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Invasive Procedures for Prenatal Diagnosis in Salmaniya Medical Complex in Bahrain: A Retrospective Cross-Sectional Descriptive Study

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Abstract

Background: Prenatal diagnosis is the process of evaluating the presence of disease or potential disease in the fetus, this enables families to be better prepared before the birth of the baby. There are non-invasive prenatal diagnosis procedures and invasive prenatal diagnosis procedures. The invasive prenatal diagnosis procedures are CVS (chorionic villus sampling) and amniocentesis. The American College of Obstetricians and Gynecologists states that invasive diagnostic testing should be available to all women, regardless of age or risk. **Objective:** To determine the indications, outcome and results of diagnostic invasive prenatal procedures. **Study setting**: The obstetrics and Gynecology Department in Salmaniya Medical Complex in Kingdom of Bahrain. **Study design:** Retrospective descriptive study. **Study subjects and Methods:** This retrospective descriptive study was conducted on 175 pregnant women who underwent invasive prenatal procedures (CVS and amniocentesis) between January 2013 and December 2018 at SMC in Kingdom of Bahrain. All medical records of the participants were reviewed and entered the study. According to the implemented procedures, medical records were categorized into two chorionic villus sampling (CVS) and amniocentesis groups. The study subject will include indications of the procedures which are advanced maternal age, hematological disorders, genetic disorders, metabolic disorders, abnormal structural findings in fetal ultrasound and previous child with aneuploidy. In addition, the study will address the complications, outcome and results of procedures. **Results:** About half of our indications of the procedures were due to hematological disorders (47.6%) followed by abnormal structural findings in fetal ultrasound (30.1%) then genetic disorders (15.7%), metabolic disorders (4.8%) and advanced maternal age (1.8%). Regarding complications

of the procedure; threatened miscarriage or loss of pregnancy within 3 weeks was (2.3%), amniotic fluid leakage (0.7%), abdominal cramps (0.7%) and Insufficient or contaminated sample (6.2%). Regarding outcome of the pregnancy, our results showed that the loss of pregnancy was (4.8%), intrauterine fetal death or still birth was (13.9%), live birth was (63.9%), preterm delivery was (7.8%), preterm premature rupture of membrane (PPROM) was (1.8%), limbs reduction was (0.0%). Termination of pregnancy outside the country was (7.8%) of chorionic villus sampling and amniocentesis. **Conclusion:** CVS and amniocentesis are useful outpatient procedures to detect diagnosis or to assess whether a patient is at increased risk of having an affected fetus and that will minimize the psychological impact on the patient and to provide a proper antenatal care to the pregnant women by her obstetrician and follow up to the baby by pediatrician. In this study it was observed that most of the patients who underwent the procedure were couples either carrier or affected to sickle cell disease or Beta thalassemia.

Keywords

Invasive Procedures, Prenatal Diagnosis, Chorionic Villus Sampling, Amniocentesis

1. Introduction

Prenatal diagnosis is the process of evaluating the presence of disease or potential disease in the fetus, this enables families to be better prepared before the birth of the baby. There are non-invasive prenatal diagnosis procedures and invasive prenatal diagnosis procedures. The invasive prenatal diagnosis procedures are CVS (chorionic villus sampling) and amniocentesis. The American College of Obstetricians and Gynecologists states that invasive diagnostic testing should be available to all women, regardless of age or risk [1].

CVS enables prenatal diagnosis of any condition in which diagnostic cytogenetic, biochemical/molecular, or DNA analysis is possible [2].

CVS is an ambulatory procedure performed under real-time ultrasound guidance, usually at tertiary care centers or facilities specializing in prenatal diagnosis. CVS is typically performed between 11 and 13 + 6 weeks of gestation. The procedure is delayed until 10 weeks of gestation because most spontaneous pregnancy losses will have occurred by this time and performance very early in pregnancy is associated with an increased risk of limb-reduction defects. The number of procedures that should be carried out annually to maintain competency is unclear; the Royal College of Obstetricians and Gynecologists (RCOG) suggests an arbitrary minimum of 30 procedures per annum [3].

