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PRACTICE GUIDELINE

SFM Clinical Practice Recommendations for Prenatal Invasive Diagnostic Procedures

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Abstract Diagnostic prenatal invasive testing currently forms an integral and extremely significant component of the practice of obstetric care and has a twofold purpose. The primary aim is to offer management options and informed decision making to pregnant women and their companions. The secondary aim is to ensure that every fetus has an optimal outcome. Currently, most professional societies offer guidelines on prenatal invasive testing based on specific indications. Society of Fetal Medicine (SFM) clinical practice recommendations are developed for use by all practitioners of fetal and maternal healthcare. They are intended to facilitate a reasonable standard of care by the entire medical community. Practitioners are encouraged to go beyond these standards in relevant clinical situations. This document has been drafted after extensive inputs and discussions by practitioners and experts, followed by a consensus.

Keywords Prenatal · Invasive · Diagnostic procedures · Guidelines · Training · Society of fetal medicine

Introduction

Diagnostic prenatal invasive testing currently forms an integral and extremely significant component of the practice of obstetric care and has a twofold purpose. The primary aim is to offer management options and informed decision making to pregnant women and their companions.

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The secondary aim is to ensure that every fetus has an optimal outcome.

The risks of fetal loss following prenatal diagnostic invasive testing have now dramatically reduced and consequently, amniocentesis, chorion villus sampling and cordocentesis can be carried out by personnel with requisite expertise and equipment, within a framework of standard guidelines that include specific and valid indications, counseling, informed consents, local legal requirements, checklists, recommended procedure and complications.

Currently, most professional societies offer guidelines on prenatal invasive testing based on specific indications [1–7]. Society of Fetal Medicine (SFM) clinical practice recommendations are developed for use by all practitioners of fetal and maternal healthcare. They are intended to facilitate a reasonable standard of care by the entire medical community. Practitioners are encouraged to go beyond these standards in relevant clinical situations. This document has been drafted after extensive inputs and discussions by practitioners and experts, followed by a consensus.

India specific stipulations of the Pre Conceptional-Prenatal Diagnostic Techniques (PC&PNDT) Act have been paraphrased in the relevant sections. For practitioners outside India, an approach appropriate to local legal, religious and cultural parameters is recommended.

For the sections requiring evidence review, the modified Grade system was used for classifying the quality of evidence as 1, 2, 3 or 4 (Table 1) [8]

Grading of recommendations:
GRADE AStrongly recommended "**RECOMMENDED**" GRADE BWeaker recommendation "**SUGGESTED"**
Classification of level of evidence
1. High quality evidence backed by consistent results from well-performed randomized controlled trials or overwhelming evidence from well executed observational studies with strong effects
2. Moderate quality evidence from randomized trials
3. Low quality evidence from observational evidence or from controlled trials with several serious limitations
4. Not backed by sufficient evidence; however, consensus reached by expert panel group (Practice based on clinical experience and expertise point)

These points reflect what is considered by SFM to be the best practice at the time at which they are issued, and the user is advised to periodically check for updates and revisions on the SFM website and the Journal of Fetal Medicine, the official journal of the Society.

Indications

Common indications for performing prenatal invasive diagnostic procedures include (but are not restricted to):

a. Abnormal results of aneuploidy screening
b. Thick nuchal translucency
c. Abnormal structural findings on ultrasound
d. Parental carrier of chromosomal balanced translocation
e. Both parents are carriers of a known genetic disorder
f. Advanced maternal age
g. Maternal transmissible infectious diseases
h. Maternal request
i. Previous child/children with chromosomal disorders, metabolic disorders, congenital anomaly, intellectual disability
j. Haemoglobinopathies
k. Sex linked disorders

This a representative list and the indications in practice may extend to conditions beyond those mentioned in this list.

Regulations for Invasive Diagnostic Procedures

The following section is paraphrased from the PC&PNDT Act in the Constitution of India, first introduced in 1994 and revised frequently since then. For practitioners outside India, an approach appropriate to local legal, religious, educocultural and personal parameters is recommended.

Where Should Invasive Diagnostic be Performed?

