

# MAMC, Issue 4, December 2021





### Preventive Care in Obstetrics.....A Stitch in Time



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### **From The President's Pen**



Dear friends,

Warm Greetings to all !

First and foremost, I thank all the esteemed NARCHI members for making the 27<sup>th</sup> annual NARCHI e-conference held in august 2021 a grand success. It was the hard work of the core NARCHI team coupled with all your support and co operation which made this possible. My heartiest congratulations to you all.

I also congratulate Dr Manju Puri and Dr Reena Yadav for being elected as president and vice president for NARCHI 2022-2024. I am sure their tenure will see the association rise to new heights and we offer them our full support.

As the Covid crisis continues and the threat of the third wave looms large upon us, we release this issue of the NARCHI bulletin on 'Preventive care in Obstetrics'. When we talk about 'prevention' in obstetrics the first thing to strike us all is 'preventing maternal mortality', an important indicator of the health care delivery system of any nation. Reduction in the preventable causes of maternal mortality will help us in achieving the SDG target of maternal mortality ratio (MMR) of less than 70 maternal deaths per 100,000 live births by the year 2030 from the current status of 113 maternal deaths per 100,000 live births...This issue provides an insight into the preventive aspects of some important causes of maternal and perinatal morbidity and mortality like anemia, hypertension, prematurity, fetal growth restriction, genetic disorders and congenital anomalies. 'Immunization' during pregnancy and Newborn screening methods have also been dealt with.

I am sure you will find the bulletin useful.

Wishing you all a 'Merry Chirstmas' & a very 'Happy and safe New Year'!

**Dr Asmita Muthal Rathore** 

President NARCHI Delhi

### From The Secretary's Desk



Dear Members,

Warm Greetings!

We extend our sincere thanks to all our members for making 27<sup>th</sup> NARCHI Annual Conference- NARCHIDELCON-2021, a grand success. The conference committee did a spectacular job of organizing five preconference workshops and 22 scientific sessions. The other highlights were over 120 paper presentations, Sheela Mehra quiz and oration by Sir S Arulkumaran. The conference was well received with overwhelming response for the handpicked scientific sessions delivered by eminent faculty.

In co-ordination with Health and Family Welfare Training Centre, New Delhi; our team has been instrumental in conducting training sessions for trainers to promote family planning services at the primary healthcare level also. A successful TOT program was conducted over two days where nearing seventy trainers were trained.

Furthering our endeavor to fulfil our motto of promoting women and child health, we congratulate our editorial team for having this bulletin on 'Preventive care in Obstetrics' a topic which covers many vital aspects important for clinicians and academicians alike.

Preventive Obstetrics is imperative for promoting maternal and neonatal health through prevention and early detection of complications during pregnancy. This involves screening and periodic examinations and detecting congenital anomalies in-utero along with newborn screening. We hope this bulletin will be instrumental in laying a road map for preventive care in Obstetrics and Gynaecology.

Happy reading!

Secretary

Dr Sangeeta Gupta

**Dr Niharika Dhiman** 

**Dr Chetna Arvind Sethi** 

### **From The Editorial Board**



Hello Friends,

Greetings of the winter season!!

To begin with, we would like to sincerely thank all NARCHI members for making the 27<sup>th</sup> annual NARCHI conference a huge success. Your constant support and encouragement and the complete dedication of the organizing team did it all and a thunderous applause are in order.

As we inch towards the twilight of our tenure, we bring to you the fourth issue of the NARCHI e-bulletin on 'Preventive care in Obstetrics'. The bulletin begins with some comprehensive information on "Preconceptional and antenatal preventive care in medical and obstetric disorders "put forth by Dr. Devender Kumar. Evidence-based, crucial preventive and screening strategies in obstetric conditions like prematurity and fetal growth restriction and medical conditions like anaemia, gestational diabetes mellitus and hypertension have been very well described by him. The important topic of Prevention and early detection of genetic disorders", aneuploidies and congenital anomalies, a topic of great concern in this medicolegal age has been justly written by Dr Chittala Kiran. 'Immunisation in Obstetrics and Gynecology' has been beautifully described by Dr YM Mala. Newborn screening for various disorders has been covered by Dr Seema Kapoor and her team, renowned faculty from the department of Paediatrics, MAMC. As knowledge is insufficient without recent updates, the same have been included with each topic. WHO recommendations on Labour Care Guide have been given a special corner. As always, a quiz for youngsters and snippets related to women path breakers have also been included.

We hope you will find these articles as interesting and valuable as we have found them.

Wishing you all a 'Merry Christmas' and a 'Happy New Year' filled with life and laughter. Happy reading....

#### **Narchi Editorial Team**

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# Preconception and Antenatal Preventive Care: Medical and Obstetric Disorders

#### **Devender Kumar**

Professor, Department of Obstetrics and Gynaecology, MAMC and Associated LNH

Preconception and antenatal care are essential biomedical, behavioral and community help to couples planning conception and continuing with pregnancy. Preconceptional anxiety and antenatal tensions are high if there is history of congenital malformations, pregnancy loss or hereditary disorders in the family. Most of these may be avoided or markedly reduced if appropriate preconceptional counseling and effective antenatal care are available. Preconception care will have positive impact on maternal and child health outcomes. A few such clinical conditions are discussed here with latest updates.

#### **Hypertensive Disorders**

Hypertensive disorders are most challenging during pregnancy especially pre-eclampsia. Gestational hypertension and preeclampsia (PE) are seen in 5 -10 % of gestations. It forms a deadly triad of maternal morbidity with hemorrhage and sepsis. Hypertensive disorders during pregnancy particularly pre-eclampsia have acute and long-term consequences for the mother and the fetus.<sup>1,2</sup> That include risk of chronic hypertension, cardiovascular disease, stroke, and metabolic syndrome for the mother and complications of prematurity for the neonate, along with increased risk of hypertension, diabetes, and neurological impairment later in their lives.<sup>3-7</sup> Psychological consequences from experiencing preeclampsia, especially in severe cases, also have been reported for the woman and her family.8

Obstetricians have a challenge to early diagnose the disorder and predict the severity for prognosis. Along with that, obstetricians also have to plan the management for optimal growth of the fetus and least morbidity to mother. Risk of recurrence of gestational hypertension or pre-eclampsia are 16% if delivered at term, 25% if delivered before 34weeks, 55% delivered before 28 weeks.<sup>9</sup>

#### **Prediction of Pre-eclampsia**

Pre-eclampsia syndrome is predominantly considered as the consequence of impaired placentation. Placenta

is mature and functional by 18 – 20 weeks so this condition is diagnosed after 20 weeks of pregnancy. There are two types, early onset PE, requiring delivery before 34 weeks' gestation and late onset PE, with delivery at or after 34 weeks, because the former is associated with a higher incidence of adverse outcome.<sup>10-13</sup>

#### Age of the Mother and Urinary Tract Infections

Mothers who are <20 years of age and  $\geq$ 30 years old are 5 to 7 times more likely to develop preeclampsia compared to the 20-29 age group.<sup>14-19</sup> Presence of a history of UTI increases the risk of pregnant women of developing preeclampsia by 3 times. It has also been hypothesized that renal damage related to preeclampsia may also underlie the patient's predilection to kidney infections.<sup>18-19</sup>

#### Mean Arterial Pressure<sup>20</sup>

In low-risk populations a mean arterial pressure in the second trimester best predicted pre-eclampsia. Mean arterial pressure is a better predictor for preeclampsia than systolic and diastolic blood pressure. In a normotensive case, blood pressure measurements at the first antenatal visit in the first and second trimester does not help predict pre-eclampsia.

*Roll-over test* had been recommended as a routine test for every pregnant patient between 28 – 32 weeks' gestation for the early diagnosis of hypertension of pregnancy<sup>21,22</sup> but was later found to have low sensitivity.<sup>23</sup>

#### **Calcium Excretion and Creatinine Clearance**

Calcium excretion has been found to be reduced in preeclampsia.<sup>24,25,26</sup> Rodriguez et al, found a sensitivity of 70% and specificity of 95% for the development of PE using a Ca/Cr ratio of 0.04 (conventional units) in a fasting spot urine from 88 normal pregnant women. Using a urinary calcium concentration threshold of 12 mg/dL, Sanchez-Ramos et al found a sensitivity of 85% and specificity of 91% for predicting preeclampsia.

#### **Uterine Artery Doppler**

Uterine artery Doppler ultrasonography predicts pre-

eclampsia, the maternal consequence of placental disease, more confidently than intrauterine growth restriction. Specifically, an increased pulsatility index with notching in the second trimester best predicted overall pre-eclampsia in low-risk and high-risk patients. An increased pulsatility index or bilateral notching best predicted severe pre-eclampsia.