The transcervical approach, the first to be used clinically in Europe and Northern America, the woman is placed in the lithotomy position, the external and internal genitalias are prepped with an antiseptic solution, and a speculum is inserted into the vagina. A single-toothed tenaculum or ring forceps is used to

grasp the anterior lip of the cervix and gently pull it toward the operator to bring the uterus into a more axial configuration. If the uterus is sharply anteverted, filling the bladder may help to straighten the angle between the endocervical canal and the anterior uterine wall. The transcervical cannula is bent to assume a similar curve and then inserted under ultrasound guidance through the canal and into the placenta. The obturator of the cannula is removed and a 20-mL syringe containing medium is attached to the catheter. Chorionic villi are aspirated as the catheter is moved back and forth inside the placenta. After an adequate specimen is obtained, the catheter is withdrawn while keeping the syringe under negative pressure. An alternative transcervical method uses a biopsy forceps to obtain the placental sample. The sample material is placed onto a plastic tissue culture dish and the content evaluated at a nearby microscope [4].

In 1984, the alternative transabdominal approach was introduced. The woman is placed in the supine position, the placenta is localized by transabdominal ultrasonography, and her lower abdomen is prepped with antiseptic solution. Transabdominal CVS procedures are associated with minor pain, which is not significantly reduced by prior administration of analgesia or local anesthesia since use of a local anesthetic provides dermal but not uterine wall anesthesia [5].

Amniocentesis is an alternative to CVS as both procedures provide essentially the same genetic information. Amniocenteses are performed to obtain amniotic fluid for karyotyping from 15 weeks (15 + 0) onwards. Amniocentesis performed before 15 completed weeks of gestation is referred to as "early amniocentesis" [3].

The choice of procedure depends upon the woman's personal appraisal of the risks and benefits of each technique. CVS results (fetal karyotype) are available four to six weeks earlier in gestation than amniocentesis results. Although amniocentesis for prenatal diagnosis can be performed in the first trimester (*i.e.* early amniocentesis, typically at 11 to 13 weeks of gestation but before 15 weeks), early amniocentesis is not recommended for most women because it is associated with a higher rate of pregnancy loss and complications than CVS or mid-trimester procedure. CVS may be associated with a higher risk of fetal loss than mid-trimester amniocentesis and a higher risk of diagnostic uncertainty. Although not diagnostic, noninvasive prenatal testing using cell-free DNA has high sensitivity and specificity for trisomy 21. For this reason, many women are reassured by a cell-free DNA screening test negative for Down syndrome and choose not to undergo an invasive diagnostic procedure [2].

The most common reasons for prenatal genetic diagnosis include: [6]

- Maternal age 35 years or older at estimated date of delivery
- Previous child with a chromosome abnormality or genetic disorder
- Parent is a carrier of a balanced translocation or other structural chromosome disorder
- Parent is a carrier of a monogenic (*i.e.*, single gene or Mendelian) disorder
- Both parents are carriers of autosomal recessive disease

- Female parent is a carrier of a sex-linked disease
- Congenital anomaly on first trimester ultrasound examination
- Abnormal results at aneuploidy screen (eg, maternal serum analytes with/without sonographic markers of aneuploidy, cell-free DNA)

Prior to a prenatal diagnostic procedure, pretest counseling of the couple is required regarding benefits and risks of invasive prenatal diagnosis screening differences between CVS and amniocentesis in terms of accuracy of results, complications and risks of procedure-related pregnancy loss, accuracy and limitations of the laboratory test being performed. [7]

2. Methods

As no study have been done in kingdom of Bahrain regarding invasive prenatal diagnostic procedures, this study investigated the 5 years experiences of prenatal diagnosis in Salmaniya medical complex in the period of January 2013 till December 2018 and the aims were to determine the indications, outcome and results of diagnostic invasive prenatal procedures.

2.1. Study Design

Retrospective cross-sectional descriptive study.

2.2. Study Area

Obstetrics and Gynecology department in Salmanyia Medical Complex in kingdom of Bahrain (Tertiary center experience).

2.3. Study Subjects and Sample Size

175 pregnant women who underwent invasive prenatal procedures (CVS and amniocentesis) between January 2013 and December 2018 at SMC in Kingdom of Bahrain.

