Prenatal Diagnosis

Pages with reference to book, From 127 To 128

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Growing recognition of frequency and importance of congenital disorders, with current social trends towards smaller families and delays in child bearing, prenatal diagnosis has become very important in the management of many pregnancies. Counselling before prenatal diagnosis is important, prospective parents should understand that a specific diagnosis can be excluded or established with a high degree of reliability but not with complete certainty. One of the most important goals is to help parents understand the reproductive options available to them. Person's previous experience, ethics, cultural background and religious beliefs will affect the acceptability of prenatal diagnosis and choice to be made, if any abnormality is detected. Congenital defects account for a high mortality in newborn and serious morbidity in infancy and childhood[1]. The identification of pregnancies in which there is an increased chance of diagnosable fetal disorder involves a search for general and specific risk factors. Age is identified as one of the important general risk factors. Prenatal cytogenetic diagnosis should be offered to all women who will be 35 years of age or over, at their expected date of delivery, as the frequency of numerical chromosomal abnormality increases with advancing age[2]. Tests for biochemical markers in maternal serum identify babies at risk for certain cytogenetic and structural abnormalities . Alpha-fetoprotein is synthesized in fetal liver and yolk sac in early fetal life. Its level is increased in maternal serum and amniotic fluid if the fetus has open neural tube or ventral wall defects associated with the exposed fetal membranes or blood vessels[3]. Invasive procedure such as amniocentesis elevates the maternal serum level of alpha-fetoprotein, so blood sample for screening should be collected before such procedure. Low levels of serum alpha-fetoprotein and unconjugated estriol are associated with trisomy 21 and trisomy 18[4]. Significantly elevated levels of human chorionic gonadotropin is the single marker that yields the highest detection rate for Down's syndrome. Combined use of maternal serum, human chorionic gonadotropin and unconjugated estriol levels, alpha- fetoprotein level and maternal age can identify approximately 60% of Down Syndrome cases with a false positive rate of 6.6 which is reduced to 3.8 by use of ultrasonography to verify gestational age[5]. Specific risk factors may be identified in the family history, history of previous pregnancies or the mothers' medical history. After the birth of one child with trisomy 21, for example, the likelihood that a subsequent child will have a similar chromosomal abnormality is approximately 1 percent, the rate of recurrence of a neural tube defect is 2-5 percent as compared with arate of 2 per 1000 births in general population[6]. If the parents have spinabifida, congenital heart disease or any known chromosomal translocation, there is an increased chance that child will have related defect[7]. Prenatal diagnosis is important for many inborn errors of metabolism, almost all of which are transmitted in an autosomal recessive fashion. Diabetes mellitus or phenylketonuria in the mother are associated with an increased risk of fetal malformation. Known teratogens include ionizing radiation, therapeutic and illicit drugs and maternal infections. Important procedures for prenatal diagnosis include amniocentesis, chorionic villous sampling, percutaneous umbilical blood sampling, fetal biopsy and ultrasonography. Amniocentesis with ultrasound guidance is done in 18th week of gestation in outpatient facilities. Chromosomal studies are carried out by culturing few viable cells present in amniotic fluid and results are generally available in 10 to 14 days[8]. The fetal mosaicism diagnosed by chromosomal culture studies is rare but clinically very important[9]. This can be further confirmed by karyotyping fetal blood sampling, which provides results within 48 hours[10]. Chorionic villous sampling can be done through a transcervical catheter or transabdominal needle with ultrasound guidance. Choice of location depends upon the location of

placenta and operator's experience and performance. Main advantage of chorionic villous sampling over amniocentesis is the earlier availability of results because procedure is done at 9-12 weeks of gestation. The greater frequency of contamination by maternal cells and pseudomosaicism in chorionic villous sampling contribute to the reduced cytogenetic accuracy of this procedure as compared with amniocentesis. A woman assigned to villous sampling has a lower chance of successful pregnancy outcome than a woman having 2nd trimester amniocentesis[11]. The clinical disadvantages of increased risk and potential diagnostic error with chorionic villous sampling should thus be weighed against the disadvantages of later timing of amniocentesis. Percutaneous umbilical blood sampling was developed for the diagnosis of toxoplasmosis. It is done at about 18th week of gestation with 20-22 gauge spinal needle inserted under ultrasound guidance into umbilical cord. Access to the fetal circulation permits the prenatal evaluation of many fetal haematologic abnormalities, including isoimmunization, haemoglobin-opathy, thrombocytopenia and coagulation factor abnormalities[12]. Fetal blood can be used for prenatal diagnosis of some inborn errors of metabolism, assessment of viral, bacterial and parasitic infection and to clarify whether chromosomal mosaicism detected by amniotic fluid or chorionic villous sampling is truly present or not. As percutaneous umbilical blood sampling entails a substantially greater risk of pregnancy loss than amniocentesis, it should be reserved for cases in which rapid diagnosis is essential or diagnostic information cannot be obtained by safer means. Fetal biopsy is a rare procedure performed with ultrasound guidance for the diagnosis of genetic disorders like epidermolysis bullosa and Duchenne's muscular dystrophy[13]. Ultrasound is an important and most commonly used aid now-adays, specially in our country, for the assessment of gestational-age, fetal growth monitoring, placental site, detection of multiple gestation and the diagnosis of major fetal anomalies. Some teratogens and infections produce only structural abnormalities which are potentially detectable with ultrasound only, visualization of fetal anatomy is essential in diagnosis of anatomical defects inherited in polygenic on multifactorial fashion. Ultrasound has also shown impressive achievement in diagnosing renal and bladder anomalies, hydrocephaly, neural tube and ventral wall defects[14]. It is also useful in mandelian's disorders characterized by certain anatomical defects, such as skeletal dysplasias. The most common congenital abnormalities are cardiovascular malformations, that is commonly missed in prenatal ultrasound examination. A four chamber view of the fetal heart is suggested for ultrasound examination in pregnancy and its sensitivity, for the detection of congenital heart defect is reported to be very high in referred population[15]. When any fetal anomaly is diagnosed ultrasonographically, echocardiography should be performed because such fetuses have 23% risk of cardiac defect[16], conversely fetuses with cardiac defect have 25-45% risk of having any other anatomical defect. One third of such fetuses will have chromosomal disorder. When fetal abnormalities are detected at any stage of prenatal period, consultation can be sought with a multidisciplinary team of physicians, ethicists, nurse specialist and psychologist to plan management The appropriate personnel, location and mode of delivery should be determined to reduce the risk of complications and danger to mother's and fetal life as much as possible.

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