The predictive accuracy of first-trimester uterine artery Doppler is better in the detection of early-onset preeclampsia than late-onset disease. The sensitivities and specificities of uterine artery Doppler is not effective and low, that limits its utility as a disease marker in isolation.<sup>27</sup>

### Maternal Serum PAPP-A, PIGF and Glycosylated Fibronectin (Biochemical Markers)

In pregnancies that develop PE, MoM values of UtA-PI and MAP at 11–13 weeks' gestation were increased and the values of serum PAPP-A and PIGF were decreased. The best individual biomarker for preterm PE was PIGF, followed by UtA-PI and MAP and then PAPP-A. The performance was better in combination of maternal factors, MAP, UtA-PI and serum PIGF. Screening for preterm PE at 11–13 weeks' gestation identifies a group of pregnancies that would benefit from prophylactic use of aspirin. Screening for preterm PE should be universal rather than selective. Placental growth factor (PIGF) is the most discriminating biomarker for PE. PIGF levels are significantly lower in pregnant women who develop PE, and PIGF combined with other factors has 93% detection rate for the risk of developing PE in the first trimester with a false-positive ratio of 5%. The other factors included maternal history, prior and family history of PE, maternal blood pressure, uterine artery pulsatility index, and pregnancy-associated plasma protein A (PAPP-A).<sup>28</sup> Maternal serum glycosylated fibronectin levels in the first trimester have also been found to be significantly higher in women with preeclampsia (P < .01) and remain higher throughout pregnancy (P < .01).<sup>29</sup>

#### **Prevention of Preeclampsia**

#### Calcium Therapy

High-dose calcium supplementation ( $\geq$  1 g/day) may reduce the risk of pre-eclampsia and preterm birth, particularly for women with low calcium diets (low-quality evidence). The treatment effect may be overestimated due to small-study effects or publication bias. It reduces the occurrence of the composite outcome 'maternal death or serious morbidity', but not stillbirth or neonatal high care admission.<sup>26</sup>

#### Low-dose Aspirin therapy<sup>30,31</sup>

Administering low-dose aspirin to pregnant women leads to small-to-moderate benefits, including reductions inpre-eclampsia (16 fewer per 1000 women treated), preterm birth (16 fewer per 1000 treated), the baby being born small-for-gestational age (seven fewer per 1000treated) and fetal or neonatal death

Risk factor	Score	Risk Factor	Score	Risk Factor	Score
Age older than 35 years	1	Inter pregnancy interval more than 7 years	1	Multifetal pregnancy	2
Age younger than 19 years	1	Conceived with Assisted Reproductive (IVF/ ICSI) Treatment	1	Hypertensive disease during previous pregnancy	2
Maternal Anemia	1	MAP>85 mm of Hg	1	Pregestational diabetes mellitus	3
Obesity (BMI >30)	1	Chronic vascular disease (Dyslipidemia)	1	Chronic hypertension	3
Primigravida	1	Excessive weight gain during pregnancy	1	Mental disorders\$	3
Short duration of sperm exposure (cohabitation)	1	Maternal hypothyroidism	2	Inherited / Acquired Thrombophilia	3
Woman born as small for gestational age	1	Family history of preeclampsia	2	Maternal chronic kidney disease	3
Family history of cardiovascular disease	1	Gestational diabetes mellitus	2	Autoimmune disease (SLE / APLAS / RA )	3
Polycystic ovary syndrome	1	Obesity (BMI > 35 kg/M2)	2	Pregnancy with Assisted Reproductive (OD or Surrogacy) Treatment	3

**Table 1:** Scoring system for Hypertensive Disorders of Pregnancy Gestosis Score

Ensuring management using following factors will ensure optimum management of women at high risk for Preeclampsia

- 1. Corelate gestational age of previous pregnancy associated with preeclampsia and its severity
- 2. Assess for any other comorbidities including lifestyle disorders
- 3. Complete evaluation of medical conditions
- 4. Multi-professional team management will provide better outcomes
- 5. Update patient and relatives about realistic management and their options
- 6. Avoid pregnancy till comorbidities are under control
- 7. Case-based management protocols along with clear hospital policies are essential. These cases should be advised about calcium supplementation and role of low dose aspirin
- 8. Blood pressure should be monitored along with urine test for albuminuria on every antenatal visit
- 9. Patient should be counseled to monitor their BP at home regularly and report if 140/90 mm Hg or more
- 10. Patient should be educated about warning signs like headache, blurring or loss of vision, epigastric pain

(five fewer per 1000 treated). Overall, administering antiplatelet agents to 1000 women has been found to translate to 20 fewer pregnancies with serious adverse outcomes. The quality of evidence for all these outcomes was high.

The ASPRE trial<sup>31</sup> has shown that, in pregnancies identified at 11–13 weeks' gestation by screening with maternal factors and biomarkers as being at high-risk for pre-eclampsia (PE), administration of aspirin (150 mg/day from 11–14 to 36 weeks' gestation) reduces the rate of early PE with delivery at < 32 weeks' gestation by about 90% and that of preterm PE with delivery at <37 weeks by 60%. In the ASPRE study, eligible women with an estimated risk for preterm PE of > 1 in 100 were invited to participate in a double-blind trial of Aspirin (150 mg per day) vs placebo from 11–14 weeks until 36 weeks' gestation. In the aspirin group, the incidence of preterm PE was reduced by 62%.

High risk factors for preeclampsia are essential hypertension, history of preeclampsia in previous pregnancy, obesity, renal disorders, diabetes, thyroid disorders, hyperaldosteronism, multiple pregnancy, underlying APLA syndrome or family history. Table 1 gives the risk scoring for preeclampsia. This HDP-Gestosis score has been proposed jointly by FOGSI and ICOG<sup>32</sup>

All women with score equal/ more than 3 should be started with Aspirin 75-150 mg 12 weeks onwards.

#### Anemia<sup>33-36</sup>

India is facing a serious burden of anemia where more than half of the women (51%) of reproductive age suffer from anemia (Global Nutrition Report 2017). According to the National Family Health Survey 4 (NFHS-4), 53.1% of non-pregnant women aged 15-49 years, 50.3% of pregnant women aged 15-49 years, and 53% of all women aged were anemic in India.<sup>37</sup> National Nutritional Anemia Prophylaxis Program was launched by Maternal and Child Health (MCH) division of Ministry of Health and Family Welfare (MOHFW) in 1970 to prevent nutritional anemia in mothers and many other initiatives were taken but it was observed during the period 2005 to 2015, the reduction of anemia was less than 1% per annum. This slow and ineffective change is matter of concern and taken seriously. Along with PMSMA, The Anemia Mukta Bharat (AMB) was launched in 2018 to reduce prevalence of anemia all over India. It is initiative of the Ministry of Health and Family Welfare (MoHFW) & United Nations Children's Fund (UNICEF). The scheme is part of the Intensified National Iron Plus Initiative (NIPI) Program and comes under the Prime Ministers overarching scheme for holistic nutritional Nourishment (POSHAN) Abhiyan. It focusses on six target beneficiary groups, through six interventions and six institutional mechanisms to achieve the envisaged target under the POSHAN Abhiyan(6x6x6):

- 1. Prophylactic Iron and Folic Acid supplementation
- 2. Deworming
- 3. Intensified year-round Behaviour Change Communication Campaign (Solid Body, Smart Mind) including ensuring delayed cord clamping in newborns
- 4. Testing of anemia using digital methods and point of care treatment
- 5. Mandatory provision of Iron and Folic Acid fortified foods in government-funded health programmes
- 6. Addressing non-nutritional causes of anemia in endemic pockets, with special focus on malaria, haemoglobinopathies and fluorosis

Complying with the targets of POSHAN Abhiyaan and National Nutrition Strategy set by NITI Aayog, the Anemia Mukt Bharat strategy has been designed to reduce prevalence of anemia by 3 percentage points per year among children, adolescents and women in the reproductive age group (15–49 years), between the year 2018 and 2022. It aims to reduce iron deficiency anemia in pregnancy from 50%(NFHS 4) to 32% as National target 2022.

As per the guidelines of this Andolon, daily one iron and folic acid tablet must be started from the fourth month of pregnancy (that is from the second trimester) and continued throughout pregnancy (minimum 180 days during pregnancy). Each tablet contains 60 mg of elemental iron + 500 mcg of folic acid and it is sugarcoated, red-color now. All pregnant women must have Hb and hematocrit estimation in first trimester and at term.

#### **Fetal Growth Restriction**

Fetal growth restriction (FGR) is defined as failure of the fetus to reach its potential to grow in the womb. Approximately 10% of pregnancies suffer from impaired fetal growth. Fetal growth is evaluated by using standard references of population based estimated fetal weight or birth weight for different gestational ages. FGR is diagnosed when estimated fetal weight or birth weight is less than 10<sup>th</sup> percentile to population standards. FGR is associated with increased fetal and neonatal mortality and morbidity. It is linked to perinatal adverse events (prematurity, cerebral palsy, intrauterine fetal death, neonatal death). It is also associated with adult pathologic conditions (obesity, hypertension, type-2 diabetes).

FGR is associated with low levels of pregnancy associated plasma protein A (PAPPA), an Insulin–like Growth Factor Binding Protein Protease.<sup>37</sup> Increased resistance in the uterine arteries is another important investigation as it is associated with poor obstetric outcome like preeclampsia, IUGR or prematurity, the positive predictive value was found to be only 15% for IUGR. Gomez et al. in 2006 examined the changes in the uterine flow between the first and second trimester. It correlated with occurrence of FGR and persistent low vascular indices had highest risk. Doppler assessment is not advised for low-risk population to screen FGR.<sup>38</sup>

For risk stratification, high-risk mothers are evaluated with maternal and familial history, maternal anthropometry (maternal pre-pregnancy weight and height), maternal nutritional status, exact gestational dating, serial fundal height estimation, non-stress test (NST), ultrasound with Doppler, and accurate fetal weight measurements. An abnormal HC/AC ratio is more specific and have negative predictive value for asymmetric FGR. Biophysical profile (BPP) reflects the fetal acid–base status and has been used to assess the risk for FGR. NST is abnormal in FGR and reactivity disappears followed by fetal breathing. Amniotic fluid reduction is the last event. Doppler studies are helpful to assess placental insufficiency. For FGR, uterine artery Doppler, umbilical artery Doppler, middle cerebral artery Doppler, Cerebro-placental ratio (CPR), ductus venosus Doppler, and aortic isthmus Doppler are used to define the prognosis.