Our study subject included the:

1) Demographic parameters

- Maternal age
- Nationality
- Gestational age

2) Indications for invasive prenatal procedures

- Advanced maternal age
- Hematological disorders (Thalassemia, sickle cell carrier or disease, sickle-thalassemia disease)
- Metabolic disorders
- Abnormal structural findings in fetal ultrasound (Thickened nuchal fold, thickened nuchal translucency, cystic hygroma, structural anomalies)
- Genetic disorders and Previous child with aneuploidy or any disorders

3) Complications of the procedures

- Amniotic fluid leakage

- Temperature > 38
- Abdominal cramps
- Threatened miscarriage or loss of pregnancy within 3 weeks
- Insufficient sample or contaminated

4) Outcome of the pregnancy

- Loss of pregnancy or spontaneous miscarriage
- Intrauterine fetal death or still birth
- Live birth
- Preterm delivery
- Preterm premature rupture of membrane (PPROM)
- Limb's reduction
- Termination of pregnancy outside the country

5) Results of the procedures

2.4. Ethics

All pregnant patients who underwent invasive procedures signed an informed consent form followed by explanation of risk, benefit and limitation of the invasive test.

2.5. Study Method

In this study both (CVS and Amniocentesis) were considered. The CVS were used by two methods transabdominal under local anesthesia and transcervical approach. Real time ultrasound guidance was used during the procedure. An 18G spinal needle was used and introduced transabdominal and aspiration of chorionic villus tissue were done and sent for analysis. Through transcervical approach chorionic villus sampling biopsy forceps were used and obtained tissue and sent for laboratory. The amniocentesis was carried out under real time ultrasound guidance by A 20G spinal needle inserted transabdominal and aspirated of amniotic fluid. For these procedures signed an informed consent. Most of the CVS procedures were done between (11 - 13) weeks of gestation, while the amniocentesis between (14 - 28) weeks of gestation.

2.6. Data Collection Method

Ethical approval for this research has been taken from the health research committee. Data was collected by recording form that designed by obstetrics and gynecology department in SMC. This form always was filled out before the procedure and included women's personal identification number, gestational age, date, blood group, type and indication of the procedure. The remaining information and outcome follow up were obtained through a newly designed form and was through contacting the patient directly.

2.7. Data Management and Analysis Plan

Descriptive statistics were reported as graphs and charts in the form of numbers

and percentages. Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

2.8. Statistical Analysis

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean ± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

3. Results

The table shows the ranged age 20 - 47 and mean age 31.1 ± 5.99, while 20 - 26 years (29.7%), 27 - 33 years (29.7%), 34 - 42 years (27.0%), as well as 43 - 50 years (13.5%) of age (years) (Table 1).

Table 1. Distribution of women of prenatal diagnosis in Bahrain according to their demographic data regarding age (years) (n = 166).

Age (years)	Total (n = 166)		Chorionic villus sampling		Amniocentesis	
	No.	%	No.	%	No.	%
20 - 26 years	45	27.1%	34	26.4%	11	29.7%
27 - 33 years	70	42.2%	59	45.7%	11	29.7%
34 - 42 years	42	25.3%	32	24.8%	10	27.0%
43 - 50 years	9	5.4%	4	3.1%	5	13.5%
Total	166	100.0%	129	100.0%	37	100.0%

The table shows that the indications of the procedures were advanced maternal age (1.8%), abnormal structural findings in fetal ultrasound (30.1%), Hematological disorders (47.6%), Genetic disorders (15.7%) and Metabolic disorders (4.8%) (Table 2).

Table 2. Distribution of women of prenatal diagnosis in Bahrain according to their indication of the procedures.

