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Pó para solução oral

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RESTABELECE O EQUILÍBRIO ELECTROLÍTICO

CRIANÇAS

200ml
(após cada dejecção)
1 Saqueta

ADULTOS e IDOSOS

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(após cada dejecção)
1 a 2 Saquetas

LACTENTES

150ml/Kg peso
O conteúdo de cada saqueta deve ser dissolvido em 200ml de água potável

Regime sugerido para o tratamento da diarreia infantil, baseado no peso corporal em Kg.

Dia	Volume da solução de Dioralyte (ml)	Volume total em 24 h (ml)
1	150 ml x kg de peso	150 ml x kg de peso
2	120 ml x kg de peso	
3	90 ml x kg de peso	
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INFORMAÇÕES ESSENCIAIS COMPATÍVEIS COM O RESUMO DAS CARACTERÍSTICAS DO MEDICAMENTO. DENOMINAÇÃO DO MEDICAMENTO: Dioralyte, pó para solução oral. **COMPOSIÇÃO QUALITATIVA E QUANTITATIVA: Substâncias activas** g/saqueta: Glicose 3,56; Cloreto de sódio 0,47; Cloreto de potássio 0,30; Citrato dissódico 0,53. **INDICAÇÕES TERAPÊUTICAS:** Correcção da perda de líquidos e electrólitos nos lactentes, crianças e adultos. Tratamento da diarreia aquosa de várias etiologias, incluindo as gastrenterites, em todos os grupos etários. **POSOLOGIA E MODO DE ADMINISTRAÇÃO:** Cada saqueta deve ser sempre dissolvida em 200 ml de água. O volume de Dioralyte reconstituído a tomar deve ser decidido pelo médico assistente, tendo em consideração o peso do doente e o estado e gravidade da situação. Um princípio básico no tratamento da diarreia é a substituição da perda de líquidos e a manutenção de uma ingestão de líquidos suficiente para repor a sua perda nas fezes. A ingestão diária deve ser baseada num volume de 150 ml/Kg de peso nos lactentes e 20–40 ml/Kg de peso nos adultos e crianças. Uma aproximação razoável é a seguinte: -lactentes – 1 a 1,5 vezes o volume alimentar habitual; - crianças – 1 saqueta após cada dejecção diarreica; - adultos – 1 ou 2 saquetas após cada dejecção diarreica. Inicialmente, podem ser necessárias maiores quantidades de Dioralyte para assegurar uma reposição precoce do equilíbrio hidro-electrolítico. Nos estadios iniciais do tratamento da diarreia, todos os alimentos, incluindo o leite de vaca e o leite artificial, devem ser interrompidos. Não se deve no entanto interromper o aleitamento materno. Nas crianças amamentadas sugere-se que se dê à criança o mesmo volume de Dioralyte do que o da alimentação normal, seguindo-se o aleitamento. Pode ser necessário, durante este período, a expressão do leite residual da mama. Após 24-48 horas, quando os sintomas desaparecerem, a dieta normal deve ser retomada gradualmente para evitar o agravamento da situação. O regime sugerido para o tratamento da diarreia infantil grave baseado no peso corporal em Kg é apresentado no quadro anterior. Quando a diarreia é acompanhada de vómitos, sugere-se ingestão frequente de pequenas quantidades de Dioralyte. No entanto, é importante que seja tomado o volume total necessário de Dioralyte. Quando o funcionamento dos rins é normal torna-se difícil superhidratar por via oral e quando existem dúvidas acerca da dosagem correcta, mais vale tomar a mais do que a menos. **CONTRA-INDICAÇÕES:** Não se conhecem contra-indicações ao Dioralyte. No entanto, existem algumas situações em que o tratamento com Dioralyte é inapropriado, tais como por exemplo, situações de oclusão intestinal requerendo intervenção cirúrgica, ou em caso de vómitos persistentes e desidratação grave ou diarreia infantil grave em que será necessária uma terapêutica por via intravenosa. **ADVERTÊNCIAS E PRECAUÇÕES ESPECIAIS DE UTILIZAÇÃO:** O Dioralyte só deve ser reconstituído com água. Cada saqueta deve ser sempre reconstituída em 200 ml de água. Uma solução mais fraca do que a recomendada não contém a concentração óptima de glicose e electrólitos e uma solução mais forte do que a recomendada pode provocar desequilíbrio electrolítico. Se a diarreia não melhorar rapidamente, os doentes deverão ser reavaliados. Nos idosos, a administração de soluções contendo glucose e electrólitos deve ser cuidadosa em caso de alterações renais ou hepáticas graves ou em outras situações em que o balanço electrolítico normal se encontre alterado. Nos lactentes, deve interromper-se durante 24 horas a alimentação com leite de vaca ou leite artificial, que deverão ser reintroduzidos gradualmente quando a diarreia tiver diminuído. Não se deve interromper o aleitamento materno. **EFEITOS INDESEJÁVEIS:** Podem ocorrer náuseas ou vómitos após a administração da solução, em particular quando esta é ingerida com demasiada rapidez. Estão também descritos casos isolados de desconforto abdominal e de obstipação.Data da revisão do texto: Janeiro de 2004.**TITULAR DA AUTORIZAÇÃO DE INTRODUÇÃO NO MERCADO: KORANGI - Produtos Farmacêuticos, Lda. Medicamento não sujeito a receita médica. Para mais informações contactar o Titular da Autorização de Introdução no Mercado**