The procedures should be performed in a centre that has been officially registered as a 'Genetic Clinic/ultrasound clinic/imaging centre'. This requires obtaining a valid certificate of registration known as FORM B (as per the PC&PDNT Act and Rules). The following are the prerequisites in the PC&PNDT Act for the grant of such a registration:

a. A room with an area of 20 m^2 with appropriate aseptic arrangements
b. Should have or acquire such of the following equipment, as may be necessary for carrying out the tests or procedures:
i. Equipment and accessories necessary for carrying out a clinical examination
ii. An ultrasonography machine including a mobile ultrasound machine, imaging machine or any other equipment capable of conducting fetal ultrasonography

Table 1 Genetic tests following prenatal diagnostic invasive procedures

Technique	Uses	Resolution	Advantages	Limitations
Karyotyping	Views the entire genome for numerical and structural chromosome abnormalities	> 5mb	It can view the entire genome; individual cells and chromosomes	An actively growing source of cells is required
FISH	Views the entire genome for numerical and structural chromosome abnormalities	> 50 kb	1. It can turn almost any DNA into a probe 2. A much higher resolution compared to G-banding for identifying deletions, insertions, and translocation breakpoints 3. It can use cells in any stage of the cell cycle as well as archived tissue. (metaphase not essential) 4. It can analyse results on a cell-by cell basis 5. Shorter turn around time	One can see only the region of the genome complementary to the probe used
Arrays	Compares the patient's genome against a reference genome (normal control or standard) and identifies differences between the two genomes and hence locates regions of genomic imbalance (copy number variations (CNVs) in the patient	< 1 kb	Depending upon the resolution of the array and the number of DNA probes being used, it is possible to detect changes greater than 1 Mb (one million base pairs) at low resolution or changes as small as 10 kb (10 thousand base pairs) at high resolution	Cannot detect balanced translocation. Also, it can detect mosaicism only if atleast 20% of the cells show mosaicism
NGS	Single base resolution of DNA across millions of fragments in a massively parallel fashion, providing enhanced coverage of the genome and higher throughput. There is an option of rapidly sequencing the entire genome or deeply sequencing targeted regions	1 base pair	Can detect abnormalities across the entire genome including substitutions, deletions, insertions, duplications, copy number changes (gene and exon) and chromosome inversions/translocations using less DNA than required for traditional DNA sequencing approaches	For many of the identified abnormalities, the clinical significance is currently unknown. Also this requires sophisticated bioinformatics systems, fast data processing and large data storage capabilities, which can be expensive

iii. Appropriate catheters and equipment for carrying out chorionic villi aspirations per vagina or per abdomen
iv. Appropriate sterile needles for amniocentesis or cordocentesis
v. A suitable fetoscope with appropriate accessories for fetoscopy, fetal skin or organ biopsy or fetal blood sampling shall be optional
vi. Equipment for dry and wet sterilization
vii. Equipment for carrying out emergency procedures such as evacuation of uterus or resuscitation in case of need
viii. Genetic Workstation if needed

c. Clinic/Centre should maintain a register showing, in serial order, the names and addresses of the women given genetic counseling, subjected to pre-natal diagnostic procedures or pre-natal diagnostic tests, the names of their husband or father and the date on which they first reported for such counseling, procedure or test.
d. Centre to ensure that all case related records, forms of consent, laboratory results, microscopic pictures, sonographic slides, recommendations and letters should be preserved by the centre for a period of two years from the date of completion of the procedure. In the event of any legal proceedings, the records shall be preserved until the final disposal of legal proceedings, or the expiry of the said period of two years, whichever is later.
e. Also, the centre should send a complete report mentioning all procedures conducted by them each month by the 5th day of the following month to the concerned Appropriate Authority.

Who can do the Procedure

Qualifications:

a. A gynecologist having experience of performing at least 20 procedures in chorionic villi aspirations, amniocentesis, cordocentesis, or fetal blood sampling etc. under supervision of an experienced gynecologist in these fields, or
b. A sonologist, Imaging Specialist, Radiologist having Post Graduate degree or diploma in sonography or image scanning, or
c. Registered Medical Practitioner having six months training or one year experience in sonography or image scanning, or
d. A medical geneticist may set up a genetic clinic/ultrasound clinic/imaging centre.

The person performing the procedure needs to follow the following:

a. He/she should be registered with the clinic/centre (Can be registered with a maximum of two such clinics/centres within a district with consulting hours mentioned)
b. Display his/her name and designation prominently on the dress worn by him/her
c. Write his/her name and designation in full under his/her signature

*(For more information regarding regulations, refer to PC&PNDT BOOKLET edition 2020) [9]