Indication of the procedures	Chorionic villus sampling (*n* = *129*)		Amniocentesis (*n* = *37*)		Total	
	No.	%	No.	%	No.	%
Advanced maternal age	**1/129**	0.8%	**2/37**	5.4%	3/166	1.8%
Abnormal structural findings in fetal ultrasound	**24/129**	18.6%	**26/37**	70.3%	50/166	30.1%
Thickened ND	0/24	0.0%	11/26	42.3%	11/50	22.0%

Continued

Thickened NT	18/24	75.0%	1/26	3.8%	19/50	38.0%
Cystic Hygroma	4/24	16.7%	1/26	3.8%	5/50	10.0%
Structural anomalies	2/24	8.3%	13/26	50.0%	15/50	30.0%
Hematological disorders	**78/129**	60.5%	**1/37**	2.7%	79/166	47.6%
Sickle cell disease	62/78	78.5%	0	0.0%	62/79	78.5%
Beta thalassemia	16/78	20.5%	1/1	100.0%	17/79	21.5%
Genetic disorders	**18/129**	14.0%	**8/37**	21.6%	26/166	15.7%
Previous baby with SMA	4/18	22.2%	2/8	25.0%	6/26	23.1%
Previous baby with Tay-sachs disease	1/18	5.6%	0/8	0.0%	1/26	3.8%
Previous baby with pyruvate carboxylase deficiency	1/18	5.6%	0/8	0.0%	1/26	3.8%
Previous baby with trisomy 21 (Down syndrome)	10/18	55.6%	4/8	50.0%	14/26	53.8%
Previous baby with trisomy 18	2/18	11.1%	2/8	25.0%	4/26	15.4%
Metabolic disorders	**8/129**	6.2%	0/37	0.0%	8/166	4.8%
CEDNIK Syndrome	2/8	25.0%	0/0	0.0%	2/8	25.0%
L2HGDH Gene deficiency	1/8	12.5%	0/0	0.0%	1/8	12.5%
Previous Baby with Propionic Acidemia	2/8	25.0%	0/0	0.0%	2/8	25.0%
Previous Baby with Very Long Chain fatty acid	3/8	37.5%	0/0	0.0%	3/8	37.5%

The table shows that the Amniotic fluid leakage (0.7%), Temperature > 38 (0.0%), Abdominal cramps (0.7%), Threatened Miscarriage or loss of pregnancy within 3 weeks (2.3%) and Insufficient sample or contaminated (6.2%) of complications of the procedures in CVS, while in amniocentesis no complication recorded (Table 3).

Table 3. Distribution of women of prenatal diagnosis in Bahrain according to their complications of the procedures.

	Chorionic villus sampling		Amniocentesis	
	No.	**%**	**No.**	**%**
Amniotic fluid leakage	1	0.7%	0	0%
Temperature > 38	0	0.0%	0	0%
Abdominal cramps	1	0.7%	0	0%
Threatened Miscarriage or loss of pregnancy within 3 weeks	3	2.3%	0	0%
Insufficient sample or contaminated	8	6.2%	0	0%

The table shows that the Loss of pregnancy (6.2%), Intrauterine fetal death or still birth (10.9%), Live birth (65.9%), Preterm delivery (7.8%), preterm premature rupture of membrane (PPROM) (2.3%), Limbs reduction (0.0%). Termination of pregnancy outside the country (7.0%) of Chorionic villus sampling. The table shows that the Loss of pregnancy (0.0%), Intrauterine fetal death or still birth (7.0%), Live birth (16.3%), Preterm delivery (2.3%), preterm premature rupture of membrane (PPROM) (0.0%), Limbs reduction (0.0%). Termination of pregnancy outside the country (3.1%) of Amniocentesis. The table shows that the total cases of chorionic villus sampling and amniocentesis loss of pregnancy were (4.8%), intrauterine fetal death or still birth were (13.9%), live birth were (63.9%), preterm delivery were (7.8%), preterm premature rupture of membrane (PPROM) were (1.8%), limbs reduction were (0.0%). Termination of pregnancy outside the country were (7.8%) (Table 4).

Table 4. Distribution of women of prenatal diagnosis in Bahrain according to their outcome of the pregnancy.