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EDITORIAL

Beyond pain and death: incorporating humanization into pediatric care

Para além da dor e da morte: integrando a humanização no cuidado pediátrico

Cândida Cancelinha

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Few experiences challenge pediatric professionals more deeply than witnessing a child's pain or death. Both moments reveal the limits of biomedical intervention and the true essence of care. They remind us that pediatrics is not only about curing disease, but essentially about relieving suffering and accompanying families through the most vulnerable period of life.

In this issue, two original studies bring these dimensions into focus. One explores the perceptions and experiences of healthcare providers facing pediatric death in a level II Portuguese hospital[1]. The other analyzes professionals' knowledge and practices regarding pain assessment in children[2]. Together, they complement the same perspective: the need for competence and compassion for those who deal with suffering in childhood.

The study by Costa et al. reveals the profound personal and professional impact of pediatric death on healthcare teams. Although death in childhood is rare, 82% of respondents had faced it, mostly in emergency contexts. Sadness and compassion were the most commonly reported emotions, transcending professional experience. Yet the study also uncovers important fragilities: younger professionals reported more anxiety and sleep disturbance; few had received specific training in palliative or bereavement care; and there were no structured debriefing protocols after a child's death. The findings echo what many pediatricians intuitively know, that behind the clinical assessment lies an emotional background that often remains unmentioned and unsupported[3].

Saraiva et al. address a different dimension of pediatric suffering: pain. Their survey, conducted in another Portuguese hospital, shows encouraging levels of theoretical knowledge and confidence among doctors and nurses. However, important gaps persist, particularly in the use of pain scales for younger children and in the safe use of opioids. The study also highlights a discrepancy between recognition and treatment: while most professionals felt pain was often identified, only two-thirds believed it was well treated, which is also confirmed by other international studies[4]. Nurses tended to use non-pharmacological strategies more consistently than physicians, and both groups expressed the need for continuous education. These findings mirror international data showing that, despite advances, one in three hospitalized children still experiences moderate or severe pain[5,6].

These two studies are not about exceptional moments – they are about everyday pediatric hospital care. Pain and death are part of the same continuum of human experience, and both require a multidimensional approach that conjugates clinical expertise with emotional intelligence, communication competence, and ethical reflection.

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Pediatric Palliative Care (PPC) embodies this integration. It is never too much to reinforce that PPC is not constrained to the final days of life, but that it begins at diagnosis and accompanies the child and family throughout the course of the illness, seeking to relieve suffering in all its forms[7].

In Portugal, the development of PPC has made significant progress in recent years, with growing awareness, training initiatives, and the creation of specialized and generalist teams within the National Palliative Care Network. Yet the findings of these two articles remind us that the principles of palliative care – effective pain control (as well as the control of other complex symptoms), emotional support, and reflection on loss – must extend beyond these teams to all pediatric care environments. Every pediatrician, nurse, and allied professional should feel prepared to recognize pain, to communicate difficult news, and to support both families and colleagues in times of loss.

Moving forward, three key priorities stand out. First, education: incorporating PPC, communication skills, and grief support into undergraduate and postgraduate pediatric training. These must be core, not optional competencies[8].