Pretest Counseling of the Couple

The information listed below should be presented and discussed. Although information leaflets and videos are useful, the patient and companion should have at least one onsite/virtual counseling session prior to the procedure [10, 11]. The counseling should include:

a. Indications for the procedure in a format that the patient and companion can understand and acknowledge. The indication must fall into one of the categories mentioned in FORM F
b. Verbal descriptions/illustrations of the planned procedure including complications.
c. Level of genetic testing analysis that the patient needs and what they opt for: the need for a second tier of genetic testing must be conveyed, for example, the need for exome sequencing if the microarray is clear.
d. Detection rates and limitations of the particular laboratory test(s) being performed, information on the chances of inconclusive results and test failure rates, time taken by the laboratory for testing and reporting, cost options, and plan of approach to unfavorable test results. Patients should be specifically informed if the laboratory work-up is in-house or outsourced.
e. Method/s of communication of results.
f. The need for seeking medical advice after test results become available, and, management options following the results
g. The need for anti-D passive immunization post-procedure if the woman is Rhesus negative and non-immunized.
h. At the end of this detailed informative process, written consent forms should be obtained from the woman and witnessed by a signatory. Both Form G and the general consent form should be obtained.

Consent Forms

Pregnancy is no exception for respecting a woman's autonomy. Consequently, valid informed consents for medical and surgical procedures must be obtained. Additionally, since any invasive procedure performed during pregnancy carries a propensity for adverse fetal and maternal events, appropriate consents need to be obtained before performing such procedures [7]. This is unequivocally applicable for all prenatal diagnostic procedures. Additional documentation is required under the PC&PNDT Act that governs the performance of such procedures in India [12].

The consent documents to be completed before prenatal diagnostic procedures are, therefore, of two types:

Form F and G

The PC&PNDT Act 1994 requires filling of sections A, C and D of form F, and all parts of form G prior to any invasive procedure during pregnancy. Section B of form F is spared. The purpose of PC&PNDT forms F and G is to document the performance of the prenatal procedure while ensuring adherence to the principle of non-disclosure of the fetal gender in any manner. Form G should bear the name of the institution and its PC&PNDT registration number. One side of Form G should be in English while the other side should be in the local language. Form G should be filled in duplicate, with the original retained in the institutional records and the copy handed over to the mother once the procedure is over. Form G should bear the signature of the performing doctor with his/her signature and registration number with the regional medical council along with the signature of the woman who underwent the procedure.

General Consent Form

Since prenatal diagnostic procedures have potential risks for the fetus and pregnant woman, it becomes prudent to have a separate consent form encompassing the following aspects of valid informed written consent.

For a consent to be valid, firstly the antenatal woman undergoing the procedure should be competent, implying that she should be able to understand, retain and weigh the information provided to her leading to decision making [13]. Since the procedure involves women who are adults, it is generally presumed that they are competent unless proved otherwise. The second requirement for a valid consent is that the woman must have sufficient information to make a choice. The performing physician or a counselor should provide the woman the information. Information should cover all aspects mentioned in Sect. 3 of this document. Thirdly, for qualifying as a valid consent the woman should be able to give her consent freely without pressure or coercion. They must be provided with adequate time before making a decision.

A prototype of a consent form is shown in the annexures.

(English and Hindi consent forms as downloadable pdf).

Pre-Procedure Requirements

Specific History

This should include information relevant for assessment and counseling including age (and ovum donor's age where relevant), chronic health conditions, infectious conditions, obstetric history, family history of genetic diseases and medication history [2]. Details of IVF, ovum donation and surrogacy should be mentioned where appropriate.

Rhesus Status of the Mother

The Rhesus status of the mother and the presence of alloantibodies in the serum should be checked. In case the patient is Rhesus negative, she needs to be counseled about the administration of prophylactic anti-D immunoglobulin within 72 h of the procedure unless the father of the fetus is known to be Rhesus negative [14].

(Grade A, Level 3).

Maternal Screening

Maternal Screening for Hepatitis B Surface Antigen, Hepatitis C Antibodies and HIV 1 & 2 status is advisable [15–17].

(Grade B, Level 3)

Presence of Hbe antigen in mothers who are HBsAg positive increases the chances of transmission of HBV. Amniocentesis in a HCV positive woman has not been shown to increase the risk of vertical transmission. Data, however, in this regard is limited. In a woman who is HIV positive, the risk of vertical transmission is considerably reduced if the woman is on antiretroviral therapy (ART) with a low/undetectable viral load. At least two weeks of ART is preferred before performing the procedure [18].

Thromboprophylaxis

Sufficient data is not available for discontinuation of thromboprophylaxis prior to fetal invasive procedures. Data from other periprocedural coagulation management of percutaneous procedures suggest that it may be prudent to continue aspirin and a prophylactic dose of low molecular weight heparin before the procedure but a single dose of therapeutic heparin may be withheld before the procedure [19, 20].

