

- The two options available include BRCA1 and 2 gene mutations or a multigene panel testing that include BRCA and other breast cancer susceptible genes
- *Both forms of testing have advantages and limitations*. In panel testing there are challenges of identifying variants of unknown significance for which there is limited data to guide for cancer risk and management (10). Hence genetic counselling prior to mutation testing is essential.
- If a mutation is previously identified in an affected patient, family at risk screening is performed by testing that one specific mutation. Whole gene sequencing / panel testing for this is not to be performed.
- *It is important to note that the testing should also include looking for rearrangements in the gene in addition to point changes.*
- Genetic testing is rapidly evolving with new information and knowledge of mutations. It is *important to relook at patients and families where the genetic basis was not established previously.*
- *Genetic counselling should be offered to all families with hereditary cancer syndrome.*

C. **Relevance of mutation testing:**

This is two fold:

1. ***Screening for at-risk individuals in the family:***

   Once a mutation is identified for a familial cancer syndrome in the family, targeted screening in at-risk individuals is possible. This will identify asymptomatic persons who harbour the mutation for appropriate counselling and management. Secondly for the affected person, the risk for development of additional cancers can be ascertained and managed appropriately[4].

   *For example, a pathogenic variant in BRCA1/2 genes confer a cumulative lifetime risk of 60 – 80% for developing breast cancer, 40 – 50% for ovarian cancer for BRCA1 mutation carriers and 10-20% for BRCA2 mutation carriers*. BRCA1 gene mutation is also associated with 20% risk of a second breast cancer and increased risk for males breast cancer. BRCA1 & BRCA2 mutations are also associated with increased risk for prostate cancer while BRCA2 mutations are associated with increased risk for pancreatic & stomach cancer and melanoma. Hence the information of the gene causing the cancer will allow the family to institute appropriate protocols for screening and management[4].

2. ***Risk reducing procedures:***

   Screening protocol in mutation positive carriers are mostly as per the NCCN guidelines, Version 1:2020[4]. Knowledge of genetic alteration would help the individual to undertake high risk screening and risk reduction options. The option of risk reducing mastectomy can be discussed in patients with BRCA1 and 2 mutations. As an example, women with BRCA1/2 mutations could consider risk reducing salpingo-oopherectomy (RRSO) after childbearing age or between 35-40 years to reduce the risk of ovarian cancer. Women with BRCA2 mutations can mostly delay RRSO to 40-45 years except for in unusual circumstances.

   Similarly screening recommendations vary for the different genes that are known to be associated with the hereditary cancer syndromes and will have to be referred to based on the genetic testing report.

3. ***Mutation guided treatment protocols:***

   Higher likelihood [7-28%] of BRCA1 and [1-17%] BRCA2 mutation carriers to have triple negative breast cancer and with younger age of affection. There are guidelines for the use of PARP (poly ADP-ribose polymerase)

inhibitors in BRCA1 /2 mutation positive patients.

There are reports of a more favourable outcome for ovarian cancer in mutation carriers.

## The Way Forward: Widening The Testing Net

Mary-Claire King, PhD, the American Cancer Society Professor of Genome Sciences at the University of Washington, discovered the two BRCA 1 and 2 genes in 1994. Based on her long experiences of dealing with breast cancer, she suggests ***that all*** women over 30 be offered testing for the breast cancer panel of ge*nes*. She notes that mutations are identified in many women after their first cancer as the family history did not warrant testing. The cancer gene can run silently through a family if the family is small, most members are young or some are males. Two recent papers also allude to a similar concept[11,12]. Beitsch et al., observed that testing all patients with a personal history of breast cancer *identified an actionable gene mutations in double the number of patients who* otherwise would not have qualified for testing based on the NCCN guidelines[12].

Easy access to reasonably cheap cancer genetic panel tests should allow for less stringent screening criteria. The benefits of a known germline mutation for screening, treatment and cascade family testing for the identified variant, would far outweigh the lost opportunities to testing based on existing guidelines[12]. Of course appropriate genetics support and counselling is mandatory to allow correct interpretation of the results of the genetic test.

**In summary,** genetic testing is important to identify mutations in highly penetrant genes for hereditary cancer syndromes as this information impacts clinical management protocols. The benefit for patients, at-risk family members and utility for instituting personalized management guidelines are well documented.

