NARCHI DELHI BULLETIN

SJH, Issue 7, March 2020

REACHING THE UNREACHED

NARCHI

Delhi Branch

An Update on Prenatal Diagnosis

NARCHI Delhi Secretariat
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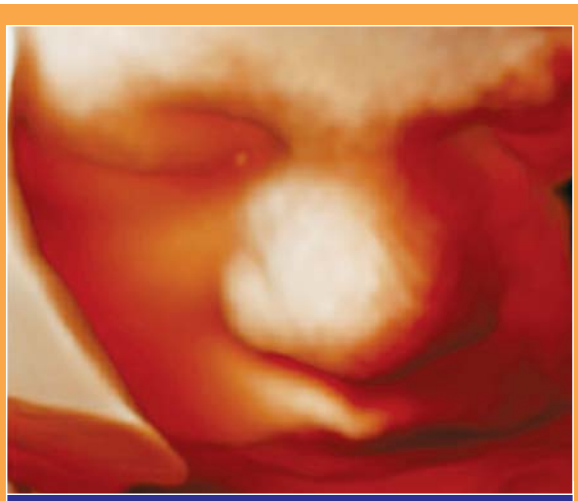

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NARCHI Bulletin

SJH, Issue 7, March 2020

Contents

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Dr Jyotsna Suri & Dr Rekha Bharti on behalf of National Association for Reproductive & Child Health of India, Delhi Branch.

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President's Message

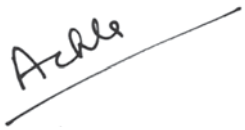
Greetings to my dear NARCHI members,

I would like to welcome you to this edition of NARCHI bulletin by wishing everyone of you a safe year ahead. While everybody is busy doing their bit in this lockdown, pregnancy and deliveries do not follow any lockdown restrictions. So, we must continue to provide optimal care during pregnancy. As is an old adage "prevention is better than cure", we begin this bulletin with one of the most pertinent topic, the prenatal diagnosis.

The frequency of inherited malformations as well as genetic disorders in newborns account for around 3-5%. Prenatal diagnosis allows identification of malformations and/or some genetic syndromes in fetuses during the first trimester of pregnancy. The severity of the disorders help in deciding subsequent course of the pregnancy taking into account the possibilities of treatment, parent's acceptation of a handicapped child and also possibility of termination of the pregnancy. In prenatal testing, both screening and diagnostic procedures are included. The first and second trimester biochemical and ultrasound, chorion villi sampling, amniocentesis, fetal blood sampling are promising procedures (e.g. fetal cell and DNA isolation from maternal blood).

Before we end here I would like to mention that, we may not be able to hold the 15th NARCHI World Congress this year. We will get back to you all with the conference dates in our next issue and till then, we will continue to do our academic activities through webinars.

Stay safe!



Dr Achla Batra

Vice President's Message

Dear Friends,

Knowing how well is your unborn child is always an anxiety for parents, which makes them undergo all possible tests. This issue reviews updates on all prenatal diagnostic tests-indications, predictive value and usefulness essential for counselling in regular practice.

Hope, you enjoy reading this issue.

Dr Saritha Shamsunder

Secretary's Message

Greetings from NARCHI Delhi Branch!

We meet you again through this bulletin after the 26th Annual NARCHI Delhi Conference Souvenir issue. I thank you all from the bottom of my heart for making the NARCHI Delhi conference a huge thumping success.

In continuum with our motto of 'Reaching the Unreached' we have been organizing health camps, public forums and CMEs on important aspects of mother and child health. In addition to this, the first of its kind endeavour was workshop on Menstrual Hygiene Management (MHM) which witnessed extensive brainstorming by 23 experts from leading institutes and hospitals of Delhi and protocols and guidelines for MHM were discussed and later presented by NARCHI president Dr Achla Batra. Dr Ajay Khera, Commissioner, Maternal and Child Health, GOI also participated and shared his opinions as well as his initiatives taken by his ministry. This was in addition to workshops on "Knotting and Suturing (Basic And Advanced)", "Post Partum Haemorrhage Management" and "Basic Infertility" which were equally appreciated by all.

It gives me immense pleasure to introduce this seventh quarterly issue of NARCHI Delhi bulletin dedicated to yet another crucial topic "Prenatal Diagnosis" Once again I congratulate our dedicated editorial team for bringing out this issue on such a vital topic which is cause of concern to both practitioners and academicians.

This issue showcases the best of 'Prenatal Diagnosis' with articles contributed by experts. In today's scenario with women putting careers before pregnancy, prenatal diagnosis definitely has special place in current Obstetrics. Hope you find this issue useful and all our bulletins find a special place on your desk as a ready reckoner.

You must be aware that we were to bring forth another wonderful conference for all of you, the "15th NARCHI World Congress" with the theme, "Reaching Beneath the Tip of Iceberg". But we are not sure when we'll be able to hold the conference in view of ongoing COVID 19 pandemic.

A hearty welcome and happy reading to every one of you!!

Dr Monika Gupta
Secretary

Dr Divya Pandey
Joint Secretary

Editor's Message

Greetings from the editorial team!

Welcome to another issue of NARCHI bulletin. Pregnant women and their families are concerned about the wellbeing of the growing fetus. Every woman wants her pregnancy to be normal, and prenatal testing provides us an opportunity to screen these women and do timely interventions. Prenatal diagnosis involves testing the unborn fetus to determine certain abnormalities that include hereditary and spontaneous genetic disorders.

These tests assess the degree of risk to the fetus but they cannot, with certainty, diagnose the affected fetus. Therefore, it is important to carefully analyze the results of the prenatal tests to reduce the anxiety of the patients. At the same time, it is important for the obstetricians to identify in time the women that need referral to the fetal medicine department. In most of the cases reassurance and follow up of the fetus is needed, however, in few cases timely detection of fetal anomalies provides option of either termination of pregnancy or in some cases in-utero treatment of the fetus.

We are thankful to the authors for simplifying the basic concept of prenatal diagnosis, interpretation of screening results and options of fetal therapy available.

We apologize for not being able to reach you in time due to the ongoing COVID-19 pandemic.

Happy reading!

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First Row: Dr Jyotsna Suri & Dr Rekha Bharti (The Editors)
Second Row: Dr Prachi Gupta (Assistant Editor), **Dr Sarita Singh** (Co-Editor), **Dr Megha Mittal** (Assistant Editor)

Making Sense of Biochemical and Soft Markers in First and Second Trimester

Chanchal Singh
Senior Consultant, Fetal Medicine, Birthright, by Rainbow Children's Hospital, New Delhi

Introduction

Prenatal screening by ultrasound and serum biochemistry is now an integral part of standard antenatal care. The main aim is detection of chromosomal abnormalities, Down syndrome being the most common with a reported prevalence of 1 in 800 live births. Serum biomarkers may also be useful in predicting obstetric complications like early preeclampsia and morbidly adherent placenta. However, in the absence of a uniform protocol and use of multi-tiered approach can make interpretation of these screening tests difficult.

First Trimester 'Dual Marker'

The two most extensively evaluated maternal serum markers in the first trimester are free beta human chorionic gonadotropin (beta hCG) and pregnancy associated plasma protein A (PAPP-A). hCG is glycoprotein formed by the developing embryo and later by the placenta. It can be assayed in both free and total forms. PAPPA is a complex high molecular weight glycoprotein. Both can be measured between 9 weeks to 13 weeks and 6 days and are effective screening test for Down syndrome. The risk is generated by converting the maternal test result into MoMs (multiple of median) and by adjusting it for maternal age, maternal weight, gestational age, ethnicity, smoking, type of conception, diabetes, number of foetuses and chorionicity. This adjustment is essential for calculation of accurate risks. The expected changes in these levels with the common aneuploidies are given in table 1.

Table 1: Expected biochemistry levels in euploid and aneuploid fetuses

Study population	Median free beta hCG (MoM*)	Median PAPPA (MoM)
Euploid	1.0	1.0
Trisomy 21	2.0	0.5
Trisomy 18	0.2	0.2
Trisomy 13	0.5	0.3
Turner syndrome	1.0	0.4

*MoM: multiple of median

Combined First Trimester Screening

When first trimester dual marker is combined with ultrasound markers especially an accurately measured nuchal translucency (NT), the detection rate for Down syndrome is 85% for a false positive rate of 5%. Addition of more ultrasound markers further improves the detection rate and brings down the false positive rate. The combination of maternal age-related risk, fetal NT, and serum markers yields a trisomy 21 detection rate of 90% for a false positive rate of 3–5%. The detection rate in screening for trisomy 18 and 13 is about 95%.

