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Entering Our Third Year: Building Bridges in Pediatric Surgery

Dear Colleagues, Friends, and Fellow Travelers on the Path of Children's Surgical Care,

As we proudly step into the third year of *Surgery on Children*, we pause for a moment not only to celebrate what has been achieved, but also to renew the promise that brought us together in the first place: to create a common home for everyone whose daily work revolves around the surgical care of infants, children, and adolescents.

Two years ago we started with a simple belief: pediatric surgery is not the monopoly of surgeons alone. Anesthesiologists who gently guide a neonate through a complex procedure, intensive care specialists who guard fragile lives hour by hour, pediatricians who prepare families and follow them for years, nurses who translate fear into trust, operating-room teams who turn chaos into precision; every one of these professionals shapes the outcome as decisively as the hand that holds the scalpel. We wanted a journal that would reflect this reality, a place where all voices could be heard equally.

Today that vision is no longer just a hope; it is a growing reality. Manuscripts now reach us from six continents. Our pages carry original studies from Latin America, challenging case series from Southeast Asia, thoughtful reviews from Scandinavia, and quality-improvement projects from Africa. Being indexed in EBSCOhost and Index Copernicus International has widened our reach and, more importantly, has brought new authors who might otherwise never have considered submitting to a young journal. We are deeply grateful for the trust placed in us.

We are equally aware of the roads still less traveled. Submissions in pediatric ophthalmological surgery, congenital cardiac surgery, and pediatric neurosurgery remain scarce; yet these fields are rich with questions that only multicenter collaboration and shared experience can answer. We therefore extend a special invitation to colleagues in these subspecialties: your perspective is needed, your data are precious, and *Surgery on Children* is ready to be your platform.

Our scope, however, continues to broaden in the most encouraging way. We now regularly receive papers on perioperative pain management, ethical dilemmas in adolescent surgery, long-term outcomes of minimally invasive techniques, psychological support for children and parents, and innovations in surgical education; exactly the multidisciplinary conversation we dreamed of fostering.

None of this would have been possible without you; the authors who entrusted us with their work, the reviewers who gave countless unpaid hours to improve every manuscript, the editorial board members who believed in the project from day one, and the readers who keep coming back. On behalf of the entire editorial team, I offer our deepest thanks.

As we begin volume three, our commitment remains unchanged: to publish rigorous, useful, and inclusive science that ultimately serves one purpose; helping the child on the operating table today and improving the care of the child who will lie there tomorrow.

We look forward to walking the year ahead together.

With warmest regards,

Atilla ŞENAYLI

Editor-in-Chief

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Views of anaesthesia technicians in Turkiye on paediatric anaesthesia: a survey study

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ABSTRACT

Aims: The aim of this study is to evaluate the opinions of anesthesia technicians about pediatric anesthesia.

Methods: Our study is a descriptive and cross-sectional study. The universe of our research is made up of people who graduated as Anesthesia Technicians in Turkiye. There are a total of 29 questions in the online questionnaire, 8 of which are sociodemographic. The data were collected between 15.10.2024-01.11.2024 via social media platforms. The collected data were analyzed with IBM SPSS version 20.0 program.

Results: The average age of the participants was 29.36±7.44, 74% were women, 53% were single, 72% did not have children and 72%. Decently worked between 1 and 10 years. 61% of the participants reported that they did not receive training about pediatric age group patients, only 51.9% considered themselves adequate about the drug doses used in pediatric patient anesthesia, 67.3% did not feel safe when giving anesthesia in non-operating room anesthesia environments, 69.6% experienced stress in pediatric patient anesthesia, 48.8% did not want to work in the pediatric operating room.

Conclusion: As a result of our study, it was determined that anesthesia technicians did not receive training such as NRP (Neonatal Resuscitation Program), CHILYAD (Advanced Life Support Training for Children), EPALS (European Pediatric Advanced Life Support), in-service, and about half of them did not consider themselves adequate about pediatric anesthesia. It has been determined that pediatric patients experience stress and increased anxiety during anesthesia, do not want to work in the pediatric operating room, and do not feel safe in non-operating room anesthesia environments. It is thought that providing training to anesthesia technicians to increase their knowledge about pediatric anesthesia may be beneficial, and stress and increased anxiety levels may be reduced.

Keywords: Pediatric anesthesia, anesthesia technician, stress

INTRODUCTION

Paediatric anaesthesia is a field that covers patients between the ages of and 0 and 18, sensitive to the special needs of this age group, where patient safety and comfort are kept at the highest level, different and special equipment are used and knowledge, attention and experience are required.[1] Psychological, physiological, pharmacological and anatomical characteristics of this sensitive age group are different from those of adults. Even children of the same age show different developmental characteristics from each other.

Respiratory system anatomy of the paediatric age group shows significant differences when compared with adults. The neck and trachea are shorter, the jaw is smaller and the head and tongue are larger compared to adults. The position of larynx is higher and moves downwards with increasing age. Especially the epiglottis of new-borns is longer and more protruding.[2] Due to all these characteristics and the position of the larynx, straight slides (Miller) are preferred instead of curved slides (Macintosh) in laryngoscopy of new-borns.

Paediatric patients have high oxygen demand and respiratory rate. While the diaphragm and intercostal muscles are weak, type 1 muscle fibres are few and lung compliance is low. Therefore, the risk of hypoxia and apnoea is high in childhood. Problems related to the respiratory tract occur rapidly. It is vitally important to intervene quickly to airway

problems that may occur.[3] The heart rate of 0-18 age group is the highest at birth and reaches the level of adults in time. Their blood pressure is low. They have high blood volume per kilogram and their fluid electrolyte balance is sensitive. Their circulatory system works faster and therefore anaesthetic drugs dissolve and metabolize faster. However, since their kidney and liver functions are not fully developed, their capacity of metabolizing drugs is lower. For this reason, drug dose adjustments, fluid electrolyte balance and blood loss management should be carried out more meticulously and carefully. Bone and muscle tissue of paediatric patients are not fully developed. Care should be taken against pressure damage in surgical positions. In addition, more care should be taken during mask ventilation because of the sensitivity of soft tissues.

Paediatric patients have difficulty in maintaining their body temperature because they have less subcutaneous fat layer. Therefore, additional measures should be taken for hypothermia. When all these anatomical and physiological differences are considered, anaesthesia team assumes a critical role to ensure patient safety and comfort in this environment which is naturally riskier and more stressful than adult anaesthesiology.[4]

In the present study, anesthesia technicians who are part of the team in the preparation and control of anesthesia equipment, preparation of drugs and anesthetic agents, monitoring and observation, emergency response during preparation of drugs and equipment, knowledge of pediatric anesthesia, stress caused by taking pediatric patients, their mastery of pediatric patient drugs and materials, operating room conditions, training they received, etc. we have examined the issues about the pediatric patient.

METHODS

The present study is a descriptive and cross-sectional study. This study has been approved by the Ethics Committee of the Faculty of Social and Human Sciences at Yozgat Bozok University with specific attention to the inclusion of vulnerable participants (e.g., children, pregnant women, individuals with disabilities) (Date: 13.09.2024, Decision No: 251964). Additional safeguards were reviewed and approved by the committee. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Population of the study consisted of all anaesthesia technicians in Turkiye. First anaesthesia technician trainings started in vocational health schools in 1984-1985 academic year. The total number of graduates and students has reached 63763 so far. Considering this number (n=63763), a sample group of 382 people was predicted with 95% interval confidence and 0.05 margin of error. Survey method was preferred in order to reach all anaesthesia technicians. Participants were reached through social media platforms with the survey form prepared in Google form. A total of 385 individuals filled in the survey forms.

Statistical Analysis

The survey form consists of 29 questions and two parts. The first part consists of 8 questions including age, gender, marital status, number of children, educational status, years of employment, institution of employment and the region of employment. The second part consists of 21 questions including the views of anaesthesia technicians about paediatric anaesthesia. The data collected were analysed in IBM SPSS version 20.0. Percentage, frequency, Mann-Whitney U and Kruskal-Wallis H test were applied to the data.

RESULTS

A total of 385 individuals were reached in the present study. Mean age was found as 29.36±7.44 years. It was found that 74% of the participants were female, 53% were single, 72% did not have children, 57% had associate degree, 72% had a working experience between 1 and 10 years, 25% were working in a private hospital and 31% were living in Marmara region. Sociodemographic characteristics of the participants are shown in **Table 1**.

Table 1. Distribution of participants' sociodemographic characteristics

Sociodemographic characteristics		**n**	**%**
Gender	Male	100	26
	Female	285	74
Age	20-24 Years	107	28
	25-29 Years	146	38
	30-34 Years	47	12
	35 Years and higher	85	22
Marital status	Married	182	47
	Single	203	53
Number of children	0	279	72
	1	56	15
	2	50	13
Educational status	Vocational health school	10	3
	Associate degree	220	57
	Undergraduate degree	138	36
	Postgraduate degree	17	4
Years of employment	1-10 years	276	72
	11-20 years	78	20
	21-30 years	31	8
Institution of employment	Unemployed	10	2
	State hospital	93	24
	Education and research hospital	93	24
	Private hospital	95	25
	City hospital	46	12
	University hospital	46	12
	Foundation university hospital	2	1
Region of employment	Marmara region	120	31
	Aegean region	42	11
	Mediterranean region	41	11
	Central Anatolia region	116	30
	Black Sea region	34	9
	Eastern Anatolia region	12	3
	South Eastern Anatolia region	20	5

In order to explore critical aspects of paediatric anaesthesia safety and workforce preparedness, two survey questions were selected for in-depth statistical analysis: (1) "Do you consider yourself competent about the drug doses used in emergency situations in paediatric patients?" and (2) "Do you experience stress, increased anxiety when anaesthetising paediatric patients?" These questions were prioritised because they reflect both technical competence and emotional readiness, two key components for delivering safe and effective paediatric anaesthesia.

The responses of the participants to survey questions about paediatric anaesthesia are shown in **Table 2**.

When the responses of participants to the question "Do you consider yourself competent about the drug doses used in emergency situations in paediatric patients?" were examined, it was found that 78% of women, 39% of participants between

Table 2. Responses of the participants to survey questions.

Survey questions			n	%
9. Are paediatric/neonatal surgeries performed in the hospital where you work?		Yes	344	89.4
		No	41	10.6
10. Is there an age and/or body weight restriction for anaesthesia of paediatric patients in your institution? (You can choose more than one option)	No restrictions. There are no age or weight restrictions.	Yes	270	70.1
	Neonatal patients are not anaesthetised.	Yes	47	12.2
	Patients under 3 years of age are not anaesthetised.	Yes	41	10.6
	Patients born prematurely are not anesthetized	Yes	16	4.2
	Patients under 10 kg are not anaesthetised.	Yes	10	2.6
	Other		1	0.3
11. Is anaesthesia given to paediatric patients outside the operating room in the institution where you work?		Yes	169	43.9
		No	216	56.1
12. Have you received in-service training on paediatric anaesthesia?		Yes	89	23.1
		No	296	76.9
13. Which of the following training(s) have you received for paediatric age group patients? (You can choose more than one option)	I haven't.	Yes	235	61
	Neonatal Resuscitation Programme (NRP)	Yes	122	31.7
	Training on Advanced Life Support in Children (CHILYAD)	Yes	77	20
	European Paediatric Advanced Life Support (EPALS)	Yes	5	1.3
14. Do you consider yourself competent about the drug doses used in emergency situations in paediatric patients?		Yes	133	34.5
		No	107	27.8
		Undecided	145	37.7
15. Do you consider yourself competent about the drug doses used in paediatric patient anaesthesia?		Yes	200	51.9
		No	72	18.7
		Undecided	113	29.4
16. Do you have enough information about consumables in different sizes according to age used in paediatric patients?		Yes	306	79.5
		No	20	5.2
		Undecided	59	15.3
17. How many people monitor the maintenance of anaesthesia in 'PEDIATRIC ANESTHESIS' at the same time in your work environment?		1	149	38.7
		2	186	48.3
		3	42	10.9
		≥4	8	2.1
18. As an anaesthesia technician in paediatric anaesthesia in the institution where you work, do you ever have or have you ever had to monitor patients alone?		Yes	333	86.5
		No	52	13.5
19. Do you have a premedication room for only paediatric patients in your work environment?		Yes	89	23.1
		No	296	76.9
20. Is premedication given to paediatric patients in your work environment?		Yes	228	59.2
		No	157	40.8
21. Are paediatric patients able to stay with their families in the premedication room in your work environment?		Yes	186	48.3
		No	199	51.7
22. Where is the pre-operative vascular access performed for paediatric patients?	Operating room	Yes	194	50.4
	Clinic	Yes	134	34.8
	Premedication room	Yes	56	14.5
	Emergency room	Yes	1	0.3
23. Which anaesthesia method is most preferred for paediatric patients in your work environment? (You can choose more than one option).	Sedation	Yes	384	99.7
	General anaesthesia	Yes	335	87
	Local anaesthesia	Yes	52	13.7
	General+aegional anaesthesia	Yes	38	9.9
	Regional anaesthesia	Yes	10	2.6
24. Write down the name of the most common paediatric surgeries in your work environment	Circumcision	Yes	229	59.5
	Inguinal Hernia	Yes	117	30.4
	Tonsillectomy	Yes	90	23.4
	Adenoidectomy	Yes	78	20.3
	Undescended testicle	Yes	67	17.4
	Appendectomy	Yes	64	16.6
	Hypospadias	Yes	49	12.7
	Fracture	Yes	27	7
	Shunt	Yes	21	5.5
	Tooth	Yes	18	4.7
25. What are the most common operational problems you experience during paediatric surgeries? (You can select more than one option).	Vascular access	Yes	285	74
	Material preparation	Yes	34	8.8
	Fluid management	Yes	22	5.7
	Other	Yes	19	4.9
	Intubation	Yes	13	3.4
	Ventilation with a mask	Yes	12	3.1
26. Would you feel safe giving anaesthesia to paediatric patients in non-operating room settings (MRI, angio, urodynamic, etc.)?		Yes	46	11.9
		No	259	67.3
		Undecided	80	20.8
27. Do you experience stress, increased anxiety when anaesthetising paediatric patients?		Yes	268	69.6
		No	68	17.7
		Undecided	49	12.7
28. Would you like to work in paediatric operating room?		Yes	118	30.6
		No	188	48.8
		Undecided	79	20.6
29. Reasons for not wanting to work in paediatrics operating room (Grouped)	Stressful working environment	Yes	58	15.1
	Considering oneself inadequate	Yes	33	8.6
	High risk	Yes	31	8.1
	Other	Yes	38	4.7
	Difficult working conditions	Yes	16	4.2
	Monitoring patients alone/ insufficient number of staff	Yes	12	3.1

The table continues

the ages of 25 and 29, 59% of participants who had associate degree, 74% of participants who had worked for 1-10 years and 29% of participants working in training and research hospital had responded as "no". Statistically significant difference was found when compared with the other groups ($p<0.05$). The distribution of the responses given by participants to the question about emergency drugs are shown in **Table 3**.

When the participants' responses to the question "Do you experience stress, increased anxiety when anaesthetising paediatric patients?" were examined, it was found that 71% of women, 36% of participants between 25 and 29 years of age, 58% of participants with an associate degree, 71% of participants who had been employed for 1-10 years and 26% of participants working in a state hospital responded as "yes". Statistically, no significant difference was found compared to other groups (p0,05). Distribution of participants' responses to the question related with stress and increased anxiety is shown in **Table 4**.

