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Delayed Presentation of Cryptorchidism, What's Behind?

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ABSTRACT

Background: Delayed presentation of cryptorchidism, or undescended testis (UDT), is still a common problem worldwide, despite the clear recommendations of most international guidelines for early referral and correction at 6–12 months of life. Identifying the underlying causes of this delayed presentation is an important step in overcoming this problem. .
Objectives: To identify the causes and risk factors associated with delayed UDT presentation.
Materials and methods: A cross-sectional study was conducted over 17 months, and included patients with UDT up to 14 years old age. Patients were divided into two groups according to their age at the time of presentation, early ($\leq$ 1 year) and late ($>$ 1-14 years) groups. The causes of delayed UDT presentation were identified in the late group. Both groups were compared regarding possible risk factors of delayed UDT presentation.
Results: Of 204 cases with UDT, there were 121 (59.3%) patients presented beyond the recommended age of orchiopexy.. The main causes of delayed presentation were parental ignorance and unawareness in 43 (35.5%) patients, false advice from medical and nonmedical personnel in 17 (14.1%) and 28 (23.1%) patients, respectively, the presence of another medical disease in 18 (14.9%) patients, and poverty in 15 (12.4%) patients. Patients in the late group had a significantly less urbanized level of residency (P-value = 0.036), a lower maternal education level (P-value = 0.012), less parent information about UDT (P-value = 0.013), more likely to be first-born boys in their families (P-value = 0.036), and to have another medical disease(s) (P-value = 0.049). We found insignificant differences between the two groups regarding family history of UDT (P-value = 0.300), paternal education level (P-value = 0.288), side (P-value = 0.759), and site (P-value = 0.073) of UDT.
Conclusion: Delayed presentation of UDT was attributed mainly to the limited knowledge of the community and medical care providers about its management. Increasing public awareness about UDT and establishing effective measures for earlier detection and referral of patients with UDT are important initial steps to solving this problem in our society.
Keywords: Undescended testis; Cryptorchidism; Delayed presentation; Orchiopexy.

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INTRODUCTION

Cryptorchidism, or undescended testis (UDT), is the failure of one or both testicles to descend to their normal anatomical position in the scrotum. It is a common congenital anomaly of the urogenital system in male newborns, affecting about 1–4% of term, and up to 45% of preterm babies [1]. Normally, the testis is located at least at the midpoint of the scrotum or below, and any testicular position above this level, and within the normal pathway of testicular descend from the abdomen to the scrotum, with the inability to manually pull the testis down to the scrotum, is regarded undescended [2].

Differentiating true UDT from retractile and ectopic testes is crucial. In retractile testis, the testis can be brought down to the bottom of the scrotum and remains there for some time, while ectopic testis is located outside both the scrotum and the normal pathway of descent [2]. After birth, spontaneous testicular descend is an expected event in most patients borne with UDT in the first three months of life, but this possibility declines thereafter, and becomes unlikely after the sixth

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month of life [3].

Normal testicular growth, germ cell differentiation, and subsequently spermatogenesis require a temperature less than body temperature by about 3–4°C, and this lower temperature is provided mainly by the intrascrotal position of the testis [4]. As a result, UDT has a less optimal environment for development, which will affect the fertility potential of patients, causing subfertility or infertility in the future. Other possible morbidities of UDT include an increased risk of testicular malignancy in comparison to the normal population, increased risk of testicular trauma, testicular torsion, and high association with an inguinal hernia with its possible complications as bowel obstruction and strangulation [1]. Direct correlations were identified years ago between the risks of infertility and testicular malignancy with the duration by which the testis remains in an undescended position [5]. For all the aforementioned risks and consequences of UDT, most international guidelines recommend early referral to specialists at about the sixth month of life, and surgical relocation of the UDT to the scrotum, or orchiopexy within the next year, preferably before the child's first birthday and maximally at the age of 18 months [6–8]. Despite these clear recommendations, a considerable portion of patients with UDT still presented beyond the recommended age of referral and treatment worldwide. In an Iraqi study, public health workers' limited knowledge about UDT, a parent's neglect, and low socioeconomic status contributed to the presentation of about three-quarters of UDT patients after their first birthday [9]. Another study in the United States (US) found that poor family education and a lack of routine genital examination by the referring care providers led to the referral of about 64% of patients after the age of 18 month [10]. Thus, highlighting the causes of delayed UDT presentation is an important step to overcome this problem.