First Trimester 'Quadruple Marker'

The addition of maternal serum markers, i.e. alphafetoprotein (AFP) and placental growth factor (PlGF) has also been shown to improve detection rates to 93% while bringing down the false positive rate to 1-1.5%. Addition of PlGF is of particular importance as it has been proven to be an effective screening tool for development of early preeclampsia (necessitating delivery before 34 weeks). This assumes greater significance in light of the fact that there is level I evidence that low dose aspirin (150 mg once a day) can prevent 80% of early preeclampsia in women who are screen positive using the FMF algorithm.

Second Trimester Triple and Quadruple Marker

Women who present late in the pregnancy and/or have missed their dual marker can be offered either a triple or a quadruple test up to 22 weeks. Triple marker includes serum total beta hCG, estriol and AFP and has the least detection rate of 60-65%. Quadruple marker adds inhibin A to the previous three hormones with an improved detection rate of 75-80%. AFP in the second trimester may have the added advantage of picking up women with open neural tube defects; however the ultrasound detection rate for open neural tube defects is nearly 100%. It is important to note that the detection rate for Down syndrome on second trimester anomaly scan is a dismal 58% and hence addition of

serum biochemistry is recommended despite the high false positive rates.

Soft Markers in Second Trimester

Ultrasound findings that are not structural abnormalities but are seen more often in fetuses affected with Down syndrome have been termed 'soft markers. Majority of these would be normal variants. As mentioned earlier, the detection rate of the genetic sonogram in the second trimester is merely 58%. Thus, the value of most soft markers in the setting of a prior low risk on first trimester screening is debatable. This becomes even more important with the advent of noninvasive prenatal screening (NIPS) which has a detection rate of more than 99% for Down syndrome. In case first trimester screening was not done, adding quadruple marker to the ultrasound improves the detection rate to 85%.

Not all soft markers have the same (in) significance: markers that may warrant invasive testing even when present in isolation include nuchal edema, absent/ hypoplastic nasal bone, ventriculomegaly and aberrant right subclavian artery (ARSA).

Absent/hypoplastic Nasal Bone

An absent or hypoplastic nasal bone on ultrasound is considered an important 'soft marker' for Down syndrome with a positive LR of 23.27. There can be a constitutional variation in the length of nasal bone and using population based cut off is preferable when labelling a nasal bone hypoplastic. Also, majority of fetuses with an isolated absent/ hypoplastic nasal bone in the first trimester will show a normally ossified nasal bone at subsequent second trimester ultrasound. Thus, if the combined risk in first trimester is low, it is reasonable to call the patient for a follow up scan at 16-17 weeks. If the nasal bone is still hypoplastic or absent, amniocentesis for fetal karyotype should be offered as the main abnormality associated with isolated hypoplastic/absent nasal bone is Down syndrome alone.

Ventriculomegaly

The posterior horn of lateral ventricle of the brain is measured in the transventricular axial plane of fetal head. Correct technique is essential in doing this measurement. Value of more than 10 mm is considered ventriculomegaly (VM). Ventriculomegaly may be associated with chromosomal abnormalities and/ or genetic syndromes. Thus, the finding of this 'soft' marker warrants a referral to a fetal medicine unit for a detailed anomaly scan, fetal echocardiography and invasive testing for fetal microarray.

Nuchal Edema

Nuchal fold thickness of more than 6 mm in the second trimester is an important marker for Downs syndrome with a likelihood ratio of 11-18.6. Thus, it warrants offering amniocentesis for karyotype. Microarray should be offered as it may be associated with other subtle chromosomal abnormalities which may not be picked on conventional karyotype.

Aberrant Right Subclavian Artery (ARSA)

ARSA may be seen in 1 in 100 fetuses. It was given a positive likelihood ratio of 21.48 for Down syndrome and invasive testing is suggested; however, some recent papers has not found an increased risk for aneuploidy or pathogenic copy number variants when ARSA is present in isolation.

Hydronephrosis

The new preferred term is 'urinary tract dilatation' (UTD) rather than hydronephrosis. The anteroposterior renal pelvis diameter should be measured in the transverse section with fetal spine at either 6'o clock or 12'o clock position. Value less than 4mm in the second trimester is considered normal. This finding has a likelihood ratio of 1.5 for Down syndrome. When present in isolation, biochemical screening should be offered if it has not been done before. Even when screening is low risk, UTD should be followed up 4-6 weekly to assess progression. Measurement more than 7 mm after 28 weeks would warrant neonatal evaluation after birth as 10-20% of these fetuses may have an underlying pelviureteric junction obstruction (PUJO) or vesicoureteric reflux (VUR).

Echogenic Bowel

Echogenic bowel can be a subjective finding and is also dependent on transducer frequency. When the bowel appears as bright as or brighter than bone using a low frequency transducer, it should be labelled as echogenic bowel. It may be associated with Down syndrome, fetal infections especially CMV, meconium peritonitis, bowel abnormality or cystic fibrosis. Bowel may also appear echogenic if there has been an intrauterine bleed or if there is fetal growth restriction.

Thus a detailed history and maternal testing for TORCH IgM and IgG and carrier screening for cystic fibrosis should be done.

Short Femur/Short Humerus

Short femur and short humerus may be a constitutional feature or it may be associated with Down syndrome. Truly short femur, ie, less than the 3rd centile is known to be a predictor of maternal preeclampsia, fetal growth restriction and stillbirth. A detailed anomaly scan should be done to exclude skeletal dysplasia.

Intracardiac Echogenic Focus

ICEF is one of the most commonly reported markers in the second trimester ultrasound. It represents mineralization within the papillary muscle. Most are single and in the left ventricle but they can be is seen in the right ventricle or as bilateral or multiple foci. It is seen in 8-15% of Indian fetuses and has no impact on either the structure or function of the heart. It has a weak association with Down syndrome and screening (quadruple marker) should be offered if it has not been done before. Isolated ICEF with low risk on combined first trimester screening does not warrant further testing.

Choroid Plexus Cysts (CPC)

CPCs may be seen in 1-2% of fetuses. They may be associated with trisomy 18 but in the absence of any other structural abnormality, isolated CPCs are of no consequence.

Single Umbilical Artery (SUA)

SUA may be seen 1 in 100 fetuses. It may be associated with cardiac structural abnormalities. Thus, a detailed anomaly scan with fetal echocardiogram should be done. Isolated SUA has a good outcome and in the setting of low risk on prior screening, does not warrant invasive testing. It may be associated with fetal growth restriction; thus serial growth monitoring from 28 weeks onwards is recommended.

Presence of Multiple Markers

Many a times, several soft markers may co-exist; eg echogenic focus and urinary tract dilatation. A composite risk assessment based on maternal age along with all markers should be done and further testing should be based on accepted cut-offs to decide high, intermediate or low risk.

AOGD Good Clinical Practice Recommendations on Aneuploidy Screening in Pregnancy have been drafted by the AOGD Fetal Medicine Subcommittee (2017 – 2019). The suggested flowcharts by the subcommittee for desirable screening protocols in Indian population are given in figures 1 and 2.

