Editorial

Role of Obstetricians in Prevention of Genetic Disorders

Suhaib Ahmed

Professor of Haematology, Riphah International University, Islamabad

Address of Correspondence: *Prof Suhaib Ahmed*
Professor of Haematology
suhaib.ahmed@riphah.edu.pk

Genetic disorders are broadly classified as single gene, polygenic, and cytogenetic disorders. Thalassaemia and Downs syndrome are the commonest single gene and cytogenetic disorders respectively in Pakistan. The burden of disease due to genetic disorders is generally hidden under the very high mortality and morbidity due to infectious diseases. Since most of these disorders are not treatable or their treatment is very expensive, these lead to very high morbidity and mortality. The affected families have to bear the brunt of severe health and socio-economic burden. There is a consensus of opinion that the best way to tackle the genetic disorders is through prevention of the new births of affected children.[1]

Prevention of genetic disorders involves carrier screening, prenatal diagnosis and genetic counselling.[2] In this triad of prevention, obstetricians have a key role to play because they are the ones who first come across a woman who could be carrying an affected fetus. Therefore, an obstetrician must have the basic knowledge about the common genetic disorders and the way a woman can be helped if the risk is discovered.

A family history of genetic disorders should be included in the routine antenatal checkup. Thalassaemia and Downs syndrome, being the commonest disorders, should be at the top of the list. All women in the first trimester should have thalassaemia screening.[3] Detection of thalassaemia trait is technically more difficult in pregnancy because of the confounding Iron deficiency that is fairly common at this stage. But knowing the significance of not missing thalassaemia trait haemoglobin electrophoresis should be advised to all women with Hb around 10.0 g/dL and MCV <75 fl or MCH <25 pg.[4] If the women is confirmed to have thalassaemia trait then her husband should be tested and if he also a carrier then the couple should be referred for prenatal diagnosis. Approximately 3% of the thalassaemia carriers in Pakistan are silent in nature i.e. they have completely normal red cell indices and haemoglobin electrophoresis. Their carrier status can only be discovered by PCR.[5] Therefore, it is advisable to test the spouse of a known thalassaemia carrier by PCR. Screening for Downs syndrome should be routinely done with increasing paternal for maternal age or history of a previously affected child. Nuchal translucency more than 3.0 mm or other soft tissue markers on ultrasound or positive triple test on maternal blood should lead to confirmation by fetal sampling and genetic analysis.[6] In case of positive history of an uncommon genetic disorder the couple should be referred to a reference center.

Prenatal diagnosis has given a new dimension to the prevention of genetic disorders. It is done to see the presence or absence of a genetic disorder in the fetus. The test should be done with a definite indication that could be the history of a previously affected child or a positive screening test. In case of a known single-gene disorder, the test should be done in every pregnancy because of the high risk of recurrence. The fetal sample may be obtained by Chorionic Villus Sampling (CVS) or amniocentesis.[7] The latter is less commonly used because it cannot be done before 15 weeks of gestation and the material obtained is often not adequate. CVS, on the other hand, is the best method because it can be done at any time after the 10th week of gestation and plenty of fetal material is obtained. Doing a CVS earlier than 10 weeks has no advantage and may cause fetal limb reduction defects.[8] CVS may be done through the trans-abdominal or the trans-cervical route.[9] The trans-abdominal route is more convenient for the patient and the operator. It is an outdoor procedure requiring a basic ultrasound machine, a set of special needles and a well-trained operator. A typical CVS needle comprises a 23 gauge

outer needle with sharp end and an inner 23 gauge aspiration needle with blunt end. The aspiration needle is slightly longer than the outer needle that ensures placental disruption at the time of aspiration. The patient needs no special preparation. The best approach is the freehand technique in which the operator holds the USG probe in one hand and the needle in the other.[10] This ensures the best-coordinated view of the needle and its track. The procedure is done under local anesthesia. Anterior placentae are best approached with a filled bladder while an empty bladder helps in a fundal or a posterior placenta. In a twin pregnancy two separate samples should be taken unless one is absolutely sure of the mono-zygosity. Giving prophylactic antibiotics after the procedure is usually not required, however, anti-D prophylaxis is mandatory in all Rh-D negative women whose husbands are Rh-D positive. The patient is advised to restrict strenuous activities for a day or two after CVS. Most women complain of uterine cramps after the procedure. Pregnancy loss is the most feared complication of CVS but in experienced hands its incidence is 1-2%.[11] The risk of miscarriage after CVS tends to increase with increasing gestational age.[12]