Table 3. Competence of participants on drug doses used in emergency situations in paediatric patients

Sociodemographic characteristics			Yes	No	Undecided	p**
Gender	Male	n/%*	48 (36%)	24 (22%)	28 (19%)	0.004
	Female	n/%*	85 (64%)	83 (78%)	117 (81%)	
Age	20-24 years	n/%*	17 (13%)	31 (29%)	59 (41%)	0.000
	25-29 years	n/%*	50 (38%)	42 (39%)	54 (37%)	
	30-34 years	n/%*	20 (15%)	12 (11%)	15 (10%)	
	35 years and higher	n/%*	46 (35%)	22 (21%)	17 (12%)	
Educational status	Vocational health school	n/%*	5 (4%)	1 (1%)	4 (3%)	0.001
	Associate degree	n/%*	57 (43%)	63 (59%)	100 (6%9)	
	Undergraduate degree	n/%*	62 (47%)	37 (35%)	39 (27%)	
	Postgraduate degree	n/%*	9 (7%)	6 (6%)	2 (1%)	
Years of employment	1-10 years	n/%*	76 (57%)	79 (74%)	121 (83%)	0.000
	11-20 years	n/%*	40 (30%)	20 (19%)	18 (12%)	
	21-30 years	n/%*	17 (13%)	8 (8%)	6 (4%)	
Institution of employment	Unemployed	n/%*	2 (2%)	5 (5%)	3 (2%)	0.000
	State hospital	n/%*	31 (23%)	29 (27%)	33 (23%)	
	Education and research hospital	n/%*	33 (25%)	31 (29%)	29 (20%)	
	Private hospital	n/%*	27 (20%)	15 (14%)	53 (37%)	
	City hospital	n/%*	19 (14%)	17 (16%)	10 (7%)	
	University hospital	n/%*	21 (16%)	10 (9%)	17 (12%)	

* %s are percentages of column. ** Gender was tested with Mann-Whitney U, others were tested with Kruskal-Wallis H

Table 4. Stress and increased anxiety of participants during anaesthesia of paediatric patients

Sociodemographic characteristics			**Yes**	**No**	**Undecided**	**p****
Gender	Male	n/%*	77(29%)	13(19)	10(20%)	0.173
	Female	n/%*	191 (71%)	55 (81%)	39 (80%)	
Age	20-24 years	n/%*	76 (28%)	21 (31%)	10 (20%)	0.319
	25-29 years	n/%*	97 (36%)	25 (37%)	24 (49%)	
	30-34 years	n/%*	38 (14%)	4 (6%)	5 (10%)	
	35 years and higher	n/%*	57 (21%)	18 (27%)	10 (20%)	
Educational status	Vocational health school	n/%*	6 (2%)	3 (4%)	1 (2%)	0.909
	Associate degree	n/%*	154 (58%)	40 (59%)	26 (5%3)	
	Undergraduate degree	n/%*	95 (35%)	23 (34%)	20 (41%)	
	Postgraduate degree	n/%*	13 (5%)	2 (3%)	2 (4%)	
Years of employment	1-10 years	n/%*	190 (71%)	50 (74%)	36 (74%)	0.424
	11-20 years	n/%*	52 (19%)	16 (24%)	10 (20%)	
	21-30 years	n/%*	26 (10%)	2 (3%)	3 (6%)	
Institution of employment	Unemployed	n/%*	7 (3%)	1 (2%)	2 (%4)	0.442
	State hospital	n/%*	69 (26%)	12 (18%)	12 (25%)	
	Education and research hospital	n/%*	60 (22%)	21 (31%)	12 (25%)	
	Private hospital	n/%*	62 (23%)	21 (31%)	12 (25%)	
	City hospital	n/%*	34 (13%)	4 (6%)	8 (16%)	
	University hospital	n/%*	36 (13%)	9 (13%)	3 (6%)	

*%s are percentages of column. ** Gender was tested with Mann-Whitney U, others were tested with Kruskal-Wallis H

DISCUSSION

Paediatric anaesthesia is a field that requires special knowledge, more attention, sensitivity and skill to provide safe anaesthesia for paediatric patients during diagnostic, surgical and therapeutic procedures. A good knowledge of the paediatric differences of the patients, starting from the anaesthetic consent to the termination of anaesthesia, is known as the most basic rule of successful and safe anaesthesia practice. A coordinated team work of the process of premedication and taking patients to the operating rooms, daily paediatric anaesthesia method, drug and dose adjustments appropriate to the anaesthesia method selected, selection of appropriate equipment for the paediatric patient, initiation, maintenance and termination of anaesthesia are important points of the field. Due to all these characteristics, paediatric anaesthesia can cause extra stress and anxiety in the working team. One of the members of this team is anaesthesia technician.

"Anaesthesia technician" title was given to individuals who graduated the department of anaesthesia in vocational health schools before the year 2017 and to individuals who got a two-year associate degree starting form year 2017. In European countries, the title of 'anaesthesia nurse' is awarded after undergoing various trainings.[5] In our literature review, there was only a limited number of scientific studies on the clinical approaches and knowledge levels of anaesthesia technicians.

Almost all of the participants in the present study stated that paediatric/neonatal surgeries were performed in the hospital where they worked and that there was no specific age or weight restriction. In a study conducted in a public hospital on postoperative pain in paediatric patients, 56.5% of the 2420 paediatric patients included in the study were in the 3-6 age group.[6]

Of the participants in the present study, it was found that 76.9% had not received in-service training on paediatric anaesthesia, while 61% reported that they had not received trainings called NRP, CHILYAD, EPALS. Drzymalski[7] stated that although most of the anaesthetist working in obstetrics were involved in resuscitation of a new-born baby, most of them did not receive NRP training. According to a study conducted in low- and middle-income countries, the paediatric skills of the anaesthesia workforce, including non-physician anaesthesia workers, should be improved.[8] Boyd et al.[9] tried to meet the need in education by organising "The Safer Anaesthesia from Education (SAFE)®" course in five countries in Eastern and Central Africa due to inadequate training of paediatric anaesthesiologists. According to a study conducted in Italy, most of the health professionals who took the Advanced Paediatric Life Support (APLS) course, those working in hospital settings, thought that the systematic methods learned had a great impact on clinical practice.[10]

In the present study, 27.8% of the participants stated that they considered themselves incompetent in knowing about the doses of drugs used in emergencies for paediatric patients. It was reported that 51.9% considered themselves competent about drug doses used in paediatric anaesthesia. Kaufmann et al.[11] reported that 60% of the paediatric anaesthetists experienced at least one paediatric error in a year and 15% had a higher rate of error at least once a month. However, it is emphasized that there are problems about reporting errors and an exact number cannot be determined. In another study conducted with an anaesthetics team of senior anaesthetists, nurse anaesthetists and operating room nurses, it was reported that errors of medication were not few in paediatric general anaesthesia, at least one medication error occurred in 38 general anaesthesia cases and these errors were mostly errors of incorrect dose and dilution errors.[12]

In the study, 48.3% of the participants reported that monitoring anaesthesia maintenance in paediatric anaesthesia was made with 2 people at the same time, while 86.5% reported that they sometimes had to monitor patients alone. Newton[13] reported that paediatric anaesthesia was mostly performed by anaesthesia workers who were non-physician anaesthesiologists. In another study, it was reported that at least one adverse event related to sedation of children was experienced in 20.1% of the practices performed by non-anaesthetists for diagnostic and therapeutic purposes and risks related with children's sedation was emphasized, drawing attention to the importance of appropriate monitoring by educated staff.[14]

It was found that 69.9% of the participants and 71% of female participants stated they experienced stress and anxiety during paediatric patient anaesthesia. Kızılcı[15] reported that dentists who took care of paediatric patients experienced more stress while treating patients under deep sedation. In another study, anaesthetists reported that burnout was common and workplace factors had a great role.[16] In a study conducted with anaesthesia assistants, women were reported to have high burnout risk.[17] Similar stress and anxiety were reported in the present study, in parallel with other studies, and it was reported that 48.8% of the participants did not want to work in paediatric surgery rooms.

Limitations

As with most studies, our current study has limitations. Participants in our survey may not have participated in the study due to the fact that elderly anesthesia technicians use social media less because they participated in the survey form via social media. The inability to reach the opinions of this group, which is especially experienced, about pediatric patients can be considered among the limitations of our study.

CONCLUSION

In terms of sociodemographic characterises, it was found in the present study that a great majority of the participants were female and within the 25-29 age group, more than half were single, more than two thirds did not have children, more than half had associate degree, more than two thirds had worked between 1 and 10 years. In terms of hospitals the participants worked in, there were participants from all hospital groups and in terms of regions where the participants lived in, there were nurses from all regions of the country.

As a result of the present study, it was found that anaesthesia technicians had not received in-service training such as NRP, CHILYAD, EPALS and almost half did not consider themselves sufficient in terms of paediatric anaesthesia. It was determined that anaesthesia technicians experienced stress and increased anxiety during anaesthesia of paediatric patients, did not want to work in paediatric operating rooms, and they did not feel safe in environments where anaesthesia was given outside the operating room. It is thought that giving trainings to anaesthesia technicians to increase their knowledge about paediatric anaesthesia, arranging the anaesthesia environment outside the operating room according to ASA (American Society of Anaesthesiologists) criteria, making it closest to the operating room conditions with adequate equipment and materials may be beneficial and stress and increased anxiety levels may be reduced.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study has been approved by the Ethics Committee of the Faculty of Social and Human Sciences at Yozgat Bozok University with specific attention to the inclusion of vulnerable participants (e.g., children, pregnant women, individuals with disabilities) (Date: 13.09.2024, Decision No: 251964). Additional safeguards were reviewed and approved by the committee.

Informed Consent

Informed consent was obtained from a parent or legal guardian. Where appropriate, age-adjusted assent was also obtained from the child. The inclusion of vulnerable populations in this study adhered to national and international ethical guidelines. Extra care was taken to ensure voluntary participation, understanding, and protection of participant dignity and autonomy.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

The authors received no financial support for the conduct or publication of this research.

Author Contributions

Concept: N.U.K., S.S., Y.A.Ş.; Design: N.U.K., S.S.; Control/Supervision: Y.A.Ş.; Data collection and/or processing: N.U.K., S.S.; Analysis and/or interpretation: S.S., Y.A.Ş.; Literature review: N.U.K., S.S.; Article writing: N.U.K., S.S., Y.A.Ş.; Critical review: All authors

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MHA MEDIHEALTH ACADEMY

Surgery on Children

Original Article

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Outcome of partial glandurethral disassembly in distal penile hypospadias repair

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ABSTRACT

Aims: Several surgical techniques have been described for distal penile hypospadias (DPH) repair, including meatal advancement and glanuloplasty incorporated (MAGPI), tubularized incised plate (TIP), Mathieu, and glandular urethral disassembly (GUD). TIP is widely performed but has notable complications such as urethrocutaneous fistula and meatal stenosis, particularly in cases with a narrow glans or urethral plate. Urethral mobilization, first described by Beck (1898) and popularized by Koff (1981), avoids urethroplasty and reduces fistula risk, but traditional methods mobilize the urethra up to 1.5 cm. The GUD technique emphasizes minimal urethral mobilization with wide glandular dissection. To evaluate the outcomes of the GUD technique in different types of DPH.

Methods: This prospective study was conducted at Zagazig University Hospitals from April 2022 to April 2023. Thirty patients with primary or recurrent DPH or urethral fistula underwent repair using urethral mobilization. Patients with severe chordee, mid-penile, or proximal hypospadias were excluded. Operative details, complications, and follow-up findings were analyzed.

Results: The mean age at surgery was 2.7 years, mean operative time 38.1 minutes, mean hospital stay 12.8 hours, and mean catheter duration 4.6 days. Follow-up averaged 3.6 months. Types included 10 (33.3%) coronal, 7 (23.3%) recurrent DPH, 6 (20%) subcoronal, 3 (10%) glandular, 2 (6.6%) urethral fistula, and 2 (6.6%) megameatus with intact prepuce. Complications occurred in 5 patients (16.6%): meatal stenosis (6.6%), dehiscence (3.3%), meatal retraction (3.3%), and fistula (3.3%). No bleeding, infection, or iatrogenic chordee occurred.

Conclusion: The GUD technique with minimal urethral mobilization is a simple, safe, and effective approach for selected DPH cases, yielding low complication rates.

Keywords: Hypospadias, urethral mobilization, glandular disassembly, urethral advancement, distal penile hypospadias

INTRODUCTION

Hypospadias is one of the most common congenital anomalies of the male genitourinary tract, with an estimated incidence of 1 in 300 live births. Approximately 60%–76% of cases are classified as distal penile hypospadias (DPH).[1]

Several surgical techniques have been described for DPH repair, including meatal advancement and glanuloplasty (MAGPI), tubularized incised plate urethroplasty (TIP), Mathieu repair, and glans-urethral disassembly (GUD).[2,3] Among these, TIP has become the most widely performed technique. However, TIP is associated with complications such as urethrocutaneous fistula, meatal stenosis, and urethral stricture.[4,5] Furthermore, its success depends on urethral plate quality, and optimal outcomes generally require a glans width greater than 14 mm.[6,7]

To overcome these limitations, the GUD technique has been introduced as an alternative. It is based on minimal urethral mobilization combined with wide glandular dissection, aiming to achieve satisfactory functional and cosmetic outcomes while reducing complication rates.

The novelty of our series lies in applying GUD specifically for DPH primary and complicated cases and systematically reporting both surgical and parent-reported outcomes. While previous reports have mainly focused on complications, our

study emphasizes the cosmetic and functional aspects in addition to complication rates.

METHODS

Ethics

This prospective study was conducted at Zagazig University Hospitals between April 2022 and April 2023 to evaluate the outcomes of the GUD technique for different types of DPH. This study has been approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University, with particular attention paid to the inclusion of vulnerable participants (e.g., children, pregnant women, individuals with disabilities) (Date: 12.01.2025, Decision No: ZU-IRB#9634). Additional safeguards were reviewed and approved by the committee. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Written informed consent was obtained from the parents/guardians of all participants.

Inclusion Criteria

Primary cases of DPH, recurrent distal hypospadias, and urethral fistula cases.

Exclusion Criteria

Presence of moderate or severe chordee, mid-penile, proximal, or perineal hypospadias.

All patients with DPH, categorized by age (<2 vs ≥2 years) and by type (primary vs complicated). This stratification allowed evaluation of outcomes according to both age and complexity of the condition.

Preoperative evaluation included full medical history, physical examination, and routine laboratory tests (CBC, PT, PTT, INR, urinalysis).

Parental-reported cosmetic and functional satisfaction was assessed at follow-up using a structured questionnaire.

Surgical Technique

Under aseptic conditions, a stay suture was placed in the glans (4/0 silk), followed by a circumferential incision 2–3 mm below the meatus. The incision site was infiltrated with diluted adrenaline (1:100,000). A size 6 feeding tube was inserted into the urethra, and the penis was degloved with chordee release. A tourniquet was applied at the base of the penis, and artificial erection was performed to assess any residual chordee. The corpus spongiosum was dissected from below the visible bifurcation. The glans was incised in the midline and configured into an inverted Y around the meatus. The urethra was mobilized 1-2 cm with wide glandular dissection (**Figure 1, 2**). It was fixed to the glans tip and underlying corpora using 6/0 Vicryl, covered with a dartos flap, and the glans was approximated with 5/0 Vicryl. Circumcision and skin closure were completed with 5/0 rapid Vicryl (**Figure 3**). A compression dressing was applied, and the catheter was secured for four days.

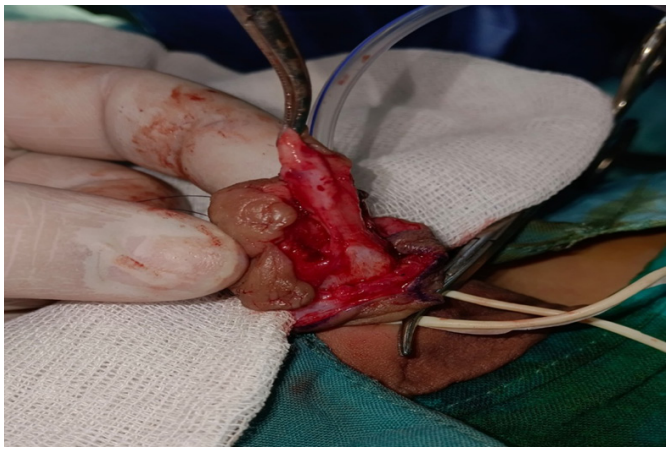

Figure 1. Corpus spongiosum dissection urethral mobilization

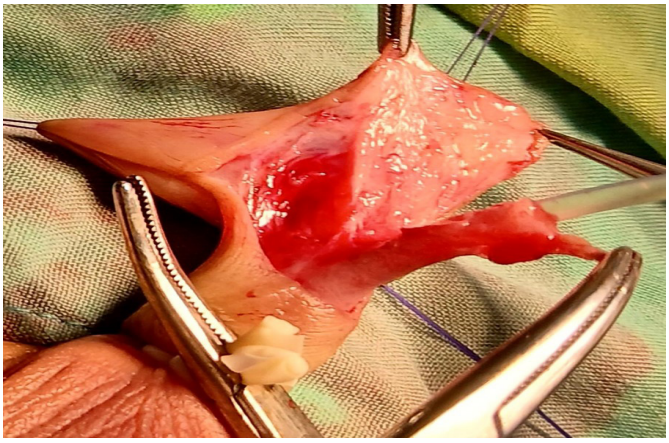

Figure 2. Wide glandular dissection and minimal urethral mobilization

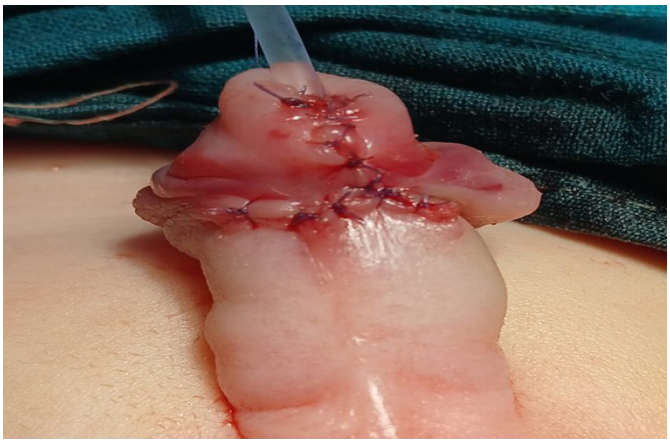

Figure 3. Final glans closure and reconstructed meat

Postoperative Care and Follow-up

Broad-spectrum intravenous antibiotics were administered 30 minutes before surgery and continued orally till removal of the catheter. The catheter was removed on postoperative day 4, urethral calibration began on day 7, and follow-up was scheduled weekly for one month, then monthly for six months.