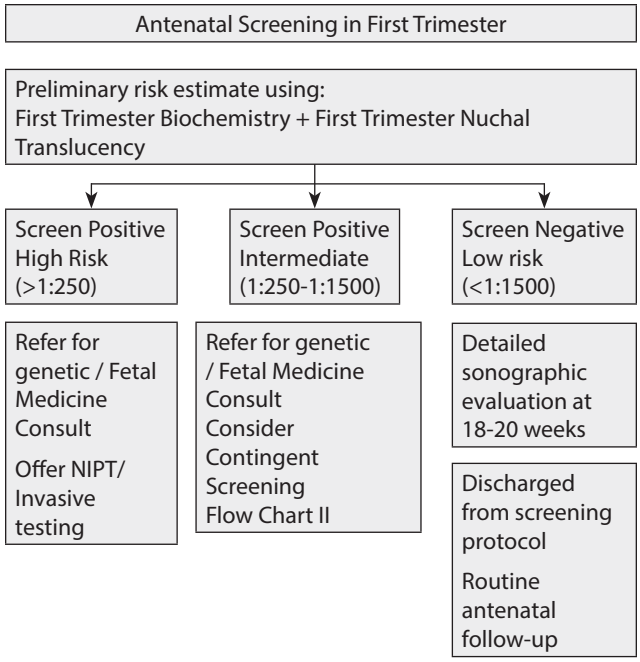


Figure 1: Desirable screening protocol in the first trimester

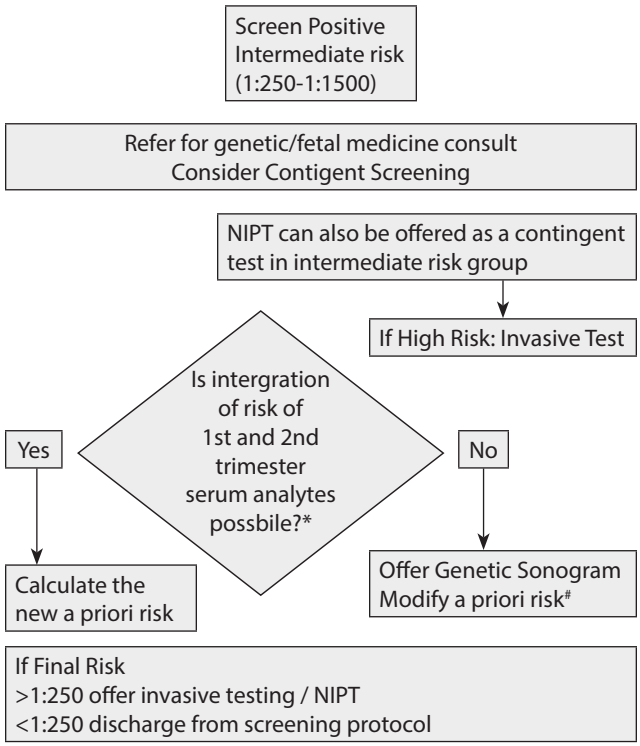


Figure 2: Contingent Screening in Intermediate Risk Group

Conclusion

Combined first trimester screening seems to be the most acceptable primary screening method in our country with a high detection rate for Down syndrome. Women who miss the first trimester screening should be offered a quadruple marker and genetic sonogram. All tests must be interpreted in the context of a priori risk that considers both maternal age as well as risk modification by previously performed screening tests.

References

1. Kagan KO, Wright D, Spencer K et al. First-trimester screening for trisomy 21 by free beta-human chorionic gonadotropin and pregnancy-associated plasma protein-A: impact of maternal and pregnancy characteristics. Ultrasound Obstet Gynecol 2008. May;31(5):493-502.
2. Wagner P, Sonek J, Hoopmann M et al. First-trimester screening for trisomies 18 and 13, triploidy and Turner syndrome by detailed early anomaly scan. Ultrasound Obstet Gynecol 2016 Oct;48(4):446-451.
3. Malone FD, Canick JA, Ball RH, et al. First- and Second-Trimester Evaluation of Risk (FASTER) Research Consortium. First-trimester or second-trimester screening, or both, for Down's syndrome. N Engl J Med 2005;353:2001e11.
4. Santorum M, Wright D, Syngelaki A et al (2016) Accuracy of first trimester combined test in screening for trisomies 21, 18 and 13. Ultrasound Obstet Gynecol.
5. Pandya P, Wright D, Syngelaki A et al (2012) Maternal serum placental growth factor in prospective screening for aneuploidies at 8–13 weeks' gestation. Fetal Diagn Ther 31:87–93.
6. Rolnik DL, Wright D, Poon LCY, et al. ASPRE trial: performance of screening for preterm pre-eclampsia. Ultrasound Obstet Gynecol. 2017 Oct;50(4):492-495.
7. Benn P, Borrell A, Chiu RW, et al. Position statement from the Chromosome Abnormality Screening Committee on behalf of the Board of the International Society for Prenatal Diagnosis. Prenat Diagn. 2015 Aug:35(8):725-34.
8. Winter TC, Rose NC. How to integrate cell-free DNA screening with sonographic markers for aneuploidy: an update. AJR Am J Roentgenol. 2018 Apr;210(4):906-912.
9. Agathokleous M, Chaveeva P, Poon LC, et al. Meta-analysis of second trimester markers for trisomy 21. Ultrasound Obstet Gynecol. 2013 Mar;41(3):247-61.
10. Svirsky R, Reches A, Brabbing-Goldstein D, et al. Association of aberrant right subclavian artery with abnormal karyotype and microarray results. Prenat Diagn. 2017 Aug;37(8):808-811.

Events held under aegis of NARCHI, Delhi Branch

1. An awareness talk by Dr Kusum Chopra, on cervical cancer, breast cancer and menstrual hygiene was organized by the Rotary club, Panchsheel park, RCD Ridge at Pitambar Public School, Kishan Garh on 16th November, 2019. Blood sugar testing and eye check-up was done for more than 100 people. Cloth bags and Sanitary Napkins were distributed to more than 70 women.
2. As a Pre-congress activity of 26th NARCHI Delhi Annual conference, an Expert Group Meeting and workshop on Sustainable Menstrual hygiene management (MHM) was organized on 21st November, 2019, by Department of Obstetrics and Gynecology, VMMC & Safdarjung Hospital. 23 senior gynaecologists from the private and public sector discussed protocols and guidelines for MHM. Dr Ajay Khera, Commissioner, Maternal and Child Health, GOI also participated and shared his opinions as well as the initiatives taken by his Ministry. The discussion was followed by a workshop which covered varied topics from "Innovations in MHM" to "Menstrual disorders in adolescents". The highlight of the workshop was a role Play on MHM conversations in Gynae OPD.
3. Another Pre-conference Workshop on "Knotting and Suturing" was conducted on 21st November 2019, at Safdarjung hospital. Workshop had video presentation on Knotting and Suturing followed by practical training which was hugely appreciated by all the participants.
4. Sir Ganga Ram Hospital, New Delhi, organized another Pre-congress Workshop of 26th NARCHI Annual Conference on 22nd November 2019, "Learning and Unlearning Infertility Practice". The workshop was attended by over in place of about 100 delegates. There were 5 lectures and 3 panel discussions followed by an interactive Question Answers session.
5. The fourth Pre-congress Workshop of 26th NARCHI Annual Conference was on "Post-Partum Hemorrhage Management", organized on 22nd November 2019, by Railway Hospital, New Delhi. Different Modalities of PPH management from medical to surgical, including all recent advances were discussed at this workshop.
6. 26th Annual NARCHI Delhi Conference was organized by the Department of Obstetrics & Gynaecology, VMMC & Safdarjung Hospital at Atal Vihari Bajpai Institute of Medical Science and Dr. Ram Manohar Lohia Hospital on 23rd-24th November 2019. The Conference was inaugurated by Dr. Sanjay Tyagi, Director General Health Services, Ministry of Health and Family Welfare, Government of India. The theme of the conference was **"The postpartum period: The crucial six weeks"** where experts and doyens of the field from the premier institutes and hospitals all over Delhi, participated & discussed the disorders and their management in the post-partum period. Dr S K Das Oration on "Quality of Care in Pregnancy" was delivered by Dr Sunita Malik and Smt. Lilawati Ghai Oration on "Antimicrobial Resistance: Smart Use of Antibiotics" was delivered by Dr Manju Puri. Key Note Address on "Postpartum Surgical Emergencies" and "Revisiting Breastfeeding and Lactation Failure" was delivered by Dr Vijay Zutshi and Dr Sadhana Gupta, respectively.
7. The motto of NARCHI Delhi is "Reaching the Unreached" for promotion of reproductive and child health. Catering to this motto, NARCHI has conducted 15 CMEs, 4 health camps, 11 Public forums and 5 Awareness programmes in the year 2019, especially for general masses who are not usually part of the mainstream institutional programs. There were many cervical and breast cancer screening camps in the peripheral part of Delhi where many positive cases were screened and treatment could be started at early stages of disease.
8. A cervical cancer screening camp was organized for teachers and mothers of the students in place of children in Green Field Public School on 7th December, 2019 by Rotary club, Delhi Ridge. 41 women got breast cancer screening and 28 Pap's smear tests were done by a in place of the team from Rajeev Gandhi Cancer Hospital.
9. A CME was conducted on 14th February, 2020. Deliberations were held on "Current trends in management of recurrent pregnancy loss" by Dr Mala Arora and "Drugs in Pregnancy and their Safety" by Dr Sonia Naik.
10. Another CME was organized on 24th February, 2020. Vivid lectures on "Advance protocol of IVF" by Dr Anup Gupta and "Overview on Yamuna Yatra for clean Environment and population control" by Dr Shirin were delivered.

