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The Risk Factors and Frequency of Congenital Anomalies in Neonates Born after Assisted Reproductive Technique in Baghdad

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Abstract

Background Assisted reproductive technique (ART) has helped couples all over the world. There have already been over 3,500,000 births resulting from ART, and with falling fertility in some countries.

Objective To identify the frequency and types of congenital anomalies among neonates born after ART, and to identify the probable fetal and maternal predisposing factors that may associated with these congenital anormalities and neonatal complications.

Methods This prospective study was performed in the Neonatal Intensive Care Unit in 3 teaching hospitals in Baghdad, from 1st day of January to day 31 of December 2015, and 306 live birth neonates were delivered by ART, and evaluated by the researcher and his residence pediatricians' doctors, and other congenital anomalies were assessed by ultrasonography, x-ray and echocardiography. Information about each neonate were taken from the records and families which includes: gestational age (term ≥ 37 week and preterm < 37 week) no post-term case were reported, body-weight (≥ 2.5 kg and < 2.5 kg), sex, system affected, age of the parents, consanguinity, residence, job of the parents, level of education, health condition of the parents, causes of infertility, any family history of congenital anomalies, death in the family. Exclusion criteria included mothers' age above 40, any maternal chronic diseases and chronic drugs taken. Congenital anomalies were classified into systems according to WHO recommendation.

Results Three hundred and six neonates were delivered, from which, 30 (10%) had congenital anomalies with male to female ratio (1.2:1), (20 (67%) twins and 10 (33%) were singletons), a significant association between congenital anomalies in ART products and male sex, consanguinity, and gestational age, as the p-value is significant (< 0.05), and the most common system affected was the gastro-intestinal tract (3%), but there was no significant association with body-weight.

Conclusion The ART born neonates are more prone for congenital anomalies. Gastrointestinal anomalies, especially esophageal atresia, are the commonest type of congenital anomalies followed by neurological anomalies. Male sex, consanguinity, and gestational age are significant risk factors for congenital anomalies. While body weight had no significant association with congenital anomalies.

Keywords Assisted reproductive technique (ART), intensive care unit, gastro-intestinal tract.

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List of abbreviations: ART = Assisted reproductive technique, IVF = In vitro fertilization

Introduction

The first successful human in vitro fertilization (IVF) attempt resulted in the 1978 delivery of Louise Brown in England and is considered the beginning of a new era for the treatment of infertility [1]. Birth defects (congenital anomalies) according to World Health Organization are structural, functional, and/or biochemical-molecular defects present at birth [2]. Early intrauterine period during 3rd-8th weeks of gestation is the vital period of life for the normal development of organs and organ system or organogenesis

[3]. On most health indicators, children born after ovulation induction (OI) seem to perform worse compared with spontaneously conceived children [4] or defined more widely to include functional disturbance as a defect, any irreversible condition exiting in a child before birth [5,6]. Birth defects are still the leading cause of perinatal mortality and childhood disability in developed countries [7]. However, birth defects in the developing world are largely underreported by deficiencies in diagnostic capabilities and lack of reliability of medical records and health statistics [8]. Factors may increase the risk of birth defects include the relatively advanced age of infertile couples, the underlying cause of their infertility, the medications used to induce ovulation or to maintain the pregnancy in the early stages, and factors associated with the procedures themselves, such as the freezing and thawing of embryos, the potential for polyspermic fertilization, and the delayed fertilization of the oocyte [9].

This study aims to identify the frequency and types of congenital anomalies among Assisted Reproductive Technologies (ART) born infants and to assess the probable fetal and maternal predisposing factors that may associated with congenital abnormalities and neonatal complications in ART.

Methods

This is a prospective study performed in Al-Imamein Al-kadhimein Medical City, Baghdad Teaching Hospital, and Al-Yarmook Teaching Hospital at the Neonatal Intensive Care Unit in a period from the 1st of January 2015 to the 31st of December 2015 during the first week of the neonate's age.