Parental-reported cosmetic and functional satisfaction was assessed at follow-up for complications and cosmetic results (slit-like meatus, straight penis, satisfactory urinary stream). using a structured questionnaire.

Statistical Analysis

Data were analyzed using SPSS version 20. Quantitative variables were expressed as mean±standard deviation and compared using Student's t-test. A p-value <0.05 was considered statistically significant. Statistical analysis included descriptive data as well as subgroup comparisons.

RESULTS

Patient Characteristics

A total of 30 patients undergoing distal hypospadias repair using the GUD technique were included. The mean age at surgery was 2.7 years, with a mean hospital stay of 12.8 hours. Catheter duration averaged 4.6 days, and patients were followed up for a mean of 3.6 months (Table 1).

Table 1. Postoperative patient characteristics

Parameter	Value
Mean age	2.7 years
Mean hospital stay	12.8 hours
Catheter duration	4.6 days
Mean follow-up	3.6 months

Types of Hypospadias

Coronal hypospadias was the most common type (33%), followed by recurrent (23.3%), subcoronal (20%), glandular (10%), urethral fistula (6.6%), and megameatus intact prepuce (6.6%). Distribution across age groups (<2 years vs ≥2 years) did not show a statistically significant difference (p=0.497) (Table 2).

Table 2. Types of hypospadias by age group

Type of hypospadias	<2 years	≥2 years	Total	p-value
Coronal	3 (30%)	7 (70%)	10 (33%)	
Recurrent	2 (28.6%)	5 (71.4%)	7 (23.3%)	
Subcoronal	3 (50%)	3 (50%)	6 (20%)	
Glandular	2 (66.7%)	1 (33.3%)	3 (10%)	
Urethral fistula	0 (0%)	2 (100%)	2 (6.6%)	
Megameatus intact prepuce	0 (0%)	2 (100%)	2 (6.6%)	
Total	10 (33.3%)	20 (66.7%)	30 (100%)	0.497 (NS)

NS: Non-significant

Postoperative Complications

Overall, complications were observed in 16.7% of patients (5/30). Meatal stenosis occurred in 2 patients which respond well with dilatation, wound dehiscence, meatal retraction, and urethrocutaneous fistula each occurred in 1 patient Which required redo surgery. No statistically significant difference in complication rates was noted between age groups (<2 years vs ≥2 years, p=1.00) (Table 3).

Table 3. Postoperative complications by age group

Complication	<2 yrs (n=10)	≥2 yrs (n=20)	Total (n=30)
Meatal stenosis	1	1	2
Wound dehiscence	0	1	1
Meatal retraction	0	1	1
Urethrocutaneous fistula	0	1	1
p-value	–	–	1.00 (NS)

NS: Non-significant

Patients with distal shaft meatal location had a significantly higher complication rate compared to coronal/subcoronal locations (25% vs 11.1%, p=0.04). The presence of mild chordee (12.5% vs 18.2%, p=0.71) and postoperative edema (20% vs 15%, p=0.74) were not significantly associated with increased complications (Table 4, 5).

Table 4. Complication rates by meatal location

Meatal location	n	Complications (n)	Complication rate	p-value
Coronal /subcoronal	18	2	11.1%	
Distal shaft	12	3	25%	
Total	30	5	16.7%	0.04*

*Distal shaft location significantly associated with increased risk of fistula formation

Table 5. Relationship of other factors with complication rates

Factor	Category	n	Complications (n)	Complication rate	p-value
Presence of mild chordee	Yes	8	1	12.5%	0.71 (NS)
	No	22	4	18.2%	
Postoperative edema	Yes	10	2	20.0%	0.74 (NS)
	No	20	3	15.0%	

NS: Non-significant

DISCUSSION

The primary objective of any hypospadias repair is to reconstruct a penis that is both functionally and cosmetically acceptable, while minimizing the complications.[8] Among the different procedures described, the TIP urethroplasty has emerged as one of the most frequently performed operations for DPH worldwide. In our institution, TIP remains a standard technique, particularly due to its relative technical simplicity and satisfactory outcomes. However, it is well recognized that TIP results are significantly influenced by the anatomical characteristics of the urethral plate and glans.[9] Factors such as plate depth, plate width, and glans diameter determine whether the neourethra will heal without tension and whether the suture line will remain intact. Several authors have suggested restricting TIP to patients with favorable anatomy, particularly those with a deeply grooved urethral plate (>6 mm) and glans width >14 mm, in order to reduce the risk of complications such as fistula, stenosis, and dehiscence.[10] Conversely, when these parameters are unfavorable, TIP has been associated with higher complication rates, reaching up to 15–20% in some series.[11,12]

In recent years, urethral mobilization–based approaches have regained attention as a valuable option for distal hypospadias repair. The key principle of these techniques lies in mobilizing the native urethra to bring it to the tip of the glans, thereby avoiding urethroplasty, flaps, or grafts.[13] The main advantages of this technique include preservation of the native tissue, less suture line, and avoiding the incision or tubularization of the urethral plate. Moreover, the operation tends to be technically straightforward, with reduced operative time. However, this technique is not without risks. Excessive mobilization to the urethra may compromise vascularity, leading to complications such as meatal stenosis,

stricture, or fistula formation.[14] To avoid this, Macedo Jr and colleagues[13] described a modification with minimal urethral mobilization and wide glans dissection, which emphasizes careful preservation of urethral blood supply. This concept is closely aligned with the approach adopted in the present study.

The GUD technique offers a unique approach by combining minor urethral mobilization with significant glans deconstruction, facilitating precise urethral reconstruction. This method has been proposed as an alternative to traditional techniques, aiming to achieve optimal functional and cosmetic results in distal hypospadias repair.

Complication rates remain the most critical measures for evaluating the outcomes of any hypospadias repair. Urethrocutaneous fistula is consided to be the most frequently encountered complication after hypospadias surgery. In our study, the incidence of fistula was 3.3%, which compares favorably with previously reported rates. Most of the published data show fistula rates of approximately 3.8% following TIP and 5.3% after Mathieu repair,[15,16] while Macedo Jr et al.[13] reported a 3% fistula rate with their mobilization technique.

Wang et al.[14] conducted a systematic review on outcomes of DPH repair using different techniques and reported that the incidence of urethral fistula was 3.8% following TIP repair. Similarly, Wilkinson et al.[15] performed a meta-analysis evaluating postoperative outcomes in distal hypospadias repair and found that the incidence of urethral fistula after TIP repair was 13%.

This suggests that urethral mobilization can achieve outcomes comparable to the best-established procedures while preserving the native urethra. Importantly, the low fistula rate in our series supports the principle that limited and careful mobilization does not compromise urethral integrity.

Meatal stenosis was reported in 6.6% of cases in our study. This incidence is in line with several earlier reports,[17,18] and notably lower than the 15% reported by Edan.[18] One explanation for our relatively low stenosis rate may be the avoidance of suture urethroplasty and preservation of native urethral tissue and careful calibration of the meatus during the procedure. Furthermore, avoiding an incised plate (as in TIP) may reduce the risk of secondary scarring and contracture.

Meatal retraction was occurred in one patient (3.3%), which falls within the reported literature range of 2.7%–6.7%.[20] Glandular dehiscence encountered in one patient secondary to severe wound infection. This finding emphasizes the well-recognized effect of infection on wound breakdown, as documented by other authors.[20,21] Therefore adequate infection prophylaxis, meticulous hemostasis, and careful dressing remain importantly in minimizing such infection.

The optimal role and duration of postoperative urinary diversion after distal hypospadias repair remain matters of debate. Some authors advocate prolonged catheterization to protect the repair, whereas others recommend early removal or even stentless approaches to reduce discomfort, bladder spasms, and infection risk.[21] In our series, urethral catheters were maintained for four days, which provided sufficient time for wound stabilization without significantly prolonging hospitalization. The satisfactory results observed in our patients support the feasibility of this regimen. Nevertheless, randomized controlled trials are needed to establish an evidence-based consensus regarding stenting protocols.

Postoperative characteristics, including mean hospital stay (12.8 hours), catheter duration (4.6 days), and operative time (38.1 minutes), indicate that the GUD technique is efficient and associated with early recovery. Stratification by age and chordee showed no significant increase in complications, reinforcing the technique's applicability across different patient profiles.

Although this study primarily focused on complication rates, parent-reported outcomes were generally favorable. All parents reported satisfaction with the cosmetic appearance of the reconstructed glans and meatus. Functional outcomes, including urine stream and continence, were satisfactory in the early postoperative period. Future studies should incorporate standardized scoring systems such as HOSE or PPPS to quantify both cosmetic and functional outcomes.

Limitations

Although our study is limited by sample size and follow-up duration, our findings support GUD as a technique that allows glans mobilization with reduced closure tension, which may lower complication rates. Evidence from systematic reviews shows variable outcomes among distal hypospadias repairs, highlighting the need for larger, multicenter studies with extended follow-up. Incorporating standardized functional and cosmetic scores in future research will enable more thorough evaluation of surgical success.

CONCLUSION

The GUD technique represents a straightforward and safe option for managing DPH in carefully selected patients, offering satisfactory outcomes with a low rate of complications.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study has been approved by the Institutional Review Board of the Faculty of Medicine, Zagazig University, with particular attention paid to the inclusion of vulnerable participants (e.g., children, pregnant women, individuals with disabilities) (Date: 12.01.2025, Decision No: ZU-IRB#9634). Additional safeguards were reviewed and approved by the committee.

Informed Consent

Informed consent was obtained from a parent or legal guardian. Where appropriate, age-adjusted assent was also obtained from the child. The inclusion of vulnerable populations in this study adhered to national and international ethical guidelines. Extra care was taken

to ensure voluntary participation, understanding, and protection of participant dignity and autonomy.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

Concept: K.H.M., Y.A.R.; Design: K.H.M., Y.A.R.; Control: K.H.M.; Data collection and/or processing: K.H.M., Y.A.R.; Analysis and/or interpretation: K.H.M., Y.A.R.; Literature review: K.H.M., Y.A.R.; Article writing: K.H.M., Y.A.R.; Critical review: All authors.

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MHA MEDIHEALTH ACADEMY

Surgery on Children

Original Article

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Cytochrome C in in vitro fertilization: a promising tool for distinguishing spent embryo culture fluids of normoresponder, diminished ovarian reserve, and polycystic ovarian syndrome

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ABSTRACT

Aims: Cytochrome C (Cyt C) is a small heme protein located in the mitochondria, playing a dual and crucial role in cellular physiology as cellular respiration and apoptosis. This study aimed to investigate Cyt C gene expression in spent embryo culture fluid (SECF) as a non-invasive biomarker for distinguishing between normoresponder (NOR), early-diminished ovarian reserve (E-DOR), advanced-diminished ovarian reserve (A-DOR), and polycystic ovarian syndrome (PCOS) patients undergoing in vitro fertilization (IVF).

Methods: SECF samples were collected from patients at Bahçeci Health Group Umut IVF Laboratory, İstanbul, with informed consent and ethical approval (2023/19-22). Forty-eight samples from each group (NOR, E-DOR, A-DOR, PCOS) were analyzed. Ovarian stimulation followed an antagonist protocol, and embryos were cultured individually. On day 3, embryos were morphologically graded. Total RNA was isolated from SECF, converted to cDNA, and Cyt C gene expression was quantified using RT-PCR, with GAPDH as an internal control. Statistical analyses included Kolmogorov-Smirnov and Shapiro-Wilk tests for normality, Sidak for multiple comparisons, and Pearson correlation test for group relationships.

Results: Compared to NOR samples, Cyt C gene expression was significantly upregulated in A-DOR samples, while E-DOR samples showed downregulation ($p<0.001$). No statistical difference was observed between NOR and PCOS samples ($p>0.05$). Pearson correlation revealed a significant relationship only between NOR and A-DOR SECF samples ($r<0.01$).

Conclusion: These findings suggest that Cyt C expression in SECF can differentiate between early and advanced stages of diminished ovarian reserve, with age-related differences in apoptosis mechanisms. PCOS cases, characterized by a high quantity but low quality of oocytes, showed no significant variation in Cyt C expression, likely due to less active apoptotic pathways. Monitoring Cyt C in SECF may provide a valuable, non-invasive tool for assessing embryo quality and optimizing IVF outcomes. Further research is needed to validate these findings and establish clinical protocols.

Keywords: Cytochrome C, diminished ovarian reserve, in vitro fertilization, normoresponder, polycystic ovarian syndrome, spent embryo culture fluid

INTRODUCTION

Cytochrome C (Cyt C) is a small heme protein found loosely associated with the inner membrane of the mitochondrion. It plays a crucial role in the electron transport chain, which is a series of complexes that transfer electrons from electron donors to electron acceptors via redox reactions. This process is essential to produce ATP, the energy currency of the cell. Cyt C is also involved in the intrinsic pathway of apoptosis, where it is released from mitochondria into the cytosol in response to pro-apoptotic signals, leading to the activation of caspases and cell death.[1]

Spent embryo culture fluid (SECF) is the medium that surrounds embryos during in vitro culture. This fluid contains a variety of biomolecules, including proteins, metabolites, and nucleic acids, which are secreted by the embryos.[2] The analysis of SECF can provide valuable insights into embryo metabolism, viability, and developmental potential. It has been suggested that the composition of SECF can be used as a non-invasive biomarker for selecting the most viable embryos for transfer in assisted reproductive technologies (ART).[3]

Recent study has explored the presence and role of Cyt C in SECF. It has been hypothesized that Cyt C levels in SECF could be indicative of mitochondrial activity and embryo quality. For instance, a study by Smith et al.[4] found that higher levels of Cyt C in SECF were associated with better embryo development and higher implantation rates. This suggests that Cyt C could serve as a potential biomarker for embryo selection in ART.

This study aims to investigate the identification of the similarities and differences between NOR, early- and advanced- diminished over reserve and polycystic over syndrome patients as a perspective of Cyt C gene expression by using SECF samples.

METHODS

Human spent embryo culture medium samples donated to research were obtained with informed consent from patients undergoing IVF at the Bahçeci Health Group Umut IVF Laboratory, İstanbul. Forty-eight samples were collected from SECF for each NOR, early and advanced reduced response, and polycystic ovary syndrome. This study has been approved by the Ethics Committee of Maltepe University (Date: 09.11.2023, Decision No: 2023/19-22). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Ovarian stimulation (OS) was started on day 2 of the menstrual period by employing the antagonist protocol. The dosage of gonadotropins was individualized based on the cases' parameters (**Figure 1**). NOR, early- and advanced-diminished over reserve and polycystic over syndrome cases received 250 µg of human chorionic gonadotropin (hCG; Ovitrelle, Serono) or 0.2 mg of triptorelin (Gonapeptyl, Ferring) for the final oocyte maturation when at least two follicles reached 18 mm in diameter, and transvaginal ultrasound-guided follicle aspiration was performed for oocyte retrieval after 35 h. The oocyte retrieval, denudation, and ICSI procedures were performed as previously described.[5] After microinjection, oocytes were cultured individually in a unique, pre-equilibrated culture dish. Single-step media-

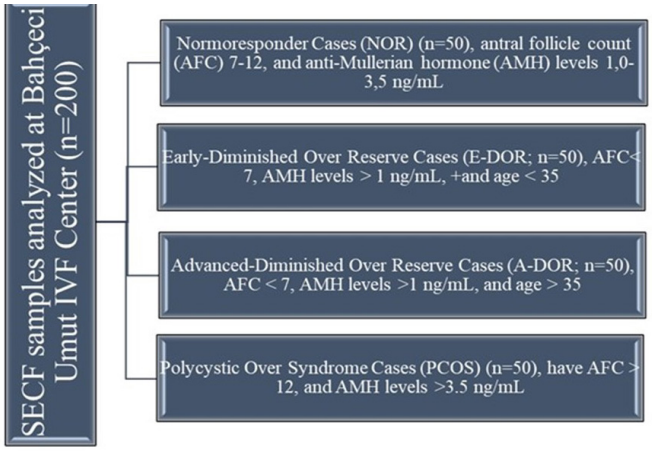

Figure 1. The properties of normoresponder, early- and advanced- diminished over reserve and polycystic over syndrome cases.

namely, single continuous culture complete (CSCM-C) with human serum albumin (Irvine Scientific, Santa Ana, CA, USA)-was used for the embryo cultures throughout the culture period in our study. All embryos were kept in benchtop incubators (MIRI, ESCO Medical, Singapore) and cultured until day 5 or 6 of embryo development. SECF materials were transferred into a PCR tube and kept frozen at 20° C until analysis.

On day 3 of embryo development, a division stage morphological score was assigned based on a three-point grading system using characteristics such as cell number, fragmentation, symmetry, and shape (**Figure 2**).