Uterine arteries are predictors of maternal circulation, whereas the umbilical and middle cerebral arteries provide information about the fetal circulation. Uterine artery Doppler are not sensitive and specific to predict adverse outcome in SGA fetuses. Umbilical artery (UA) Doppler provides both diagnostic and prognostic knowledge in the management of FGR. The various Doppler abnormalities seen in IUGR are increased resistance in blood vessels or absent and reverse end diastolic flow (AREDF). Increased umbilical artery Doppler perfusion index (PI) has shown good correlation of early identification of FGR, both alone or with the Cerebro-placental ratio (CPR) ratio. AREDF is usually associated with injury to various fetal organs or death.

#### Prediction Prevention and Treatment of Preterm Labor

Preterm is referred to gestation age less than 37 weeks and in no circumstances, it should be considered as normal labor. Preterm labor is 5-18% prevalent among live births worldwide.<sup>39,40</sup> It is ironical that Obstetrician has to predict and prevent premature births, vis a vis will deliver a preterm baby due to medical conditions like eclampsia, Rh isoimmunization or FGR. Most of the preterm labor are spontaneous (80%).<sup>41</sup> As an expert he/she has to ensure the fetal survival and prevent perinatal morbidity mortality. Preterm labor is associated with complications which not only affects the baby but parents and attending physicians (obstetrician or neontologist) too. It is psychological and financial burden on family and community. "Going home" chances of preterm baby depends on gestational age, birth weight, lung maturity and neural protection at birth. Surfactant and modern neonatal ICU (NICU) have improved the survival of 24-week baby but their neural development is still guestionable.<sup>42,43</sup>

The common causes of preterm births are multiple gestation, preterm, hypertensive disorders like severe

pre-eclampsia or eclampsia, pre-labor rupture of membranes, antepartum hemorrhage, hydramnios, congenital malformations etc. Preterm births can be divided in three categories as extremely preterm (less than 28 weeks), very preterm (28 to 32 weeks) and moderate to late preterm (32 to 37 weeks).

Maternal causes like previous obstetric history of preterm birth, multiple gestation, periodontal disease, obesity, heart disease, antepartum hemorrhage or hypertensive disorders are risk factors for preterm birth. The most common predictor of preterm birth is past history of preterm labor. Preterm birth is also seen among smokers, drug abusers, history of cervical amputation or LEEP procedure. It can occur in cases with fibroid uterus or genitourinary infections.44-45 Other than past history of preterm birth, other predictors are cervical length, uterocervical angle (anteversion), Placental alpha-microglobulin-1 (PAMG-1), fetal fibronectin, and insulin-like growth factor binding protein-1 (IGFBP-1) are also associated with preterm labor. Maternal serum calponin 1 and ratio of maternal serum alpha fetoprotein (AFP) to amniotic fluid AFP are also potential predictor of preterm birth. The Preterm SAMBA study results will throw more light on preterm birth prediction. It is based on metabolomics techniques, and well-defined protocols for sample collection among multi-ethnic populations.<sup>46</sup> Cervix length of 2.5 cm or less has 55% sensitivity and 10% false positive rate. Concentration of more than 50 ng/ ml of fetal fibronectin is positive considered as positive predictor of preterm labor.

Good antenatal care is the single most effective way to prevent or decrease the complications of preterm labor. All cases with history of preterm labor before 34 weeks should be offered vaginal progesterone supplementation from 16 weeks onward (likelihood decrease of preterm labor by 45%).47 Prophylactic as well as rescue cerclage is useful if cervical length is 25 mm or less between 16 – 24 weeks of pregnancy. Consider tocolysis (preferably nifedipine and avoid betamimetics) for all cases of threatened preterm labor from 24 weeks or more till 34 weeks of pregnancy. This does not prevent preterm births but definitely help in providing the corticosteroids for fetal lung maturity. Best tocolysis is oxytocin receptor antagonists. Tocolytics (prostaglandin inhibitors and calcium channel blockers) are must for antenatal corticosteroids and magnesium sulfate administration.<sup>47</sup> In some cases, it will give time to transfer the mother to a tertiary facility where neonatal intensive care unit is available. Intravenous magnesium sulfate has neuroprotective effects on preterm births and should always be used between 24+0 and 33+6 weeks of pregnancy. It decreases the risk of cerebral palsy in infants born at less than 32 weeks' gestation. It should be given in established preterm labor cases too during this period of gestation.

#### Conclusion

Medical and obstetric disorders are related to high maternal and perinatal morbidity and mortality. Preeclampsia, anemia, fetal growth restriction and prematurity are important disorders amongst these. Many complications may be avoided or markedly reduced if appropriate preconceptional counseling with identification of high risk factors and antenatal care with right preventive measures are available.Every couple must have a choice to plan their pregnancy and get good preconception counseling. It is not only the health education and promotion for society but for community and nation too. It can play a major role in reduction of maternal as well as perinatal morbidity.

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### The prevention of disease today is one of the most important factors in line of human endeavor.

- Charles Mayo

### Prevention and Early Detection: Genetic Disorders, Aneuploidy, Congenital Anomalies

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The introduction of prenatal care is a major advance in the care of pregnant women and has played a pivotal role in the substantial reduction in maternal and perinatal mortality achieved during the last century.

Few decades ago, antenatal care visits were concentrated during the third trimester, as most common complications occur towards the end of pregnancy. With introduction of early trimester ultrasound and reliable biochemical markers, for the last two decades, we are able to screen and diagnose various genetic disorders, congenital anomalies and foetal aneuploidies in prenatal period. The advances in prenatal care play a major role in the care of pregnant women and result in the substantial reduction in maternal mental stress and perinatal mortality.

#### **Screening for Aneuploidies**

Screening for aneuploidies is an important part of routine antenatal care. The most common screening markers in first trimester are maternal age, biochemical analytes and the various sonographic measurements. In second trimester the assessment of multiple serum markers and genetic sonogram are used for aneuploidy screening. Cell-free DNA is the most sensitive and specific, but expensive, screening test for the common foetal aneuploidies but not a diagnostic test. It may be performed as primary screening or as a follow-up test to abnormal findings on first or second-trimester screenings.

A negative screening test substantially decreases the risk of the targeted aneuploidy but does not ensure that the foetus is unaffected. A positive screening test requires genetic counselling, comprehensive ultrasonographic evaluation and diagnostic testing by chorionic villi sampling and/or amniocentesis for foetal genetic analysis.

All patients should be offered an anomaly sonogram between 18 and 22 weeks of gestation for foetal structural defects, since these may occur with or without foetal aneuploidy.

Soft markers are minor ultrasound findings which may be normal variants but are noteworthy because of their association with an increased aneuploidy risk.

When an isolated soft marker is identified after negative screening results, patients may be reassured that the risk of foetal aneuploidy remains low. However, the identification of soft markers remains important to evaluate for associated conditions that are unrelated to foetal aneuploidy.

#### **Genetic Disorders**

Hemoglobinopathies are inherited disorders of red blood cells which impose a heavy burden on families and the health sector due to associated morbidity and mortality. The carrier frequency of beta thalassemia in India 3-17%, whereas, that of the sickle cell gene varies from 1 to 35 %.<sup>3</sup>

In India because of cultural barriers and stigma, premarital testing poses a significant challenge. However, it has improved in recent times. Although the ideal time to screen for hemoglobinopathies is premarital period/ preconceptional period, couple testing at 8 weeks of gestation is advised.<sup>4</sup> Extended family screening is recommended for all known and detected carriers and patients.

Screening method	Gestational age of screening (in weeks)	Detection rate	False positive rate	Analytes
Nuchal Translucency alone	10 to13 6/7	70%	5%	
First trimester screening	10 to 13 6/7	82-87%	5%	NT+PAPPA, free beta hCG
Quad test	15 to 22	81%	5%	hCG, AFP, uE3, DIA
Cell free fetal DNA	10 to Term	99%	2-4% (lowest)	Fetal DNA extracted from the maternal blood

<b>ble 2:</b> Various soft ultrasound markers and their likelihood ratio of aneuploidy <sup>2</sup>	

Marker	USG finding	Likelihood ratio (Isolated marker)
Intracardiac echogenic foci	A small (<6mm) echogenic area in either of the cardiac ventricle and visualized in at least 2 separate planes	0.95
Ventriculomegaly	Lateral ventricular dilatation >10mm	3.81
Increased nuchal fold	A thickened nuchal fold is defined as > 6 mm between 15 and 20 weeks of gestation.	3.79
Echogenic bowel	The fetal bowel displays echogenicity equal to or greater than that of the surrounding fetal bone.	1.65
Mild hydronephrosis	Anterior - posterior renal pelvis diameter, with > 4 mm (16 and 27 weeks of gestation ) and >7mm after 28weeks	1.08
Short humerus	The ratio of the observed to expected humeral length is <0.90.	0.78
Short femur	The ratio of the observed femoral length to expected femoral length is <0.92.	0.61
Aberrant Right Subclavian Artery	Presence of aberrant right subclavian artery	3.94
Absent or hypoplastic Nasal Bone	Nasal bone length <2.5 mm, or <2.5 <sup>th</sup> centile for gestational age	6.58

The screening test recommended for detection of carrier state of Beta thalassaemia is cation exchange high performance liquid chromatography (CE - HPLC) and it is also helpful for detection of other haemoglobin variants such as HbS, HbC and HbE. Naked Eye Single Tube Red Cell Osmotic Fragility Test (NESTROFT) though simple and less costly, is not sensitive and has a significant error rate. Isolated use of red cell indices [mean cell volume (MCV) < 80 fl and mean cell Hb (MCH) < 27 pg], has been found to miss a significant proportion of beta-thalassaemia carriers during pregnancy.<sup>5</sup>

Detection of causative mutation is the confirmatory test for diagnosis of hemoglobinopathies. Several PCR based methods most commonly Reverse Dot Blot Hybridization, and amplification refractory mutation system (ARMS) are used for detection of a limited number of known mutations and DNA sequencing for unknown mutations.