Parameters	Chorionic villus sampling		Amniocentesis		Total	
	No.	%	No.	%	No.	%
Loss of pregnancy	8	6.2%	0	0.0%	8	4.8%
Intrauterine fetal death or still birth	14	10.9%	9	7.0%	23	13.9%
Live birth	85	65.9%	21	16.3%	106	63.9%
Preterm delivery	10	7.8%	3	2.3%	13	7.8%
preterm premature rupture of membrane (PPROM)	3	2.3%	0	0.0%	3	1.8%
Limbs reduction	0	0.0%	0	0.0%	0	0.0%
Termination of pregnancy outside the country	9	7.0%	4	3.1%	13	7.8%
Total Cases	129	100.0%	37	28.7%	166	100.0%

The table shows that the affected (5.1%), carrier (39.2%) and normal (26.6%) of sickle cell disease, also beta thalassemia, of affected (3.8%), carrier (16.5%) and normal (8.9%). the total cases results of hematological disorders that the affected (8.9%), carrier (55.7%) and normal (35.5%) (Table 5).

Table 5. Distribution of women of prenatal diagnosis in Bahrain in relation to hematological disorders.

Hematological disorders	Affected		Carrier		Normal	
	No.	%	No.	%	No.	%
Sickle cell disease	4	5.1%	31	39.2%	21	26.6%
Beta thalassemia	3	3.8%	13	16.5%	7	8.9%
Total cases	7	8.9%	44	55.7%	28	35.5%

The table shows that the previous baby with SMA (spinal muscular atrophy) were affected (11.5%) while normal (11.5%), previous baby with Taysachs disease were affected (3.8%) , previous baby with Trisomy 21 (Down syndrome) were affected (3.8%) while normal (50%), previous baby with pyruvate carboxylase deficiency were affected (3.8%) and previous baby with trisomy 18 were affected (7.7%) while normal (7.7%) (Table 6).

Table 6. Distribution of women of prenatal diagnosis in Bahrain in relation to their genetic disorders.

Genetic Disorders	Affected		Carrier		Normal	
	No.	%	No.	%	No.	%
Previous baby with SMA (spinal muscular atrophy)	3	11.5%	0	0.0%	3	11.5%
Previous baby with Tay-sachs disease	1	3.8%	0	0.0%	0	0.0%
Previous baby with trisomy 21 (Down syndrome)	1	3.8%	0	0.0%	13	50.0%
Previous baby with pyruvate carboxylase deficiency	1	3.8%	0	0.0%	0	0.0%
Previous baby with trisomy 18	2	7.7%	0	0.0%	2	7.7%

The table shows that the CEDNIK syndrome (cerebral dysgenesis, neuropathy, ichthyosis, and palmoplantar keratoderma syndrome) were affected (25.0%), L2HGDH gene deficiency were affected (12.5%), previous baby with very long chain fatty acid were affected (12.5%) while carrier (25%) and previous baby with propionic acidemia were normal (25%) (Table 7).

Table 7. Distribution of women of prenatal diagnosis in Bahrain in relation to their metabolic disorders.

Metabolic Disorders	Affected		Carrier		Normal	
	No.	%	No.	%	No.	%
CEDNIK Syndrome	2	25.0%	0	0.0%	0	0.0%
L2HGDH Gene deficiency	1	12.5%	0	0.0%	0	0.0%
Previous Baby with Propionic Acidemia	0	0.0%	0	0.0%	2	25.0%
Previous Baby with Very Long Chain fatty acid	1	12.5%	2	25.0%	0	0.0%

The table shows that the advanced maternal age (33.3%) of affected (Table 8).

Table 8. Distribution of women of prenatal diagnosis in Bahrain in relation to their advanced maternal age (n = 3).

	Affected	Carrier	Normal
Advanced Maternal age	1 (33.3%)	0 (0%)	2 (66.7%)

The table shows that the Thickened nuchal fold (2.0%), Thickened nuchal translucency (0.0%), Cystic Hygroma (8.0%), Structural abnormalities (2.0%) of Turner syndrome; Thickened nuchal fold (0.0%), Thickened nuchal translucency (4.0%), Cystic Hygroma (2.0%), as well as Structural abnormalities (6.0%) of Trisomy 18; Thickened nuchal fold (10.0%), Thickened nuchal translucency (8.0%), Cystic Hygroma (0.0%), as well as Structural abnormalities (6.0%) of Trisomy 21; Thickened nuchal fold (0.0%), Thickened nuchal translucency (2.0%), Cystic Hygroma (0.0%), as well as Structural abnormalities (0.0%) of Trisomy 13, of Abnormal structural findings in fetal ultrasound (Table 9).