(Grade B, Level 4)

Antibiotic Prophylaxis

A single RCT has reported improved outcomes with Azithromycin but several methodological issues were raised regarding the study. Another smaller retrospective study did not find any difference with the use of antibiotics [21].

There is not enough evidence to recommend antibiotic prophylaxis before an invasive procedure and these need not be administered routinely [3].

(Grade A, Level 3)

Ultrasound

Every prenatal diagnostic procedure should invariably be preceded by ultrasound for locating the placenta, confirming gestational age, assessing the amount of amniotic fluid and documenting fetal heart rate [9].

(Grade A, Level 4)

Procedure Guidelines

Amniocentesis

Amniocentesis is the most commonly performed prenatal diagnostic procedure and is defined as a technique that involves the aspiration of amniotic fluid from the amniotic cavity under ultrasound guidance.

a. The procedure can be carried out from 16 completed weeks onwards [2, 10, 19]. If done early, such as

15 weeks, culture can fail due to low cell count. **(Grade A, Level 1).** In the RCT performed by the CEMAT group, performing amniocentesis before 13 weeks gestation was the major predictive factor for adverse outcome [22].

b. Early amniocentesis should not be done as it is associated with complications such as tenting and higher rates of pregnancy loss and talipes [10]. **(Grade A, Level 1)**

Technique

a. The procedure is performed under aseptic precautions. Using real time ultrasound guidance, a 22-gauge [19], 9 cm long needle is inserted transabdominally into a pocket of amniotic fluid that is free of fetal parts and the umbilical cord.
b. Transplacental insertion of the needle is preferably avoided [7, 10, 19, 23]. Although some studies have suggested an increased rate of fetal loss in transplacental procedures, this has not been substantiated. The advantage of transplacental entry is a lower incidence of tenting of membranes [10, 19, 23]. ***(Grade B, Level 2)***
c. The initial 2 ml of amniotic fluid aspirated is discarded to avoid maternal contamination. Maternal cell contamination has also been seen to increase with placental penetration, an increased number of needle passes, and operator inexperience [24]. ***(Grade B, Level 4)***
d. Subsequently, around 20 ml of amniotic fluid is aspirated, transferred to sterile tubes, labeled with the name of the patient and sent to the genetic laboratory for analysis). More fluid may be aspirated depending on the indication of the test.
e. Fluid can be aspirated either by the operator or the assistant during the procedure depending on the distribution of tasks of real time ultrasound guidance, needle placement and aspiration. A freehand method without a needle guide is used.
f. Local anesthesia is usually not necessary as there is only minimal pain during amniocentesis and there is no evidence to support the use of analgesia. A Cochrane review analysed five different RCTs which applied four different strategies for pain reduction during amniocentesis: usage of infiltrative local anesthesia, subfreezing needles, analgesic cream and light leg rubbing. The review concluded that infiltrative local anesthesia provided no significant reduction of pain [5]. ***(Grade A, Level 1)***

Chorion Villus Sampling (CVS)

CVS involves withdrawal of trophoblastic cells from the placenta under ultrasound guidance.

The procedure is recommended to be performed from 10 completed weeks onwards. It is not recommended to perform CVS earlier as there is a higher risk of pregnancy loss and limb reduction defects [10, 19, 23].

(Grade A, Level 3)

Technique

a. The procedure is performed under aseptic precautions, most commonly via a transabdominal method. The procedure may also be performed transcervically, subject to the clinician's expertise and in an abdominally inaccessible posterior placenta. The risk of fetal loss and sample adequacy is comparable in both approaches [25]. (***Grade A, Level 2)*** A recent survey has shown a decreasing trend towards performing transcervical CVS as this is technically demanding [26].
b. Since a wider gauge needle is used local anesthesia may be administered at the intended point of entry prior to needle insertion [10]. (***Grade B, Level 4)***
c. Under ultrasound guidance, an 18 G needle is inserted into the placenta, a vacuum is created with the help of a 10 ml syringe prefilled with 2–3 ml of normal saline/nutrient media. ***(Grade A, Level 2)***
d. Maintaining the vacuum manually with help of an assistant or with the help of a vacuum adaptor, back and forth movements within the placenta are used to obtain villi [6].
e. The adequacy of the amount of villi obtained is done visually. In general, 5–10 mg of villi are adequate for a microarray or karyotyping [3].

Advantages of CVS Over Amniocentesis

a. Biochemical or DNA analysis can usually be carried out directly on villi obviating the need for cell culture as is required after amniocentesis.
b. The yield of DNA from the CVS sample is much greater than 20 ml of amniotic fluid
c. CVS provides a shift towards early diagnosis and this provides valuable time for the couple for decision making. When termination of pregnancy is an option, this is safer in the first trimester than the second trimester. Issues of privacy and maternal–fetal bonding are also easier to manage with a first trimester decision.