The total number of delivery from ART was 306 live births, from these deliveries, there were 30 (10%) neonates have obvious congenital anomalies, (20 twins and 10 as singletons) evaluated in the Neonatal Unit by researcher and his residence pediatricians' doctors, and other congenital anomalies were assessed by ultrasonography, x-ray and echocardiography study. Information list for each newborn, taking the detail from the neonatal records and families which includes: gestational age (the neonates were classified into term $\geq$ 37 week and preterm < 37 weeks); no post-term was reported, bodyweight (the neonates were classified into $\geq$ 2.5 kg and < 2.5 kg), sex, system affected, age of the parents, consanguinity, residence, job of the parents, level of their education, health condition of the parents, causes of infertility, any family history of congenital anomalies and if there is death in the family. Exclusion criteria included mother's age above 40, any maternal chronic diseases or drugs taken. Congenital anomalies were classified into systems according to World Health Organization recommendation [10]. We compare the different variables with control cases of normal conception (1000 cases) that has been taken at the Neonatal Unit from them 10 cases have congenital anomalies with matching age group (20-40) years for the mothers and gravidity (primigravida).

Statistical analysis was done using SPSS version 20 software program, chi-square test was used and a p-value <0.05 was considered significant.

Results

The study included 306 neonates (168 males and 138 females) with male to female ratio (1.2:1), from which, 30 cases (18 males and 12 females) had congenital malformation, (20 twins and 10 as singletons), with frequency of 10%, as shown in table (1), while in normal conception the frequency (1%) and p value (< 0.001), which is significant.

Table 1. Distribution of neonates with congenital malformation in both groups according to their sex

Sex	Total Live Birth By ART*	Congenital Malformation No. (%)	Total Live Birth By N C**	Congenital Malformation No. (%)	P Value
Male	168	18 (6%)	514	6 (0.6%)	<0.001
Female	138	12 (4%)	486	4 (0.4%)	
Total	306	30 (10%)	1000	10 (1 %)	

ART*= Assisted reproductive technique. N C**= Normal conception

Gastro-intestinal tract (GIT) anomalies was the commonest system 9 (3%) affected with (50%, was esophageal atresia, 33. %, imperforated anus, and 7%, of diaphragmatic hernia), followed by Central nervous system (CNS) anomalies 8 (2.7%), (40% hydrocephaly, 40% spinabifida, 20% anencephaly). Cardiovascular system (CVS) 6 (1.9%), (50%, ventricular septal defect (VSD)+ patent ductus arteriosus (PDA), 25% PDA, 25% dilated cardiomyopathy). Musculoskeletal system 4 (1.4%), (75% developmental dysplasia of the hip, 25% high arched palate), while the renal system was the least one 3 (0.9%), (67% polycystic kidney disease, 0.33% hydronephrosis), and with comparison with normal conception group the p-value=0.004 as in table 2.

Table 2. The relationship between congenital anomalies and system affected

System affected	No. of cases ART*	male No.	Female No.	%	No. of cases N C**	Male No.	Female No.	%
Gastrointestinal	9	6	3	3	2	2	0	0.2
Central nervous system	8	6	2	2.7	3	2	1	0.3
Cardiovascular	6	2	4	1.9	2	1	1	0.2
Musculoskeletal	4	2	2	1.4	1	0	1	0.1
Renal	3	2	1	0.9	2	2	0	0.2
P value				0.004				

ART*= Assisted reproductive technique. N C**= normal conception

Consanguinity showed significant association with congenital anomalies 70%, and p-value = (0.0228), as shown in table 3.

Gestational age had a significant association with congenital anomalies the p-value (0.002). As in table 4.