**Salient points in conclusion** include:

- Genetic testing is traditionally offered based on current guidelines
- Latest published literature alludes to the need to test young women with breast cancer to allow for maximal benefits from identification of a germline mutation.
- Appropriate tests should include gene sequencing and testing for gene rearrangements.
- Patients must undergo adequate pre-test and post-test genetic counselling with referral to genetic specialist with expertise in cancer genetics principles.
- The role of cascade screening in families where a pathogenic / likely pathogenic mutation is identified must be emphasized.
- The increasing role of precision medicine based on the gene causing the cancer.
- This is a rapidly advancing field. The testing and management guidelines must be reviewed frequently so as to keep abreast with the latest protocols for evidence based management of hereditary cancer syndrome.

## References


1. Choi DH, Lee MH, Bale AE, Carter D, Haffty BG. Incidence of BRCA1 and BRCA2 mutations in young Korean breast cancer patients. J Clin Oncol. 2004;22(9):1638-1645. doi:10.1200/JCO.2004.04.179
2. "My family health portrait. A tool from Surgeon General". *Public Health Genomics and knowledge database (v6.2.4).* Center for Disease control and prevention. Atlanta (USA): CDC; 2020. Available at https://phgkb.cdc.gov/FHH/html/index.html. Retrieved June 3, 2020)
3. Hereditary Cancer Syndromes and Risk Assessment: ACOG (American College of Obstetricians and Gynaecologists Committee) OPINION SUMMARY, Number 793. Obstet Gynecol. 2019; 134(6):1366-1367.
4. NCCN guidelines-version1.2020. Genetic/familial high risk assessment: Breast, Ovarian and pancreatic (https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf)
5. Pal T, Agnese D, Daly M, et al. Points to consider: is there evidence to support BRCA1/2 and other inherited breast cancer genetic testing for all breast cancer patients? A statement of the American College of Medical Genetics and Genomics (ACMG). Genet Med. 2020;22(4):681-685
6. Robson M, Domchek S. Broad Application of Multigene Panel Testing for Breast Cancer Susceptibility-Pandora's Box Is Opening Wider [published online ahead of print, 2019 Oct 3]. JAMA Oncol. 2019
7. LaDuca H, Stuenkel AJ, Dolinsky JS, et al. Utilization of multigene panels in hereditary cancer predisposition testing: Analysis of more than 2,000 patients. Genet Med. 2014; 16:830–837.
8. Maxwell KN, Wubbenhorst B, D'Andrea K, *et al*. Prevalence of mutations in a panel of breast cancer susceptibility genes in BRCA1/2-negative patients with early-onset

breast cancer. Genet Med. 2015; 17:630–638.

9. Sharma Bhai P, Sharma D, Saxena R, Verma IC. Next-Generation Sequencing Reveals a Nonsense Mutation (p.Arg364Ter) in *MRE11A* Gene in an Indian Patient with Familial Breast Cancer. Breast Care (Basel). 2017; 12(2):114-116. doi:10.1159/000457786
10. Committee on Practice Bulletins–Gynecology, Committee on Genetics, Society of Gynecologic Oncology. Practice Bulletin No 182: Hereditary Breast and Ovarian Cancer Syndrome. Obstet Gynecol. 2017;130(3):e110-e126.
11. Patel AP, Wang M, Fahed AC, et al. Association of Rare Pathogenic DNA Variants for Familial Hypercholesterolemia, Hereditary Breast and Ovarian Cancer Syndrome, and Lynch Syndrome With Disease Risk in Adults According to Family History. *JAMA Netw Open*. 2020;3(4):e203959.
12. Beitsch PD, Whitworth PW, Hughes K, et al. Underdiagnosis of Hereditary Breast Cancer: Are Genetic Testing Guidelines a Tool or an Obstacle? *J Clin Oncol*. 2019;37(6):453-460

# Proceedings of Virtual AOGD Monthly Clinical Meeting held at Lady Hardinge Medical College New Delhi on 26th March, 2021