Table 9. Distribution of women of prenatal diagnosis in Bahrain in relation to their abnormal structural findings in fetal ultrasound.

Abnormal structural findings in fetal ultrasound	Turner syndrome		Trisomy 18		Trisomy 21		Trisomy 13		Normal	
	No.	%	No.	%	No.	%	No.	%	No.	%
Thickened nuchal fold (ND)	1	2.0%	0	0.0%	5	10.0%	0	0.0%	5	10.0%
Thickened nuchal translucency (NT)	0	0.0%	2	4.0%	4	8.0%	1	2.0%	12	24.0%
Cystic Hygroma	4	8.0%	1	2.0%	0	0.0%	0	0.0%	0	0.0%
Structural abnormalities	1	2.0%	3	6.0%	3	6.0%	0	0.0%	8	16.0%

4. Discussion

In Saudi Arabia M. Anwar Iqbal *et al.* [8] done study similar to our study but their main indication was advanced maternal age (86.7%), followed by a previous child with abnormal chromosome (6.6%) and metabolic disorders (1.3%). While compared to this study, metabolic disorders are higher by (3.5%).

Brambati *et al.* [9] performed CVS on 1844 women aged 18 - 48 years, at 13 - 20 weeks gestation whose primary indication was chromosomal anomalies and single gene defects in 85% and 15% of cases respectively. The majority of invasive prenatal diagnostic procedures in the west are performed for individuals deemed to be at high risk for Down's syndrome. Habib F *et al.* [10] increase in the incidence of down syndrome with maternal age and the incidence in Saudi Arabia is reported to be 1.80 to 2.34 per 1000 births. The total number of down syndrome pregnancies is increasing, probably due mainly to the increasing proportion of older mothers. Most of the studies their main indication was advanced maternal age as compared to this study the majority of invasive prenatal diagnostic procedures was hematological disorders.

Regarding complications of the procedures our results showed that the Amniotic fluid leakage (0.7%), Temperature > 38 (0.0%), Abdominal cramps (0.7%), Threatened Miscarriage or loss of pregnancy within 3 weeks (2.3%) and Insufficient sample or contaminated (6.2%) of complications of the procedures. Silver *et al.* [11] reported that loss rates are to be higher when practitioners perform

fewer procedures, and when larger gauge needles are used. Culture failure is the most encountered problem. With good culture technique this can be limited to 0.3% - 0.6%. Persutte and Lenke [12] suggested that culture failure is higher in aneuploidy pregnancies, thus further diagnostic testing should be offered. Firth [13] stated that maternal cell contamination is rare with ultrasound guidance, an inaccurate diagnosis occurs in <0.2% of cases. CVS can be performed between 10 and 13 weeks. Sampling earlier than this gestation is possibly associated with a higher risk of fetal abnormality. Bringman [14] study found that the most feared risk from both invasive testing modalities is pregnancy loss. Overall, the risk of a complication that would lead to the loss of pregnancy ranges from 1 in 300 to 1 in 500 for both procedures. Hogge *et al.* [15] the major complications include bleeding, infection and rupture of membranes. Active vaginal/cervical infection is an indication for a transabdominal approach. Light vaginal bleeding is seen frequently after transcervical, but uncommonly after transabdominal procedures, this is usually self-limiting. The incidence of post-procedure chorioamnionitis is low occurring in only 0.3% of cases. As compared to our study no cases documented with chorioamnionitis, as temperature > 38 was (0.0%).

Regarding outcome of the pregnancy of the total cases of chorionic villus sampling and amniocentesis were loss of pregnancy were (4.8%), intrauterine fetal death or still birth were (13.9%), live birth were (63.9%), preterm delivery were (7.8%), preterm premature rupture of membrane (PPROM) were (1.8%), limbs reduction were (0.0%) and termination of pregnancy outside the country were (7.8%).