Fetal Blood Sampling (FBS)

FBS or percutaneous umbilical blood sampling or cordocentesis involves aspiration of blood from the umbilical vein under ultrasound guidance.

The procedure is recommended to be performed from 18 completed weeks [27] onwards for specific indications, such as to rule out chromosomal mosaicism after amniocentesis, hematological assessment of the fetus or when anomalies are detected late in pregnancy. This test is technically more difficult and complication rates are also higher.

Technique

a. The procedure is performed under aseptic precautions. Using ultrasound guidance, a 20- or 22-gauge needle is inserted transabdominally into the umbilical vein.
b. The umbilical vein can be approached at the placental insertion site, free loop or the intrahepatic portion depending upon experience and accessibility [27]. The placental site has an advantage of stability and shorter duration of procedure but has the disadvantage of maternal contamination [28]. ***(Grade A, Level 3)***
c. Care should be taken not to puncture the umbilical artery as this can lead to sudden bradycardia and death of the fetus. Blood is aspirated into the syringe by the assistant.
d. Around 2–4 ml of blood in a heparinized vacutainer is sufficient for analysis. Blood should be collected in an appropriate container and sent for analysis. Blood should be collected in an EDTA vacutainer for DNA extraction to rule out single gene disorders, in a plain vacutainer to diagnose fetal infections and in a heparinized vacutainer to rule out chromosomal abnormalities.

Post Procedure Requirements

a. *Ultrasound* Document fetal heart rate, inspect the placenta for any hematoma and assess the liquor volume [19].
b. **Instructions**:
i. Limiting physical activity for 12–24 h is optional and there is no evidence of clinical benefit [3, 19].
ii. Antibiotic prophylaxis or administration of progesterone or a tocolytic agent before or after the procedure is currently not recommended [3, 21, 23].
iii. Prophylactic dose of Anti-D immunoglobulin should be administered to all Rh negative, ICT negative women within 72 h post procedure. A dose of 150 mcg is usually recommended when procedures are performed at less than 20 weeks of gestation. In situations where there is suspicion of excessive bleeding, quantification of the amount of bleeding is recommended and the required dose can be administered acoordingly [4, 14].
c. A detailed report [19] regarding the procedure must be provided to the managing healthcare provider that includes:
i. Indication for the invasive procedure
ii. Ultrasound findings prior to the procedure
iii. Procedure description
iv. Instrument used
v. Quantity of sample
vi. Appearance of amniotic fluid (in case of amniocentesis)
vii. Viability of fetus
viii. Appearance of the procedure and amniotic fluid volume after the procedure
ix. Rhesus status and prophylaxis
x. Laboratory exams requested

Complications of Prenatal Diagnostic Procedures

Serious Risks

a. *Miscarriage* The most dreaded complication of invasive testing is miscarriage. Reported rates vary between one in 100 to one in 1000 for amniocentesis and one in 100 to 3 in 1000 for CVS [29]. It is a good practice that when risks less than one in 100 are quoted these should be supported by robust local data [19]. A recent study has quoted the risk of miscarriage in women undergoing CVS as about 1% higher in comparison with women who do not undergo CVS. The increased risk, however, is not entirely related to the invasive procedure but also to the demographic and pregnancy characteristics of the patients. The authors concluded that the risk of miscarriage after CVS remains low and similar to, or slightly higher than, that in the general population [30]. In a systematic review to estimate the procedure-related risk of miscarriage after amniocentesis and chorionic villus sampling, it was seen that the weighted procedure-related risk of miscarriage following amniocentesis was 0.30% (95% CI, 0.11–0.49%; I2 = 70.1%) while that of CVS was 0.20% (95% CI, −0.13–0.52%; I2 = 52.7%). They observed that the procedure-related risks of miscarriage following amniocentesis and CVS are lower than those currently quoted to women. The risk

appears to be negligible when these interventions were compared to control groups of the same risk profile [29]. A higher risk of 1–2% is reported for fetal blood sampling [31]. Factors affecting this risk are:

i. Operator experience
ii. Multiple entries (3 or more)
iii. If amniotic fluid is bloodstained.
iv. When there is chorioamniotic separation
v. Maternal BMI $\geq$ 40 kg/m2
vi. Vaginal bleeding during the current pregnancy
vii. Past history of miscarriage (spontaneous or induced)

b. Vaginal bleeding following CVS can occur in up to 10% of patients. Risk is higher with transcervical procedures [19].
c. Amniotic fluid leakage can occur in 1–2% procedures; however, in most cases, the leakage stops by itself due to spontaneous sealing of the membranes. Leakage following amniocentesis has better prognosis than spontaneous preterm prelabour rupture of membranes (PPROM) as it usually seals spontaneously [19].
d. Chorioamnionitis: The risk of infection is less than 1 in 100 [10]

Frequent Risks

Frequent risks include mild discomfort at needle puncture site similar to that experienced during venepucture.