## Rudimentary Horn – Miseries of Inaction at primary surgery - A case series

**Anuradha Singh, Manju Puri**

Unicornuate Uterus with non communicating Rudimentary Horn is a rare uterine anomaly. The reported Incidence in literature is 1 in 1 lakh cases. The usual presentation is often asymptomatic but they can have catastrophic sequelae and long-term morbidity if not diagnosed on time or remain unattended. Here we discussed, a case series of 3 cases with varied clinical presentation of noncommunicating rudimentary horn. All of them had undergone a primary surgery wherein rudimentary horn was either unattended or undiagnosed and later on, they had to suffer with grave consequences or long-term morbidities due to complications related to non communicating rudimentary horn. All had to undergo repeat surgery for definitive management

**Case 1:** 32 yr old lady P2L1A1, presented to gynecology OPD with severe secondary dysmenorrhoea which was not relieved with medical treatment. She had full-term LSCS in her first pregnancy done for breech presentation, which was uneventful. The second pregnancy resulted in spontaneous first-trimester abortion. In her third conception, she had laparotomy for a ruptured uterus at 34 weeks period of gestation with rupture and delivery of a stillborn baby at a government Hospital. After third pregnancy, she started having intractable secondary dysmenorrhea. MRI was done which showed the possibility of a rudimentary horn. The patient underwent laparotomy, non-communicating rudimentary horn was identified on the left side and was excised and the patient became symptom-free thereafter and later had successful full term pregnancy

**Case 2:** A 23 yr old lady, G2E1 presented to emergency with ruptured rudimentary horn pregnancy with a unicornuate uterus and underwent laparotomy with rudimentary horn excision and right salpingectomy. Both the tubes were found to be normal intraoperatively. She gave a history of laparotomy for ectopic pregnancy at a private hospital 1 yr back for which no papers were available and the condition was not diagnosed. She subsequently had rudimentary horn pregnancy, which ruptured and she had to undergo laparotomy with rudimentary horn excision

**Case 3:** A 27-year-old lady P2L2A1 presented with complaints of severe intractable secondary dysmenorrhoea for 2 years. She had a history of MTP followed by IUD vaginal delivery of the anencephalic fetus. It was followed by full-term LSCS for breech presentation in her third pregnancy. A provisional diagnosis of endometriosis/ rudimentary horn was made. MRI confirmed the diagnosis of a rudimentary horn. The patient underwent corrective surgery and was cured of her symptoms.

### Discussion

A unicornuate uterus with a rudimentary horn is the rarest variety of type 2 Mullerian anomalies, with a frequency of 1 in 1 lakh cases. Most of these women with rudimentary horn are asymptomatic till menarche or first pregnancy or present with dysmenorrhoea immediately after menarche or in the reproductive age group with secondary dysmenorrhoea and /or chronic pelvic pain. It can also lead to obstetric complications like habitual abortions, preterm labor, and malpresentation, rupture uterus in case of pregnancy in horn. Early diagnosis is important to avoid consecutive damage to the reproductive system, life-threatening complications like a rupture in pregnant state or long-term morbidity in terms of debilitating pelvic pain. All three patients had undergone previous primary surgery where the anomaly could not be diagnosed and these patients had to undergo repeat surgery which could have been easily avoided.

### Conclusion

It should be a routine for gynecologist and surgeon

to look for normal anatomy of the uterus and position of uterine appendages, insertion of round ligaments in any pelvic surgery, and common operations like caesarean sections. Index of suspicion should be high for timely detection and intervention, to avoid future morbidity and life-threatening complications.

## Indiscriminate Use of Folic Acid Among Women of Reproductive Age Group: Time to revisit

**Manju Puri, Kanika Chopra**

Folate is an important factor in DNA synthesis, its stability, integrity and repair requires Vit B12 as a cofactor. In the presence of VitB12 deficiency, folate is not metabolized and can result in aberrations of DNA synthesis and epigenetic aberration. Epigenetics is defined as the changes in the periphery of the DNA and not in the sequence of DNA. Imbalance between folic acid-vitamin B12 levels have been found to be associated with breast, non-colorectal cancers and impaired neurocognitive development, fetal anomalies and fetal growth retardation.