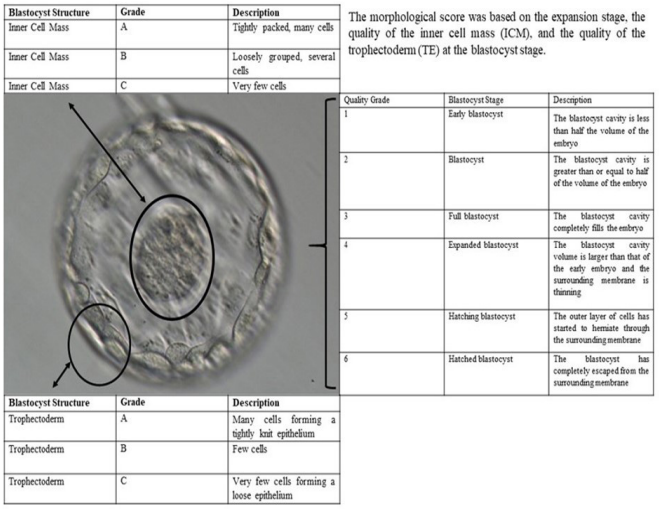

Figure 2. Morphological classification of normoresponder, early and advanced diminished over response, and polycystic over syndrome embryos

Total RNAs were isolated from the collected samples according to the manufacturer protocol (AnalytikJena, Germany). Total RNAs are converted to cDNA (Nucleogene, Turkiye) and then Cyt C; (BmLabosis, Turkiye) gene expression was detected by using real time- polymerase chain reaction (RT-PCR; Kogene, South Korea). As an internal control, glyseraldehide-3-phosphate dehydrogenase (GAPDH) was used. The primer sequences are shown in **Table 1**. ΔCT method was used to determine the Cyt C gene expression.[6] Kolmogorov-Smirnov and Shapiro-Wilk tests were used for normal distribution, and Sidak was used to determine multiple comparisons. *p<0.01; **p<0.05, and ***p<0.001 values were indicated as a result of statistical evaluations for gene expressions while ##r<0.01 value was used for correlations between experimental groups.

RESULTS

Compared to the NOR samples (-2.21±1.957), the gene expression of Cyt C was upregulated in the A-DOR samples (2.751±1.902) while the Cyt C gene expression of E-DOR (-4.969±3.69) was downregulated (p<0.001). There couldn't be observed any statistical difference between NOR and PCOS samples (-2.324±2.328; p>0.05). According to the Pearson correlation test, there is only a correlation between NOR and A-DOR SECF samples (r<0.01, **Figure 3**).

Table 1. Forward and reverse primer sequences used in RT-PCR

Gene	Forward sequence	Reverse sequence
Cyt C	5'-TCGTTGTGCCAGCGACTAAA-3'	5'-TCTTGTGCTTGCCTCCCTTT-3'
GAPDH	5′-CGAGGGGGGAGCCAAAAGGG-′3	3′-GAAACTGCGACCCCGACCGT-′5

Cyt C: Cytochrome C, GAPDH: Glyseraldehide-3-phosphate dehydrogenase

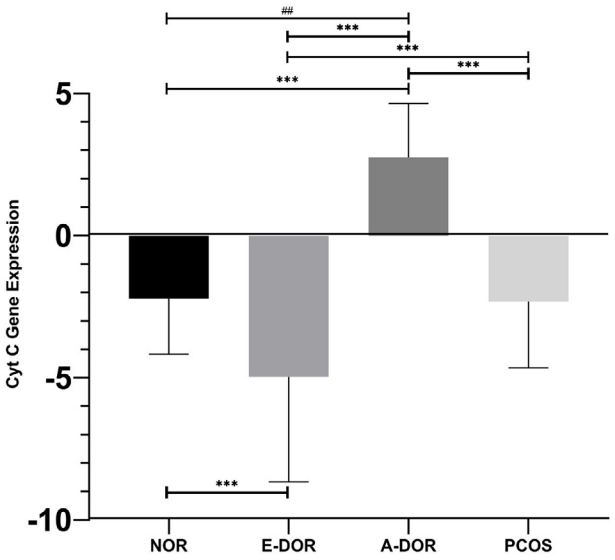

Figure 3. The Cyt C gene expression of normoresponder (NOR; p<0.001), early-diminished over response (E-DOR; p<0.001), advanced-diminished over response (A-DOR; p<0.001), and polycystic over syndrome (PCOS;p>0.05).

DISCUSSION

Cyt C is a mitochondrial protein that transfers electrons to the respiratory chain and sustains ATP production to perform life-supporting functions. Cyt C is also central to the intrinsic pathway of apoptosis. When cells receive pro-apoptotic signals, Cyt C is released from the mitochondria into the cytosol, triggering a cascade that activates caspases and leads to controlled cell death. This process is vital for tissue homeostasis, development, and the elimination of damaged or abnormal cells.[7]

Recently, embryo waste culture fluid has been used to analyze various parameters, especially biochemical and genetic. In contrast to trophectoderm biopsy, Shitara et al.[8] discovered that cell-free DNA (cf-DNA) in spent culture medium accurately reflects the chromosomal condition of embryos after culturing past implantation.In a study, to help choose a viable embryo with high implantation potential, metabolic analysis of spent embryo culture medium may be a useful supplement to morphological characteristics in assessing the embryonic viability and attachment potential of preimplantation embryos.[9] Furthermore, Zhang et al.[10] predicted embryo development potential by using digital PCR detection of mtDNA/gDNA ratio in SECF. It was reported that granulosa cell (GC) apoptosis is a physiological phenomenon in the follicle and may cause a decrease in follicle number by inducing follicular atresia.[7,11]

Limitations

The detection of Cyt C in SECF could also provide insights into the metabolic state of the embryo. Mitochondrial dysfunction is known to impair embryo development and is a common cause of infertility. By monitoring Cyt C levels in SECF, clinicians could potentially identify embryos with compromised mitochondrial function and avoid their transfer, thereby improving the success rates of ART procedures. This study has some limitations, one of these being that the number of samples taken represents only a single population, there is a possibility that the sample is not representative of the entire population. Furthermore, given the resources available to us, fund, only a single gene could be examined. Therefore, further genetic studies could be conducted for the same study group.

In the study, SECFs from advanced-diminished ovarian reserve (A-DOR) patients showed significantly upregulated Cyt C expression, suggesting higher apoptosis and potentially lower viability (p<0.001). Early-diminished ovarian reserve (E-DOR) embryos had downregulated Cyt C, indicating less apoptosis and possibly better viability (p<0.001). NOR and polycystic ovarian syndrome (PCOS) embryos showed no significant difference in Cyt C levels, suggesting similar apoptotic activity and viability.

The absence of variation in Cyt C within the PCOS group, coupled with the divergent expression profiles of DOR throughout early and late ages, indicates that SECF may serve as a valuable tool for differentiating between early and late stages of DOR. PCOS cases are characterized by a high quantity of oocytes, although their quality is inadequate. In such a situation, apoptotic pathways would not be effective and therefore Cyt C expression would be low, or no difference would be expected. According to our findings, cases with low Cyt C expression indicate E-DOR, while cases with high Cyt C expression are A-DOR individuals. One of the main reasons is thought to be the age of the cases. E-DOR individuals are younger than A-DOR individuals. Therefore, it is known that the apoptosis mechanism normally seen in various tissues and cells of these individuals is more active than in young individuals. In addition, the apoptosis rate in A-DOR cases was significantly higher than in E-DOR cases. It is thought that one of the reasons for the number of oocytes being less than 7 in the A-DOR cases may be that Cyt C exits from the mitochondria to the cytosol and initiates the apoptotic cascade.

In the context of in vitro fertilization (IVF), Cyt C levels in SECF can reflect the metabolic and apoptotic status of embryos. Elevated or reduced expression of Cyt C may indicate mitochondrial dysfunction or altered apoptosis, which can affect embryo viability and developmental potential. Furthermore, Monitoring Cyt C in SECF offers a non-invasive method to assess embryo quality, helping clinicians select embryos with higher implantation potential and optimize IVF outcomes. It can also help differentiate between ovarian response types, such as NOR, diminished ovarian reserve, and PCOS, providing insights into

underlying cellular mechanisms. Balanced Cyt C levels are associated with healthy mitochondrial function and controlled apoptosis, both of which are crucial for embryo viability. Abnormal levels, either too high (excessive apoptosis) or too low (mitochondrial dysfunction), can negatively impact embryo development and reduce the likelihood of successful IVF. Thus, Cyt C measurement in SECF is a promising tool for optimizing embryo selection and improving reproductive outcomes.

CONCLUSION

As a result, Cyt C is a vital protein involved in both cellular respiration and apoptosis. Its presence in SECF offers a promising avenue for non-invasive assessment of embryo quality and viability in ART. By identifying embryos with compromised mitochondrial function or abnormal apoptotic activity, Cyt C measurement may improve the success rates of ART and contribute to personalized treatment strategies. Further research is needed to fully understand the implications of Cyt C levels in SECF and to develop reliable protocols for its use in clinical practice.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study has been approved by the Ethics Committee of Maltepe University (Date: 09.11.2023, Decision No: 2023/19-22).

Informed Consent

Written informed consent was obtained from all individual participants prior to their inclusion in the study. Participants were fully informed about the study's aims, procedures, potential risks and benefits, and their rights-including the right to withdraw at any time without consequence. All participants voluntarily signed a written informed consent form.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

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Author Contributions

Concept: D.K., N.Ö.K., Ç.Ö.; Design: D.K., N.Ö.K., Ç.Ö.; Control: D.K., N.Ö.K., Ç.Ö.; Resources: D.K., N.Ö.K., Ç.Ö.; Materials: D.K., N.Ö.K., Ç.Ö.; Data Collection and/or Processing: D.K., N.Ö.K., Ç.Ö., E.Ç.; Analysis and/or Interpretation: E.Ç., Ç.Ö.; Literature Review: D.K., N.Ö.K., Ç.Ö.; Writing The Article: D.K., N.Ö.K., Ç.Ö., E.Ç.; Critical Review: E.Ç., Ç.Ö.

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MHA MEDIHEALTH ACADEMY

Surgery on Children

Original Article

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Intrathyroidal ectopic thymus in childhood: ultrasound features for accurate diagnosis

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ABSTRACT

Aims: To characterize the ultrasonographic features of intrathyroidal ectopic thymus (IET) in pediatric patients and emphasize the role of ultrasound (US) in its accurate identification to prevent misdiagnosis.

Methods: Eighty-four pediatric patients (aged 3–12 years) were referred for neck US due to cervical lymphadenopathy, during which incidental lesions in the thyroid gland were detected. These lesions, identified within normal thyroid parenchyma, were classified as IET. In such cases, color Doppler US (CDUS) was also performed without additional cost or workload..

Results: Among 84 pediatric patients, all IET lesions appeared as solid nodules with smooth margins and no mass effect. Ten lesions were uniformly hypoechoic, while 74 showed scattered internal bright echoes. Lesions measured 4–12 mm and were predominantly fusiform (59.5%), followed by triangular and round shapes. IET was unilateral in most cases (88%), with a marked left-lobe predominance, and all lesions were localized to the mid-to-lower thyroid lobe. CDUS demonstrated reduced or normal vascularity without suspicious flow patterns. Follow-up imaging in 62 children showed stable findings, with gradual size reduction in 8 adolescents and complete regression in one child. Echogenicity (p=0.001), lesion shape (p=0.01), and location (p=0.03) were significantly associated with IET characteristics, supporting their diagnostic relevance.

Conclusion: The presence of internal echogenicities and mid-to-lower lobe localization, especially in the left lobe, are key diagnostic indicators. IET is more prevalent than previously recognized. Recognition of its US features may prevent unnecessary interventions. Routine US monitoring is recommended, while further diagnostic procedures are generally unwarranted.

Keywords: Intrathyroidal ectopic thymus, thyroid gland, thyroid nodule, thyroid ultrasonography

INTRODUCTION

The thymus is a bilobed organ situated in the anterior superior mediastinum, superior to the heart and posterior to the sternum, with essential roles in immune regulation and endocrine function. Embryologically, it primarily originates from the third pharyngeal pouch, with minor contributions from the fourth pouch, developing between the fifth and sixth weeks of gestation. The thymus comprises tissues derived from all three embryonic germ layers. Around the eighth week, bilateral thymic primordia fuse at the midline and migrate caudomedially to their definitive location. Incomplete migration or arrested development can result in residual thymic tissue along this pathway. Given their adjacent embryologic origins-specifically the third pharyngeal pouch and thyroid diverticulum-the migration patterns of the thymus and thyroid are closely linked. Cervical thymic remnants are often underrecognized due to their asymptomatic nature and incidental discovery during surgical procedures.[1,2]

Ultrasound (US) is widely used for thyroid evaluation in pediatric patients, capable of detecting minor anomalies even in asymptomatic individuals.[2] Although thyroid nodules are rare in children, they carry a higher malignant potential compared to those in adults.[3-5] Ectopic thymic tissue can sonographically mimic a thyroid nodule, often presenting as a hyperechoic lesion that may raise suspicion of malignancy.[6-8] It is therefore essential to recognize the distinct sonographic features of ectopic thymic tissue in order to differentiate it from potentially malignant nodules and thus avoid unnecessary fine-needle aspiration biopsies.[9-11]

The main purpose of this article is to draw attention to the ultrasonographic detection of this intrathyroidal ectopic thymus (IET) lesion, especially in the pediatric age population, without the need for interventional procedures.

METHODS

Ethics

This retrospective study was approved by the Non-interventional Ethics Committee of Gaziosmanpaşa Training and Research Hospital with specific attention to the inclusion of vulnerable participants (e.g., children, pregnant women, individuals with disabilities) (Date: 28.05.2025, Decision No: 65). Additional safeguards were reviewed and approved by the committee. All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Study Design

This retrospective study was conducted in the US Unit of the Radiology Department at Gaziosmanpaşa Training and Research Hospital (İstanbul) and included pediatric patients who underwent ultrasonographic examinations between August 2019 and October 2025. Among those referred for neck US due to cervical lymphadenopathy, cases with incidentally detected thyroid lesions suggestive of ectopic thymus-initially described in the reports as possible IET-were identified through a comprehensive review of archived US reports. Only cases with adequate image quality and optimal visualization were included in the study.

Lesions identified from the reports were further evaluated on corresponding US images. Sonographically, these lesions were located within otherwise normal-appearing thyroid parenchyma and exhibited finely granular (speckled or hyperechoic) internal echotexture with delicate linear echogenic strands, resembling normal thymic tissue. None of the cases demonstrated suspicious sonographic features indicative of malignancy, such as irregular margins, marked or heterogeneous hypoechogenicity, increased intralesional vascularity on color Doppler US (CDUS), or mass effect. The consistency between sonographic reports and imaging findings was thereby confirmed.

Population

Over the six-year study period, a total of 84 pediatric patients (46 boys and 38 girls) aged between 3 and 12 years were included. All patients had available follow-up ultrasonography records at 6, 12, and 18 months. Only those with normal thyroid function test results were enrolled. Patients with a known thyroid disorder, a history of thyroid surgery, palpable thyroid nodules, abnormal or unavailable thyroid function test results, or a history of radiation exposure to the head and neck region were excluded from the study.

Ultrasound Examination and Image Interpretation

All examinations were performed in the US unit of the radiology department using high-resolution linear transducers (5–10 MHz and 10–14 MHz) on Toshiba Aplio 300 or Siemens Acuson S300 systems. All studies were conducted and interpreted by a single experienced radiologist, ensuring technical and interpretive consistency across the cohort.

Operational Diagnostic Criteria for IET

To ensure diagnostic consistency and reproducibility, lesions were classified as IET when they demonstrated a constellation of characteristic sonographic and clinical features derived from established descriptions of thymic tissue in pediatric imaging literature. Specifically, IET was identified when a lesion was located in the mid-to-lower portion of a thyroid lobe and exhibited a finely granular or speckled internal echotexture with delicate linear echogenic strands, closely resembling the classic “starry-sky” appearance of normal thymic parenchyma. The margins were smooth and well defined, without distortion or displacement of adjacent thyroid tissue, and no suspicious features suggestive of malignancy-such as irregular borders, marked hypoechogenicity, microcalcifications, or extrathyroidal extension-were present. CDUS showed either decreased or normal vascularity compared with the surrounding thyroid parenchyma, with no focal intralesional hypervascularity. Clinically, lesions were non-palpable, asymptomatic, and detected in children with normal thyroid function. In a subset of patients, the diagnosis was further strengthened by the presence of direct anatomical continuity between the intrathyroidal lesion and an elongated cervical or mediastinal thymus. The final diagnosis of IET was established by integrating these imaging features with longitudinal sonographic stability during follow-up.

Follow-Up

US follow-up at 6, 12, and 18 months was available for 62 children. Lesions were assessed for changes in size, echogenicity, margins, and vascularity. Regression or stability was recorded as part of the natural evolution of thymic tissue.