Events held under aegis of NARCHI

Awareness Talk by the Rotary Club,
Panchsheel park

Cervical Cancer Screening Camp
at Green Field Public School

CME on RPL Management
& Safety of Drugs in Pregnancy

CME on IVF Protocols
& Overview on Yamuna Yatra

Round Table Discussion & Workshop on Menstrual Hygiene

Pre-congress Workshop on
"Knotting and Suturing"

Pre-congress Workshop on
Infertility at Sir Ganga Ram Hospital

Pre-congress Workshop on PPH
at Railway Hospital, New Delhi

26th Annual NARCHI Delhi Conference, Inaugural Ceremony

Inaugural Ceremony

Events held under aegis of NARCHI

Presidential Address and Report

Vote of Thanks by Secretary

Souvenir Release




Patrons NARCHI Delhi Branch with Chief Guest & Guests of Honour at Annual Conference


Key Note Address by Dr Vijay Zutshi


Key Note Address by Dr Sadhana Gupta


Dr S K Das Oration by Dr Sunita Malik


Dr Manju Puri: Smt Lilawati Ghai Oration


Dr Shiela Mehra Quiz

Valadictory Ceremony


मासिक धर्म में पर्यावरण अनुकूल उत्पादों को बढ़ावा देगी सरकार

सफदरजंग अस्पताल में दिल्ली के 23 अस्पतालों के विशेषज्ञों की हुई बैठक


दैनिक भास्कर

24-Feb-2019
फरीदाबाद Page 4

राजधानी के अस्पतालों में आने वाली गर्भवती महिलाओं में करीब 75 फीसदी महिलाएं होती हैं एनीमिया की शिकार


गर्भावस्था में मधुमेह-हाइपरटेंशन से बदल सकता है शिशु का आकार

75 फीसदी एनीमिया की शिकार
Press Coverage of Conference

Approach to a Case with Ventriculomegaly/ Hydrocephalus Spectrum

Manisha Kumar[1], Ramya Mishra[2]
[1]Professor, [2]Resident, Department of Obstetrics and Gynecology, Lady Hardinge Medical College, New Delhi

Introduction

Ventriculomegaly is said to occur when the atrial diameter of the lateral ventricle is more than 10 mm which is 2.4 SD above mean. The incidence is 1 in 100 fetus at 20 weeks of gestation but decreases to 1 in 1000 at birth, due to its resolution in most of the cases. The ventricular atrial diameter remains constant from 18 weeks to 40 weeks. When the atrial diameter is between 10 to 12 mm it is defined as mild ventriculomegaly. The measurement between 13 to 15 mm is considered moderate and the diameter of more than 15mm is said to be severe ventriculomegaly. Hydrocephalus is the pathologic dilatation of the brain ventricular system, usually due to obstruction.

Normal Ventricular System

The ventricular system is responsible for the production and circulation of the cerebrospinal fluid (CSF). It is a system of four interconnected cavities (ventricles) in the brain where CSF is produced and then circulated to the central canal of the spinal cord. Choroid plexus in the lateral ventricles produce CSF which in turn is connected to third ventricle by inter ventricular foramen of Monro. The third ventricle and fourth ventricle are connected by aqueduct of Sylvius. Fourth ventricle is connected to subarachnoid space via the cisterna magna through median aperture, Magendie and to subarachnoid space via the cistern of great cerebral vein through right and left lateral aperture of Luschka. Ventriculomegaly is not a disease but a manifestation of various intracranial disease processes.

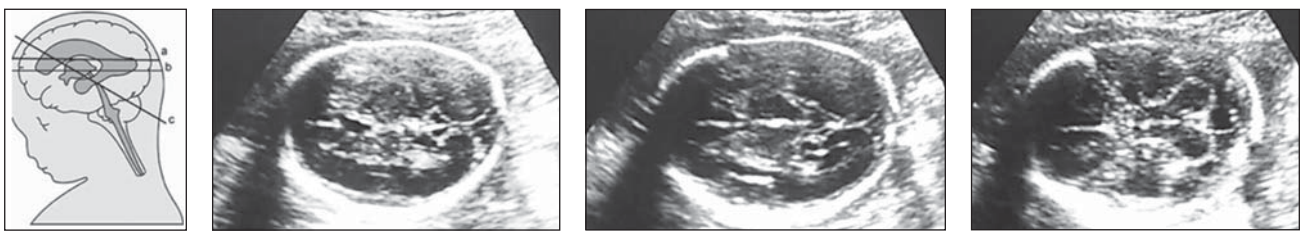
Assessment of Intracranial anatomy on Ultrasound is shown in figure 1 & 2.

Work Up of Case with fetal Ventriculomegaly

History: A detailed history which includes family history of any congenital anomaly or developmental delay, past history of infection, drug intake or diabetes should be taken.

Targeted ultrasound: The incidence of additional CNS and non-CNS sonographic abnormalities identified in fetuses with mild or moderate ventriculomegaly is nearly 50%. When ventriculomegaly is identified, a detailed ultrasound should be performed by a practitioner experienced in the diagnosis of fetal anomalies. Careful attention should be given to intracranial anatomy including the lateral, third, and fourth ventricles, corpus callosum, thalami, germinal matrix region, cerebellum and the cerebellar vermis. Ventriculomegaly is a nonspecific finding and careful attention to all fetal anatomic structures, both CNS and non-CNS, is important.

The fetal heart should be carefully examined, and fetal biometry should be assessed for evidence of growth restriction. Finally, a thorough inspection should be performed for signs of fetal infection, including intracranial or extracranial calcifications, hepatosplenomegaly, ascites, and fetal growth restriction. Cerebro-mantle thickness if less than 10 mm shows poor prognosis, but if more cannot ensure normal mental functions.



A B C

Figure 1: The intracranial anatomy is studied on ultrasound in three different views. First view is an axial section in which we see frontal horn, cavum septum pellucidum, atrium and choroid plexus (A). In the second axial view we can see thalamus and hyppocampal gyrus (B) and in the third view we see cerebellum and cisterna magna (C).

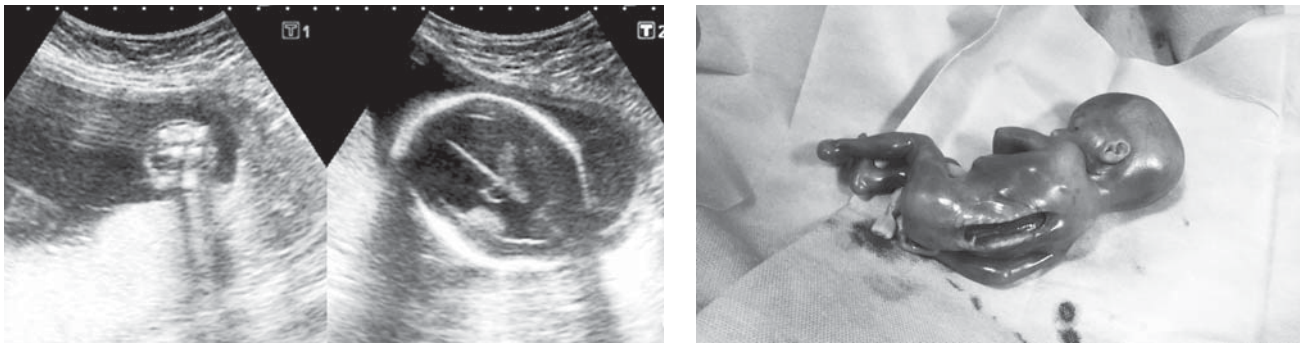


Figure 2: The antenatal ultrasound and photograph of baby with Spina bifida and ventriculomegaly, it is the most common anomaly associated with ventriculomegaly.

Blood investigations: Approximately 5% of cases of mild to moderate ventriculomegaly are reported to result from congenital fetal infections, including CMV or toxoplasmosis. The blood investigations advised are TORCH serology, OGTT, VDRL test.

Invasive testing: It must be advised after counselling, sample is to be sent for karyotyping and Microarray. Approximately 5% of fetuses with apparently isolated mild to moderate ventriculomegaly have an abnormal karyotype, most commonly trisomy 21. Another 10 -15% have abnormal findings on chromosomal microarray.

Fetal MRI: Fetal MRI can be useful in the evaluation of ventriculomegaly because it can identify significant abnormalities not easily detected by ultrasound. It is useful particularly in certain abnormalities like Lissencephaly, a neuronal migration disorder. Fetal MRI is best done after 32 weeks of gestation.