#### **Foetal Congenital Anomalies**

First trimester anomaly scan at 11-13 weeks helps to identify CNS anomalies with good sensitivity. Its detection rate for major anomalies is 49%.<sup>6</sup> In case of open spina bifida, the smaller biparietal diameter, absent intracranial translucency and posterior displacement of cerebellum are the early markers. Cystic abnormalities of the posterior fossa (Dandy-Walker complex) can be occasionally detected. First trimester diagnosis of conditions like acrania, alobar holoprosencephaly and encephalocele is possible, and these anomalies should actively be excluded at every early scan using transvaginal sonography. Screening for spina bifida is feasible in specialist centres with detection rates of 50% to 100% and very low-false positive rates (FPRs). Measuring Alpha fetoprotein levels and ultrasound at 18-20 weeks are the standard practice at some centres to detect neural tube defects. Supplementation of folic acid during periconceptional period is recommended to prevent NTDs.

Congenital heart defects (CHDs) are the most common malformations (8–10/1000 live births). Early ultrasound markers of congenital heart disease are increased nuchal translucency (three fold increase in CHD). An abnormal ductus venosus flow and presence of tricuspid regurgitation are more commonly seen in foetuses with CHDs. In a retrospective study, 57% was the detection rate for major cardiac defects during the first trimester. High detection rates were achieved for hypoplastic left heart syndrome (HLHS) (100%), and for atrioventricular (AV) canal (80%) and right heart (71%) defects.<sup>6</sup>

#### Conclusion

Screening for carrier status for beta-thalassaemia and other haemoglobinopathies should be offered to all couples. The first trimester aneuploidy screening and anomaly scan can detect majority of abnormal foetuses. Second trimester is still an opportunistic window to screen for anomalies.

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True prevention is not waiting for bad things to happen, it's preventing things from happening in the first place .....

- Don McPherson

### **Immunization in Obstetrics and Gynaecology**

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Immunization is the process of stimulating a protective adaptive immune response against microbes by exposure to either non-pathogenic forms or components of the microbes. Therefore, encouraging and ensuring vaccination in women is a quintessential component of preventive care for women so as to immunize them against preventable diseases before and during pregnancy.<sup>1,2</sup> Here, we elaborate on immunization of women in obstetric and gynaecology.

The recommendations for vaccination during pregnancy according to CDC are listed in the Table 1.<sup>3</sup>

Table	1: Vaccines	in obstetrics-	CDC
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Recommended before pregnancy (Preconceptional)	1. MMR 2. Hepatitis B
Recommended for routine use in pregnancy (Antenatal)	1. TdaP 2. Influenza 3. Covid vaccine
Recommended for special circumstances in pregnancy	<ol> <li>Hepatitis A and B</li> <li>Pneumococcal</li> <li>Meningococcal</li> <li>Travel Vaccination-Yellow fever</li> <li>Zoonotic vaccine preventable diseases-Rabies</li> </ol>
Contraindicated in pregnancy	1. BCG 2. MMR 3. Varicella 4. Herpes Zoster 5. HPV

#### Table 2: Vaccines in obstetrics- FOGSI

Vaccination before pregnancy	Catchup Vaccination 1. MMR 2. Varicella
	Sickle Cell Diseas/Splenectomy 1. Pneumococcal 2. Meningococcal 3. H. Influenza
Vaccination during pregnancy	1. Tdap 28-32 weeks 2. Influenza
Vaccination during pregnancy under special conditions	<ol> <li>Yellow Fever Vaccine</li> <li>Pneumococcal</li> <li>Meningococcal</li> <li>Hepatitis A</li> <li>Hepatitis B</li> <li>Typhoid</li> </ol>

FOGSI (2020), recommendation for vaccination during pregnancy are similar to the recommendations as per CDC as stated in Table 2.

#### Td/Tdap in Pregnancy<sup>4</sup>

Td(Tetanus-diphtheria) vaccine has replaced Tetanus toxoid vaccine in pregnancy in Universal Immunization Program of India. Immunization schedule (Table-3) of Td is as follows:

Table 3: Immunization schedule-Td

Early in pregnancy	Td-1
4 weeks after Td-1	Td-2
Pregnant within 3 years of last pregnancy with both doses of Td received	Td-B

Tetanus and diphtheria(Adsorbed) vaccine is administered as 0.5 ml deep i.m. in upper arm. It is suggested that available TT is to be used first before starting use of Td.

**TDAP VACCINE** can prevent diphtheria and pertussis in neonate in addition to tetanus. It can be given at 7 years of age or older.<sup>5</sup> According to CDC, all pregnant women should get a dose of Tdap during every pregnancy, to protect the newborn from pertussis. Young infants are at increased risk for death from pertussis and are entirely dependent on passive immunization from maternal antibodies until the infant vaccine series is initiated at 6 weeks (pentavalent-1). It is one of the most cost-effective strategies in protecting the newborn/young infants from neonatal pertussis. Since maternal antipertusis antibodies are relatively shortlived, to maximize passive transfer to the fetus, a dose of Tdap is ideally given between 27 and 36 weeks gestation. However, if received early in pregnancy due to a sustained wound or community outbreak, then it is not to be repeated at 27-36 weeks.

Other than CDC, RCOG, ACOG and FOGSI have also recommended this vaccine in third trimester. However, Universal Immunisation Program of India advocates Td as of now.

#### Influenza Vaccine in Pregnancy

ACOG-2018 recommendation advocates women who are or will be pregnant during influenza season to receive an inactivated influenza vaccine as soon as it is available, during any trimester, (CDC and ACOG). Due to the high potential for morbidity, recommendation regarding postexposure prophylaxis has been given (75mg of Oseltamivir once daily for 10 days) - for pregnant women and those who are upto 2 weeks postpartum.<sup>6</sup> If Oseltamivir is unavailable, Zanamivir can be substituted, two inhalations once daily for 10 days.6 FOGSI in 2019 recommended that INACTIVATED INFLUENZA VACCINE (Quadrivalent: Dosage- 0.5ml IM) can be given any time during pregnancy, and is very important to give between October and January. Table 4 describes the differences between Quadravalent and Trivalent influenza vaccines.

Table 4: Types of influenza vacc	ne
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	Quadrivalent Vaccine	Trivalent Vaccine
Composition	Split virions- disruptions of viral membrane	Subunit- disruption of viral membrane and removal of interval subviral core
Response	Cellular and antibody response as core proteins are maintained	Only antibody response as core proteins are removed
No. of subtypes of influenza vaccine	2A and 2B	2A and 1B
Clinical efficiency	Better	Less effective

#### **COVID Vaccine in Pregnancy**

Pregnant women with COVID-19 are at increased risk for preterm birth and might be at added risk of other adverse pregnancy outcomes<sup>7</sup> including higher chances of neonatal morbidity.<sup>8</sup> Over and above pre-existing co-morbidities, advanced maternal age and high body mass index are risk factors for severe COVID-19 disease in pregnancy.<sup>9</sup>

According to MOHFW in India, three vaccines have received approval for restricted use in emergency situation at present. One of them is an inactivated vaccine (Covaxin) and two other are based on nonreplicating viral vector platform (Covishield and Sputnik V).

A pregnant woman who opts for vaccination, could be vaccinated at anytime of pregnancy and lactation. As per the latest studies experts believe that COVID-19 vaccines are unlikely to pose a risk to the pregnant person or foetus.<sup>10</sup> According to The Royal College of Obstetricians and Gynecologists (RCOG) all pregnant women should be offered the vaccine as the general population.<sup>11</sup>

#### **Vaccination in Special Conditions**

#### **Hepatitis A Vaccine (HAV)**

CDC and ACOG have recommended that pregnant women at high risk of infection should receive HAV vaccine. Risk factors include travel to endemic areas, outbreaks and exposure to individuals with HAV infection. Vaccine available is HAVRIX, dosage is 1.0 ml IM, 2 doses given 6-12 months apart.

#### **Hepatitis B Vaccine**

HBV vaccination is the best preventive measure, including administration preconceptionally and during pregnancy. The 3 dose HBV vaccine (Recombivax 1.0 ml IM 0, 1, 6 months) series should be initiated for pregnant women who are at high risk and who have not been vaccinated previously. As per FOGSI, Hepatitis B vaccination during pregnancy is safe and does not warrant a termination.