Statistical Analysis

Data analyses were performed to examine distribution patterns and internal variability among IET lesions. Three clinically meaningful subgroup categories were predefined within the cohort: echogenicity (hypoechoic lesions vs. lesions containing bright internal echoes), lesion shape (fusiform vs. non-fusiform, the latter including round and triangular configurations), and lobe involvement (right, left, or bilateral). Continuous variables such as lesion size were assessed for normality using the Shapiro-Wilk test. Depending on distribution characteristics, normally distributed variables were compared using the Student’s t-test, whereas non-normally distributed variables were analyzed with the Mann-Whitney U test. Categorical variables-including echogenicity patterns, shape classifications, lobe involvement, and vascularity-were compared using the Pearson Chi-square test or Fisher’s exact test when expected cell counts were small. A two-sided p-value <0.05 was considered statistically significant. All analyses were conducted using IBM SPSS Statistics (Version 25.0). Importantly, because the aim of the study was to characterize internal features of IET rather than compare IET to non-IET nodules or estimate prevalence, all statistical tests were restricted to comparisons within the IET cohort, and no diagnostic accuracy assessments or prevalence calculations were performed.

RESULTS

A total of 84 children met the inclusion criteria, all demonstrating an intrathyroidal lesion with smooth margins, absence of mass effect, and benign sonographic morphology. Lesion size ranged from 4 to 12 mm, with a mean±SD of 8.2±2.4 mm. Most lesions exhibited bright internal echoes

(74/84, 88.1%) (**Figure 1**), whereas a smaller subset appeared hypoechoic (10/84, 11.9%) (Figure 2). In terms of shape, the majority were fusiform (50/84, 59.5%), followed by triangular (18/84, 21.4%) and round configurations (16/84, 19.1%). Lesions predominantly involved the left thyroid lobe (50/84, 59.5%), with fewer located in the right lobe (24/84, 28.6%) or bilaterally (10/84, 11.9%). Color Doppler ultrasonography demonstrated decreased vascularity in 40 children (47.6%) and vascularity similar to surrounding thyroid tissue in 44 (52.4%) (**Figure 2**). In 16 children (19.0%), the intrathyroidal lesion showed direct anatomical continuity with an elongated cervical thymus, providing strong supportive evidence for the diagnosis of IET. These descriptive ultrasonographic features are summarized in **Table 1**.

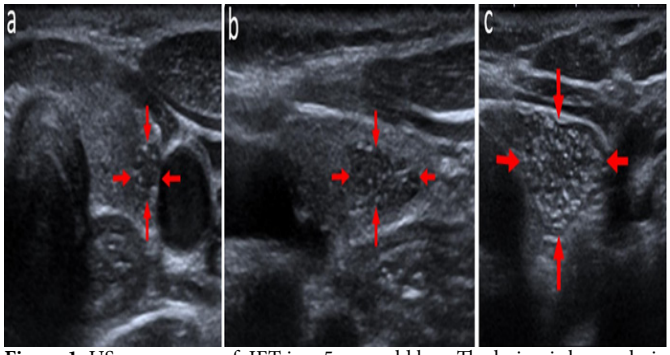

Figure 1. US appearance of IET in a 5-year-old boy. The lesion is hypoechoic compared with the surrounding thyroid parenchyma and contains punctate echogenic foci, showing a characteristic ultrasonographic similarity to normal thymic tissue (marked with red arrows).

(a) Axial image demonstrating the lesion lateral to the left thyroid lobe. (b) Longitudinal image showing the lesion near the inferior aspect of the left thyroid lobe. (c) US image of normal thymic tissue. (IET: Intrathyroidal ectopic thymus, US: Ultrasound)

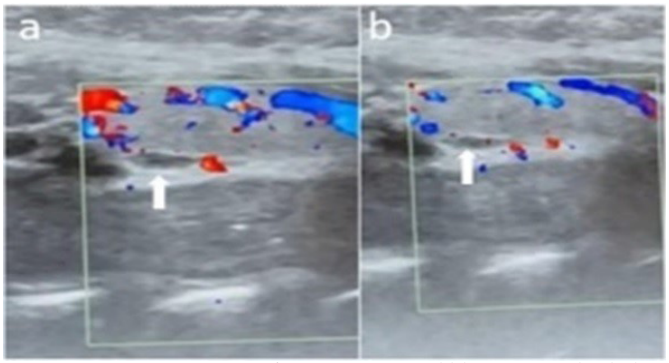

Figure 2. CDUS appearance of IET in a 6-year-old boy. Longitudinal plane ultrasound images of a patient with an incidental IET located in the posterior region of the left thyroid lobe (marked with white arrows)

CDUS evaluation at two separate time points (a, b) demonstrates vascularity comparable to the surrounding thyroid parenchyma. (CDUS: Color Doppler ultrasound; IET: Intrathyroidal ectopic thymus, US: Ultrasound)

Subgroup analyses revealed several notable internal distribution patterns. When echogenicity was considered, lesion size did not differ significantly between hypoechoic lesions (mean 7.6±2.1 mm) and those with bright internal echoes (mean 8.3±2.4 mm; p>0.05). However, lesions with bright internal echoes were significantly more likely to be located in the left lobe (46/74, 62%) compared with hypoechoic lesions (4/10, 40%), indicating a non-random distribution (p<0.05). Vascularity did not differ between these groups (p>0.05). Detailed comparisons between echogenicity subgroups are presented in **Table 2**.

In the analysis of lesion shape, fusiform lesions demonstrated a slightly larger mean size (8.4±2.3 mm) compared with non-fusiform lesions (7.9±2.5 mm), although this difference was not statistically significant (p>0.05). Bright internal echoes were significantly more common in fusiform lesions (47/50, 94%) than in non-fusiform lesions (27/34, 79%) (p<0.05). Furthermore, fusiform lesions exhibited a stronger left-lobe predominance (35/50, 70%), again supporting a non-uniform lobe distribution pattern (p<0.05). These shape-based subgroup comparisons are shown in **Table 3**.

When lobe involvement was evaluated independently, lesions located in the left lobe demonstrated the highest prevalence of bright internal echoes (46/50, 92%), followed by bilateral lesions (10/10, 100%) and right-lobe lesions (18/24, 75%), yielding a statistically significant overall difference (p=0.03). Lesion size did not differ significantly among the right, left, and bilateral groups (p>0.05). While fusiform morphology appeared more common in left-lobe lesions (33/50, 66%) compared with right-lobe lesions (12/24, 50%) or bilateral involvement (5/10, 50%), this trend did not reach statistical significance (p>0.05). Lobe-based subgroup analyses are

Table 1. Descriptive characteristics of IET lesions (n = 84)

Characteristic	Value
Lesion size, mm (mean±SD, range)	8.2±2.4 (4-12)
Echogenicity	
Bright internal echoes	74 (88.1%)
Hypoechoic	10 (11.9%)
Shape	
Fusiform	50 (59.5%)
Triangular	18 (21.4%)
Round	16 (19.1%)
Lobe involvement	
Left lobe	50 (59.5%)
Right lobe	24 (28.6%)
Bilateral	10 (11.9%)
CDUS	
Decreased	40 (47.6%)
Similar to parenchyma	44 (52.4%)
Continuity with cervical thymus	16 (19.0%)

CDUS: Color Doppler ultrasound, IET: Intrathyroidal ectopic thymus, SD: Standard deviation

Table 2. Comparison according to echogenicity subgroups

Parameter	Hypoechoic (n=10)	Bright internal echoes (n=74)	p-value
Lesion size, mm (mean±SD)	7.6±2.1	8.3±2.4	>0.05
Left lobe involvement	4 (40%)	46 (62%)	<0.05
Decreased vascularity	6 (60%)	34 (46%)	>0.05

*Statistically significant at p<0.05, SD: Standard deviation

Table 3. Comparison according to lesion shape

Parameter	Fusiform (n=50)	Non-fusiform (n=34)	p-value
Lesion size, mm (mean±SD)	8.4±2.3	7.9±2.5	>0.05
Bright internal echoes	47 (94%)	27 (79%)	<0.05
Left lobe involvement	35 (70%)	15 (44%)	<0.05

*Statistically significant at p<0.05, SD: Standard deviation

summarized in Table 4. Collectively, these findings indicate that bright internal echoes and fusiform morphology are the dominant sonographic phenotypes of IET and that left-lobe localization is disproportionately represented across these patterns.

Table 4. Comparison according to lobe involvement

Parameter	Right (n=24)	Left (n=50)	Bilateral (n=10)	p-value
Bright internal echoes	18 (75%)	46 (92%)	10 (100%)	0.03
Lesion size, mm (mean±SD)	Similar across groups	Similar across groups	Similar	>0.05
Fusiform morphology	12 (50%)	33 (66%)	5 (50%)	>0.05

*Statistically significant at p<0.05, SD: Standard deviation

Follow-up ultrasonography was available in 62 children. During longitudinal assessment, the vast majority of lesions (53/62, 85.5%) remained morphologically stable, while 8 children (12.9%) demonstrated gradual reduction in lesion size. Complete resolution occurred in a single 6-year-old girl, with disappearance of the lesion documented 18 months after initial identification. Importantly, none of the lesions developed suspicious sonographic features over time, and no child required biopsy or surgical intervention. These follow-up findings reinforce the benign nature of IET and underscore the safety of conservative sonographic surveillance in typical cases.

DISCUSSION

IET is an uncommon but clinically relevant entity in pediatric thyroid imaging, primarily because of its potential to mimic thyroid nodules and thereby prompt unnecessary invasive procedures. The present study provides a comprehensive ultrasonographic characterization of IET in a relatively large pediatric cohort and reinforces the role of high-resolution US as a reliable, noninvasive tool for its identification and follow-up.

Thyroid nodules are rare in children but carry a substantially higher malignancy risk compared with adults, reported to range between 22% and 26%.[4,12] Consequently, any intrathyroidal lesion detected on US in the pediatric population often raises concern and leads to further diagnostic workup. In this context, ectopic thymic tissue represents a well-recognized diagnostic pitfall. Several previous reports have described IET being misinterpreted as suspicious thyroid nodules, resulting in fine-needle aspiration or surgical excision for definitive diagnosis.[7,8,14,15] Our findings support the growing body of evidence that careful assessment of sonographic morphology can reliably distinguish IET from true thyroid nodules, thereby avoiding unnecessary interventions.

Embryologically, the thymus originates primarily from the third pharyngeal pouch and descends caudally toward the mediastinum during early fetal development. Given the close developmental relationship and migration pathways of the thymus and thyroid, remnants of thymic tissue may persist along this route and become embedded within or adjacent to the thyroid gland.[7,10,16] This embryologic background explains the characteristic mid-to-lower lobe localization observed in our cohort and reported consistently in prior studies.[9,17,19]

In the present series, IET lesions demonstrated a highly consistent ultrasonographic appearance: smooth margins, absence of mass effect, and a finely granular or "starry sky" echotexture with punctate or linear echogenic foci corresponding to thymic septa and Hassall's corpuscles.[10,17] These features closely mirrored the appearance of the normally positioned cervical or mediastinal thymus, and in nearly one-fifth of cases, direct anatomical continuity between the intrathyroidal lesion and an elongated thymus was observed. This continuity provides particularly strong imaging evidence for the diagnosis of IET and has been emphasized as a key confirmatory feature in the literature.[19]

Color Doppler ultrasonography in our cohort demonstrated either decreased vascularity or vascularity comparable to the surrounding thyroid parenchyma, with no suspicious flow patterns. While Segni et al.[19] reported an absence of detectable vascularity in their series,other studies have similarly described reduced or normal vascularity rather than hypervascular patterns.[9,17] These findings suggest that Doppler characteristics should be interpreted as supportive rather than decisive features and always considered in conjunction with grayscale morphology.

Importantly, although certain sonographic features-such as fusiform shape, bright internal echoes, and left-lobe predominance-were frequently observed in our cohort, these characteristics should not be interpreted as standalone diagnostic criteria. Rather, they represent common phenotypic patterns within IET lesions. Their diagnostic value lies in their combined presence alongside typical location, benign morphology, lack of mass effect, and clinical context, rather than in isolation. This distinction is essential to avoid overinterpretation of descriptive findings as definitive diagnostic indicators.

Longitudinal follow-up further supported the benign nature of IET. Most lesions remained stable over an 18-month period, while a subset demonstrated gradual size reduction, consistent with physiological thymic involution during late childhood and adolescence. Complete regression, although uncommon, was documented in one patient. These observations align with previous longitudinal studies and reinforce conservative US surveillance as an appropriate management strategy for typical IET lesions.[19]

The present study does not aim to estimate the prevalence of IET in the general pediatric population or among all children undergoing neck US. Rather, it characterizes the imaging features of lesions already identified as IET within a specific referral population. In this context, our findings suggest that IET may be encountered more frequently in routine pediatric neck US practice than is often appreciated, particularly when careful attention is paid to thymus-like echotexture and typical localization. However, any inference regarding prevalence should be made cautiously and within the limitations of the study design.

Overall, the principal contribution of this study lies in its relatively large sample size, systematic documentation of sonographic features, demonstration of internal distribution patterns within IET lesions, and confirmation of benign behavior on follow-up. Together, these findings provide practical guidance for radiologists and pediatric clinicians and support a noninvasive, observation-based approach in typical cases.

Limitations

This study has several limitations that should be acknowledged. First, its retrospective design introduces inherent selection bias. The study population consisted exclusively of children referred for neck US due to cervical lymphadenopathy, rather than a general pediatric or thyroid-specific screening population. As a result, the findings may not be fully generalizable to other clinical settings or referral indications.

Second, no histopathological confirmation was available, as the diagnosis of IET was based on characteristic ultrasonographic features and longitudinal stability or regression. While this may be considered a limitation, it also reflects real-world clinical practice and aligns with current recommendations to avoid invasive procedures in lesions with a clearly benign imaging profile. The presence of direct continuity with cervical thymus in a subset of cases further strengthens the imaging-based diagnosis.

Third, although subgroup analyses were performed to explore internal distribution patterns within the IET cohort, the study did not include a non-IET control group. Therefore, the findings should be interpreted as descriptive rather than diagnostic accuracy or comparative results.

Finally, the follow-up period, while sufficient to demonstrate stability or regression in most cases, may not capture very long-term evolution of all lesions. Longer follow-up studies could further clarify the natural history of IET across different pediatric age groups.

CONCLUSION

IET is a benign developmental variant that can closely mimic thyroid nodules in children. Recognition of its characteristic ultrasonographic features-particularly thymus-like echotexture with internal echogenicities, smooth margins, absence of mass effect, and typical mid-to-lower lobe localization-allows confident, noninvasive diagnosis in most cases. Although certain features such as fusiform shape and left-lobe predominance are commonly observed, they should be regarded as supportive rather than definitive diagnostic markers.

In children with non-palpable, asymptomatic intrathyroidal lesions and normal thyroid function, typical sonographic findings consistent with IET warrant conservative management with US follow-up rather than immediate biopsy or surgery. Awareness of this entity and its imaging characteristics is essential to prevent unnecessary invasive procedures and to promote appropriate, patient-centered care in pediatric thyroid imaging.

ETHICAL DECLARATIONS

Ethics Committee Approval

This retrospective study was approved by the Non-interventional Ethics Committee of Gaziosmanpaşa Training and Research Hospital with specific attention to the inclusion of vulnerable participants (e.g., children, pregnant women, individuals with disabilities) (Date: 28.05.2025, Decision No: 65). Additional safeguards were reviewed and approved by the committee.

Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

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Author Contributions

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MHA MEDIHEALTH ACADEMY

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A new scheme for risk stratification of pregnancy complicated by fetal anomalies

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ABSTRACT

Fetal anomalies are being increasingly detected during pregnancy with the increased adoption of sonological screening, advances in fetal imaging and genetic testing. The optimal use and factual interpretation of fetal diagnostic modalities and therapeutic decision-making constitute a significant challenge to the concerned specialists. This article aims to review the topic of management concerns in pregnancy complicated by fetal anomaly (PCFA), with the objective of proposal of a risk stratification system that can guide evaluation and therapy. The general management principles in common fetal disorders, the concept of 'soft markers' and the importance of a multidisciplinary approach to therapy are also analyzed. A narrative review of the management principles in PCFA on the basis of analysis of current literature, clinical guidelines and recommendations, in the light of clinical experience, is presented here. A novel risk stratification approach to PCFA is proposed that would reflect the severity, prognosis and possible outcome. The critical parameters in characterization of a prenatally detected fetal anomaly are its physiological/ pathological nature, the severity and associated risk factors, possible progression and complications, and its effect on the gestation and the fetus. These factors determine the need for detailed fetal imaging, invasive fetal diagnosis, fetal therapy, changes in perinatal management and even the option to terminate pregnancy in severe anomalies. All these key parameters are integrated in the new system of risk stratification of PCFA proposed here. The need for categorization of PCFA arises from the variegated nature of fetal disorders that range from benign physiological alterations or minor defects to major, multi-systemic anomalies. Though the management of fetal anomalies has to be highly individualized, proper risk stratification would help bring clarity to the decision-making process.