Counselling Regarding Outcome

- **Isolated ventriculomegaly of <12mm (mild):** Incidence of neurodevelopmental delay is 7.9%, similar to that noted in general population.
- **Moderate ventriculomegaly (13-15 mm):** The likelihood of normal neurodevelopment is 75-93%.
- **Severe ventriculomegaly (>15mm)**: There is 80-87% survival at birth, severe disability is seen in 40%, mild to moderate disability seen in 20%, no disability seen in 40%. However study done in the present setup showed only 40% survival.
- **Ventriculomegaly with associated malformations**: In the presence of associated malformations mortality is 50-70%.

Management of Pregnancy

- Counselling from a fetal medicine specialist/ neurosurgery should be sought.
- If the period of gestation is less than 20 weeks and ventriculomegaly is severe or with associated malformation, the termination of pregnancy can be offered.
- Ultrasound and investigations should be aimed at identifying associated abnormalities as the prognosis is poor with associated malformations.
- Serial ultrasonography is to be done at regular intervals to monitor its evolution
- The timing and mode of delivery is based on standard obstetric indications.

Route of Delivery

- All decisions have to be taken after counselling and informed choice to the couple regarding the prognosis.
- There is no evidence that the preterm or Caesarean delivery improves maternal or neonatal outcome in the setting of mild to moderate ventriculomegaly.
- If the baby is regarded, CSF drainage is avoided and delivery can be done by lower segment Caesarean section if fetal head circumference is >40 cm.
- In cases where prognosis is dismal, cephalocentesis is advised where fetal head is decompressed to allow vaginal delivery and avoid maternal morbidity due to surgery.

Counselling about Risk of Recurrence

Recurrence risk of isolated ventriculomegaly in the future pregnancy is low in most of the cases. If the aetiology of ventriculomegaly is attributed to infections like toxoplasma or CMV, there is no increased risk of recurrence. If it is a part of a genetic syndrome, the recurrence risk depends upon the type of inheritance. Half of the male fetuses may be affected in X-linked hydrocephaly.

Our Experience

A study was done at Lady Hardinge Medical College to find out the outcome of fetal ventriculomegaly (VM) in terms of survival after two years and to evaluate the antenatal factors which influence the postnatal outcome. Fetal VM was seen in 263/648(40.6%) cases with central nervous system malformation. VM was severe in 85.9% and was associated with other anomalies in 56.3% of the cases. Total 40.3% cases with VM were liveborn. The survival at birth was poorest with severe VM (40.7%) and in cases associated with multiple defects (30%). Only 23.6% survived beyond 2 years of age. There was developmental delay in 24.2% among those survived. Logistic regression analysis showed that, the presence of associated defect and severe VM were significant poor prognostic factors for survival at birth (p=0.001) and after 2 years of age (p=0.002). It was concluded that in a low resource setup the problems associated with fetal VM were compounded by late referral. The outcome in the present set up was far lower than that quoted in western studies. The knowledge of the outcome in existing setup provides data for realistic counselling to the couple.

Key Points

- When enlargement of the lateral ventricles (≥10 mm) is identified, a thorough evaluation should be performed, including detailed sonographic evaluation of fetal anatomy.
- Amniocentesis for karyotype/chromosomal microarray analysis, and a workup for fetal infection must be done.
- Follow-up ultrasound examination should be performed to assess for progression of the ventricular dilation.
- Ventriculomegaly is characterized as mild (10-12 mm), moderate (13-15 mm), or severe (>15 mm) for the purposes of patient counselling given that the chance of an adverse outcome and potential for other abnormalities are higher when the ventricles measure 13-15 mm vs 10-12 mm.
- In isolated mild ventriculomegaly of 10-12 mm, after a complete evaluation, women can be counselled that the outcome is favourable, and the infant is likely to be normal.
- In isolated moderate ventriculomegaly of 13-15 mm, after a complete evaluation, women can be counselled that the outcome is likely to be favourable but that there is an increased risk of neurodevelopmental disabilities.
- In cases of severe ventriculomegaly and associated anomalies, prognosis is worse.
- Both intracranial and extra cranial anomalies might be associated with occurrence of ventriculomegaly.
- The timing and mode of delivery should be based on standard obstetric indications.
- Vaginal delivery should be preferred in cases of poor prognosis; parents are advised to take informed decision.

Suggested Reading

1. International Society of Ultrasound in Obstetrics and Gynecology Education Committee. Sonographic examination of the fetal central nervous system: guidelines for performing the 'basic examination' and the 'fetal neurosonogram.' Ultrasound Obstet Gynecol 2007;29: 109-16.
2. Griffiths PD, Reeves MJ, Morris JE, et al. A prospective study of fetuses with isolated ventriculomegaly investigated by antenatal sonography and in utero MR imaging. AJNR Am J Neuroradiol 2010;31:106-11
3. Sethna F, Tennant PW, Rankin J, C Robson S. Prevalence, natural history, and clinical outcome of mild to moderate ventriculomegaly. Obstet Gynecol 2011;117:867-76.
4. Pasquini L, Masini G, Gaini C, et al. The utility of infection screening in isolated mild ventriculomegaly: an observational retrospective study on 141 fetuses. Prenat Diagn 2014;34:1295-300.
5. Donnelly JC, Platt LD, Rebarber A, Zachary J, Grobman WA, Wapner RJ. Association of copy number variants with specific ultrasonographically detected fetal anomalies. Obstet Gynecol 2014;124: 83-90
6. Griffiths PD, Bradburn M, Campbell MJ, et al. MERIDIAN Collaborative Group. Use of MRI in the diagnosis of fetal brain abnormalities in utero (MERIDIAN): a multicenter, prospective cohort study. Lancet 2017;389: 538-46.
7. Society for Maternal-Fetal Medicine (SMFM); Nathan S. Fox, MD; Ana Monteagudo, MD; Jeffrey A. Kuller, MD; Sabrina Craigo, MD; and Mary E. Norton, MD. Mild fetal ventriculomegaly: diagnosis, evaluation, and management. Society for Maternal-Fetal Medicine (SMFM) Consult Series I #45 smfm.org
8. S. Carta, A. Kealin Agten, C. Belcaro And A. Bhide. Outcome of fetuses with prenatal diagnosis of isolated severebilateral ventriculomegaly: systematic review and meta-analysis Ultrasound Obstet Gynecol. 2018 Aug;52(2):165-17.
9. Kumar M, Garg N, Hasija A, Pritam A, Shukla P, Vanamail P, Roy Choudhury S. Two-year postnatal outcome of 263 cases of fetal ventriculomegaly. J Matern Fetal Neonatal Med. 2018 Oct 1:1-7.

Emerging Role of Microarray in Prenatal Diagnosis

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Chromosomal Microarray Analysis (CMA) is a molecular technique for screening whole genome at high resolution. It detects most of the chromosomal aberrations seen on conventional karyotype as well as smaller submicroscopic deletions and duplications. These smaller submicroscopic deletions and duplications are known as copy number variants (CNVs). CMA is recommended as the first-tier test in the postnatal evaluation of congenital abnormalities and neurodevelopmental disorders. It has become an important diagnostic tool in prenatal and postnatal evaluation.

Technique

It is performed on DNA extracted from chorionic villi, amniocytes or fetal blood unlike karyotype where cell culture is required. Two techniques used in prenatal microarray are comparative genomic hybridisation (CGH) and single neucleotide polymorphism (SNP). Most of the platforms of CMA use a combination of both.

In CGH the fetal DNA and control or reference DNA are labelled with different colored fluorescent dyes, mixed and hybridised on array platform consisting of DNA probes. The relative intensities of the colors indicate duplication or deletions. These signals are interpreted by bioinformatics.

In SNP, only fetal DNA is hybridized on array platforms. A SNP is a variation at a single position in a DNA sequence among individuals.

While CGH arrays can detect CNVs, SNP can detect triploidy, and regions on the 2 homologous chromosomes that are identical to each other, as occurs with uniparental disomy (UPD) and consanguinity. SNP arrays also can detect some cases of maternal cell contamination, mosaicism and parent of origin.

Arrays may include probes that cover the whole genome, or may be targeted with concentrated coverage in known disease-causing regions of the genome and more limited coverage of the rest of the genome. An advantage of targeted arrays is that they decrease the chance of identifying a variant of uncertain significance (VUS). In general, arrays used for prenatal diagnosis have lower resolution than those used for postnatal testing for this reason.