Table 3. The relationship between consanguinity and congenital anomalies

System affected	ART* No.	Consanguinity +ve	Consanguinity -ve	NC** No.	Consanguinity +ve	Consanguinity -ve
Central nervous system	8	6	2	3	2	1
Cardiovascular	6	4	2	2	2	0
Renal	3	2	1	2	1	1
Gastrointestinal	9	6	3	2	1	1
Musculoskeletal	4	3	1	1	0	1
Total No.	30	21 (70%)	9 (30%)	10	6 (60%)	4 (40%)
P value			0.0228			

ART*= Assisted reproductive technique. N C**= normal conception

Table 4. The relationship between gestational age and system affected

System affected	Total no. of ART*	Term ≥ 37 weeks	Preterm < 37 weeks	No. of NC**	Term ≥ 37 weeks	Preterm < 37 weeks
Central nervous system	8	3	5	3	1	2
Cardiovascular	6	2	4	2	0	2
Renal	3	1	2	2	2	0
Gastrointestinal	9	3	6	2	1	1
Musculoskeletal	4	3	1	1	0	1
P-value			0.002			

ART*= Assisted reproductive technique. N C**= normal conception

Body weight had no significant association with congenital anomalies, as the p= value (0.6446) as in table 5.

Discussion

The current study showed that the frequency of congenital malformation among the ART born neonates 10%, which was in agreement with Allen et al. study done in Canada (9%) [11], but higher than study done by Mozafari Kermani et al. (7%) [12], while in general population (2-3%) [13,14], which similar to study in Finland (5.5-6.6%) [15], Netherlands (2.3%,3.7%) [16,17], England (4.8%) [18], Australia (4.3%) [19], Sweden (5%) [20], Germany (8.6%) [21] and Australia (8.9%) [22]. The variation in results probably because of small mass and short duration of the current study.

Current study shows a higher predominance of male gender (males 5.88%: females 3.92%), which in accordance With Iranian study done by Movafagh et al. [23].

Table 5. The relation between the body Weight and system affected

System affected	Total no. of ART*	Body weight ≥ 2.5kg	Body weight < 2.5kg	No. of NC**	Body weight ≥ 2.5kg	Body weight < 2.5kg
Central nervous system	8	5	3	3	1	2
Cardiovascular	6	2	4	2	0	2
Renal	3	2	1	2	1	1
Gastrointestinal	9	5	4	2	2	0
Musculoskeletal	4	2	2	1	0	1
P-value	0.6446					

ART*= Assisted reproductive technique. N C**= normal conception

The current study showed predominance of GIT anomalies 2.94% followed by CNS anomalies 2.45%, CVS anomalies 1.96%. Musculoskeletal 1.47% then Renal 0.98%. A study done by Allen et al. showed the predominance of musculoskeletal 3.3%, Renal 2.6%, CVS 1.8%, GIT 0.6% and CNS 0.4% [11], this difference may related to study mass or regional variation and may be due to genetic factor.

Consanguinity among neonates was found in 21 (70%), which in accordance with study by Khatemi and Mamorri (67%) [24], and Chaturvedi and Banerjee (71%) [25]. The current study showed a significant statistical association between gestational age and congenital anomalies, which was in agreement with Davies et al. [26].

This study recommended that the ART neonates have high frequency of congenital anomalies, with high frequency in males than females. Gastrointestinal anomalies, especially esophageal atresia was the commonest type of congenital anomalies followed by neurological anomalies. Consanguinity and gestational age had significant association with congenital anomalies in ART neonates. There is no significant association between body weight and congenital anomalies in ART neonates.

This study recommends that ART contributes to significant risk of congenital malformation and may be more pronounced for multiple pregnancies so accurate counseling for parents considering ART and multidisciplinary coordination of care prior to delivery are warranted. Discussion of options for prenatal screening for congenital structural abnormalities in pregnancies achieved by ART is recommended, including appropriate use of Biochemical and sonographic screening. Further scientific research is needed to determine the relation between specific type of ART (as far as there are different methods of ART), and congenital abnormalities.

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Conflict of interest

The author declares no conflict of interest.

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