

Evaluation of External Genital Anomalies and the Underlying Factors in Male Newborns

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ABSTRACT

Background: External genital anomalies are the most common congenital disorders in male infants with unknown etiology in the majority of cases. According to recent reports, incidence rate of these anomalies is rising in different countries. This study aimed to evaluate the prevalence of external genital anomalies and possible underlying factors in male newborns.

Methods: This cross-sectional study was conducted on all the male neonates born in Motahari Hospital of Urmia during October 2009-June 2010. Neonatal screening results and demographic data were recorded separately in a questionnaire for each neonate. Data analysis was performed in SPSS V.20 using descriptive statistics (mean, frequency, percentage, and standard deviation) and Chi-square test to evaluate the correlations between quantitative variables.

Results: In this study, external genital anomalies were identified in 83 male neonates (8.3%). Moreover, 59 infants (5.9%) had cryptorchidism, 18 (1.8%) had hypospadias and 12 infants (1.2%) had microphallus. Moreover, a significant correlation was observed between the incidence of cryptorchidism and maternal comorbidities, low birth weight, prematurity, maternal gestational hypertension, and diabetes mellitus.

Conclusion: According to the results of this study, cryptorchidism is the most prevalent external genital anomaly in male newborns, followed by hypospadias. Occurrence of these anomalies is associated with several risk factors, such as prematurity, low birth weight, maternal diseases (e.g., diabetes and hypertension), and use of medications during pregnancy. In addition, cryptorchidism had a significant correlation with smoking habits, and further studies with larger sample sizes are required in this regard.

Keywords: Cryptorchidism, Genital anomaly, Hypospadias, Newborn, Male

Introduction

External genital anomalies are the most prevalent congenital disorders in male newborns with unknown etiology in the majority of cases (1-3). Genetic and environmental factors are commonly involved in the incidence of genital anomalies, including maternal age, maternal comorbidities during pregnancy, prematurity, low birth weight, and white race (1, 4). Most of these anomalies could be identified in neonatal screening examinations and might be associated with severe diseases, such as congenital adrenal hyperplasia (5). Therefore, early diagnosis and treatment of these anomalies is of paramount importance. According to the literature, there is a significant

correlation between infertility and the occurrence of undescended testis and testicular cancer (6). Recent reports have suggested that the incidence of these abnormalities is rising in different countries (7-9). Nevertheless, this increase has been reported to be insignificant by some researchers (10). Variations in the findings of different studies in this regard could be due to genetic and environmental factors, as well as different methods of data collection (7).

This study aimed to evaluate the prevalence of external genital anomalies and possible underlying factors in male newborns.

Methods

This cross-sectional study was conducted on

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all the male neonates born in Motahari Hospital of Urmia, Iran during October 2009-June 2010. Neonatal examinations were performed within the first 24 hours of birth by a trained intern, and if the neonates were suspected of genital anomalies, they were re-examined and received necessary paraclinical evaluations by a urologist.

Neonatal screening results (birth weight, gestational age, and external genital examinations) and demographic data were separately recorded in a questionnaire for each infant. Microphallus was defined as a stretched penile length of less than 2.5 standard deviations (SDs) below the mean for age (11). Undescended testis was considered if either testicle was absent in the scrotum of the neonate.

This study was conducted based on the principles of the Declaration of Helsinki, and the study protocol was approved by the Ethics Committee of Urmia University of Medical Sciences. Moreover, written informed consent was obtained from the parents of all the newborns.

Data analysis was performed in SPSS V.20 using descriptive statistics (mean, frequency, percentage, and standard deviation) and Chi-square test to evaluate the correlations between quantitative variables. P value of less than 0.05 was considered significant.

Results

During October 2009-June 2010, 1,940 infants were born in Motahari Hospital of Urmia. In total, 1,001 male newborns were enrolled in this study. Among the studied infants, 83 cases (8.3%) had at least one anomaly, 59 neonates (5.9%) had cryptorchidism, 18 infants (1.8%) had hypospadias, 12 cases (1.2%) had microphallus, and 10 neonates (1%) had chordia (Table 1).

Birth weight and gestational age were recorded for the newborns, and the results were indicative of a significant correlation between the gestational age and birth weight of male newborns with the incidence of external genital anomalies ($P < 0.05$) (Tables 2 & 3).