Most Islamic scholars in Pakistan and elsewhere have a consensus of opinion on the permissibility of termination of pregnancy before 120 days (17 weeks) of gestation if the fetus is affected by a serious genetic disorder or a malformation.[13, 14] Over 90% of the couples in Pakistan accept termination of pregnancy when the fetus is affected by serious genetic disorder.[13]

Non Invasive Prenatal Testing (NIPT) is a relatively new entry in the field of prenatal genetic testing. It is based on the fact that a very small amount of fetal DNA circulates in the maternal blood. The test is technically difficult, expensive and is mostly limited to the screening of fetal Trisomies.[15] In a Pakistani setting CVS is far more feasible option than NIPT. Pre-implantation genetic diagnosis (PGD) is another fascinating development in the recent past. A blastomere or a trophoectoderm biopsy of an embryo can be tested for genetic disorders.[16] But the procedure is expensive, technically demanding and unsuitable for Pakistan.

Thalassaemia being the commonest and a completely preventable genetic disorder in Pakistan should be the priority number one. Obstetricians are one of the most important components of preventive strategies. Basic education on the carrier screening and CVS should be included in syllabi at all levels including those for the doctors, nurses and the midwives. Training courses on CVS should be conducted at frequent intervals all over the country. The facilities of CVS should be made available at the Tehsil headquarter hospital level from where the samples may be referred to a central DNA lab.

References

1. Alwan AD, Modell B, Bittles AH, Czeilel A, Hamamy H. Community control of genetic and congenital disorders. World Health Organisation. Office for the Eastern Mediterranean; 1997.
2. Cao A, Kan YW. The prevention of thalassemia. Cold Spring Harbor perspectives in medicine. 2013: 3: a011775.
3. Cousens NE, Gaff CL, Metcalfe SA, Delatycki MB. Carrier screening for beta-thalassaemia: a review of international practice. Eur J Hum Genet 2010; 18(10):1077-1083.
4. Ahmed S. Genetic Haemoglobin Disorders in Pakistan. Nat J Health Sci 2017; 2: 95-99. doi.org/10.21089/njhs.23.0095.
5. Ahmed S. Genetic Haemoglobin Disorders in Pakistan. GRC Publication 2018.
6. Snijders RJ, Noble P, Sebire N, Souka A, Nicolaides KH. UK multicentre project on assessment of risk of trisomy 21 by maternal age and fetal nuchal-translucency thickness at 10–14 weeks of gestation. The Lancet 1998; 352(9125): 343-346.
7. Ball RH. Invasive fetal testing. Curr Opin Obstet Gynecol 2004; 16: 159-162.
8. Golden CM, Ryan LM, Holmes LB. Chorionic villus sampling: a distinctive teratogenic effect on fingers? Birth Defects Res A Clin Mol Teratol 2003; 67(8): 557-562.
9. Levy R, Arfi JS, Daffos F. Fetal sampling techniques. Gynecol Obstet Fertil 2003; 31(6): 550-555.
10. Ahmed S. Trans-abdominal chorionic villus sampling (CVS) for prenatal diagnosis of genetic disorder. J Col Phys Surg Pak 2006; 16: 204-207.
11. Alfirevic Z, Navaratnam K, Mujezinovic F. Amniocentesis and chorionic villus sampling for prenatal diagnosis. Cochrane Database of Systematic Reviews 2017(9). CD003252 https://doi.org/10.1002/14651858.CD003252.pub2
12. Mujezinovic F, Alfirevic Z. Procedure-related complications of amniocentesis and chorionic villous sampling: a systematic review. Obstetrics & Gynecology 2007; 110(3): 687-694.
13. Ahmed S, Saleem M, Sultana N, Raashid Y, Waqar A, Anwar M, Modell B, et al. Prenatal diagnosis of beta-thalassaemia in Pakistan: experience in a Muslim country. Prenatal Diagnosis Prenatal Diagnosis. 2000; 20(5): 378-383.
14. Al-Matary A, Ali J. Controversies and considerations regarding the termination of pregnancy for foetal anomalies in Islam. BMC medical ethics. 2014;15(1): 10-19.
15. Morain S, Greene MF, Mello MM. A New Era in Noninvasive Prenatal Testing. N Engl J Med. 2013; 369(6): 499-501.