Uncommon/Rare Risks

a. Culture failure is reported in 1 in 1000 samples (higher after 28 weeks).
b. Bloody tap: Bloodstained samples are seen in less than 1% of procedures. The blood is almost always of maternal origin and does not adversely affect amniotic cell growth. The incidence of bloody tap for an experienced operator is 0.8% of procedures [10].
c. Confined placental mosaicism (CPM) is more commonly seen following CVS and can occur in 1 in 100 samples. Amniotic fluid mosaicism is also reported in 0.25% of procedures.
d. Maternal cell contamination (MCC) may occur and is more common with CVS samples. This can be prevented by sending a sample of maternal blood in an EDTA container along with the fetal sample.
e. Rh isoimmunization can occur if Anti D is not given to Rh negative women following invasive procedures [10].
f. There is a risk of mother-to-child transmission of maternal infection during invasive procedures, for example in women with HIV not on HAART (Highly Active Antiretroviral Therapy), women with Hepatitis B infection and high viral load.
g. Technical difficulties in obese women: The procedure may be difficult in women with high body mass index (BMI) especially regarding clarity of views on ultrasound and the ability of the needle to reach amniotic fluid. Thus, appropriate probe, machine settings and needle length should be used.
h. Dry tap: Failure to obtain a sample during the procedure is termed as a 'dry tap'. It is seen more frequently when amniocentesis is attempted prior to 15 weeks of gestation due to incomplete 'fusion' of amnion and chorion. When done at the correct gestation, an experienced operator will get it in the first attempt in 94% of procedures [10].
i. Rarely there may be a small risk of fetal injury and maternal bowel injury.

Suggestions to Minimize this Risk

a. A checklist such as included in this document should be used before and during the procedure.
b. All procedures should be performed at appropriate gestation.
c. All procedures must be done under real time continuous ultrasound guidance and the needle tip should be kept in view at all times.
d. The needle should be chosen appropriately: 22G for amniocentesis and 18 or 20G for CVS. Appropriate choice of needle size can minimize the risk of procedure related miscarriage.
e. In amniocentesis, transplacental entry should be avoided as far as possible.
f. Choose appropriate length of needle. Women with high BMI may need a longer needle.
g. Practice strict asepsis. There is no evidence that routine antibiotic cover decreases risk of infection.
h. Discard the first 2 ml of amniotic fluid while performing amniocentesis to minimize the risk of maternal cell contamination. Send an EDTA sample of maternal blood along with the fetal sample, with appropriate labeling.
i. A documented blood group report should be checked prior to the procedure. Women with an Rh negative blood group should receive Anti D after the procedure [11]. A prophylactic dose of anti D immunoglobulin should be administered to all Rh negative, ICT negative women within 72 h post procedure. A dose of 150 mcg is usually recommended when procedures are performed at less than 20 weeks of gestation. In situations where there is