This study aimed to identify the main causes and some possible predisposing factors behind the delayed presentation of UDT at our institution to optimize the time of referral and treatment and, subsequently, the outcomes of this anomaly.

MATERIALS AND METHODS

A cross-sectional observational study carried out at a tertiary Pediatric Surgery Center in Baghdad, Iraq over a period of seventeen months, from July 2022 to the end of November 2023. The inclusion criteria included any patient with confirmed UDT, ranging in age from birth to 14 years.

The exclusion criteria included patients with retractile, ascending, ectopic testes, UDT following previous inguinal surgery including orchiopexy, patients older than 14 years old, and patients whose families refused to participate in the study.

Our institution recommends orchiopexy at one year of age. Our institutional protocol involves a physical examination in supine, standing, and squatting positions to diagnose UDT. We first performed sonography for impalpable UDT to determine the presence or absence of the testis. Should sonography fail to visualize the testis, we scheduled the patient for a laparoscopic assessment.

A questionnaire form was designed and reviewed by the Scientific and Ethical Committee of Al-Mustansiriyah Medical College, Department of Surgery, which approved the study (Ref. No.182, on June 2022). The questionnaire involved information about patients and their families. Patient information included age at the time of presentation, side and site of UDT, birth sequence among male births, and presence or absence of another medical disease(s). The family information encompassed the education level of the parents, their knowledge about UDT and its source, their place of residence, and their family's history of UDT. We assessed parental awareness of UDT by directly asking if they had any information about it. We assessed their knowledge by asking them three questions about the recommended age for UDT referral, the recommended age for orchiopexy, and the potential complications of UDT, if they had any. We considered parental information good when they answered at least two questions correctly, and misinformation bad when they gave at least two incorrect answers. We classified the information's sources as either nonmedical (family members, relatives, and friends) or medical (doctors, nurses, medical assistants, midwives, and paramedics). We obtained parental consent for all cases, explained the questionnaire to the parents, and had them fill it out to prevent bias during data collection, except for the side and site of UDT, where the examining doctor filled it out. A medical care administrator, blind to the study, filled out the questionnaire for illiterate families or parents with low education levels. We gave identification codes to all patients to protect their privacy, and we did not use or share their data outside of this study. We divided the patients into two groups based on their age at the time of presentation. The early group included patients who were up to one year old, and the late group included patients who were older than one year. We identified the causes of delayed UDT presentation in the late group, and analyzed and compared data from both groups to determine if the factors under study could potentially predispose to delayed UDT presentation.

We used the Statistical Package for the Social Sciences version 28 (SPSS-28) for data analysis. Categorical data was expressed as frequencies and percentages, and the age of patients as median, interquartile range (IQR (Q1–Q3)), and range (minimum-maximum values). The differences between percentages were tested by the Pearson Chi-square test (χ^2-test), and a P-value of < 0.05 was set for statistical significance.

RESULTS

A total of 204 patients with UDT were included in the study, 83 (40.7%) patients presented before their first birthday and constituted the early group, and 121 (59.3%) patients aged more than 1 year to 14 years represented the late group. In the early group, the median age of patients was 7.4 months, ranging from 2 weeks to 11.5 months, with an IQR of 4.6 (4.5–9.1 months). In the late group, the median age of patients was 28.5 months, ranging from 14.2–161 months, with an IQR of 23.5 (20–43.5 months) as shown in Table 1.

The main cause of delayed UDT presentation in the late

Table 1. Age distribution of patients with undescended testis.

Age(month)	N (%)
≤ 12	83 (40.7%)
13–24	39 (19.1%)
25–36	31 (15.2%)
37–48	23 (11.3%)
> 48–168	28 (13.7%)
Total	204 (100%)

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group was parent ignorance or unawareness, which was reported in 43 (35.5%) patients (Table 2).