A standard karyotype can detect aneuploidies (abnormalities in chromosome number), deletions or duplications of approximately 5-10 Mb, and balanced or unbalanced translocations and inversions. CMA has a greater resolution than conventional karyotyping, allowing for the detection of much smaller, submicroscopic deletions, and duplications typically down to a 50- to 100-kb level. With the advent of SNP array for CMA, it is possible to detect triploidy and uniparental disomy which is not detected with CGH array. CMA is unable to detect balanced chromosomal structural abnormalities like balanced translocation or inversions. CMA also can detect some copy number changes near the chromosomal breakpoint sites in rearrangements that appear to be balanced on a conventional karyotype.

CMA may be performed on DNA obtained from amniocentesis, CVS, fetal cord blood, and stillbirth specimens. DNA obtained from the mesenchymal core cells of the chorionic villi and uncultured amniocytes is preferable to DNA from cultured cells to allow for quicker turnaround and to avoid the possibility of culture artifacts.

Indications

1. Fetal structural abnormalities: The yield of CMA is about 6-7% more than conventional karyotype in cases with fetal structural abnormalities.
2. Stillbirths: The yield of CMA is better than conventional karyotype in macerated tissue as it does not require dividing cells and results are more likely to be available if good quality DNA is available (87% vs 70%). The detection rate of CMA for genetic disorders is also more than conventional karyotype in stillbirths (8.3% vs 5.3%).
3. Miscarriage: CMA is a better tool to evaluate abortus as there is high failure rate of culture in this tissue also. Usually low resolution panels of CMA are sufficient to evaluate abortal tissue.
4. Women undergoing invasive testing for advanced maternal age, abnormal screening results: The diagnostic yield of CMA over conventional karyotype in these cases is about 1.7%. Most of

the bodies recommend conventional karyotype as the first-tier test in these cases. However, women undergoing invasive testing for any indication may be offered CMA after proper counselling of its advantages and limitations.

Advantages

1. Higher diagnostic yield: The higher detection rate of CMA for genetic disorders in various situations has been discussed in the above section. This is attributed to its better resolution (50-100kb) than conventional karyotype (5-10Mb).
2. Faster turnaround time: CMA does not need cell cultures or dividing cells for analysis and hence results are usually available in a week.
3. Macerated tissue: It has higher yield in stillbirths and products of conception for the same reason that dividing cells are not required and good quality DNA is used for CMA.
4. Identifies consanguinity and parents of origin.

Limitations & Disadvantages

1. Inability to detect balanced translocations, however most of these are benign.
2. CMA does not provide information about mechanism of chromosomal imbalance, whether it is trisomy or an unbalanced Robertsonian translocation defect. Unbalanced translocations if inherited have a higher recurrence risk. These cases need further evaluation by karyotype to look for translocation.
3. Diseases may be identified for which the clinical presentation may vary greatly and range from mild to severe. It may not be possible to predict what the outcome will be in a given patient.
4. Does not identify single gene mutations as for hemoglobinopathies, spinal muscular dystrophy or cystic fibrosis.
5. VUS: Copy number variants of uncertain significance (VUS) are copy number changes that have not been reported and thus have an unknown phenotype. These small changes are not detectable by G-banding, but are identified by CMA in 1 to 2 percent of cases. The additional information provided by CMA can be challenging to interpret, particularly if a phenotypically normal parent carries the same change. In the absence of clear prognostic information, parents may find it difficult to make a decision about continuing the pregnancy. The patients in whom a fetal VUS is detected receive counselling from experts who have access to databases that provide updated information concerning genotype-phenotype correlations. In prenatal testing, low resolution platforms of CMA are used to minimise VUS.
6. Information not sought for may come forth during evaluation by CMA: CNVs with severe neurological phenotypes or mild or severe adult onset diseases may be detected. It also may disclose consanguinity and non-paternity. This may cause parental anxiety and difficult decisions regarding reproductive choices.

Counselling

Pre and post-test counselling be performed by trained genetic counsellors, geneticists or other providers with expertise in the complexities of interpreting CMA results. The couple should be informed about indications, advantages, limitations, disadvantages and VUS. The patients in whom a fetal VUS is detected receive counselling from experts who have access to databases that provide updated information concerning genotype-phenotype correlations.

Conclusion

There is abundant evidence indicating the added detection of pathogenic abnormalities with CMA in comparison to the traditional karyotyping. It is the test of choice in fetuses with ultrasound abnormalities and for evaluation of stillbirths. However it has potential to cause clinical and ethical dilemmas in prenatal diagnosis. Thorough prenatal and postnatal counselling to apprise the patient of scope of the test helps her in making reproductive choices.

Suggested Reading

1. Dugoff L, Norton ME, Kuller JA. Society for Maternal-Fetal Medicine Consult series no. 41. The use of chromosomal microarray for prenatal diagnosis. American journal of obstetrics and gynecology. 2016; 215:B2–9.
2. Levy B, Wapner R. Prenatal Diagnosis by Chromosomal Microarray Analysis. Fertil Steril. 2018; 109(2): 201–212.
3. Oneda B, Rauch A. Microarrays in prenatal diagnosis. Best Practice & Research Clinical Obstetrics and Gynaecology 42 (2017) 53e63.
4. Committee Opinion No. 682: Microarrays and Next-Generation Sequencing Technology: The Use of Advanced Genetic Diagnostic Tools in Obstetrics and Gynecology. Obstetrics and gynecology. 2016; 128:e262–e8.

Fetal Therapy

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Definition: Fetal therapy is defined as any intervention aiming for correcting or treating a certain foetal pathology or an anomaly.

Advances in technology resulting in improved resolution of ultrasound and more refined endoscopic equipment have made the foetus more easily accessible. Consequently several fetal conditions are now amenable to both medical and surgical interventions. Due to the potential complications, the risks and benefits of the intervention must be balanced. Fetal disorders amenable to treatment with either maternal medication or surgical procedures are discussed. A consensus endorsed by the international fetal medicine and surgery society (IFMSS) has been reached on the criteria and indications for fetal therapy.

Table 1: Types of fetal therapy

Non invasive	Invasive Direct therapy	Invasive Fetal Therapy
Preventive	Intrauterine transfusion	FIGS
Therapeutic	Drug therapy	FETENDO
		Hysterotomy

Types of Fetal Therapy (Table 1)

Preventive Pharmacotherapy

Periconceptional folic acid supplementation: 400ug/day in low risk and 4mg/day in high risk pregnancies started two months preconception and continued in first trimester to prevent neural tube defects.

Antenatal steroid to enhance foetal lung maturity: Injection Dexamethasone 6 mg Intramuscular, 4 doses at an interval of 12 hrs at gestational age between 24-34 weeks.

Anti D immunoglobulin to Rh negative mothers: 300ug intramuscular at 28 weeks after confirming absence of isoimmunisation (RAADP) and within 72 hrs of delivery (300ug) if baby is Rh positive has reduced the incidence of isoimmunisation from 16% to 0.2 %.

Hydroxycholroquine to SLE mothers with positive anti Ro/La antibodies to prevent congenital heart block: HCQS 6mg/kg/d should be initiated between 6-10 wks of gestation if not already on this medication as would be in case of previous affected child or positive anti Ro/La antibodies.

Therapeutic Pharmacotherapy

Fetal goitre: Fetal cord blood should be tested for thyroid status and then treated by either transplacental carbimazole or levothyroxine.

Fetal heart block: Transplacental dexamethasone 4 mg daily till 26 weeks or term in first degree or second degree heart block.

Congenital Adrenal Hyperplasia: Oral dexamethasone 20 µg/kg/d to 1.5 mg per day divided in three doses. Critical period for external genitalia development is 7 to 12 weeks. To prevent virilization, treatment should be initiated by 9 weeks before it is known whether the fetus is at risk. It can be stopped once prenatal diagnosis establishes unaffected fetus.

Congenital cystic adenomatoid hyperplasia: Inj Dexamethasone to mother 12 mg every 12 hours, for 4 doses.

Fetal tachyarrythmias: Refer to Table 2

Fetal Infections: Toxoplasmosis, Materna l HIV, HSV and Varicella.

Table 2: Management of fetal tachyarrythmias

	First choice therapy	Second choice therapy	Third choice therapy
Short VA SVT or AFL Non hydrops	Digoxin	Digoxin and sotalol	Digoxin and flecainide
Short VA SVT or AFL hydrops	Digoxin and sotalol	Digoxin and flecainide	
Long VA SVT	Sotalol	Flecainide	

VA: Ventricular arrythmia, SVT: Supraventricular tachycardia, AFL: Atrial fibrillation. Ref: Miyoshi T, et al. BMJ Open 2017;7:e016597.