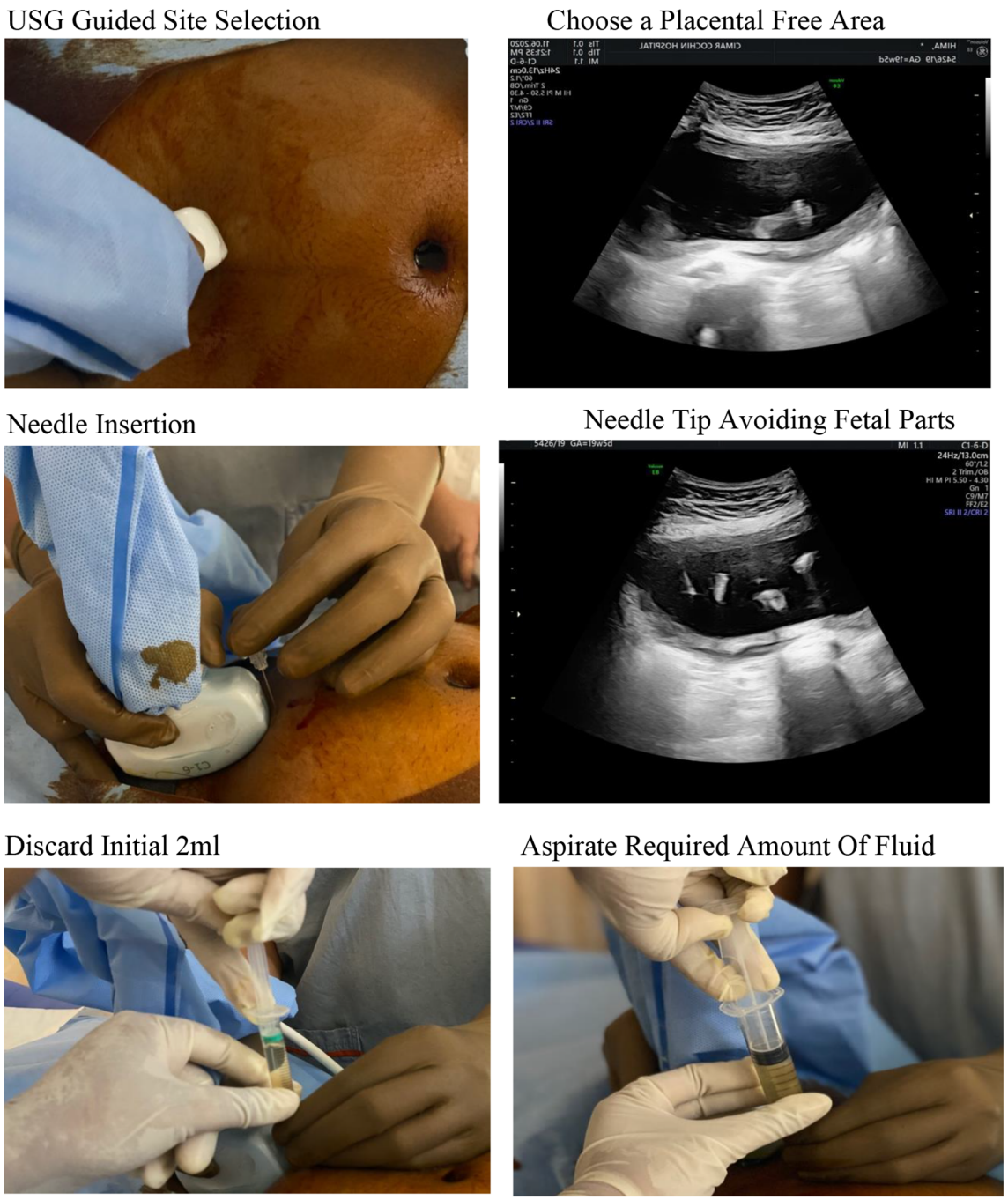

Fig. 1 Steps for performing amniocentesis

suspicion of excessive bleeding quantification of the amount of bleeding is recommended and the required dose can be administered accordingly [4, 14].

j. To minimize vertical transmission of chronic infections, ensure that the benefits of the procedure outweigh the associated risks. Non-invasive options should be considered wherever possible. If the procedure is absolutely necessary, the following precautions should be taken [10].

i. Practice universal precautions.
ii. HIV positive woman: In women on HAART (Highly Active Antiretroviral Therapy) and minimal viral load, the risk of vertical transmission is extremely low.
iii. Hepatitis B positive: Postpone procedure if HBe antigen is positive
iv. Avoid transplacental entry for all