The majority of mothers in the early group, as well as fathers, had higher education levels of learning (37 (44.6%) and 35 (42.2%), respectively), with only 8 (9.6%) mothers and 5 (6%) fathers were illiterates. While in the late group, the majority of mothers and fathers had secondary school levels of learning (45 (37.2%) and 43 (35.5%), respectively), with 15 (12.4 %) mothers and 9 (7.9%) fathers being illiterates. The difference in the level of parent education between the two groups was significant on the maternal side (P-value = 0.012), but not in the paternal side (P-value = 0.288), as illustrated in Table 3.

In terms of parents' knowledge about UDT, 38 (45.8%) parents in the early group and 28 (23.1%) parents in the late group had good information about UDT, and the rest of the parents in both groups had misinformation or no information. In the early group, the misinformation was provided by medical personnel in 7 (8.4%) patients, and nonmedical personnel in 11 (13.3%) patients. While in the late group, the misinformation was provided by medical personnel in 17 (14.1%) patients, and nonmedical personnel in 28 (23.1%) patients. The difference in parent information about UDT between the two groups was significant (P-value = 0.013). Sixty-three (75.9%) patients in the early group were living in urban areas, in comparison to 75 (62%) patients in the late group, which was significant (P-value = 0.036). Family history of UDT was reported more in the early group (8 (9.6%) *vs* 7 (5.8%)), but the difference was insignificant (P-value = 0.300) as indicated in Table 3.

In both early and late groups, the right testis was most commonly involved (50.6% and 52.1%, respectively), followed by the left side (36.1% and 38%, respectively), and bilateral disease (13.3% and 9.9%, respectively), which were insignificant (P-value = 0.759). Inguinal UDT was the most common condition among patients in the early group (53.2%), whereas high scrotal/suprascrotal testis was more common in the late group (51.1%), although this difference was not statistically significant (P-value = 0.073). Twenty (24.1%) and 46 (38%) patients in the early and late groups, respectively were the first-born boys in their families. The difference in the childbirth sequence between the two groups was significant (P-value = 0.036). Table 4 shows that the late group reported a higher prevalence of another medical disease (14.9% *vs.* 6%, P-value = 0.049).

DISCUSSION

Delayed presentation of UDT is still a major concern worldwide, despite the fact that it is a common and easily detectable congenital anomaly. Understanding the pathophysiological and morphological changes associated with UDT has led to a progressive decline in the recommended age for orchiopexy over the last few decades. In the 1950s, orchiopexy was recommended at the age of 10–15 years, which was decreased to 4–6 years in the 1970s, and 2 years in the 1980s–1990s [3]. Nowadays, orchiopexy is recommended between the ages of 6 months and 12–18 months at the latest, and it is advisable to do a genital examination in each clinical checkup visit to assess the testicular site and to diagnose any changes in testicular position as in ascending, or retractile testes [6]. Recently, harvesting testicular tissue at the time of orchiopexy to be stored by cryopreservation, is recommended for patients with bilateral UDT, to be used in the future if patients develop fertility problem [11].

Table 2. Causes of delayed presentation of undescended testis.

Cause	N (%)
Parent ignorance/unawareness	43 (35.5%)
False advice from medical personnel	17 (14.1%)
False advice from nonmedical personnel	28 (23.1%)
Poverty	15 (12.4%)
Presence of other medical disease(s)	18 (14.9%)
Total	121 (100%)

The rate of delay in our study, although it was high, coincided with most reports about delayed UDT presentations from different parts of the world [12–15]. A study in the United States (US) found that about 70% of UDT patients presented at least 6 months beyond the recommended age for orchiopexy [12]. Another Canadian study revealed that approximately 75% of orchiopexy operations took place after the recommended age for repair [15].