IFMSS Criteria for Fetal Surgery

Accurate diagnosis and staging is possible with exclusion of associated anomalies.

Natural history of disease is documented and prognosis is established.

There is currently no effective postnatal therapy at that period of gestation.

In utero surgery has proved feasible in animal models, reversing deleterious effects of the condition.

Interventions are performed in specialised multidisciplinary fetal treatment centres registered with the appropriate authorities within strict protocols and informed consent of the mother or parents.

Invasive Fetal Therapy

Fetal Direct Therapy

Intrauterine transfusion: Fetal anemia as in Rh alloimmunisation, Parvo virus B19 infection or fetal hemoglobinopathies when MCA PSV >1.5 MoM and Hb 2SD below mean for that gestational age or in presence of hydropic features between 16- 35 weeks.

Access site for intrauterine transfusion: In case of anterior placentation, umbilical vein at the placental end of the cord insertion is the preferred target. In case of posterior placentation needling of free floating loop of cord can result in 3 fold increase in procedure related complications as it readily floats away from the needle when cord penetration is attempted. Most European centres advocate use of the intra hepatic portion of the umbilical vein in an effort to prevent fetal bradycardia but it is associated with increase in fetal stress hormones. Hence umbilical cord insertion into the posterior placenta is the primary site of access for IUT. Use of the intrahepatic vein should be considered a viable option in case of poor access to the cord or may be preferred target for vascular access when transfusing a twin gestation if the corresponding placental cord insertions are difficult to identify.

Red cells to be used for IUT should be O negative, fresh (collected within the previous 72 hours), Hct 80%, leukocyte depleted, CMV seronegative and unit irradiated with 25 Gy to prevent graft vs host reaction.

Technique: Antenatal steroids should be given after 26 weeks. Procedure should be planned with all pre requisites of the need of emergency CS. Under ultrasound guidance the fetus is paralysed (Vecuronium 0.1mg/kg or Atracurium 0.4mg/kg). Once access to the fetal circulation is obtained (Figure 1) an initial sample should be sent for hematocrit and reticulocyte count. The three way stop cock is connected to the needle and packed cells transfused at the rate of 1-2 ml/min (Figure 2). Target hematocrit is 55% while in case of hydropic fetus it is 30% and a repeat procedure is performed 48 hrs later to normalise the fetal hematocrit. Hydrops typically reverses after 2 or 3 IVTs, placentomegaly being the last features of hydrops to reverse. The timing of subsequent transfusions can be calculated on the basis of an anticipated decline in fetal haemoglobin of 0.4g/dl/d, 0.3g/dl/d and 0.2g/dl/d consecutively for the first, second and third transfusion intervals. More rapid decline in hematocrit in the first transfusion interval can be anticipated in hydropic fetuses.

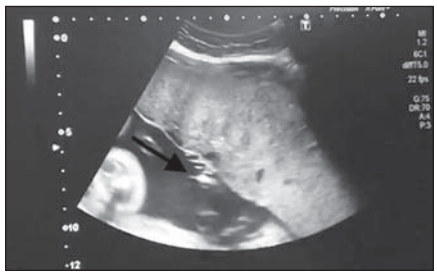

Figure 1: Needle tip in umbilical vein

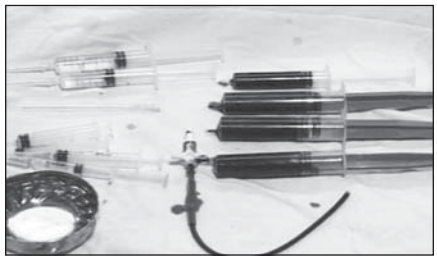

Figure 2: Blood loaded for fetal transfusion

Intraamniotic Levothyroxin 200-800 ugms/injection in Fetal Goitrous Hypothyroidism.

Fetal arrhythmias: Last resort in severe hydrops. Drugs given are Amiodarone, Digoxin, Verapamil and Adenosine. Sites are Umbilical vein, Fetal heart, Fetal peritoneum and muscle.

Direct fetal pacing: Without reported survivors. Development of new Endocardial lead for direct fetal pacing could make this feasible.

FIGS: Fetal intervention Guided sonographically

Procedures Include

Selective fetal reduction

To drain amniotic fluid (Amnioreduction), fetal urine, collections (Figure 3)

To sample fetal tissue

To place catheter shunts in fetal bladder, chest, abdomen, ventricles

RFA of acardiac twin/TRAP in TTTS

Multifetal Pregnancy Reduction (MFPR):

MFPR is performed between 11-14 wks gestation. A Nuchal translucency (NT) scan is performed to map all pregnancies and decision is based on reducing the smallest accessible fetus or fetus with abnormal NT scan. If a monochorionic pair of fetuses exists in a higher order multiple pregnancy that pair can be selected for reduction after informed consent. A 22 gauge spinal needle is placed into the thorax of the targeted fetus, 2 ml (dose can be increased if required) of potassium chloride is injected and asystole is observed for at least 3 minutes. Transvaginal MFPR is typically reserved for the rare situation in which target fetuse cannot be safely approached transabdominally because this technique is associated with significantly higher loss rates when compared with transabdominal approach (12% vs 5%). The FIGO Committee for the ethical aspects of human reproduction and women health has recommended that for triplet pregnancies and higher "it may be considered ethically preferable to reduce the number of fetuses rather than to do nothing".

Selective Termination

The phrase selective termination refers specifically to termination of an anomalous fetus in a multiple gestation typically in the second trimester. This differs from multifetal reduction which refers to a non specific reduction in the number of fetuses present in a higher order multiple pregnancy, almost always in the first trimester to lower the risk for prematurity for the remaining fetuses.

The method of selective termination depends on the chorionicity. In dichorionic pregnancies, USG guided intracardiac injection of potassium chloride is the most common technique. In monochorionic pregnancies ultrasound guided / fetoscopic / laser /RFA cord occlusion is commonly used.

Indications

1. TRAP (Twin reverse arterial perfusion) sequence
2. Selective FGR type 2
3. Discordant anomaly (lethal) in one twin
4. TTTS stage 3 or 4 can be an option other than laser. Co twin survival rates are higher with RFA performed as early as possible between 12-23 weeks.

Radiofrequency ablation (RFA): It has been used for selective fetal reduction in monochorionic pregnancies for similar indications as fetoscopic cord occlusion. It has also been used in ablating sacrococcygeal teratomas. The procedure is performed under local anaesthesia under antibiotic cover. The radiofrequency needle is inserted percutaneously under continuous ultrasound guidance into the intrafetal portion of the umbilical cord (Figure 4). The needle tip position is confirmed by color flow mapping. Radiofrequency energy is applied by the generator until an average temperature of 110°C is achieved for 3 minutes.

Thermal energy is applied until the cessation of blood flow is demonstrated in the umbilical cord by the colour flow Doppler. Cardiac asystole should be observed for 3 minutes either immediately or after 30 minutes of procedure. The advantages of RFA are that it can be performed before 16 weeks, smaller needle diameter, minimal maternal discomfort, performed under local anaesthesia and less procedure related complications.

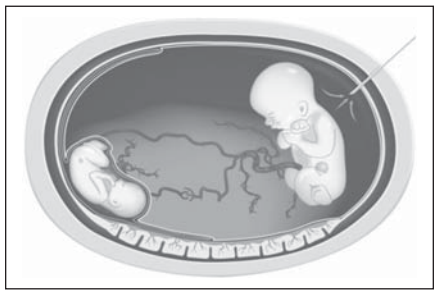

Figure 3: Amnioreduction

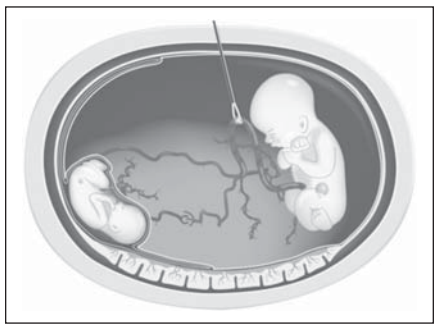

Figure 4: Cord coagulation

FETENDO: Fetoscopic Surgery

Fetoscopic laser coagulation: Laser coagulation of the vascular anastomoses was first reported by De Lia and co workers in 1990. The procedure became much more popular when Nicolaides group described a percutaneous approach, and since a randomised trial proved this to be the most effective it has become the standard of care for advanced cases of TTTS.