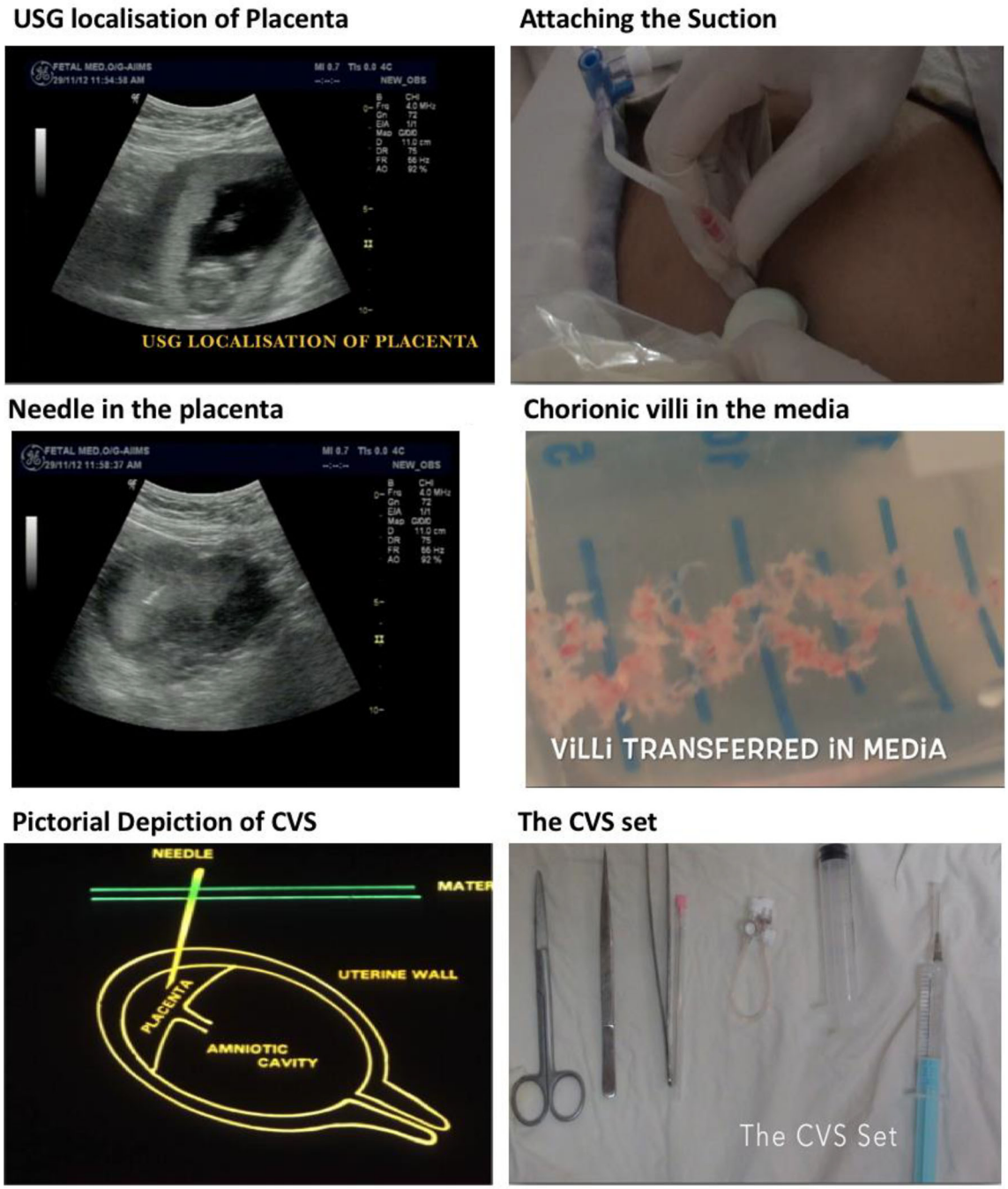

Fig. 2 Steps for performing chorion villus sampling

k. Self-audit: An operator's competence should be reviewed when pregnancy loss rates are more than 4 in 100 consecutive procedures [18].
l. Ensure maintenance of competence (minimum 30 annual invasive procedures per operator as per RCOG guidelines) [10]

Multiple Pregnancy

The increasing incidence of multiple pregnancy has also increased the number of women presenting for invasive diagnostic procedures Fig. 1.

Technique

a. The most important determinant of the technique used for diagnostic invasive procedures in multiple pregnancy is chorionicity [32].
b. Both chorionicity as well as labeling of the fetuses must be determined very carefully and documented diagrammatically in the records.
c. The procedure should be performed by an operator who can also perform selective reduction in case of an abnormal result [19].
d. Dichorionic twins/higher order multiples with separate chorionicity will require sampling from each placenta in CVS (Fig. 2) and each amniotic sac in case of amniocentesis [32]. (Grade B, Level 4)
e. In monochorionic diamniotic (MCDA) twins, CVS would be performed from the single placenta [32]. However, in MCDA twins with significant discordance in either CRLs or NTs in the first trimester, amniocentesis (from 16 weeks onwards) from both amniotic sacs should be done due to the small risk of heterokaryotypia [32]. (Grade B, Level 4)
f. MCDA twins discordant for structural anomalies should also be offered amniocentesis from both sacs for the same reason.
g. The samples must be labeled carefully as per the numbering of the fetuses.

Risks

The rate of miscarriage following an invasive procedure in multiple pregnancy is reported to be between 2–3% for both amniocentesis and CVS [12, 13, 19, 22].

Concluding Comments

There is no doubt that prenatal invasive procedures form an integral part in confirming the normalcy of a fetus. Appropriate training, adherence to protocols of this document and regular audit protocols will ensure quality control.

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