Second, institutions should provide spaces for structured debriefing and peer support, which is still far from reality in many hospitals. Acknowledging the emotional impact of pediatric work is an essential component of institutional humanization – caring for healthcare providers as an institutional responsibility[3].

Third, continuity of care: ensuring that pain management, symptom control, and psychosocial support are consistent across hospital, home, and community settings. In complex or prolonged conditions, early referral to specialized PPC teams should be standard practice – allowing shared care, coordinated support, and the prevention of avoidable suffering for children, families, and professionals[7,9].

Ultimately, both studies point to a common message: compassion must be intentional. It requires knowledge, teamwork, and reflection. It also requires caring for those who care – recognizing that the well-being of professionals is inseparable from the quality of care offered to children and families.

Humanization, in this sense, is not an abstract principle, but a daily practice, expressed in how we listen, comfort, and remain present. As pediatricians, we cannot always prevent pain or death, but we can ensure that neither occurs without presence and dedication. By acknowledging children's suffering, we honor the true essence of pediatrics: to always care, even when we cannot cure.

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ORIGINAL ARTICLE

Cross-sectional study: healthcare professionals' perspective on pediatric pain assessment and management

Bárbara Martins Saraiva[1], Inês Gomes[2], Rita Marques[2], Marta Almeida[2], Cristina Esteves[2], Cristina Ferreira[2], and Filipa Nunes[2]*

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Abstract

Introduction and Objectives: Pain is recognized as the fifth vital sign. Although guidelines on pain have increased greatly, two thirds of hospitalized children report experiencing uncontrolled pain. Our goal was to evaluate the knowledge of a pediatric healthcare team on pain assessment/management in all pediatric sectors. **Methods:** Cross-sectional study among doctors and nurses of all pediatric departments in a secondary hospital, July 2022. Statistical significance was analyzed concerning "career type" and "years of experience." Statistically significant p values were < 0.05. **Results:** A total of 81 out of 122 (66%) professionals answered (42% doctors; 58% nurses). Of these, 48% worked in the emergency department and 24% in intensive care. The median score was 12 out of 14 (86%) questions on a survey. Questions with lower scores concerned opioids. A total of 77% reported using pain assessment scales "often/always": 75% named the appropriate scale for children aged four to six/over six, but only 44% could identify that for children under four years of age. Nurses use scales more frequently ($p < 0.05$). One third of those surveyed believed pain was only "sometimes" well treated. Three quarters used non-pharmacological interventions regularly, especially nurses ($p = 0.01$). Participants were highly confident using morphine (78%), fentanyl (69%), and ketamine (63%). Experienced doctors were more confident ($p = 0.001$). The most commonly chosen for mild, moderate, and severe pain were paracetamol/ibuprofen, ketorolac/tramadol, and fentanyl/ketamine, respectively, in accordance with current guidelines. **Discussion:** Theoretical knowledge was satisfactory; however, opioid training must be prioritized. There is a lack of experience with the application of scales for evaluating pain in children under four years of age. High levels of experience were noted in sedoanalgesia. Constant training is needed to guarantee professionals are highly experienced and to ensure the best treatment and care.

Keywords: Pediatric pain. Sedoanalgesia. Pain assessment. Pain awareness. Professionals' perspective. Hospital survey.

Estudo transversal: perspectiva dos profissionais de saúde sobre a avaliação e o manejo da dor pediátrica

Resumo

Introdução e Objetivos: A dor é o quinto sinal vital. Embora a evidência em abordagem da dor tenha aumentado, 2/3 das crianças hospitalizadas refere dor não controlada. Pretendemos avaliar o conhecimento e experiência dos profissionais na abordagem/tratamento da dor pediátrica nos vários departamentos. **Métodos:** Estudo transversal, incluindo médicos e