Perinatal transmission prevention is done by identifying HBV infected pregnant mother and administration of hep B immunoglobulin and Heb B vaccine to newborn within 12 hours of birth. Further Antenatal Tenofovir is indicated if Hepatitis B viral load is more than 10,00,000/dl at 32 weeks of gestation.

#### Pneumococcal Vaccine

PNEUMOCOCCAL VACCINE (PPSV23) in the dose of 1 dose 0.5ml is indicated in high risk patients ie. women with heart disease, lung disease or sickle cell disease, Diabetic, Smoker. Single dose is sufficient for one season.

#### **Meningococcal Vaccine**

MENINGOCOCCAL VACCINE (MPSV4) Quadrivalent meningococcal conjugate vaccine(MPSV4) single 0.5ml, IM dose is given in the time of meningococcal outbreak.

#### **Yellow Fever Vaccine**

During pregnancy if a women travels (Africa and S.America) and her risk of exposure and infection is high enough to outweigh any potential theoretical risk of vaccination.

However Limited safety data is available in pregnancy.

It is a live attenuated vaccine and 0.5ml subcutaneous is given in Upper arm.

#### **Rabies Vaccine**

Rabies is nearly 100% fatal disease and there is no contraindication to Post exposure Prophylaxis. Pregnancy and lactation are no contraindications for rabies PEP in the event of an exposure. There is no adverse effect on pregnant woman, course of pregnancy, fetus or lactating mother. According to updated red cross regime doses are given on days 0,3,7 and 28 wherein two doses of 0.1ml are given on each day (total 8 doses, 4 visits)

#### **Contraindicated Vaccines**

- 1. CDC does not recommend administration of BCG vaccination (live attenuated) during pregnancy, even though no harmful effects of BCG vaccination have been observed on the fetus.
- 2. Pregnancy should be avoided for 30 days after MMR vaccination (overall theoretical risk of anomalies is up to 2.6%). However it is not an indication for pregnancy termination. It may be given to susceptible women postpartum, and breastfeeding is not a contraindication. The MMR Booster shot is a short live-attenuated vaccine. After a woman receives it, the CDC recommends waiting at least four weeks before attempting pregnancy because of theoretical risks to the fetus.
- 3. WHO and ACOG recommend avoiding HPV vaccination during pregnancy. However, when administered during pregnancy, it has not been associated with adverse pregnancy outcomes, including major malformations.
  - If administered inadvertently, termination of pregnancy should not be considered. True safety of HPV vaccination in pregnancy has yet not been established.
- 4. Varicella vaccine is not recommended for pregnant women or for those who may become pregnant within a month following each vaccine dose. Wild type varicella can cause congenital infection. The attenuated vaccine virus is not secreted in breast milk, and so postpartum vaccination can be given. An attenuated live-virus vaccine, Varivax, is recommended for nonpregnant adolescents and adults with no history of varicella: in two doses, 4 to 8 weeks apart.

#### **Vaccines Under Research**

- 1. GBS Vaccinne to protect the newborn against group B streptococcal infections through maternal immunization. It has been identified as a priority by WHO.<sup>12</sup>
- 2. RSV Vaccine: RSV can cause severe pneumonia and bronchiolitis, especially in infants less than 6 months of age. No licensed vaccine so far provides protection from it.<sup>13</sup>

#### **Vaccination During Breastfeeding**

Inactivated, subunit, recombinant, toxoids polysaccharide and conjugated vaccines pose no risk in pregnancy, and can also be given during breastfeeding. Majority of live viruses in vaccines have also not been demonstrated in human breast milk. Viral vaccines (both live and inactivated) administered to a breastfeeding woman do not affect the safety of breastfeeding for women or their infants. Lactation does not adversely affect the efficacy or the safety of the vaccination.

#### **HPV Vaccine**

Three different vaccines, which differ in the number of HPV types they contain and target, have been developed, although not all are available globally:

- Quadrivalent vaccine (Gardasil) targets HPV types ,6 16 ,11 , and 18.
- Nanovalent vaccine (Gardasil 9) targets the same HPV types as the quadrivalent vaccine (16,11,6, and 18) as well as types 52,45,33,31, and 58.
- Bivalent vaccine (Cervarix) targets HPV types 16 and 18.

Recommended age for routine HPV vaccination is 11 to 12 years. It can even be administered starting at 9 years of age.

- For adolescents and young adults aged 13 to 26 years who have not been previously vaccinated or those have not completed the vaccine series, catch-up vaccination is recommended.
- For women aged 27 years and older, catch-up vaccination is not routinely recommended; the ACIP notes that the decision to vaccinate people in this age group should be made on an individual basis.
   For pregnant patients, HPV is not recommended during pregnancy due to limited data on safety.

Breastfeeding females can receive the immunization series since subunit vaccines do not affect the safety of infant breastfeeding.

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### IN THE FUTURE.....

### **WHO Labour Care Guide: New Update**

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#### Introduction

In the past two decades, efforts have been made to encourage and support pregnant women to give birth in health facilities, where they ideally receive goodquality intrapartum care from skilled health personnel.<sup>1</sup>

The Labour Care Guide is designed to emphasise the importance of the experiential dimension of childbirth by requiring explicit recording of evidence-based practices that matter not only for women's positive birth experience but also for improving clinical outcomes for women and their newborns.<sup>2</sup>

The new WHO recommendations included in labour care guide is based on the emerging evidence on normal labour progression, as well as recommendations informed by the global shift towards improving experience of childbirth, that necessitated the design of a new labour monitoring tool called the WHO Labour Care Guide.<sup>3</sup>

### Why We Need Labor Care Guide Instead of Partograph?

In 2018 the WHO initiated a process to revise the partograph in light of recent evidences which are:

- Understanding of the individual variability of the progress of labours resulting in good perinatal outcomes
- Many women do not experience a labour that conforms to the average rate on which the partograph design was based.
- Failing to find evidence to support the use of a cervical dilatation rate of 1 cm/hour as a screening tool to predict adverse labour outcomes.
- Emerging evidence on normal labour progression, as well as recommendations informed by the global shift towards improving experience of childbirth.
- Respectful maternity care.

#### The Labour Care Guide<sup>1</sup>

The principal aims of the LCG are to:

· Guide the monitoring and documentation of the

well-being of women, babies and the progress of labour

- Guide skilled health personnel to offer supportive care throughout labour to ensure a positive childbirth experience for women
- Assist skilled health personnel to promptly identify and address emerging labour complications, by providing reference thresholds for labour observations that are intended to trigger reflection and specific action(s) if an abnormal observation is identified
- · Prevent unnecessary use of interventions in labour
- Support audit and quality improvement of labour management

#### For Whom should The LCG be Used?<sup>1</sup>

The LCG has been designed for the care of women and their babies during labour and childbirth. It includes assessments and observations that are essential for the care of all pregnant women, regardless of their risk status. Women at high risk of developing labour complications may require additional specialized monitoring and care

#### When should The LCG be Initiated?<sup>1</sup>

Documentation of the well-being of the woman and her baby as well as progression of labour, on LCG, should be initiated when the woman enters active phase of the first stage of labour (5 cm or more cervical dilatation), regardless of her parity and membranes status.

#### Where should the LCG be Used?<sup>1</sup>

The LCG is designed to be used for all births in health facilities, including primary, secondary and tertiary care settings.

The LCG has seven sections, which were adapted from the previous partograph design. The sections are as follows (see Fig. 1):

- at admission
- 2. Supportive care
- 3. Care of the baby
- 4. Care of the woman
- 5. Labour progress
- 6. Medication
- 7. Shared decision-making

#### How to use The Labour Care Guide<sup>1</sup>

#### **Labour Monitoring to Action**

To ensure the systematic and consistent application of the LCG, health providers are encouraged to use the Assess, Record, Check, Plan approach, which involves:

- Assess (assess the well-being of woman and her baby, and progress of labour)
- Record (document labour observations)
- Check reference threshold (compare labour) observations with reference values in the "Alert" column)
- Plan (decide whether and what interventions are required, in consultation with the woman, and document accordingly)

#### What has Changed in Labour Care Guide<sup>4</sup>?

As compared with the previous partograph designs, the Labour Care Guide includes the following changes:

- The 1 cm/hour 'alert' line and its corresponding 'action' line have been replaced with evidence-based time limits at each centimetre of cervical dilatation during active first stage of labour; the starting point of active first stage of labour is a cervical dilatation of 5 cm (instead of 4 cm or less)
- Normal progress of labor which was taken as cervical dilatation of 1 cm/hour is not considered as it does not account for the variability in the rates of progression between women.
- · It differs fundamentally in that the guiding parameters for labour progress are dynamic as opposed to being static as in partograph. Rather than having a fixed-rate limit over the entire active first stage of labour, consideration for intervention is guided by an evidence-based time limit for each centimetre of cervical dilatation.
- The absence of the diagonal labour progress limit lines is the most striking difference between the Labour Care Guide and the partograph.