Folic acid is indicated in reproductive age group as universal periconceptional supplementation to prevent neural tube defects in the dose of 0.4 mg/day. Supplementation should start ≥1 month prior to pregnancy in this group of women. High dose prophylaxis is required in women with either parent or personal history of NTD where the dose is 4 mg/day. In women on antiepileptic agents valproic acid or carbamazepine, on drugs that reduce folic acid activity like sulfasalazine, trimethoprim, maternal conditions associated with decreased absorption or increased clearance e.g IBD, Celiac disease, Bariatric surgery and in those with diabetes the dose is 1 mg/day. In this group of women supplementations should start ≥3 months prior to pregnancy and continued up to 12 weeks of gestation. Dose of folic acid reduces to 0.4 mg/day after 12 weeks (ACOG 187 2017). In India we routinely supplement all pregnant women preconceptionally and in first trimester with 5 mg of folic acid per day which is nearly 12.5 times higher than the recommended dose.

We conducted a study on 100 pregnant women at their first registration visit in first trimester at LHMC they had not received any supplementation prior. We estimated serum folic acid, vit B12 levels in them and found that 97% were folate replete and 60% were vitamin B12 deficient. Another study comparing serum Folic acid, Vitamin B12 in women with and without RPL was conducted in our department. 107 women of RPL and 343 controls were enrolled, and it was found that majority of women with RPL (cases) were folate replete (97.5%) and 64 % were Vit B12 deficient. Vitamin B12 deficiency was found to be a significant risk factor for RPL (OR = 16.39). Recurrent pregnancy loss cases were found to be hypermethylated with respect to MTHFR gene-specific methylation as compared to the non-pregnant controls in another study done by our department and it was found that hypermethylation of MTHFR gene was associated with imbalance between serum folic acid and Vitamin 12 level, emphasizing the possible role of epigenetic aberration resulting in disease emergence.

To conclude, indiscriminate supplementation of folate in high doses should be avoided and Vit B12 supplementation need to be considered in women deficient in Vit B12 to prevent epigenetic aberrations at both intergenerational and transgenerational levels.

## Flash Glucose Monitoring (FGM): New paradigm for glycemic monitoring in pregnant women with diabetes

**Pikee Saxena, Khushbu Kumari, Anupam Prakash Manju Puri, Sachin Jain**

This presentation was made to make the obstetricians aware about the application of Flash glucose monitoring (FGM) system to evaluate glycaemic variability (GV) and patient satisfaction in pregnant women with diabetes.

Glycaemic variability is defined as the degree of glucose fluctuations in an individual over one day (intraday GV) or between different days (interday GV). It has been observed in the Diabetes Control and Complications Trial (DCCT) that in spite of similar HbA1c levels, patients treated with conventional methods showed a significantly higher rate of complications due to higher glycemic variation. Fluctuating glucose levels result in increased oxidative stress with endothelial damage,

dyslipidaemia and increased rates of micro and macro vascular complications which may possibly result in macrosomia, sudden intrauterine death and other complications.

A woman with GDM or pregestational diabetes has to measure glucose levels 4-7 times/day by Self-Monitoring of Blood Glucose (SMBG) which still gives only a snapshot of the overall picture instead of reflecting the actual daily pattern besides being painful and inconvenient for the patient. Flash glucose monitoring system (FGM) generates Ambulatory Glucose Profile (AGP) report and is a relatively new and simple technology which provides glucose values every 15 minutes using a sensor inserted in the interstitial fluid below the skin. It is currently being used to evaluate all dimensions of glycaemia and to titrate therapeutic intervention in patients suffering from type1/type 2 diabetes.

The aim of the current pilot study was to use FGM for evaluating glycaemic variability and patient satisfaction in comparison to the conventional SMBG in pregnant women with GDM and Type1/ Type 2 diabetes in pregnancy.

This prospective study was conducted in Lady Hardinge Medical College and SSKH on 70 pregnant women with diabetes where blood sugar levels were monitored by FGM and by conventional self-monitoring of blood glucose (SMBG) using a glucometer.