Keywords: Congenital abnormalities, prenatal diagnosis, fetal therapies, pregnancy, high-risk

INTRODUCTION

Background

Fetal anomalies are being increasingly detected during pregnancy with the increased adoption of sonological screening, advances in fetal imaging and genetic testing. The newer genetic tests and markers (like cell free fetal DNA testing, and biomarker assay) have made it possible to screen for fetal disorders even from a maternal blood sample. Similarly, advances in fetal imaging have made it possible to detect, evaluate and follow up fetuses with structural anomalies of variable severity.[1-4] The clinical aspects of management like the universal applicability of maternal screening tests, the indications for invasive fetal diagnosis/ fetal therapy and termination of pregnancy for severe anomalies continue to be grey areas clouded by medical and ethical concerns.

Objective: This article aims to review the topic of management concerns in pregnancy complicated by fetal anomaly (PCFA), with the objective of proposal of a risk stratification system that can guide evaluation and therapy. The general management principles in common fetal disorders, the concept of 'soft markers' and the importance of a multidisciplinary approach to therapy are also analyzed.

Methods: A narrative review of the management principles in PCFA on the basis of analysis of current literature, clinical guidelines and recommendations, in the light of clinical experience, is presented here. A novel risk stratification approach to PCFA is proposed that would reflect the severity, prognosis and possible outcome.

The Importance of Risk Stratification of Fetal Anomalies

Many of the prenatally detected fetal anomalies are generally followed up on the basis of the organ system-specific grading systems of severity (as in the case of fetal hydronephrosis). But many of the other common organ system anomalies do not have the benefit of a severity scoring system (as in the case of many anomalies of heart, lung or nervous system). It is neither tangible nor practically feasible to have an individual risk stratification for each and every anomaly.

The wide spectrum of these defects range from minor aberrations to major genetic or structural anomalies. Moreover, many of the fetuses have disorders affecting more than one system, each with variable severity and prognosis. The natural history of the anomalies are also highly variable with possibility of spontaneous resolution in some and the propensity to progress or develop complications during pregnancy in the others. Progression during prenatal period can have an adverse effect on the fetus, the mother and the pregnancy.[3-5]

It has been observed in clinical practice that many minor physiological/anatomical alteration(s) in the fetus could be misinterpreted as more sinister conditions, leading to unnecessary investigations, interventions and unwarranted distress. This would be particularly true for anomalies of organ systems without any specific severity scoring. Conversely, there is also the likelihood of a disorder that ideally requires aggressive prenatal testing/intervention, not benefitting from the same in the absence of a proper risk stratification. Delay or failure in the appropriate decision-making regarding management would result in unwarranted complications.[3-5]

The Objectives of Risk Stratification of Fetal Anomalies

It is vital to differentiate an anomaly with low likelihood of complications, high probability of spontaneous resolution and scarce need for therapy from those where the converse is true. Once a fetal anomaly is detected on the prenatal scan, it is crucial to have clarity in this distinction, from the perspective of the obstetrician, concerned specialist(s) and the parents. This distinction has the greatest bearing on the decision-making process regarding any prenatal, perinatal or postnatal intervention.

The critical parameters in characterization of a prenatally detected anomaly are the physiological/pathological nature of the anomaly, severity of the disorder, associated problems/ risk factors, possible progression, likely complications, and its effect on the gestation and life of the fetus. These factors, in turn decide the need for detailed fetal imaging, invasive fetal diagnosis, fetal therapy, perinatal therapy, changes in obstetric management and the option to terminate pregnancy in severe anomalies.[1,3,5,6]

All these parameters and factors are integrated in the new risk stratification of PCFA proposed here. The categorization should help in structuring crucial management decisions regarding the investigative or therapeutic modalities in pregnancy. The present stratification is not intended to substitute the available organ- specific grading systems for fetal anomalies. Such grading systems can be integrated into the risk stratification to supplement the data. The classification systems can thus serve to be mutually complementary, not mutually exclusive.

Risk Stratification for Prenatally Detected Fetal Anomalies based on Severity of the Anomaly and the Necessity for Crucial Management Decisions in Pregnancy Complicated by Feta Anomaly (PCFA)

Prerequisites of categorization of fetal anomalies: The diagnosis should be based on an Ultrasound performed by a sonologist with expertise in prenatal sonology. But the categorization should be done by the maternal-fetal medicine specialist/paediatric surgeon (with inputs from other specialists where required) and not by the untrained sonologist or obstetrician. This is because the anomaly/ anomalies detected have to be assessed for severity and prognosis and management options are to be decided upon by specialists with expertise in management of these conditions (**Figure**).

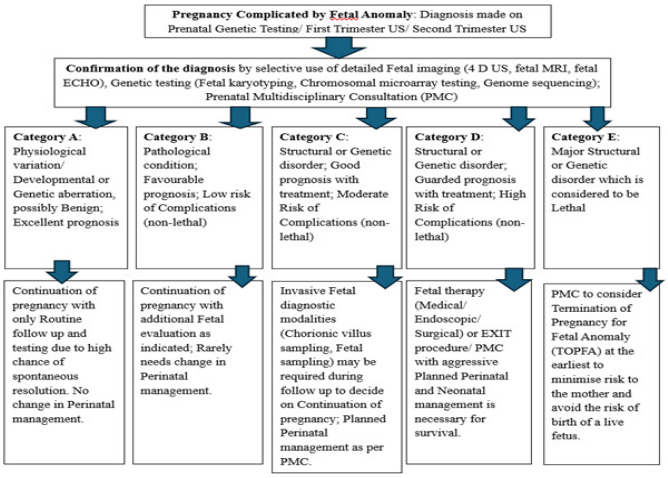

Figure. The general scheme of risk stratification approach to pregnancy complicated by fetal anomalies

If organ-specific grading systems are available for a particular anomaly, it can be integrated with the risk stratification. When more than one anomaly is detected, the severity should be assessed individually. The categorization will have to be revised, on the basis of evolution of the disorder during pregnancy/ test results of specific studies/ follow up investigations, whenever necessary (**Table**).

THE RISK STRATIFICATION OF PCFA

Category A

Physiological variation/developmental or genetic aberration; possibly benign/incidental finding; excellent prognosis; high likelihood of spontaneous resolution; low risk of complications*.

Plan: Continuation of pregnancy with only routine follow up and testing; Selective use of additional fetal evaluation**; No change in perinatal management.

Category B

Pathological condition with less likelihood of spontaneous resolution; favourable prognosis; low risk of complications* (non-lethal).

Table. The general scheme of risk stratification approach to pregnancy complicated by fetal anomalies, with examples of each category

Category of risk strata	A	B	C	D	E
Nature of the anomaly	Physiologica/minor; possibly benign	Pathological condition	Major defect	Major defect	Major defect
Chance of spontaneous resolution	High	Low	Nil	Nil	Nil
Risk of progression/ complications	Low	Low (non-lethal)	Moderate (non-lethal)	High (non-lethal)	High (lethal)
Prognosis/ Possible Outcome	Excellent	Favourable	Good, with therapy	Guarded, with therapy	Poor
Plan of evaluation	Only selective use of evaluation other than routine tests	Additional evaluation is required	Invasive fetal diagnostic modalities are required	Requires use of fetal therapy/ EXIT procedure	Evaluate to confirm diagnosis
General management plan	Continuation of pregnancy	Continuation of pregnancy	Continuation of pregnancy based on risk evaluation	Continuation of pregnancy based on risk evaluation	Termination of pregnancy for fetal anomaly
Changes in Perinatal management	Nil	May be required	Yes	Yes	-
Examples for each category	Low grade urinary tract dilatation, choroid plexus cysts	Unilateral hydronephrosis, gonadal cyst	Genetic or Syndromic disorders, posterior urethral valves	Large neck lesions, large teratoma, fetal lung lesions	Anencephaly, Trisomy 13, Infantile polycystic kidney

Plan: Continuation of pregnancy with the additional fetal evaluation as indicated** and rarely need changes in perinatal management.

Category C

Structural defect/genetic disorder; good prognosis; moderate risk of complications* (non-lethal)

Requires the use of invasive fetal diagnostic modalities** to decide on continuation of pregnancy; planned perinatal management.

Category D

Major structural defect/genetic disorder; guarded prognosis with treatment; high risk of complications* (non-lethal)

Requires fetal therapy (medical/surgical/fetal endoscopic)/ex-utero intrapartum treatment (EXIT) procedure, with planned obstetric/ perinatal management.

Category E

Major structural defect/genetic disorder (lethal) that requires termination of pregnancy for fetal anomaly (TOPFA)

***Complications:** Fetal/gestational/maternal (narrated below)

****Fetal evaluation:** Non-invasive testing includes serial ultrasound and Doppler, fetal echocardiogram, fetal MRI etc. Invasive, diagnostic testing includes amniocentesis, chorionic villus sampling (CVS), fetal blood/urine sampling etc.

Examples of each category[5-8]:

A: Isolated findings of low grade urinary tract dilatation, echogenic bowel, intracardiac echogenic focus, choroid plexus cysts etc. (Low probability of being pathological in isolation)

B: Higher grades of urinary tract dilatation; Gonadal cyst; Isolated systemic anomalies (cardiac, lung etc.) that generally carry a good prognosis etc.

C: Complex defects/ multisystemic anomalies/ Genetic disorders that require Amniocentesis/ Chorionic villus sampling/ fetal blood sampling; Posterior urethral valves requiring fetal urine sampling.

D: Fetal lung lesions requiring prenatal maternal steroids, large Teratoma requiring fetal surgery, poor risk Myelomeningocele that is a candidate for fetal surgery, large neck lesions requiring EXIT Procedure.

E: Anomalies like Anencephaly, Trisomy 13, Infantile Polycystic Kidney Disease etc.

Complications in prenatally detected fetal anomalies: The complications pertaining to prenatally detected fetal anomalies can be classified as fetal, gestational and maternal. Fetal complications will include conditions like growth retardation, fetal anemia, organ damage from progressive disease, cardiac failure, hydrops fetalis, intrauterine death etc.[4-6] Gestational (pregnancy-related) complications include amniotic fluid abnormalities, placentomegaly, chorioamnionitis, rupture of protective sacs as in exomphalos etc. and maternal complications include preeclampsia, maternal mirror syndrome, premature labour, dystocia etc.[6-9]

DISCUSSION

The Concept of Sonological "Soft Markers" Revisited

The categorization proposed here does not consider or include the concept of sonological "soft markers". The findings labelled so, as those of cerebral ventricular dilatation, thickened nuchal fold, single umbilical artery, shortened humerus/femur length and hypoplastic nasal bone could be markers of significant disorders that may mandate detailed evaluation. The other such findings like mild renal pelvic dilatation, choroid plexus cysts, echogenic bowel and intracardiac echogenic focus could be benign findings with high chance of spontaneous resolution, especially when found in isolation.[1,4,7,8] But still, they

mandate a detailed anatomical survey and even additional evaluation, especially when they occur along with other abnormalities. Hence it would be detrimental to group together these diverse conditions of variable significance under a common umbrella, that risks undermining their possible significance.[9-12]

Commonly Detected Anomalies and General Management Principles

The defects that usually need only prenatal follow up and postnatal therapy include conditions like hydronephrosis, isolated congenital diaphragmatic hernia and oesophageal atresia, intestinal atresias, anorectal malformation, enteric cysts, small and intact abdominal wall defects, small sacrococcygeal teratoma, small lymphovascular malformations, benign cysts and uncomplicated craniofacial/ limb/chest wall abnormalities.[11-14] The defects that may require induction of preterm delivery include ruptured exomphalos, gastroschisis, progressive hydrops fetalis, progressive hydrocephalus, progressive hydrothorax, fetal arrhythmias and severe growth retardation. The defects that need planned caesarian section include large sacrococcygeal teratoma, severe hydrocephalus, large myelomeningocele, conjoined twins, large exomphalos/gastroschisis, large cervical lympho-vascular malformation and the presence of inadequate labor or fetal distress. The defects that may require an ex-utero intrapartum treatment (EXIT) procedure include the conditions that require emergency upper airway access like congenital high airway obstruction syndrome (CHAOS), large neck lesions and conditions requiring immediate extracorporeal membrane oxygenation (ECMO) cannulation. The defects that require TOPFA include severe neurological defects like Anencephaly, chromosomal anomalies like Trisomy 13, bilateral renal agenesis and infantile polycystic kidney disease, metabolic disorders like Tay-Sach's disease and lethal bone dysplasias like recessive Osteogenesis imperfecta.[13-16]

The Importance of a Multidisciplinary Approach to Treatment of Fetal Anomalies

A crucial role in the management of prenatally detected fetal anomalies rests on the paediatric surgeon, who is generally responsible for the management of the majority of the congenital structural disorders that occur in the neonate. It is also important to involve other specialists like the geneticist, pediatrician, nephrologist, cardiologist, neurologist etc. in situations that require their specific expert opinion. The scarcity of well-trained maternal-fetal medicine specialists, especially in limited resource scenarios, only augments the responsibility of the paediatric surgeon to coordinate the opinions and take management decisions. Hence, it is vital for the paediatric surgeon to be well trained and updated about the concepts in evaluation and treatment of these conditions. They should have a dynamic interaction with the obstetrician, to facilitate and streamline therapy.[15-18]

The optimal use and factual interpretation of fetal diagnostic modalities and therapeutic decision-making constitute a significant challenge to the concerned specialists. There is a need for objective guidelines, multidisciplinary integration and evidence-based approach to the management of PCFA. The aspect of informed decision-making by the parents is equally vital for the optimal management of fetal anomalies. A risk stratification approach and multidisciplinary involvement can greatly help the concerned specialists and parents involved in the decision-making process.[19-22]

The science of prenatal diagnosis has evolved tremendously over the past few decades with the availability of newer genetic testing, early and advanced fetal imaging, maternal testing, advances in genetic diagnosis like chromosome microarray and genome sequencing and advanced fetal therapy. These advances have necessitated the stratification of anomalies, both isolated and multiple, for the purpose of institution of appropriate therapy.

The novel risk stratification approach proposed here has the objective of segregation of anomalies based on their severity, need for further evaluation/ therapy and possible outcome. The categorization may need revision in some cases based on the evolution of the disorder during pregnancy. The stratification proposed here needs evidence-based validation in prospective cohort studies in the next phase for clinical application. The primary purpose of this structured approach to evaluation and to ensure apt treatment at the right time where necessary and to avoid testing and therapy where it is unwarranted. This would provide a basic and broad framework for prognostication, evaluation, management and follow up.

CONCLUSION

The importance of categorization of prenatally detected fetal anomalies pertain to the need to determine the severity of the disorder, predict outcome, decide on therapy and to facilitate communication with the parents. The need for classification also arises from the variegated nature of these disorders that range from physiological changes or minor defects to major anomalies. A proper risk stratification approach would hence facilitate the diagnostic process, guide evaluation and aid prognostication and formulation of crucial management decisions.

ETHICAL DECLARATIONS

Peer Review Process

This review was externally peer-reviewed.

Conflict of Interest

The authors declare no conflicts of interest.

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Author Contributions

The author is solely responsible for the conception, data collection, analysis, and writing of this manuscript.

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Delayed recognition of perineal ectopic testis in a pediatric patient: diagnostic and surgical implications of a rare cryptorchidism variant

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ABSTRACT

Cryptorchidism is one of the most prevalent congenital urogenital anomalies in the paediatric male population. Ectopic testis cases are less frequent, with perineal localization being the rarest form. A six-year-old patient was referred to the paediatric urology outpatient clinic following the failure to palpate the right testis during a routine physical examination in primary care. The evaluation process revealed the presence of a perineal ectopic testis, a diagnosis that was subsequently confirmed through ultrasonography. The testis was surgically mobilised, placed in a dartos pouch, and fixed in the scrotum. Perineal ectopic testis is a diagnostically challenging and rare variant. Even though the diagnosis was made at an older age in this case, the surgical procedure resulted in anatomically successful outcomes. The utilisation of systematic genital examinations within primary healthcare settings facilitates the timely identification and subsequent referral of cases exhibiting similar characteristics. Early diagnosis is of pivotal importance in preserving testicular function. It is important to note that even in cases where the onset of symptoms is delayed, the implementation of appropriate surgical intervention can result in favourable outcomes. The quality of primary care follow-up is fundamental to this process.

Keywords: Cryptorchidism, perineal testis, pediatric urology, scrotal orchidopexy, primary care, delayed diagnosis

INTRODUCTION

Cryptorchidism is among the most frequently reported congenital anomalies of the male genital system. It is characterised by the failure of the testis to complete its normal descent.[1] While most cases involve the testis being located in the inguinal canal or abdominal cavity, a small subset presents with ectopic testicular placement outside the usual descent path.[2] In the context of ectopic locations, the perineal region is the least prevalent, with an occurrence rate of less than 1 in 10,000 cases.[3]

Perineal ectopic testis is a rare variant that poses significant diagnostic challenges. In instances where the testis is not palpable in the standard locations, the possibility of ectopic placement must be considered. The failure to recognise such variants in a timely manner may result in complications, including testicular atrophy, subfertility, and malignant transformation.[1,4]

Primary healthcare settings represent the fundamental framework for paediatric monitoring, and genital examination should be considered a vital component of routine assessments. Systematic physical examinations have been shown to facilitate the early detection and referral of undescended or ectopic testis cases.[5] The present report details a case of delayed diagnosis of perineal ectopic testis, addressing the diagnostic process, surgical approach, and the critical role of primary care from an academic perspective.