When analyzing the causes of delay in our study, it can be stated that more than two-thirds of delayed UDT cases were attributed to limited knowledge of community and medical personnel about this common childhood anomaly and limited adherence to guidelines and recommendations about early assessment and referral of patients with UDT. An assessment of parents' knowledge about UDT and the sources of this knowledge supported this explanation, providing insight into the understanding of community and medical care providers about UDT in our society. More than three-quarters of parents in the late group, as well as half of parents in the early group, had misinformation or no information about UDT, according to the data analysis. Nonmedical personnel, such as friends or relatives, primarily provided the misinformation in both groups. These findings may reflect the population's awareness of UDT in our community. Medical personnel, on the other hand, were responsible for parent misinformation about UDT in 8.4% and 14.1% of patients in the early and late groups, respectively. Our study did not assess the educational degree and specialty of the referring medical personnel, but this finding may indicate their understanding of UDT in our health institutions. Many studies discussed the influence of public unawareness and limited medical personnel knowledge about UDT as possible causes of delayed presentation. In one study from Africa, it was found that parent ignorance was the underlying cause of delayed UDT presentation in about half of the cases, with early neonatal assessment and thorough examination done only in about a fifth of patients, and nearly one-quarter of patients with UDT were presented to initial hospitals without explanation of the time of spontaneous testicular descend or advise for follow-up and referral to specialists, or specialized hospitals [16]. Similarly, in a Korean study, about 40% of UDT cases were presented lately due to delayed referral from primary care physicians, and parent unawareness or neglect [17]. A study in Sweden found that approximately half of patients referred for suspected UDT had normal testes on examination, with no need for surgical referral or follow-up. This rate of inaccurate referrals was more pronounced if the referrers were non-specialized physicians, especially from a child health center [18]. Given these findings, and although the study population may not reflect the actual knowledge of our community about UDT, it

Table 3. Family characteristics of patients with undescended testis.*

Family character	Early group (n = 83)	Late group (n = 121)	P-value
Parents´ education level:			
Mother:			
Illiterate (%)	8 (9.6%)	15 (12.4%)	0.012*
Primary school (%)	10 (12%)	31 (25.6%)	
Secondary school (%)	28 (33.8%)	45 (37.2%)	
Higher education (%)	37 (44.6%)	30 (24.8%)	
Father:			
Illiterate (%)	5 (6%)	9 (7.4%)	0.288
Primary school (%)	16 (19.3%)	33 (27.3%)	
Secondary school (%)	27 (32.5%)	43 (35.5%)	
Higher education (%)	35 (42.2%)	36 (29.8%)	
Parental knowledge about UDT and source of information:			
Good information (%):	38 (45.8%)	28 (23.1%)	0.013*
- Medical personnel (%)	28 (33.7%)	19 (15.7%)	
- Nonmedical Personnel (%)	10 (12.1%)	9 (7.4%)	
Misinformation (%):	18 (21.7%)	45 (37.2%)	
- Medical personnel (%)	7 (8.4%)	17 (14.1%)	
- Nonmedical personnel (%)	11 (13.3%)	28 (23.1%)	
No information (%)	27 (32.5%)	48 (39.7%)	
Residency:			
Urban (%)	63 (75.9%)	75 (62%)	0.036*
Rural (%)	20 (24.1%)	46 (38%)	
Family history of UDT:			
Positive (%)	8 (9.6%)	7 (5.8%)	0.300
Negative (%)	75 (90.4%)	114 (94.2%)	

* Significant difference between percentages using Pearson Chi-square test (χ^2-test) at 0.05, UDT: Undescended testis.

Table 4. Characteristics of patients with undescended testis (UDT).*

Patient character	Early group (n= 83 patients, 94 UDT testes)	Late group (n=121 patients, 133 UDT testes)	P-value
Side of UDT			
Right (%)	42 (50.6%)	63 (52.1%)	0.759
Left (%)	30 (36.1%)	46 (38%)	
Bilateral (%)	11 (13.3%)	12 (9.9%)	
Site of UDT			
High scrotal/Suprascrotal (%)	37 (39.4%)	68 (51.1%)	0.073
Inguinal (%)	50 (53.2%)	48 (36.1%)	
Abdominal (%)	5 (5.3%)	11 (8.3%)	
Absent (%)	2 (2.1%)	6 (4.5%)	
Patient's birth sequence among male births			
1st (%)	20 (24.1%)	46 (38%)	0.036*
2nd or more (%)	63 (75.9%)	75 (62%)	
Presence of medical disease(s)			
Positive (%)	5 (6%)	18 (14.9%)	0.049*
Negative (%)	78 (94%)	103 (85.1%)	

* Significant difference between percentages using Pearson Chi-square test (χ^2-test) at 0.05, UDT: Undescended testis.

is clear that community education about UDT, and updating medical personnel information with the latest guidelines and recommendations about UDT referral and management; are essential steps to overcome delayed UDT presentation in our society.