FGM generated 19,950 readings versus 1470 readings by SMBG over 3 days. Glucose values measured by FGM and SMBG had significant positive correlation ($r > 0.89$; $p<0.001$). Significant difference ($p<0.001$) was present between minimum glucose values by FGM (52.49±15.42 mg/dl and SMBG (72.74±18.30 mg/dl). FGM (20.9%) was able to pick exact duration of hypoglycaemia while one third of this duration was missed by conventional SMBG (14.7%; $p<0.05$). Hypoglycaemic episodes were observed in 92.9 % women by FGM compared to 45.7% by SMBG ($p<0.001$). No significant difference was observed in maximum glucose level or duration of hyperglycaemia by both methods. FGM identified hyperglycaemia in 74% women vs. 52% by SMBG ($p <0.001$). GV calculated by using MODD by FGM was 118.4±52.4mg/dl and by SMBG was 83.2±53.2 mg/dl ($p <0.001$). 100% women preferred AGP vs. SMBG. Three interesting case scenarios were discussed where FGM was used for titrating medical nutrition therapy and insulin dose for reducing glycemic variability.

This is the first study to evaluate FGM for GV and patient satisfaction in women with gestational diabetes mellitus. Significant correlation was observed in corresponding glucose values by FGM and SMBG. FGM was more sensitive in detecting GV and hypoglycaemic excursions compared to SMBG. All women preferred FGM over SMBG for monitoring glucose in pregnancy.

# Announcement

## Calendar of Virtual Monthly Clinical Meetings 2020-21

| | |
|---|---|
| 29th May, 2020 | B L Kapoor Hospital |
| 26th June, 2020 | VMMC & Safdarjung Hospital |
| 31st July, 2020 | AIIMS |
| 14th August, 2020 | Lady Hardinge Medical College & Smt. Sucheta Kriplani Hospital |
| 28th August, 2020 | Army Hospital- Research & Referral |
| 11th September, 2020 | Indraprastha Apollo Hospital |
| 25th September, 2020 | DDU Hospital |
| 27th November, 2020 | MAMC Hospital |
| 18th December, 2020 | Sir Ganga Ram Hospital |
| 1st January, 2021 | ESIC PGIMSR Hospital |
| 29th January, 2021 | Dr RML Hospital |
| 26th February, 2021 | UCMS & GTB Hospital |
| 26th March, 2021 | Lady Hardinge Medical College |
| 30th April, 2021 | Apollo Hospital |

## AOGD Events Held

On 26th February 2021 - **AOGD Virtual Monthly Clinical Meeting** organized by University College of Medical Sciences and Guru Teg Bahadur Hospital, New Delhi.

On 27th February 2021- Webinar CME on **Women's Health** by Institute of Obstetrics and Gynaecology, Sir Ganga Ram Hospital, New Delhi.

On 27th February 2021- Webinar on **Breast and Cervical Cancer Prevention** by Breast Cancer and Cervical Cancer Screening & Screening Committee AOGD in association with Asian Society of Mastology and American College of Surgeons.

On 3rd March 2021- Virtual Quiz on **Critical Care in Obstetrics** by Institute of Obstetrics and Gynaecology, Sir Ganga Ram Hospital, New Delhi under the aegis of AOGD.

On 5th March 2021- FAQs on **Multi Micro Nutrients in Pregnancy** under the aegis of AOGD.

On 6th March 2021 Webinar **Providing Quality Care in Abdominal Malformations** by Fetal Medicine Sub-Committee & QI committee of AOGD And Delhi Association of Paediatric Surgeons.

On 6th March, 2021 - Webinar on **Hormones and Cancer Interplay & Borderline Ovarian Tumours How Clinical Decisions Improve Outcome?** Under the aegis of Reproductive Endocrinology Committee AOGD and DGF-South-West.

On 8th March, 2021- FAQ on **Screening of Cervical Cancer** under the aegis of AOGD

On 6th to 8th March, 2021- **FOGSI Screening Camp and Awareness Drive on Preventable Cervical & Brest Cancer** under the aegis of AOGD.

On 9th March 2021- FAQs on **Ovulation Induction** under the aegis of AOGD.

On 16th March 2021- FAQs on **Female Sexual Disorders** under the aegis of AOGD.

On 18th March 2021- FAQs on **HIV in Pregnancy** under the aegis of AOGD.

On 1st April 2021 - Webinar on **Fibroid Focus** by DGF-outer Delhi and AOGD infertility committee organised by Dr. Jyoti Malik and Dr. Kavita Agarwal.

On 2nd April 2021- FAQs on **Care of Pregnant Women** under the aegis of AOGD

## Forthcoming Events

On 30th April 2021 **AOGD Virtual Monthly Clinical Meeting** will be organized by Apollo Hospital, New Delhi