CASE

A six-year-old male patient was referred to a specialist in paediatric urology following a routine physical examination in primary care that revealed an empty right hemiscrotum. Physical examination revealed the presence of the urethral meatus at the coronal level, in addition to a dorsally hooded prepuce. Surgery was planned for hypospadias repair in the second session. The left testis was found to be in its normal position, exhibiting the expected dimensions and consistency that are characteristic of its age. The right hemiscrotum was found to be hypoplastic, with only minimal fluid present (**Figure 1**). It was not possible to palpate the right testis in the inguinal canal.

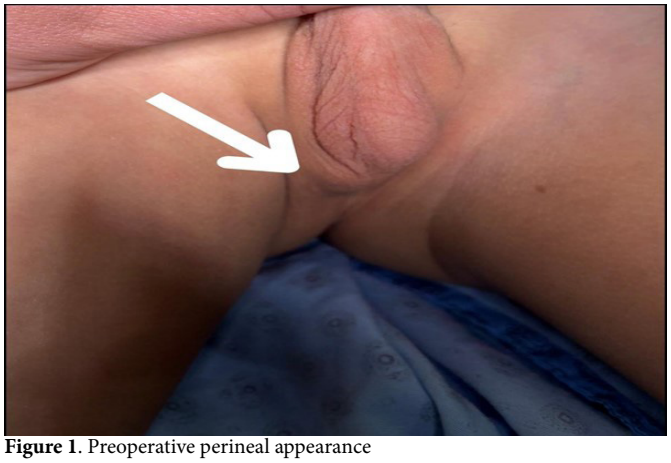

Figure 1. Preoperative perineal appearance

Upon extending the palpation area, a mobile, soft mass was detected approximately 1.5 cm inferior to the scrotum in the right perineal region, overlying muscle tissue. Ultrasonography confirmed the absence of the right testis in the scrotum and identified the perineal mass as testicular tissue.

Surgical exploration was performed through a transverse scrotal incision. After the traversal of the scrotal layers, the dissection was deepened towards the perineal area, where the testis was located. The adhesions to the surrounding tissues were meticulously released. The testis, exhibiting normal consistency and displaying a slightly reduced size in comparison with the contralateral side, was mobilised (**Figure 2**). The epididymis was then found to be separated. There was no tension when the testicle was placed in the dartos sac and fixed to the scrotum. (**Figure 3**). The postoperative course was uneventful, with no complications observed.

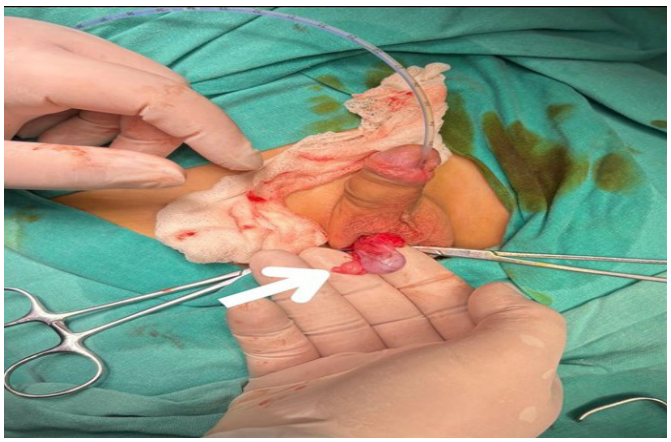

Figure 2. Dimensions of the testis

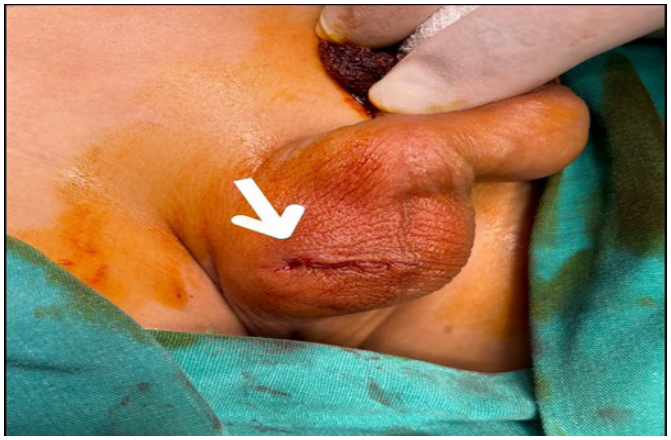

Figure 3. Postoperative single incision appearance

DISCUSSION

Perineal ectopic testis is characterised by abnormal testicular descent, deviating from the physiological route and settling in the perineal area, making it an extremely rare form of cryptorchidism.[6] While ectopic testis accounts for approximately 5-10% of all undescended testes, perineal placement is the least common variant within this group. Diagnosis is frequently challenging, as the testis is not located in the conventional palpation zones and may be misinterpreted as testicular agenesis or intra-abdominal testis.[7] Atypical anatomical positioning necessitates a careful and systematic approach during physical examination and surgical planning. This case, despite presenting typical findings associated with cryptorchidism, is diagnostically significant due to its perineal location, which represents a variant that has been rarely reported in the literature. Despite the diagnosis being delayed, the correct localisation was achieved via physical examination and successful scrotal fixation was performed through a minimally invasive approach, rendering the case clinically relevant.

In primary healthcare settings, routine genital examinations during childhood follow-ups are crucial for the early recognition of urogenital anomalies, such as undescended or ectopic testes. In this particular instance, the diagnosis was made at a relatively late stage, at six years of age. This suggests that earlier physical evaluations may have been either overlooked or not carried out in a sufficiently systematic manner. This diagnostic delay has the potential to increase the risk of complications. Consequently, structured, documented, and auditable genital examinations should be standard practice in paediatric follow-ups. Furthermore, the implementation of continuous professional development for healthcare providers, in conjunction with public education campaigns for parents, has the potential to enhance clinical awareness and societal consciousness.

Although there are different opinions in the literature about the use of routine ultrasonography in the diagnosis of undescended testis, it can be a valuable aid in cases with suspected ectopic testis.[1] Ultrasonography is a valuable tool in a range of medical contexts, including the identification of anatomical positioning, assessment of vascularization, and guidance for surgical planning. However, it should be noted that the sensitivity of the test varies, especially in cases where it is performed in an abdominal or atypical location.[8] Consequently, if clinical suspicion remains high despite inconclusive imaging, exploratory surgery should not be postponed.[9] In the presented case, the testis was not located in the inguinal canal but was identified in the perineal region via extended palpation and confirmed with ultrasonography.

From a surgical standpoint, the ability to localise the problem with precision through physical examination and targeted imaging has been shown to prevent unnecessary laparoscopic or inguinal explorations due to diagnostic uncertainty. A solitary scrotal incision facilitated the mobilisation of the testis from the perineum, achieving minimal tissue trauma. It was observed that the vascular structures were preserved, and that the testis was tension-free when placed in the dartos pouch. The length of the cord was found to be adequate, thus

enabling the procedure to be completed in a single session without the need for additional surgical intervention. As documented in the extant literature, surgical planning in ectopic testis cases should be based on a detailed physical assessment and meticulous localization, with a view to minimising unnecessary invasive procedures, operative time, costs, and patient morbidity, while optimising anatomical and functional outcomes.[10] A systematic examination is fundamental to the management of patients in whom the testis is not found in the scrotum or inguinal canal, with the aim of excluding perineal and other ectopic locations.

CONCLUSION

Perineal ectopic testis is a rare form of cryptorchidism that poses significant diagnostic challenges due to its atypical localization. This case demonstrates that, despite delayed diagnosis, favourable anatomical and functional outcomes are attainable with accurate localization and appropriate surgical management. Standardised genital examinations in primary care remain essential for the early detection and prevention of long-term complications.

ETHICAL DECLARATIONS

Informed Consent

Informed consent was obtained from the legal guardians of the pediatric patient(s) described in this report. Where developmentally appropriate, assent was also sought from the child. The inclusion of vulnerable populations in this study adhered to national and international ethical guidelines. Extra care was taken to ensure voluntary participation, understanding, and protection of participant dignity and autonomy.

Peer Review Process

This report underwent external peer review.

Conflict of Interest

The authors declare no conflicts of interest.

Financial Disclosure

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Author Contributions

Concept: K.N., T.H.; Design: K.N., T.H.; Control: K.N., T.H.; Resources: K.N., T.H.; Materials: K.N.; Data Collection and/or Processing: K.N.; Analysis and/or Interpretation: K.N.; Literature Review: T.H.; Writing the Article: K.N., T.H.; Critical Review: K.N., T.H.

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Chylous ascites as a diagnostic surprise during inguinal hernia surgery: a case report and review of literature

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ABSTRACT

Chylous ascites is a rare form of ascites characterized by the accumulation of lipid-rich lymphatic fluid in the peritoneal cavity. In children, congenital lymphovascular malformations like cystic lymphangioma and mesenteric cyst are the most common cause. However, its intraoperative detection during elective procedures like inguinal hernia repair is exceedingly rare. We report a case of 5-month-old male infant presented with reducible right inguinal hernia. During elective herniotomy milky white fluid was encountered, suspicious of chylous ascites. Fluid analysis confirmed the diagnosis with triglyceride levels >9500 mg/dl and positive chylomicrons. Subsequent imaging revealed a cystic lesion in the mesentery and the child underwent exploratory laparotomy with complete excision of the lesion and bowel anastomosis. Histopathology confirmed cystic lymphangioma. Postoperatively the child remain stable and tolerated orals well. At one-year follow-up, the child remains asymptomatic and thriving well. This case highlights the importance of maintaining a high index of suspicion for chylous ascites when atypical intra-abdominal fluid is encountered during surgery. Ruptured cystic lymphangioma presenting as chylous ascites encountered during hernia surgery is a very rare phenomena. With prompt evaluation and appropriate surgical management based on the underlying etiology we can achieve excellent outcomes. Reporting such rare intraoperative findings adds valuable insight into the etiological spectrum and surgical management of pediatric chylous ascites.

Keywords: Chylous ascites, cystic, hernia, inguinal, infant, lymphangioma

INTRODUCTION

Extravasation and accumulation of lymphatic fluid in the abdominal cavity is referred as chylous ascites. This fluid collects in the peritoneum either due to leaking lymphatics following trauma or due to obstruction of the lymphatic ducts.[1] Congenital chylous ascites remains the leading cause in pediatric age group and if a cause cannot be found after appropriate diagnostic work up, it is labelled as idiopathic. Congenital lymphatic malformations like cystic lymphangioma and chylolymphatic mesenteric cysts are the most common to cause chylous ascites.[2] Patients may present with a severe cachexic look with muscle wasting, pleural effusions, palpable abdominal masses or hernias of umbilical or inguinal region.[3] Initial management involves drainage of chylous fluid, respiratory support if needed, diet rich in medium chain triglycerides (MCT) with or without total parenteral nutrition (TPN) followed by surgical interventions in cases of failed conservative treatment.[4] Many children with congenital chylous ascites present with abdominal distension, abdominal mass or hernias. These patients are diagnosed in the pre-operative period while evaluating for the abdominal conditions. Rarely, in cases of mild ascites they are diagnosed intra-operatively while operating for inguinal hernias.[5] We have managed a similar case of congenital chylous ascites as surprize during hernia surgery and later it turned out to be cystic lymphangioma on further evaluation. This case report aims to highlight lymphovascular anomaly as the main etiological factor in majority of congenital chylous ascites in infants. Their individualized management strategies emphasizing on surgical resection and a detailed review of literature is discussed.

CASE

A 5 month old boy presented for right sided inguinal swelling. The swelling increased on coughing and crying and reduces on sleep. There was no history of fever vomiting and pain in the swelling. No feeding or respiratory difficulty was there. On examination there was a reducible, non-obstructed right inguinal hernia with palpable bowel loops as contents.

Both the testes were palpable separately and the scrotum was normal. Left side inguinal region was also normal. There was no abdominal distension and tenderness on examination. After baseline work up and pre-anaesthetic fitness, the child was taken up for hernia surgery. During surgery as soon as the hernial sac dissected and opened, there was a gush of milky white peritoneal fluid egressed from deep ring (**Figure 1a, 1b**). Around 100 ml of similar fluid was drained, sent for fluid analysis and herniotomy completed. The patient remained stable in the post-operative period with no obvious abdominal signs and tolerated orals well. Due to personal constraints, the parents took the patient home despite being counselled about the risk of serious complications of chylous ascites and the need for urgent evaluation. The patient returned for assessment after a few days." Ultrasonography was suggestive of moderate ascites with a 30x34x45 mm cystic lesion in the mesentery. Contrast CT abdomen findings were suggestive of a 32x30x48 mm sized mildly enhancing cystic lesion with internal calcifications in left paraumbilical region with ascites (**Figure 2a, 2b**). Chest X-ray was normal. The ascitic fluid (sent intra-operatively during herniotomy) analysis was consistent with chylous ascites (**Table**). Haematological and serum biochemistry parameters were within normal limits. Lymphangiography and lymphoscintigraphy studies were not done due to unavailability in nearby places. So the child was planned for surgical exploration with a working diagnosis of a cystic lesion of lymphovascular origin based on the radiological and laboratory findings. Intra-operatively there was chylous ascites of around 1200 ml with a ruptured cystic lesion of size 35x32x45 mm in the mesentery of small bowel at around 60 cm proximal to IC junction. There were spicules of calcifications in the wall of the cavity and copious amount of lymphatic fluid was leaking from the cyst wall (**Figure 2c**). The cystic lesion was resected along with the corresponding segment of bowel and end to end ileo-ileal anastomosis was done (**Figure 2d**). Post operatively the child remained stable. The abdominal drain output was initially around 200 ml (serous) per day which gradually decreased to less than 10 ml and then removed after 10 days. Histopathology was suggestive of dilated lymphatic channels and lymphoid cell aggregation along with collection of inflammatory cells and areas of hemorrhage diagnostic of cystic lymphangioma (**Figure 3a, 3b**). The child was on regular follow up after discharge from the hospital for the assessment of growth, appetite and abdominal symptoms. At one year follow up the child is symptom free and growing well.

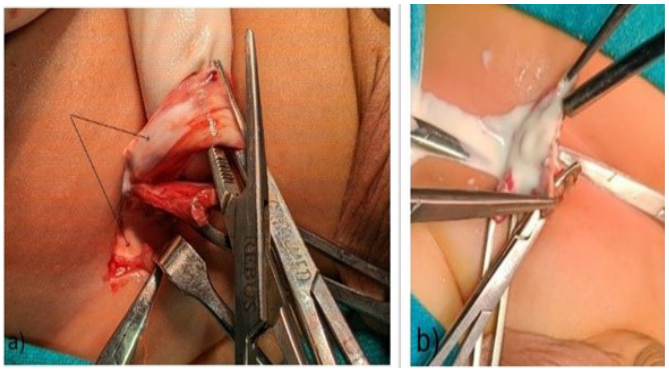

Figure 1. Intraoperative picture of chylous fluid: **a**) within and **b**) outside the hernia sac (black arrows).

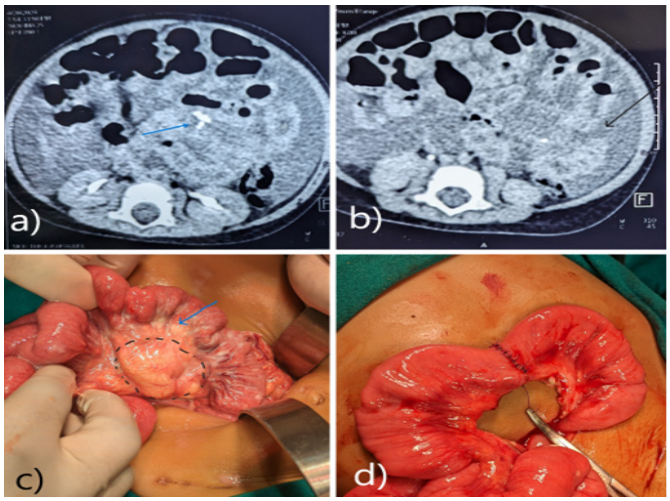

Figure 2. CT images and intraoperative photographs of the cystic lesion with chylous fluid: **a**) Axial CT cut with calcified mass in the mesentery (blue arrow) **b**) CT image with ascites (black arrow). **c**) cystic lymphatic mass in the mesentery and d) Bowel with mesenteric defect after resection and anastomosis.