In our study, the presence of another medical disease was an underlying cause of delayed UDT presentation. Another medical disease includes any chronic condition in any system in the body as cardiac, respiratory, neurological, or gastrointestinal systems, that needs evaluation and treatment. A significant difference was found between the early and late groups regarding the influence of another medical disease on

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the time of UDT referrals. Most parents in the early group stated that the presence of another medical disease gave them the insight to seek medical help and advice for UDT, as the latter was diagnosed during the assessment of another disease. This finding was similar to other studies in a Chinese study, Tian-Xin Zhao *et al.* found that patients with other comorbidities, mainly inguinal conditions such as inguinal hernia and hydrocele, were more likely to present early as the associated anomalies were the motivators for early presentation [19]. Another study revealed that the type of associated malformations influenced the presentation time, with patients with hypospadias presenting earlier than those with micropenis [20]. However, these studies included only congenital anomalies in the inguinoscrotal area and no chronic clinical problems elsewhere in the body, as in our study. In contrast, most families in the late group stated that the presence of another medical illness influenced the time of UDT presentation, and attributed this delay to two main reasons. First, most parents were busy with the treatment of another illness as they thought that UDT was less urgent and its treatment could be delayed, so gave priority for treatment to another illness, especially if the illness was affecting the quality of life as in cardiac or neurological diseases. Second, the presence of another disease carried significant morbidity regarding the risks of operation and anesthesia, as in patients with chronic respiratory problems such as asthma or tracheomalacia. As a result, the presentation of patients for UDT was delayed while controlling another medical illness to an optimal level. Therefore, we need to determine whether the presence of another medical illness is a predisposing factor for either an early or delayed presentation of UDT. In our opinion, the severity of the illness, and the affected body system may be the primary determents of the time of UDT presentation, for example, a patient with a severe cardiac problem tends to be a late presenter, while a patient with mild hydronephrosis tends to be an early presenter.

Poverty was the least reason for delayed UDT presentation in our study. The effects of financial and economic statuses of families on the time of UDT presentation were not assessed in our study. This is because most medical services, including surgical procedures, are free of fees in government hospitals, apart from the private departments, according to the instructions of Ministry of Health in our country. This was clearly reflected in our study, as less than a fifth of patients were delayed for financial problems. Many studies however documented socioeconomic factors as main causes or risk factors for delayed UDT referral [19, 21].

In addition to the main causes of delayed UDT presentation, we assessed the effects of some factors in both patients and their families as possible predisposing factors for delayed presentation, such as parent education level, residency, family history of UDT, site and side of UDT, and patient's birth sequence.

Regarding parent education level, higher levels of education in both fathers and mothers were observed in the early group in comparison to parents in the late group. This was reflected positively in parent knowledge about UDT, as parents in the early group had better knowledge about UDT than parents in the late group. The differences in parent education level between the two groups were significant for the maternal side, but not for the paternal side. This finding could be attributed to the mother's duty as a main care provider for children, and subsequently more time period of contact between them. As a result, educated mothers tend to discover the abnormal testicular position earlier, with a subsequent referral. Many studies identified a direct relation between parent education level and time of UDT presentation, i.e. increasing level of parent education was associated with earlier UDT presentation [10, 16].

In our study, the location of residency had a significant impact on the time of the UDT presentation, as living in urban areas was associated with an earlier presentation. This finding aligned with previous research, such as a US study that found patients from urban areas were approximately one year younger than those from rural areas for both referral and orchiopexy times [22]. This finding was expected, as increased levels of urbanization are associated with more advanced and modern medical services are provided by specialized and qualified physicians at specialized hospitals and medical centers. Unlike rural areas, which contain general hospitals and primary care centers that are usually managed by nonspecialized physicians and general practitioners. In addition, different levels of education are usually present between urban and rural areas, which influence the time of presentation as mentioned previously.