Alkuraya and Kilani [16] recent studies on Muslim populations revealed that education about the religion's stance on termination of pregnancy improved uptake of prenatal diagnosis and termination of pregnancies affected by thalassemia and sickle cell anemia. In Saudi Arabia, Alkuraya and Kilani (2001) found that 28 out of 32 Muslim participants refused abortion, but 13 (46.4%) changed their minds after they were given the fatwa on abortion. El-Beshlawy *et al.* [17] in Egypt, where previously there was a poor uptake of termination among pregnant mothers with affected fetuses, a recent study showed that with comprehensive in-depth counselling addressing the Islamic aspects of termination, uptake of selective abortion increased significantly. As compared to our study regarding termination of pregnancy were (7.8%) which is less by (3.5%).

The true incidence of procedure-related losses is difficult to evaluate. Brambati *et al.* [9] and Jackson *et al.* [18] suggested that transabdominal (TA) and transcervical (TC) procedures carry the same risk, but there are some data to suggest a slightly higher loss rate for transcervical (TC) procedures. In comparison to amniocentesis, Smidt-Jensen *et al.* [19] proved that loss rates do not differ. It is now accepted that the procedure-related loss from CVS is 1% above the background loss rate after 14 weeks' gestation and 2% before 14 weeks. Although most large trials of CVS demonstrated the safety of this procedure, Planteydt *et al.* [20] and Christians *et al.* [21] reported some limb defects in pregnancies that had been investigated by CVS. Firth *et al.* [22] noted a cluster of abnormalities

including transverse limb deficiency and oromandibular limb hypogenesis syndromes. Firth *et al.* [23] hypothesized that the defects were most likely to have occurred due to vascular disruption caused by hemodynamic disturbances or embolism of end arteries supplying the developing limbs. Alfirevic *et al.* [24] amniocentesis performed prior to 15 weeks had a significantly higher miscarriage rate and increased the risk of talipes equinovarus than CVS. On the other hand, CVS should not be performed before 10 weeks' gestation due to a possible increase in risk of limb reduction defects. As compared to our study no cases found to have limb defect as all the procedures were carried out between 11 - 14 weeks. Like M. Anwar Iqbal *et al.* [8] in Saudi Arabia study as no cases found to have limb defect.

Rhoads *et al.* [25] stated that the fetal loss rate following CVS has not been compared with no invasive testing in randomized studies but was found to be comparable to the fetal loss rate after amniocentesis. Alfirevic *et al.* [24] study of amniocentesis and CVS concluded that the total pregnancy loss of transabdominal CVS is comparable to that of second-trimester amniocentesis (OR 0.90, 95% CI, 0.66 - 1.23), while transcervical CVS is likely to be associated with a significantly higher risk of miscarriage (OR 1.40, 95% CI, 1.09 - 1.81).

Regarding results of the procedures according to the hematological disorders, our results showed that the affected women were (5.1%), carriers were (39.2%) and normal were (26.6%) of sickle cell disease, although beta thalassemia of affected women were (3.8%), carriers were (16.5%) and normal were (8.9%). The total cases result of the hematological disorders were the affected (8.9%), carrier (55.7%) and normal (35.5%). Referring to El-Beshlawy *et al.* [17] study which held in Egypt the results of the study regarding beta thalassemia disease showed (33.8%) were found to have affected fetuses while (66.2%) with normal or carrier fetuses for beta thalassemia.

5. Conclusion

CVS and amniocentesis are useful outdoor procedures to detect diagnosis or to assess whether a patient is at increased risk of having an affected fetus and that will minimize the psychological impact on the patient and to provide a proper antenatal care by her obstetrician and follow up to the baby by pediatrician. In this study it was observed that most of the patients who underwent the procedure were couples either carrier or affected to sickle cell disease or beta thalassemia. About half of our indications of the procedures were due to hematological disorders (47.6%) couples with sickle cell disease (carrier or affected disease) composing most hematological disorders (78.5%) followed by beta thalassemia (21.5%). Pre-marital counseling for the couples was introduced in Bahrain since 1992, a new law has been passed by the Bahrain Government which requires that all Bahraini couples, who are planning to marry, undergo mandatory premarital counseling. However, the most common indications found in this study were couples with hematological disorders (sickle cell disease, thalassemia disease) due to high rate of consanguinity marriage in the rural area of Bahrain.

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Ethical Approval

The study was approved by the Institutional Ethics Committee.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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