Table. Peritoneal fluid analysis

Test name	Results	Units
Appearance	Milky white peritoneal fluid for analysis	
Triglycerides	9528.4	mg/dl
Cholesterol	119.44	mg/dl
Chylomicrons	Positive	Negative
Amylase	26.24	U/L
Microscopy	Lymphocytes	N/A
Cytology	Moderately cellular smear showing lymphocytes, neutrophils, mesothelial cells and histiocytes	N/A
ZN stain	Negative for acid fast bacilli	N/A
Culture & sensitivity	Negative for bacterial growth	

U/L: Units per liter, N/A: Not available, ZN stain: Ziehl-neelsen stain

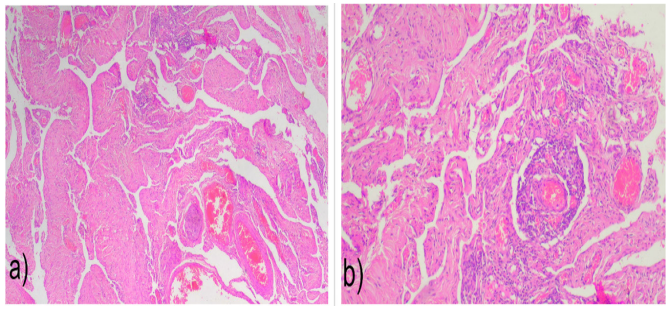

Figure 3. Histopathology (H & E stain) showing **a**) dilated lymphatic channels and cystic spaces with lymphoid aggregates and inflammatory cells (4X). **b**) Proteinaceous and hemorrhagic contents with dilated cystic spaces (10X).

DISCUSSION

Interstitial spaces of the body produce lymphatic fluid which transports nutrients, electrolytes, hormones and pathogen via a unidirectional valved lymphatic system. These vessels take lymph to the lymph nodes containing immune cells to filter the cellular waste, water, proteins and pathogens. Abdominal lymphatics absorb fat from bowel and take the lymph from abdominal organs. They join the lumbar lymphatics to form

the cisterna chyli and drain into venous circulation at the confluence between left subclavian vein and jugular vein. The lymphatic system is a one way drainage system which includes lymph, lymph vessels, lymphatic tissues and bone marrow. Any injury or obstruction to these ducts leads to chylous effusions or chylous ascites depending on the site of obstruction and this is the principle mechanism behind the chylous ascites formation.[6]

Chylous ascites has been reported since 17th century in various forms. Based on lymphangiography studies following causes have been identified.[6]

- Congenital lymphatic anomalies like lymphangioma or lymphatic hypoplasia.
- Cardiac causes such as cardiac failure, dilated cardiomyopathy and pericarditis.
- Infections like tuberculosis, Filariasis and mycobacterium avium.
- Inflammatory conditions like radiation, pancreatitis, retroperitoneal fibrosis and sarcoidosis.
- Gastrointestinal disorders like Malrotation and volvulus.
- Metabolic disorders like tyrosinemia and glycosylation disorders.
- Traumatic abdominal or thoracic injury
- Renal causes like nephrotic syndrome, liver cirrhosis and portal hypertension.
- Post-operative conditions like congenital diaphragmatic hernia, nephrectomy and fundoplication.
- Neoplastic causes like lymphangiomyomatosis and Kaposi's sarcoma.
- Drugs like calcium channel blockers
- Other causes like incarcerated inguinal hernia and obturator hernia.

Chylous ascites presents mostly as vague pain and abdominal distension in more than 90% of the patients. In infants it can present as umbilical or inguinal hernias as in the index case, though very rare. Post-surgical patients with duct injury presents as acute respiratory distress, abdominal distension, edema, cachexia, muscle wasting and effusions.[7]

Laboratory analysis of the chylous fluid is the most confirmatory investigation for the diagnosis of chylous ascites. The fluid is analysed for the cell count, gram stain, triglyceride levels, total protein, albumin, bacteria, culture, lactate dehydrogenase (LDH), amylase and glucose.[8] Chylous fluid has triglyceride levels higher than 110 mg/dl as mentioned by a few authors however, they are mostly above 200 mg/dl.[7] Our patient had triglycerides levels near 10,000 mg/dl (Table), suggesting the fluid to be chyle only.

Contrast CT scan can easily pick up and localize lymphatic mass/malformations, type of fluid (blood/ascites), thoracic duct injury and other calcified lesions if any.[7] We have done a contrast CT abdomen and found an enhancing lesion with internal calcifications in mesentery and gross ascites.

Lymphangiography is the gold-standard diagnostic modality for assessing lymphatic anatomy, locating sites of leakage or obstruction, and evaluating the retroperitoneal lymph nodes and thoracic duct. However, because it is invasive and carries risks such as hypersensitivity reactions, fat embolism, and tissue necrosis, it is increasingly being replaced by non-invasive investigations.[9] In infants with congenital lymphatic malformations, it helps distinguish between lymphatic hypoplasia, aplasia, and localize leakage. The study involves subcutaneous injection of a radiolabeled tracer (commonly Tc-99m sulphur colloid), followed by serial imaging to trace lymphatic drainage. When combined with MR lymphangiography, lymphoscintigraphy offers complementary physiologic information, aiding in accurate diagnosis and guiding surgical or interventional management. It is also used in the post-operative period to assess the effectiveness of a lymphatic bypass or thoracic duct ligation. Lymphoscintigraphy is used when lymphangiography is contraindicated to assess the lymphatic drainage and functional assessment. Although it has no specific contraindications but, it is still not used frequently due to technical challenges involved in small children.[10]

Diagnostic laparoscopy is reserved for patients with no definitive cause identified and suspicion of malignancy and tuberculosis. In post-operative patients sometimes exploratory laparotomy is required to diagnose and treat the underlying cause. It is also combined with lymphangiography intra-operatively to properly delineate lymphatic anatomy.[8]

Management of chylous ascites involves multimodality treatment involving nutritional specialist, pharmacotherapies and surgical management. In patients with an identifiable cause, treatment of primary condition is the mainstay of treatment. All the medical management strategies are based on decreasing chyle flow by bowel rest, TPN, replacing electrolytes and micronutrients. This resolves chylous ascites in majority of the patients.[11]

Dietary modifications include high protein diet enriched with MCT and restriction of long chain triglycerides (LCT). MCTs are absorbed from intestines and transported directly into liver as free fatty acids and glycerol, preventing both production and flow of chyle. Patients not responding to these measures require bowel rest and TPN.[10] Along with TPN, Somatostatin analogue octreotide has been found very effective in rapidly reducing the chylous ascites, probably by inhibition of lymph secretion from lymphatic vessels.[12] Transjugular intrahepatic portosystemic shunt (TIPS) is used in cirrhotic patients with end stage liver disease however, it has not been approved in children.[13] Peritoneovenous shunts were used in past as a rescue therapy for patients not responding to medical management and not fit for surgery.[14] Angiographic embolization is also used for resistant chylous ascites as an effective method.[15] Chylous ascites of congenital causes, neoplastic etiology or post-operative origin may need

surgical exploration however, operative interventions are not without complications.

There are a few published reports in literature on chylous ascites in infants and their management. Causes of chylous ascites in infants are mainly congenital lymphovascular disorders, incarcerated hernias, intestinal malrotation with volvulus, liver disease and thoracic duct atresia. Sometimes the ascites presents as a diagnostic surprize during hernia surgery in a previously asymptomatic child as in index case.[6]

Alnee et al.[1] in 2011, managed a similar case of chylous ascites presented with abdominal distension and bilateral inguinal hernias by repeated paracentesis and conservative management.

In 2021, Dreuning et al.[6] concluded that the chylous ascites in an infant with inguinal hernia can be due to mechanical compression of lymphatics during repeated incarceration and attempted manual reduction of contents if no other cause found on further work up. This can be managed very well with MCT diet and conservative approach.

Siddiqui et al.[16] also managed similar case with conservative approach in an infant with chylous ascites presenting with bilateral inguinal and umbilical hernia. However, they could managed to get lymphoscintigraphy done and identified the cause of chylous ascites as leak from retroperitoneal lymphatics.

Albaghdady et al.[17] published a series of four infants with chylous ascites managed by surgical interventions combined with medical management. Surgical interventions included resection of chylolymphatic cyst, resection of omental cyst and placement of peritoneovenous shunts.

Presence of calcification is another significant finding seen rarely. The differential diagnoses for calcified cystic lesion of mesentery include teratoma, meconium peritonitis cyst, dermoid cyst, hydatid cyst, pseudocyst and calcified hematoma. To the best of our knowledge only four cases of calcification in cystic lymphangioma are reported and they were managed by surgical excision. Exact etiology for the calcifications is not clear however, there is a possibility that presence of the lesion from the intrauterine life and chronic inflammation could have led to calcium deposition in the walls of the lesion.[18]

It is evident from above discussion that most of the neonates with chylous ascites responds well to medical management and very rarely surgical exploration is needed. Those who need operative treatment are the cases of either active lymphatic leak or radiologically proven lymphovascular malformations. Resection of congenital mass and involved part of bowel as in index case, closure of chyle leak and repair of retroperitoneal lymphatic fistulas are few surgical procedures used with good outcomes. Sometimes other modalities like angiographic embolization, fibrin glue peritoneovenous shunts and use of etilefrine might need to be utilized in failed surgical explorations.[9] However chylous ascites diagnosed unexpectedly during hernia surgery in an asymptomatic child is very rare. In our patient surgical intervention combined with medical management were successful in controlling the chylous ascites effectively over a period of two weeks. The uniqueness of this case lies in the rarity of the diagnosis and its incidental detection during a commonly performed procedure in an infant.

CONCLUSION

This case illustrates the importance of intraoperative awareness and rapid diagnostic evaluation when faced with atypical findings during routine procedures like herniotomy. Although chylous ascites is often associated with serious underlying conditions, it may occasionally present in otherwise asymptomatic infants, as in our case. Conservative management remains the first-line approach, with favourable outcomes in idiopathic or postoperative cases. A few might need further evaluation and surgical intervention. In infants with ruptured cystic lymphangioma, complete resection of the lesion with restoration of intestinal continuity provides the best therapeutic results and is associated with good postoperative outcomes. Reporting such rare presentations enhances our understanding and preparedness for unexpected intraoperative challenges in pediatric surgical care.

ETHICAL DECLARATIONS

Informed Consent

Informed consent was obtained from the legal guardians of the pediatric patient(s) described in this report. Where developmentally appropriate, assent was also sought from the child. The inclusion of vulnerable populations in this study adhered to national and international ethical guidelines. Extra care was taken to ensure voluntary participation, understanding, and protection of participant dignity and autonomy.

Peer Review Process

This manuscript was subject to external peer review.

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Financial Disclosure

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Author Contributions

The author is solely responsible for the conception, data collection, analysis, and writing of this manuscript.

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MHA MEDIHEALTH ACADEMY

Surgery on Children

Letter to the Editor

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Emerging advances in the utility of gabapentinoids for postoperative pain management

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Dear Editor,

Gabapentinoids have become increasingly integrated into multimodal perioperative analgesia, driven by evidence suggesting their ability to attenuate central sensitization, reduce postoperative hyperalgesia and limit opioid use. However, despite their widespread application in adults, the role of gabapentinoids in pediatric perioperative pain management remains insufficiently defined. This letter aims to summarize recent developments and persisting uncertainties regarding gabapentinoid use in children.

Although the U.S. Food and Drug Administration has not approved gabapentinoids for pediatric pain indications, their off-label use continues to rise. A tertiary children's hospital reported a 1.3 fold increase in pregabalin prescriptions between 2013 and 2019, with indications including musculoskeletal pain, neuropathic pain, visceral pain, and headaches.[1] This trend reflects growing clinical interest, despite the absence of robust pediatric-specific efficacy data.

Pharmacokinetic analyses demonstrate that children clear pregabalin more rapidly than adults, supporting weight-based dosing regimens. Current guidance recommends 2.5-10 mg/kg/day for children aged 4-16 years weighing ≥30 kg, and 3.5-14 mg/kg/day for those <30 kg, with renal elimination necessitating individualized dosing for impaired renal function.[2] These pharmacologic considerations are reinforced by phase 1 data describing predictable pharmacokinetics and acceptable tolerability in children, with sedation and dizziness being the most commonly observed adverse effects.[3]

Evidence evaluating perioperative use in children is emerging but limited. Randomized controlled trials indicate that preoperative pregabalin may reduce emergence agitation and early postoperative analgesic needs following sevoflurane anesthesia. In pediatric oncology, small cohorts report improvements in vincristine-induced neuropathic pain and reductions in opiod consumption after pregabalin initiation.[4] These findings align with adult data, where systematic reviews demonstrate modest reduction in oipoid requirements and early postoperative pain. However, concerns surrounding sedation, respiratory depression and variable clinical benefit persist, underscoring the need for cautious interpretation.

Beyond chronic pain management, pregabalin has shown potential value in perioperative settings. Marouf reported that preoperative pregabalin administration significantly reduced emergence agitation in children undergoing sevoflurane anesthesia, suggesting a role in modifying postoperative behavioral responses.[5] Although promising, these findings require confirmation in larger studies to establish optimal dosing and evaluate potential interactions with anesthetic agents.

Collectively, these studies highlight both the potential and the limitations of pregabalin use in children. Although emerging evidence supports its role in selected indications, variability in outcome assessments, limited sample sizes, and the scarcity of large, well-designed trials continue to hinder evidence-based clinical decision-making. Taken together, current evidence indicates that gabapentinoids hold promise for perioperative analgesia, particularly through mechanisms that reduce central sensitization and opioid burden. However, the variability in clinical responses, limited specific randomized data in children, and safety concerns in vulnerable populations necessitate a cautious, evidence driven approach. Priorities for the field should include multicenter randomized trials in pediatric surgical cohorts, standardized pain phenotyping, validated pediatric outcome instruments, and careful evaluation of respiratory and neurocognitive safety endpoints.

ETHICAL DECLARATIONS

Peer Review Process

This letter was externally peer-reviewed.

Conflict of Interest

The authors declare no conflicts of interest.

Financial Disclosure

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Author Contributions

The author is solely responsible for the conception, data collection, analysis, and writing of this manuscript.

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MHA MEDIHEALTH ACADEMY

Surgery on Children

Erratum

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Erratum to "Surgical results in cases of osteoid osteoma: a single-center retrospective study"

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It has been noticed that the figure numbers on page 3 of the original published article are incorrectly numbered. We request that the text "Figure 4" be completely removed and that "Figure 5" be corrected to "Figure 4". There is no change in the number of figures. This correction does not affect the content or results of the article. The authors apologize for this error.

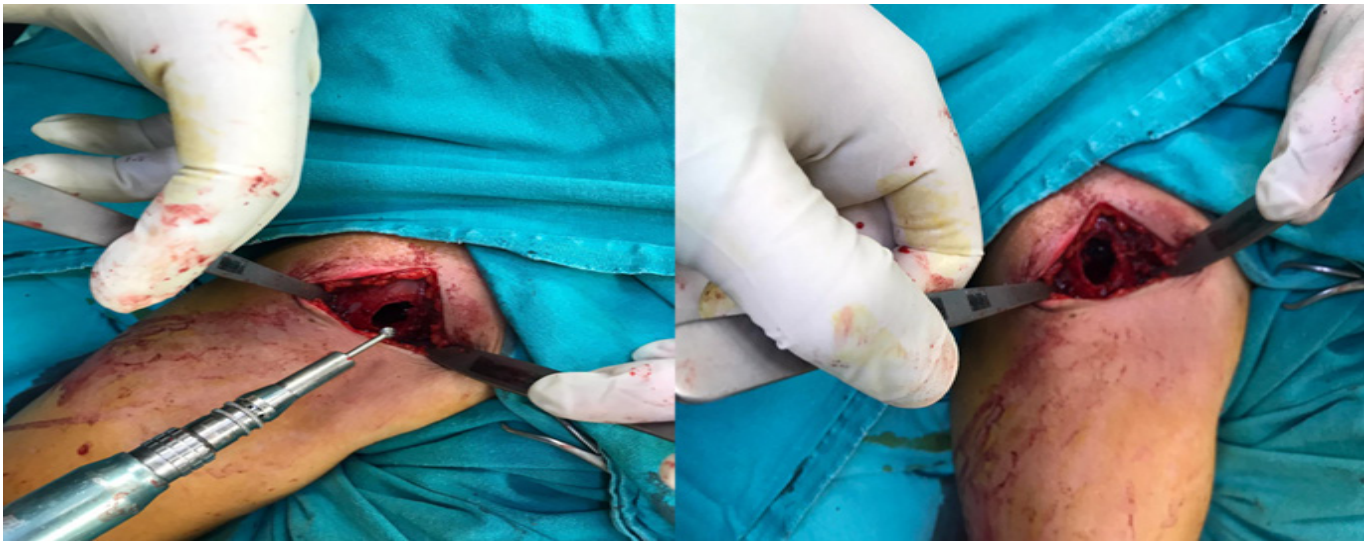

Figure 4. Burr-down-assisted intralesional curettage method in osteoid osteoma surgery

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