- 1. Identifying information and labour characteristics The Labour Care Guide includes assessment of labour companionship, oral hydration, maternal position and mobility, and pain management, with the aim of promoting the use of these evidence-based yet often neglected practices.
  - Inclusion of second stage of labour is very important feature as increased uterine activity compounded by maternal expulsive efforts make the second stage of labour a particularly critical time, and reduced vigilance at this time may lead to poor outcomes

#### Advantages of Labour Care Guide Over Modified WHO Partograph<sup>5</sup>

Modified WHO partograph	WHO Labour Care Guide
Active phase defined as starting from 4 cm of cervical dilatation	Active phase defined as starting from 5 cm of cervical dilatation
Fixed 1 cm/hour 'alert' line and 'action' lines	Evidence-based time limits at each centimetre of cervical dilatation
No second-stage section	Intensified monitoring in second stage
No recording of supportive care interventions	Explicit recording of labour companionship, pain relief, oral fluid intake and posture
Records strength, duration and frequency of uterine contractions	Records duration and frequency of uterine contractions
No explicit requirement to respond to deviations from expected observations of any labour parameter, other than cervical dilatation alert and action lines	Requires deviations to be highlighted and the corresponding response to be recorded by the provider

As a redesigned WHO partograph, the LCG has the potential to promote woman-centered care and continuous assessment and decision-making throughout labor. Implementing the LCG should be accompanied by the necessary initial and ongoing training, supportive supervision and strategies to promote an enabling environment for practitioners to use LCG efficiently.<sup>2</sup>

#### **Care Throughout Labour and Birth Recommendations**<sup>1</sup>

• Respectful maternity care: refers to care organized for and provided to all women in a manner that maintains their dignity, privacy and confidentiality, ensures freedom from harm and mistreatment, and enables informed choice and continuous support during labour and childbirth – is recommended

- **Effective communication:** Effective communication between maternity care providers and women in labour, using simple and culturally acceptable methods is recommended
- **Companionship:** A companion of choice is recommended for all women throughout labour and childbirth
- **Continuity of care:** Midwife-led continuity-of-care models, in which a known midwife or small group of midwives supports a woman throughout the antenatal, intrapartum and postnatal continuum, are recommended in settings with well-functioning midwifery programmes

The picture given below is the format of Labour care guide:

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WHO LABOUR CARE GUIDE         Name       Parity       Labour onset       Active labour diagnosis [Date       ]																				
Ruptured membranes [Date     Time     ]     Risk factors																				
Time         : <th:< th=""> <th:< th=""> <th:< th=""> <th:< th=""></th:<></th:<></th:<></th:<>						3	4	5	6	:	: 3 <u>9</u>	:	: 10 1	: 1 12		:	1	:	2	3
		ALERT						CTIVE FI	RST STAG	GE ——					-	– SE	CONI	D STA	GE -	
SUPPORTIVE CARE	Companion N																			
	Pain relief	N																		
	Oral fluid	N																		
sup	Posture	SP																		
	Baseline FHR	<110, ≥160																		
	FHR deceleratior	L																		
BABY	Amniotic flui	id M+++, B																		
ΒA	Fetal positio	n P, T																		
	Caput	+++																		
	Moulding	+++														1				$\square$
_	Pulse	<60, ≥120																		
z	Systolic BP	<80, ≥140																		
WOMAN	Diastolic BP	≥90																		
3	Temperature	°C <35.0, ≥ 37.5																		
	Urine	P++, A++																		
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NO	Oxytocin (U	I/L, drops/min)																		
MEDICATIO	Medicine																			
M	IV fluids																			
DN-MAKING	ASSESSMEN	NT								1										
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Abbrev © Wor	viations: Y – Yes, N	ANY OBSERVATION – No, D – Declined, I tion, 2021. Some rig use.	J – Unknown, S	P – Supine, MO	– Mobile, E – Ea	rly, L – Late, V –	Variable, I – Int	act, <b>C</b> – Clear, M	– Meconium, B	– Blood, A – An	terior, <b>P</b> – Poster	ior, <b>T</b> – Transve	rse, P+ – Protein	, A+ – Acetone						



### **Newborn Screening: Dried Blood Spot**

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#### Introduction

Screening is defined as identification of unrecognized disease or defects by rapidly applied tests in apparently healthy individuals on a large scale.<sup>1</sup> Newborn screening (NBS) is the practice of screening newborns shortly after birth for potentially fatal disorders that are treatable, but difficult or impossible to detect clinically. It is a coordinated comprehensive system consisting of education, screening (specimen Taking, transportation and testing), follow- up of abnormal and unsatisfactory test results, confirmatory testing and diagnosis, timely appropriate management and periodic outcome evaluation, quality assurance and program evaluation, validity of testing systems, efficiency of follow-up and intervention, and assessments of long-term benefits to individuals, families and society.<sup>2</sup> Most of the disorders which are targeted under NBS may be difficult to diagnose at birth and can lead to severe debilitating complications/ mortality in the absence of correct diagnosis. Newborn screening can help to identify these disorders in the pre-symptomatic phase, thus reducing their burden of morbidity and mortality.<sup>3,4</sup>

#### **Dried Blood Spot**

Ivar Christian Bang (1869 – 1918), the father of modern clinical microanalysis was the first to demonstrate the clinical use of filter papers for measurement of glucose.

After this discovery, dried filter paper based blood spots have been useful for detection of different analytes, toxins and drugs in toxicology and microbiological diagnosis.<sup>5</sup> At present, a special type of filter paper is used to collect blood samples from newborns for NBS.

The following steps need to be followed for collection of DBS sample in newborns:

- A. Prepare the supplies-The filter paper card (Figure 1) with key demographic data of the babies, a lancet (maximum tip length 2.4 mm), sterile swab, sterile guaze and gloves should be prepared before sampling. A barcode can be generated with patient identification and can be pasted on the filter paper.
- **B.** Prepare the sampling site-The ideal recommended site for sampling in a newborn is the heel. The lateral borders of the heel should be cleaned for sampling taking care to avoid the central part (Figure 2A). The site should be cleaned and warmed and held with a sterile guaze before collecting the sample. It can be warmed by rubbing against hands, warming with a warm towel etc.
- **C. Collect blood** The sampling site is pricked with the lancet and heel is squeezed till a drop of blood can form (time taken around 5 seconds). One drop of blood is dabbed against the filter paper against marked circles to fill these uniformly. The following precautions should be taken during collection (**Figure 2B**):

()	ALLOW BLOOD TO SOAK THROUGH AND COMPLET FILL EACH CIRCLE APPLY BLOOD ONLY TO ONE S OF THE FILTER PAPER.	Pepartment of Pediatrics, MAMC & LN Hospital         Newborn Screening Filter Paper         Networn Name         Intervision
$\bigcirc$	SIDE	Call Code         Number         Call Code         Number<

Figure 1: Filter paper for Dried Blood Spots



Figure 2: A: Site of blood sampling; B: Adequately collected DBS

- i. Wait to collect the sample till a good volume blood drop is formed and the rub the card against the hanging drop
- ii. Fill each circle with a single drop only
- iii. Do not dab/wipe the filter with repeated drops of blood
- iv. Collect at least three (preferably five) blood spots from each neonate
- v. The depth of the puncture should not exceed 2.4 mm, which is ensured using a lancet
- vi. If a second puncture is necessary, this is made a few millimeters away from the first or in other foot
- vii. The blood sport should not be touched with the finger
- **D.** Dry and pack the card- The filter paper should be dried completely before packing inside an envelope by leaving it exposed to air at room temperature. The use of heat, air blower etc is not recommended for this purpose.
- **E. Transport:** The filter paper with DBS is a potential biocontaminant which require safe transport. Few blood analytes are susceptible to extreme temperature fluctuations. The DBS should therefore be transported in thermocol boxes or biosafety cabinets till the main laboratory.
- F. Measurement of analytes The DBS cards are punched using automated machines into small circles which are then processed for measurement of different analytes.

The main advantages and limitations of using a DBS are mentioned in **Table I** below:

Table 1: Advantages and disadvantages of Dried Blood Spots

Advantages
Requires less blood volume- better acceptance in neonatal
screening
Simple and less invasive procedure over intravenous blood
sampling
Minimal risk of bacterial contamination or hemolysis
Can be preserved for long periods
Can be used to collect samples in field settings
Disadvantages
Can only measure analytes from serum
Requires temperature control for transportation
Logistic concerns of equipment for processing and
measuring the analytes

#### **Newborn Screening for Metabolic Disorders**

**Phenylketonuria** was the first metabolic disorder which was screened in 1960s. As more and more enzyme assays were developed, NBS for **congenital hypothyroidism** was made possible using TSH and later T4 in the 1970s. Screening for other endocrinal disorders namely **congenital adrenal hyperplasia** was developed by 1978. Most of the developed countries now have universal NBS program with services extended to screen for **cystic fibrosis, primary immunodeficiency, G6PD deficiency, galactosemia** and other inborn errors of metabolism.<sup>2,6</sup>

The prevalence of congenital adrenal hyperplasia (CAH)

in India is reported 1 in 5762 babies as per NBS data and overall prevalence of congenital hypothyroidism (CH) was 1 in 722 births or 1:1130 births after excluding those with transient hypothyroidism.<sup>3,7</sup> Universal newborn screening for treatable genetic disorders like congenital hypothyroidism and congenital adrenal hyperplasia, however, has still not seen the light of the day in India. Newborn screening in India is only done in a project mode, in specific medical facilities, cities or states, intermittently.89 The major challenges associated with NBS include a large birth cohort, unattended deliveries which are still common in India, lack of awareness, financial implications and absence of uniform screening guidelines makes it a challenging and arduous task to implement universal NBS. The current coverage of NBS in India is approximately 2%, with only few states like Kerala and Tamil Nadu advocating universal screening.9 The NBS program was launched in Kerala in 2012 which screens for four disorders including congenital hypothyroidism, CAH, Glucose 6 phosphate dehydrogenase deficiency and Galactosemia. Since then, the program has grown to screen more than 140,000 births per year in over 90 government hospitals of Kerala.<sup>9</sup>