Indications

TTTS (Twin to Twin transfusion syndrome) stage 2, 3

and TAPS (The anaemia polycythemia syndrome).

Fetoscopic laser coagulation is usually performed 16 weeks onwards. Preoperatively all patients undergo a detailed ultrasound study for disease staging and to exclude discordant anomalies. Prophylactic antibiotics and prophylactic tocolytics are used. For most cases it is performed percutaneously through a 3-4 mm incision with local anaesthesia. Nd:YAG laser or diode laser with fibres of 400-600 um provides optimal efficacy.

Under USG guidance, the canula or fetoscopic sheath is inserted into the recipient twin sac. Coagulation is performed at a distance of approximately 1cm using Soloman technique (Figure 5 & 6). This approach consists of first selective coagulation of anastomosis and second additional superficial coagulation on the membranes along the complete vascular equator, from one placental margin to the other. The procedure is completed by amnioreduction. The canula or sheath is removed under USG guidance to detect any significant bleeding from the uterine wall.

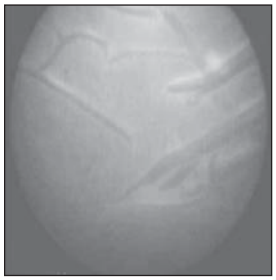

Figure 5: Identifying the vessels

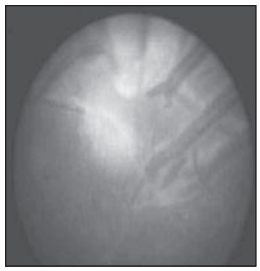

Figure 6: Laser coagulation of vessel

Complications: Postoperatively single IUFD can occur in about 33% of pregnancies and double IUFD in 4%. TAPS can occur in 13% and persistent TTTS in 14% of double survivors but with Soloman technique TTTS can be reduced to <1% and TAPS <1%.

Amnioreduction vs Laser coagulation: Laser coagulation appears to be more effective in the treatment of TTTS, with less perinatal neurologic morbidity and mortality. Use of serial amnioreduction should be restricted to cases with side by side insertion of the umbilical cords, those with large anastomosis between the umbilical cord vessels or with a gestational age of 26 weeks or more and stage 1 disease with technical limitations to visualise the equator.

In addition to utility of laser in monchorionic twins, fetal laser therapy is also used to treat amniotic bands, chorioangiomas, sacrococcygeal teratomas, lower urinary tract obstructions and chest masses (Table 3).

Table 3: Fetal Laser Therapy

	Aims of fetal therapy	Indications of fetal therapy	Alternatives to fetal laser therapy
Amniotic band syndrome	Release the band before irreversible ischemia	Evidence of compromised blood supply	Fetoscopy and section of the bands with scissors
Chorioangioma	Interruption of the vascular supply	Symptomatic hydramnios, fetal heart failure prior to viability	Endoscopic guided ligation of feeding vessel
Sacrococcygeal teratomas	Interruption of the vascular supply to mass or tumour reduction	Fetal heart failure prior to viability	Open fetal surgery Thermocoagulation RFA
LUTO- Posterior urethral valve	Fulguration of the posterior valve through fetal cystoscopy	Megacystis with increased wall thickness, hydronephrosis	Vesicoamniotic shunt
Fetal hyperechoic lung lesions- CPAM, CHAOS, BPS	Interruption of the vascular supply to the mass	Fetal hydrops prior to viability	Open fetal surgery Thoracoamniotic shunt RFA Injection of sclerosing agent or coiling
Fetal Meningomyelocoele (MMC)	Intrauterine repair of MMC	To prevent damage to spinal nerves	Endoscopic Repair (Fig 7)

LUTO: Lower urinary tract obstruction,CPAM:Congenital pulmonary airway malformation,BPS: Bronchopulmonary sequestration,CHAOS: Congenital high airway obstruction syndrome.

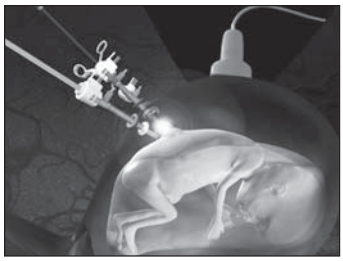

Figure 7: Endoscopic repair of MMC

Open Fetal Surgery

Open fetal surgery refers to any procedure requiring a hysterotomy in contrast to those involving only the insertion of fetoscope. Prenatal surgery can be associated with complications of PROM, PTL, oligoamnios, placental abruption and delivery by CS, table 4.

Table 4: Open Fetal Surgery

Anomaly	Pathophysiologic Consequence	Fetal Treatment
Congenital pulmonary airway malformation	Hydrops, pulmonary hypoplasia	Open surgery lobectomy
Congenital high airway obstruction sequence	Massive hyperechogenic lungs. Heart compression	CS with EXIT procedure and tracheostomy
Sacrococcygeal teratoma	High output cardiac failure	Open surgery tumour debulking
Myelomeningocele	Spinal cord damage Brain stem compression Hydrocephalus	Open surgery defect closure/ Fetoscopic repair
Posterior urethral valve	Renal dysplasia Pulmonary hypoplasia	Vesicoamniotic shunt or Cystoscopic valve ablation
Diaphragmatic hernia	Pulmonary hypoplasia	Fetoscopic endotracheal occlusion

EXIT: Ex utero intrapartum treatment

The Future of Fetal Therapy

The past three decades have seen dramatic progress in our ability to diagnose, appropriately select and treat fetuses with life threatening or quality of life impacting disease. The future includes Fetal Haemopoitic stem cell transplant and Fetal gene therapy. Despite this success, application of fetal intervention remains fairly limited. There are a number of keys that can be envisioned for the future success and expansion of fetal therapy. In the short term the single most important factor is accountability. For fetal therapy to become permanently established, the benefit to patients must be clearly established by randomised clinical trials when applicable. The second area of required progress is reduction of maternal and fetal risk. The third area is development of improved imaging technology. In addition a more developmental approach will be required to fully correct specific defects, with earlier and more discrete interventions.

Suggested Readings

1. Morris RK, Chan BC, Kilby MD. Advances in fetal therapy. The obstetrician and gynaecologist 2010;12:94-102.
2. Friedman DM1, Kim MY, Copel JA, Llanos C, Davis C, Buyon JP. Prospective evaluation of fetuses with autoimmune-associated congenital heart block followed in the PR Interval and Dexamethasone Evaluation (PRIDE) Study. Am J Cardiol. 2009 Apr 15;103(8):1102-6.
3. Mathis J, Raio L, Baud D. Fetal laser therapy: applications in the management of fetal pathologies.Prenat Diagn. 2015 Jul;35(7):623-36.
4. Dodd JM1, Crowther CA. Reduction of the number of fetuses for women with a multiple pregnancy. . Cochrane Database Syst Rev. 2012 Oct 17;10:CD003932.
5. Morris RK1, Selman TJ, Harbidge A, Martin WI, Kilby MD Fetoscopic laser coagulation for severe twin-to-twin transfusion syndrome: factors influencing perinatal outcome, learning curve of the procedure and lessons for new centres.BJOG. 2010 Oct;117(11):1350-7.
6. Dodd JM1, Windrim RC, van Kamp IL. Techniques of intrauterine fetal transfusion for women with red-cell isoimmunisation for improving health outcomes. Cochrane Database Syst Rev. 2012 Sep 12;(9):CD007096.
7. Miyoshi T, Maeno Y, Sago H, et al. Antenatal antiarrhythmic treatment for fetal tachyarrhythmias: a study protocol for a prospective multicentre trial. BMJ Open2017;7:e016597.
8. Kapagambe S, Jensen W G, Chen Y J,Vanover M,et al. Fetal surgery for Meningomyelocoele; A systematic review and metanalysis of outcomes in Fetoscopic versus open repair. Fetal Diagnosis and Therapy 2018;43:161-174.

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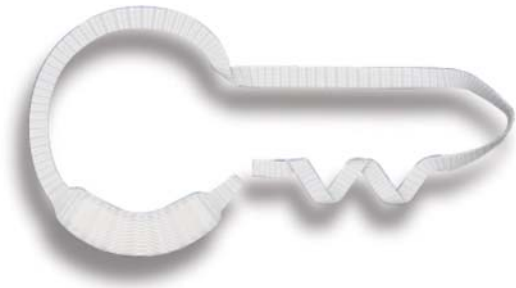

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