Table 1. Distribution of External Genital Anomalies in Male Newborns during October 2009-June 2010 in Motahari Hospital of Urmia

Anomalies	N (%)	
Cryptorchidism	Right	10 (1)
	Left	30 (3)
	Bilateral	19 (1.9)
Hypospadias	Glans	14 (1.4)
	Middle	2 (0.2)
	Pubic	2 (0.2)
Microphallus	22 (2.2)	
Cordia	10 (1)	
Hypospadias+Cryptorchidism	2 (0.2)	
Microphallus+Cryptorchidism	4 (0.4)	
Microphallus+Hypospadias	5 (0.5)	
Hypospadias+Cordia	9 (0.9)	

Table 2. Prevalence of External Genital Anomalies Based on Gestational Age of Male Newborns during October 2009-June 2010 in Motahari Hospital of Urmia

Gestational Age	Microphallus		Hypospadias		Cordia		Cryptorchidism	
	No	Yes	No	Yes	No	Yes	No	Yes
<37 Weeks	94	13	102	5	103	4	86	21
42 <Weeks	18	1	19	0	19	0	17	2
37-42 Weeks	867	8	862	13	869	6	839	36
Total	979	22	983	18	991	10	942	59
P-value	0		0.11		0.97		0	

Table 3. Prevalence of External Genital Anomalies Based on Birth Weight in Male Newborns during October 2009-June 2010 in Motahari Hospital of Urmia

Birth Weight	Microphallus		Hypospadias		Cordia		Cryptorchidism	
	No	Yes	No	Yes	No	Yes	No	Yes
2000 g >	69	14	80	3	82	1	62	21
2000-2500 g	46	3	45	4	46	3	38	11
2500-4000 g	788	4	784	8	788	4	767	25
4000 g <	76	1	74	3	75	2	75	2
Total	979	22	983	18	991	10	942	59
P-value	0.00		0.001		0.001		0.00	

Table 4. Maternal Demographic Characteristics for Male Newborns during October 2009-June 2010 in Motahari Hospital of Urmia

Variable		N (%)
Age (year)	18>	86 (8.6)
	18-35	816 (81.6)
	35<	99 (9.9)
Education Status	Illiterate	321 (32.1)
	Below Diploma	654 (65.4)
	Diploma or Bachelor's Degree	25 (2.5)
	Master's Degree	1 (1)
Language	Kurdish	598 (59.8)
	Azari	403 (40.3)
Occupation	Housewife	968 (96.8)
	Employee	8 (0.8)
	Other	25 (2.5)

In this study, mean of maternal age was 26 years (minimum=14 years, maximum=50 years), and 403 of the mothers were native Azerbaijani speakers. No significant correlation was observed between the demographic characteristics of the mothers and incidence of genital anomalies in male newborns ($P>0.05$) (Table 4). In addition, 22 mothers had smoking habits, and cryptorchidism was diagnosed in three newborns of these mothers ($P=0.065$).

Chronic or gestational diseases were reported in 279 mothers, including hypertension, gestational hypertension, diabetes mellitus, gestational diabetes, pyelonephritis, and thyroid disease. Moreover, a significant correlation was observed between maternal comorbidities and incidence of external genital anomalies ($P=0.006$). In addition, hypospadias was diagnosed in four newborns with maternal gestational hypertension ($P=0.012$), and cryptorchidism was reported in nine newborns with maternal gestational hypertension ($P=0.04$), as well as two newborns with maternal diabetes mellitus ($P=0.00$) (Table 5).

In this study, 161 unwanted pregnancies were reported, and no significant correlation was observed between the incidence of external genital anomalies and unwanted pregnancy ($P>0.05$). Among 406 neonates who were born via caesarean section, 12 cases were diagnosed with hypospadias ($P=0.046$).

Corticosteroid consumption was reported in six mothers, and one of the newborns in this group (based on the person's statement) whose was diagnosed with cryptorchidism ($P=0.21$).

Table 5. Prevalence of Cryptorchidism and Hypospadias in Newborns with Maternal Diabetes Mellitus, Gestational Diabetes, Hypertension, and Gestational Hypertension

Maternal Disease	Cryptorchidism		Hypospadias	
	No	Yes	No	Yes
Diabetes Mellitus	2	2	4	0
Gestational Diabetes	18	2	17	3
Hypertension	12	2	14	0
Gestational Hypertension	62	9	67	4

Furthermore, one of the mothers was addicted newborn was diagnosed with cryptorchidism. Consanguineous marriage was reported in 197 parents, and 20 cases had family history of external genital anomalies. Moreover, no significant correlation was observed between consanguineous marriage and family history of external genital anomalies ($P>0.05$).

Discussion

Cryptorchidism is one of the most common external genital anomalies in male newborns, which may remain undiagnosed in many cases. In general, factors such as low birth weight, prematurity, twin pregnancy, and advanced maternal age contribute to the incidence of cryptorchidism. Recent reports have noted the rising prevalence of cryptorchidism, which might be due to lifestyle and environmental factors (1-3).

In the present study, prevalence rate of cryptorchidism was estimated at 59 cases per 1,001 male newborns, which is higher than the rate determined in the study by Shiva et al., in which 23.8 of the newborns were premature, and 46.2% were diagnosed with cryptorchidism (12). In the current study, 10.7% of the male newborns were premature, and 19.6% were diagnosed with cryptorchidism.

Despite the lower frequency of prematurity in our study, prevalence rate of cryptorchidism was comparatively higher; this could be due to the presence of maternal diseases during pregnancy. Since the study setting (Motahari Hospital) was a tertiary referral hospital, there were several cases of high-risk pregnancies among the patients.