To promote the early detection and management of childhood disorders, the Government of India launched the Rashtriya Bal Suraksha Karyakram (RBSK) in 2013, which aimed to screen over 270 million children from 0 to 18 years for 4 Ds - Defects at birth, Diseases, Deficiencies and Development Delays including Disabilities. The Delhi government recently launched its flagship health programme under the vision of Rashtriya Bal Swasthya Karyakram (RBSK) called as Mission NEEV (Neonatal Early Evaluation Vision) to provide universal newborn screening for congenital hypothyroidism and congenital adrenal hyperplasia, early diagnosis of visible birth defects, critical congenital heart diseases and hearing loss. The program is being launched at 31 major birthing facilities of the city and will be expanded later to all delivery points and other birthing facilities.<sup>10,11</sup>

For every screen positive baby, it is mandatory to perform confirmatory biochemical and molecular testing. These tests should be performed at an appropriate healthcare facility in consultation with a specialist after proper counselling of the parents/ caregivers. In some disorders (like hemoglobinopathies) establishment of a correct diagnosis might involve testing the parents and/or other siblings as well. This implies that recall rates will be high for any screening test to ensure a positive baby is not missed.

#### Conclusion

Newborn screening (NBS) is a simple, inexpensive, yet an effective method to identify potentially lifethreatening conditions in pre-symptomatic neonates, enabling early treatment/institution of therapy. NBS has been demonstrated to save lives and prevent serious disability. It appears to be cost-effective and represents a public health success in most developed nations. Public awareness coupled with professional training and family education must be a part of the complete NBS system. Hence, it is important that Universal screening should be implemented as a programme at the earliest

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### **Newborn Screening: Point of Care Testing**

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#### Introduction

Newborn screening for common metabolic and genetic disorders should be an essential part of neonatal care as early detection and treatment can help prevent intellectual and physical defects and life threatening illnesses.<sup>1</sup> Conditions for which screening is done differ from country to country, based on the prevalence of the condition and available resources. Universal screening for about 40 to 50 metabolic disorders is mandatory in US, Europe and many other countries across the world. Though universal screening is a cost-intensive exercise, the benefits far surpass the cost as it helps in reducing the mortality and morbidity of these diseases. Pointof-care (POC) testing refers to those tests performed and interpreted outside of a laboratory but close to the site of direct delivery of medical care for a patient.<sup>2</sup> POC testing has been widely used in the developed world to screen for disorders with high prevalence and public health importance like hearing loss and critical congenital heart diseases, the timely detection of which can facilitate appropriate management and cause significant decrease in infant and child morbidity as well as mortality.<sup>3</sup>

#### **POC Screening for Hearing Loss**

Congenital hearing impairment occurs in approximately 1 to 5 per 1000 live births and when permanent unilateral hearing loss is included, the incidence increases to 8 per 1000 live births.<sup>4</sup> Neonatal hearing loss has a prevalence that is more than twice that of other newborn disorders detectable by screening such as congenital hypothyroidism and phenylketonuria.<sup>5</sup> Studies done in India using different hearing screening protocols have estimated the prevalence of neonatal hearing loss to vary between 1 and 8 per 1000 babies screened. Early identification and treatment for hearing loss by 6 months of age provides better prognosis in language development, academic success, social integration and successful participation in the society.<sup>6</sup>

In October 2007 the Joint Committee on Infant Hearing (JCIH) issued its eighth position statement, which continues to endorse the early hearing detection and intervention (EHDI) for infants with hearing loss with the overall goal of maximizing their linguistic competence and literacy development. The 2007 statement continues to follow the "1-3-6 EHDI Plan" according to which-(i) All infants should have access to hearing screening using a physiologic measure at no later than 1 month of age, (ii) All infants who do not pass the initial hearing screening and the subsequent rescreening should have appropriate audiological 8and medical evaluations to confirm the presence of hearing loss at no later than 3 months of age, (iii) All infants with confirmed permanent hearing loss should receive early intervention services as soon as possible after diagnosis but at no later than 6 months of age.<sup>7</sup>

POC tests widely used for screening infants for hearing loss include Oto-acoustic emissions (OAE) and automated Auditory Brainstem Response audiometry (AABR). While OAE is cost effective, quick, simple and reliable with a sensitivity of 100% and specificity of 99%, AABR has the additional advantage of identifying neonates with auditory neuropathy unlike testing for OAE, and is especially useful for babies requiring neonatal intensive care unit (NICU), with multiple comorbidities. The other advantages of AABR include rapidity, easy-to-use and high sensitivity (0.99) and specificity (0.87)

In a study conducted by Kumar et al. between Jan 2007 and Mar 2016 a total of 30,600 neonates were screened using Newborn Hearing Screening. Out of the 75 neonates who failed screening, 58 babies had a false positive result and passed the test after a week. Out of the true positive17 babies, 8 infants had hearing difficulties requiring treatment by an ENT Surgeon.<sup>9</sup>

Hence, hearing screening of apparently well newborns should become a standard of care in India like many other developed countries.

#### Screening for Critical Congenital Heart Defects (CCHD)

Congenital heart disease (CHD) is the most frequently occurring congenital disorder, responsible for 28% of all congenital birth defects<sup>10</sup>, The birth prevalence of CHD is reported to be 8-12/1000 live births.<sup>11</sup> Considering a

rate of 9/1000, about 1.35 million babies are born with CHD each year globally.<sup>12</sup>

In 2011, the US Secretary of Health and Human Services Advisory Committee on Heritable Disorders in Newborns and Children (SACHDNC) recommended that newborns be screened for critical congenital heart disease (CCHD) by pulse oximetry. This recommendation was made on the basis of evidence of the effectiveness of screening and the benefit of early intervention in improving child health.<sup>13</sup>

Newborn screening for critical congenital heart defects (CCHD) was added to the US Recommended Uniform Screening Panel in 2011. Within 4 years, 46 states and the District of Columbia had adopted it into their newborn screening program, leading to CCHD screening being nearly universal in the United States. This rapid adoption occurred while there were still questions about the effectiveness of the recommended screening protocol and barriers to follow-up for infants with a positive screen. In response, the Centers for Disease Control and Prevention (CDC) partnered with the American Academy of Pediatrics (AAP) to form an expert panel between January and September 2015 representing a broad array of primary care, neonatology, pediatric cardiology, nursing, midwifery, public health, and advocacy communities.<sup>14</sup>

Pulse oximetry screening should be ideally done at  $\geq$ 24 hours, but it may be done even at <24 hours of life, if discharge of the baby from hospital has been planned early. Any pulse oximeter screening with an oxygen saturation measure that is  $\geq$ 95% in the right hand or foot with a  $\leq$ 3% absolute difference between the right hand or foot is considered a 'passed' screen. A screen is considered 'failed' if: (i) Any oxygen saturation measure is <90% (in the initial screen or in repeat screens), (ii) Oxygen saturation is <95% in the right hand and foot on three measures, each separated by one hour, (iii)>3% absolute difference exists in oxygen saturation between the right hand and foot on three measures, each separated by one hour. Any infant who fails the screen should have an evaluation for causes of hypoxemia. In most cases this will include an echocardiogram, but if a reversible cause of hypoxemia is identified and appropriately treated, an echocardiogram may not be necessary. Concerned pediatrician should be notified immediately and the infant might need to be seen by a pediatric cardiologist.<sup>15</sup> While it is true that pulse oximeter screening will allow detection of many more newborns with CCHD, it is necessary to carefully consider the

implications of population-wide screening, particularly in low-resource environments, where making cardiac catheterisation based interventions and / or surgeries for the babies diagnosed with CCHD still remains a bottleneck.

In the Indian state of Kerala, every baby born in government facility is being screened for CCHD according to AAP guidelines, since 2018.<sup>16</sup> A large number of babies with critical CHD have been identified and managed according to the protocol developed by the State Government resulting in a significant decrease in the neonatal and infant mortality rates in the state, providing a template for the other states to emulate.

#### Conclusion

POC screening tests for hearing loss and CCHD, which are relatively easier to implement must be incorporated in the newborn screening programme, wherever feasible. Early identification of these disorders and timely intervention can prevent death or disability among the screened neonates and infants and enable them to reach their full potential, as they grow.

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### **Women Pathbreakers**

#### **Poonam Kashyap**

Assistant Professor, Department of Obstetrics and Gynecology, Maulana Azad Medical College and Lok Nayak Hospital, Delhi

'These inspiring women endured poverty and deep rooted stereotypes but they never stopped and went on to achieve great heights in their fields.

One revolutionised the field of viral oncology, the other devised ways to assess and protect the health of newborns, both dramatically improving the health of millions'.

#### Sarah Stewart: the women who revealed a missing link between virus and cancer



Stewart was born on August 16, 1906 in the state of Jalisco, Mexico. She began doctoral work at the University of Colorado School of Medicine in Denver in 1933. Two years into her doctoral studies, She took a position of research assistant at the National Institutes of Health and became the first woman scientist to work at the Public Health Services. Stewart was a pioneer in the field of viral oncology and demonstrated the basis that cancer causing viruses can spread from animal to animal. She and Bernice Eddy co-discovered the first polyoma virus, and Stewart-Eddy polyoma virus is named after them. It was her effort and initial work of understanding oncogenic viruses that led to the development of HPV vaccine.