A family history of UDT was described as a risk factor for cryptorchidism and may be related to an underlying genetic predisposition [3, 23]. The influence of positive family history on the time of UDT presentation is in favor of early presentation [24]. A previous experience with UDT, made families more aware of this anomaly and more informed about the optimal time of referral and surgical repair. In our study, a positive family history of UDT was reported more in the early group, but the difference didn't reach a significant level.

Regarding the influence of the side and site of UDT on the time of presentation, the right side was the predominant side of involvement in both groups, and bilateral disease was reported more in the early group. The latter result was expected because bilateral disease is visible and frightening to parents, which may indicate that there is something going wrong in their child's genitalia. This in turn made the family to ask for medical help and advice earlier. With respect to the site of UDT, most patients in the late group had UDT at a lower level than patients in the early group. This relatively lower site of UDT may give a false impression to parents that the position of testis was just a variation of the normal site, especially in young children, and may contribute to delayed presentation in the late group. However, the differences in the side of UDT, whether unilateral or bilateral, and site were insignificant between the two groups.

Maternal null parity, and subsequently the delivery of the first-born child in the family, was mentioned in literature as a possible predisposing factor for UDT [2]. This was explained by increased estrogen levels in primigravida women in comparison to multigravida, which will, in turn, influence the process of testicular descend during fetal life [3, 25]. We assessed the influence of the patient's birth order, among male births in the family, on the time of UDT presentation. Data analysis revealed a significant difference between the two groups, as patients in the late group were more likely to be first-born boys in their families. The parents in the late group primarily attributed the delayed presentation of their child to their apprehensions about the potential risks of surgery and anesthesia on their first and precious boy, particularly if they received misleading advice to postpone the referral until the child reached a suitable age. In our opinion, the presence of previous boys with normal testicles in the family provides adequate knowledge to parents, especially mothers, about the normal appearance of external genitalia in new-

borns and young infants. Our study demonstrated this, as the early group reported having more than one boy in the family.

Our study had some limitations. First, the required sample size for the study could not be determined due to a lack of data about a total number of patients with UDT in our community. Second, it was a single institutional study, which may not reflect the actual picture of UDT presentation in our community. Third, although we tried to reduce bias during data collection by clarifying the inclusion and exclusion criteria and filling out the questionnaire by parents themselves, parents' responses may be biased. For example, they attributed the delayed presentation of their child to the wrong medical advice to hide unawareness or neglect about the condition of their child. Finally, due to the study design, some important factors were not assessed, such as the effect of delayed presentation on the morphological features of the testes, compliance of patients and their families to medical advice as regular follow-up for young patients, and attendance for orchiopexy according to the appointment of operation for older patients.

CONCLUSION

In our institution, we reported that more than half of patients with UDT still presented beyond the recommended age for orchiopexy. The main causes of delayed UDT presentation were parent ignorance and unawareness, false advice from medical and non-medical personnel, the presence of another medical illness, and poverty. Living in rural areas, having a lower maternal education level, and being the first-born boy in the family significantly possible predisposing factors for delayed UDT presentation. Family history of the UDT, paternal education level, side, and site of UDT didn't have significant impacts on the time of UDT presentation. Improving public education about UDT, and adapting routine testicular examination during clinical checkup visits, together with quality-based interventions, are possible helpful steps to overcome the delayed presentation of UDT in our society.

ETHICAL DECLARATIONS

Acknowledgment

None.

Ethics Approval and Consent to Participate

The Scientific and Ethical Committee of Al Mustansiriyah Medical College/Department of Surgery had approved the study (Ref. No. 182, on June 2022). Parental consent was taken for all participants in the study.

Consent for Publication

Not applicable (no individual personal data included).

Availability of Data and Material

Data generated during this study are available from the corresponding author upon reasonable request.

Competing Interests

The authors declare that there is no conflict of interest.

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Authors' Contributions

All stated authors contributed directly, significantly, and intellectually to the work and consented it to be published.

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