In one study, Preiksa RT et al. reported a significant correlation between cryptorchidism, birth weight and gestational age of neonates. However, they found no significant relationship between the incidence of cryptorchidism and maternal age (6). Similarly, cryptorchidism had no

significant correlation with maternal age in the current research ($P=0.357$). In addition, we identified only one case of cryptorchidism among the male infants of six mothers who used corticosteroids during pregnancy.

In the present study, 22 mothers had smoking habits, and three cases of cryptorchidism were diagnosed in the male newborns of this group. In another research, Golduri et al. determined the odds ratios at 5.39 for smoking habits and incidence of cryptorchidism. According to the literature, incidence of cryptorchidism is significantly correlated with alcohol consumption; in the current study, none of the mothers had alcohol consumption (13).

Maternal diseases during pregnancy are one of the main risk factors for neonatal anomalies. In this regard, Weidenr et al. reported hypertension and pre-eclampsia as the major risk factors for cryptorchidism (14). Moreover, the findings were indicative of a significant correlation between cryptorchidism, diabetes mellitus and gestational hypertension of the mothers.

Recent reports have noted the rising prevalence of hypospadias (9, 15). According to statistics, prevalence of hypospadias varies between 0.4-8.2 per 1,000 male newborns in the world. This significant difference could be due to geographical, environmental, and genetic factors, as well as variable methods of data collection (7). Prevalence rate of hypospadias has been estimated at 1.03 in Denmark and 0.27 in Finland (16).

In this regard, several studies in the United States have suggested that the prevalence of hypospadias has increased from 2.2 cases in 1970 to 3.9 cases per 1,000 male live births in 1993 (7). In another study, prevalence of hypospadias was evaluated in Washington (U.S.A) during 1987-2002. According to the results, prevalence rate of hypospadias increased from 4.6 cases in 1987 to 5 cases per 1,000 male live births in 2002, which was indicative of no significant change in the incidence rate of this disorder (3).

Although several reports have confirmed the increasing rates of hypospadias in many countries, the results of one study performed in Spain were indicative of the declining rate of this anomaly (17). According to statistics, prevalence rate of hypospadias is on a rising trend in Asia (18). In the current study, incidence rate of hypospadias was estimated at 18:1,000 male newborns, while this rate was

reported to be 9:1,000 male live births in the study by Shiva et al. (12).

A number of studies have denoted associations between the incidence of hypospadias and factors such as low birth weight and low gestational age (19-21); however, confirming the relationship between hypospadias and other risk factors requires further investigation (3). High prevalence rate of hypospadias in the present study could be due to maternal comorbidities during pregnancy and different sample population since our study was conducted in a tertiary referral hospital.

Among the main risk factors for hypospadias are advanced or low maternal age during pregnancy; however, the exact cause of this correlation remains unknown (3). In this regard, the results of one study performed in New York (U.S.A) were indicative of a significant correlation between maternal age and incidence of hypospadias in newborns (10). Another research in California (U.S.A) suggested a linear relationship between maternal age (>40 years and <20 years) and incidence of hypospadias (8). Furthermore, the findings of Abdollahi et al. reported advanced maternal age as a major risk factor for the incidence of hypospadias in newborns (22). Results of the current study were indicative of no association between maternal age and the incidence of genital anomalies.

According to the literature, incidence of hypospadias is correlated with chronic diabetes (3); however, no such relationship was observed in the current study. On the other hand, presence of maternal diseases was found to be significantly correlated with the incidence of external genital anomalies, while Shiva et al. reported no associations in this regard (12).

According to the results of the present study, familial relations of parents could be a risk factor for the incidence of external genital anomalies. In this regard, the results obtained by Shiva et al. were suggestive of a significant correlation between consanguineous marriage and occurrence of microphallus (12). In the current research, no significant association was observed between the familial relation of parents and incidence of external genital anomalies.

Cryptorchidism is considered as the most common external genital anomaly in male newborns, followed by hypospadias. Occurrence of these anomalies is associated with risk factors

such as prematurity, low birth weight, maternal diseases during pregnancy (especially diabetes and hypertension), and medication use during pregnancy. According to the results of the present study, cryptorchidism was directly correlated with smoking habits; however, future studies with larger samples sizes are required in order to confirm this finding.

The current research was conducted in Motahari Hospital of Urmia located in West Azerbaijan Province, Iran. This hospital is a tertiary referral center in West Azerbaijan Province, and almost all the participants in our study had low socioeconomic status or were referred from other cities due to comorbidities during pregnancy.

Conclusion

Cryptorchidism is considered as the most common external genital anomaly in male newborns, followed by hypospadias. Occurrence of these anomalies is associated with risk factors such as prematurity, low birth weight, maternal diseases during pregnancy (especially diabetes and hypertension), and medication use during pregnancy. According to the results of the present study, cryptorchidism was directly correlated with smoking habits; however, future studies with larger samples sizes are required in order to confirm this finding.

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