#### Virginia Apgar



She was an American physician, obstetrical anaesthesiologist and medical researcher, best known as the inventor of the Apgar Score. She graduated from the College of Physicians and Surgeons at Columbia University in 1933. Virginia Apgar devised newborn's Apgar score in 1953, creating the first tool to scientifically assess a neonate's health risks and need for potentially life-saving observation. During the rubella pandemic of 1964–65, she advocated the use of universal vaccination to prevent mother-to-child transmission of rubella. Apgar also emphasized the use of Rh testing to identify at risk women who can transfer antibodies across placenta and destroy fetal RBCs leading to fetal hydrops. She conducted various workshops to highlight the importance of early detection of birth defects and the need for more research in this area.

### **Quiz - Preventive Care in Obstetrics**

#### Reena Rani

Assitant Professor, Department of Obstetrics and Gynaecology, MAMC

#### Q1. Gardasil 9 vaccine provides known protection against all HPV except

- a. 31
- b. 33
- c. 16
- d. 15

#### Q2. Mentzer index is

- a. MCV/RBC
- b. MCHC/HB
- c. HB/MCV
- d. MCV/HGB

### Q3. Which of the following confirmed values meet the diagnostic threshold for diabetes?

- a. fasting blood glucose 100 mg/dl
- b. random glucose > 160 mg/dl
- c. 2 hour post prandial glucose  $\geq$  to 126 mg/dl
- d. fasting blood glucose  $\geq$  126 mg/dl
- Q4. Only intervention which has proved its role in prevention of preterm labour in women with prior history of spontaneous preterm labour and ultrasound suggestive of normal cervical length at 20 week of gestation
  - a. Cervical cerclage
  - b. Magnesium sulfate
  - c. Progesterone supplementation
  - d. Bedrest

### Q5. Risk of miscarriage in amniocentesis after 15 weeks is

- a. 1 in 1000
- b. 1 in 10000
- c. 1 in 100
- d. 1 in 10

#### Q6. 6X6X6 STRATEGY is related to

- a. Newborn screening
- b. Prevention of anemia

- c. Prevention of hypothyroidism
- d. None of the above
- Q7. Minimum time gap required between conception and measles vaccination is
  - a. 1 month
  - b. 2 month
  - c. 3 month
  - d. 4 month

#### Q8. Spinal Muscular Dystrophy is

- a. Autosomal dominant
- b. X-linked dominant
- c. Autosomal recessive
- d. X-linked recessive

#### Q9. The father of modern clinical microanalysis is

- a. Ivar Christian Bang
- b. Károly Ereky
- c. Francis Galton
- d. Antoni van Leeuwanhoek

Q10. A newborn screen suggestive of classical galactosemia will have \_\_\_\_\_ galactose -1- phosphate uridylytransferase (GALT) enzyme and \_\_\_\_\_ erythrocyte galactose-1phosphate concentration.

- a. Elevated, reduced
- b. Reduced, elevated
- c. Normal, reduced
- d. reduced, reduced
- Q11. Detection rate of preeclampsia via universal screening tool (MAP,uterine artery PI,PLGF) is
  - a. 90-93%
  - b. 70-80%
  - c. 50-63%
  - d. 30-40 %

#### Q12. POSHAN Abhiyan started on

- a. 8th march 2016
- b. 8th march 2018
- c. 8th may 2019
- d. 8th may 2020

#### Q13. Mission NEEV (Neonatal Early Evaluation Q15. For Newborn screening by DBS method, Vision) envisages to provide universal newborn screening for

- a. congenital hypothyroidism
- b. congenital adrenal hyperplasia
- c. critical congenital heart diseases
- d. All of the above

#### Q14. WHO Labour Care Guide includes:

- a. Supportive care
- b. Care of baby and mother
- c. Labour progress
- d. All of above

### blood is usually taken from

- a. Center of heel
- b. Lateral part of heel
- c. Prominent vein on dorsum of hand
- d. Forearm fold

#### **Quiz Answers**

1:d	2:a	3:d	4:c	5:c	6:b	7:a	8:c
9:a	10:b	11:a	12:b	13:d	14:b	15:b	

## **NARCHI Activities**

1. Webinar: Panel discussion on A to Z of GDM, June 19, 2021 a Under the aegis of NARCHI In association with multidisciplinary committee AOGF and DGFSW



2. Webinar: Recurrent Pregnancy losses: Managing the Unexplained 24/06/21. Organied by FOGsd in association with NARCHI Delhi.


CME – Conversation on Mensturation, 26/6/21
 Deptt. of Obstetrics and Gynaecology, Babu Jagjeevan Ram Memorial Hospital, Delhi



4. Education series 5- 28/6/21, Kasturba Hospital and NARCHI, Delhi

Postgraduate training -Intrahepatic cholestasis of pregnancy



- World Population day and Population stabilization fortnight - NARCHI Delhi with its members and DFW, Govt of NCT Delhi.
- 6. Webinar: Hypertensive disorders in pregnancy, 30/6/21

FOGsd under aegis of NARCHI Delhi , ISCCP,IFS,AICC RCOG NZ,



7. Webinar: PCOS & Infertility, 10/7/21 FOGsd in association with NARCHI Delhi.



8. Webinar: Pregnancies following ART, 3/8/21 AOGD infertility sub-committee in association with NARCHI

- CME on Reining in the Caesarean Pandemic, 4<sup>th</sup> August, 2021
   Department of Obstetrics & Gynaecology, Lady Hardinge Medical College With NARCHI, Delhi
- 10. FIGO Session **Pregnancy and COVID-19** Maulana Azad Medical College, New Delhi and NARCHI, India
- 11. NARCHI annual conference 27<sup>th</sup>-29<sup>th</sup> August 2021.
- 12. NARCHI outreach activity: 29 sept 2021, Baba Saheb Ambedkar Medical College and hospital.

Health talks and performance of two" Nukkad Natak " on the theme of Antenatal and postnatal care, performed by residents of Dept of OBG in the OPD wing and PNC ward.



13. TOT on Family Planning Counselling Services organised by HFW Training Cell and Narchi Delhi, Dept of Obstetrics and gynecology, MAMC & LNH. 30th Nov & 1st Dec 2021



14. Male participation in Family Planning - NSV awareness fortnight 2/12/21



NSV awareness : Nukkad Natak



15. CME "Steps towards safe motherhood" - Birth Companion and VBAC, 11/12/21

Dr. Baba Saheb Ambedkar Medical College and hospital with NARCHI, Delhi



## **Annual Conference Glimpses**

- Pre-conference Workshops 5
- Sheila Mehra QUIZ
- Oration by Sir Sabaratnam Arulkumaran
- Release of E- souvenir
  - Workshops and Quiz









- 20 Scientific Sessions on Main Conference Day
- 24 Prizes Won for Paper and Poster Presentation
- 128 Paper Presented
- FIGo Complimentary Registration to Quiz Winners
  - Main Conference



• Release of E- souvenir





• Dr S Das Oration delivered by Sir S Arulkumaran







• Address by Narchi National President Dr K K Roy



Validectory



The doctor of the future will give no medication but will interest his patients in the care of the human frame, in diet and in the cause and prevention of disease.

- Thomas Edison

# **World Population Day**

#### **Activities Undertaken**

- Mass Mail sent to ~1000 NARCHI Delhi Members
- Website: Message on homepage
- Advertisement in Bulletin Full Page
- CME on Contraception

- College activity: Awareness and empowerment of the youth
- Awareness programmes including health talks, Nukadd Natak and Distribution of IEC material in various hospitals and polyclinics.



#### Webinar on Contraception

- DFW, Govt of NCT Delhi, in collaboration with Abbott, under the Aegis of NARCHI, DGF-North and AICC RCOG, NZ
- Lecture Topic: Choosing the Right Contraceptive
  Pill
- Panel Discussion: My Pill My Choice
- Date: 29th June, 2021



NARCHI Bulletin

#### College Activity: Awareness and Empowerment of the Youth

SRCC, New Delhi on 7<sup>th</sup> July 2021 3 pm onwards

Shared widely on Mass Media by instagram posts and whatsapp among the young



### Awareness Programmes Incuding Health Talk, Distribution of IEC Material in Polyclinics

- Health talk on FP: 28th June 21
- At Polyclinic keshavpuram
- Attached with DCB Hospital
- Conducted by: Dr Salam Zeliang Nodal Officer and Incharge, family Planning, DCB Hospital
- Health talk at Delhi govt polyclinic at Ballimaran on 1st july
- Conducted by Dr Rashmi Yadav









#### **Awareness Programmes in Various Hospitals**

Activities conducted in Hindu Rao Hospital over 4 days as Nukkad Natak, Health Talks, Distribution of IEC Material









Kasturba Gandhi Hospital on 14<sup>th</sup> July, 2021







Lok Nayak Hospital Over 3 Days











An ounce of prevention is worth a pound of cure.

- Henry de Bracton

### HIGH RESOLUTION AND CLEAR-CUT SEPARATION OF HEMOGLOBIN FRACTIONS BY CAPILLARY ELECTROPHORESIS



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