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enfermeiros de todos os departamentos de pediatria, num hospital secundário (julho de 2022). Análise estatística com foco na "profissão" ou "anos de experiência". P *value* estatisticamente significativo < 0,05. **Resultados:** 81/122 (66%) profissionais participaram (42% médicos; 58% enfermeiros). 48% trabalham em urgência e 24% em cuidados intensivos. Num questionário teórico, a mediana de resultados foi 12 em 14 (86%) questões. Questões sobre opióides obtiveram resultados inferiores. 77% referiram usar escalas de dor "frequentemente/sempre": 75% assinalou a correta para crianças com idades de "4-6"/ "> 6" e 44% para "< 4" anos. Enfermeiros usam escalas mais frequentemente (p < 0,05). Um terço dos inquiridos considerou que a dor era "às vezes" tratada. 3/4 utiliza medidas não farmacológicas, maioritariamente enfermeiros (p = 0,01). Os participantes mostraram-se confiantes na utilização de morfina (78%), fentanil (69%) e cetamina (63%). Médicos seniores referiram maior confiança (p = 0,001). Os fármacos escolhidos para tratamento da dor ligeira, moderada e grave foram, respetivamente: paracetamol/ibuprofeno; cetorolac/tramadol; fentanil/cetamina – de acordo com a literatura recente. **Discussão:** O conhecimento teórico revelou-se satisfatório, sendo necessário desmistificar o receio dos opióides. Observou-se menos conhecimento na utilização de escalas para avaliação da dor em idades < 4 anos. Observou-se elevada confiança em sedoanalgesia. O treino constante dos profissionais é essencial para garantir melhor reconhecimento e tratamento da dor.

Palavras-chave: Dor pediátrica. Sedoanalgesia. Reconhecimento da dor. Alerta/sensibilização para a dor pediátrica. Perspetiva dos profissionais. Questionário hospitalar.

Keypoints

What is known
- Very few surveys have analyzed professionals' perspectives and current practices in pediatric pain management, often excluding doctors.
- Despite training in objective pain assessment, it is unclear if methods chosen by professionals are age-appropriate in practice.
- Pediatric pain evidence is advancing rapidly, yet it remains uncertain whether current practices and knowledge adequately reflect this progress.

What is added
- Building on nurses' practices, doctors should enhance care by integrating non-pharmacological interventions and consistently applying pain assessment scales.
- Professionals demonstrate high confidence in sedoanalgesia management, likely reflecting the team's commitment to regular training and staying current.
- Analgesia choices for each pain level align with literature; prioritizing training in pain assessment and safe opioid management remains essential.

Background

Pain is defined as an unpleasant sensory and emotional experience associated with potential tissue damage[1]. It is one of the most common complaints reported by hospitalized patients and one of the main reasons for seeking medical help[2]. It has been recognized as the fifth vital sign for almost 30 years[3], and an increasing volume of scientific research on its routine assessment has been published[1].

Pain is a subjective symptom and must be identified, localized, quantified, and reassessed[4-6]. Children's pain is often not recognized[6,7], although it is known to have harmful physiological effects, including in newborns' brain development[8,9]. The inability to communicate verbally may exclude children from appropriate pain-relieving treatment, especially infants, neonates, and children with cognitive impairment[4,6,9,10]. Although there is no universal tool, there are several pain assessment scales which consider children's particularities and must be used accordingly[6,11,12]. Therefore, children often depend on well-trained care-providing teams to make an accurate pain evaluation and to decide on the appropriate interventions[12-15].

Pain can be a symptom but also a consequence of medical procedures. Preventing and monitoring pain is crucial, mainly in emergency departments and intensive care units[13,16,17]. Several protocols and guidelines have been published nationally and internationally[5,16-23]. It is known that an integrated approach using both pharmacological and non-pharmacological interventions increases the effectiveness of pain relief. This is displayed in current protocols of sedoanalgesia, including those for urgent procedures[5,13,16,17,22,23].

Assessment of health professionals' awareness of patients' pain has exposed serious discrepancies in practitioners' training and clinical practices[9,15,24]. Moreover, two thirds of hospitalized children still report uncontrolled pain at some point in their admission[25-27]. Although only a few enquiries have been carried out to analyze professionals' perspectives and current practices, they have shown that there are gaps in clinical knowledge and that protocols are not always followed. Since, after educational interventions, changes were

observed in both doctors' and nurses' practices, more research and investment into formal training shall be provided[1,9,24].

Fifteen years ago, a small survey was conducted in our department to promote awareness of pain and its management in pediatrics and the need for training (*data not published).* The main goal of the present study is to evaluate the current theoretical knowledge and practical experience in pain assessment and treatment of doctors and nurses working in a pediatric department of a level II hospital. It is our aim to assess the professionals' level of expertise in non-pharmacological and pharmacological interventions in sedoanalgesia, as well as their perspectives on the current pain management approach in their departments.

Material and methods

Study population

Cross-sectional study among doctors and nurses working in the pediatric department of a secondary hospital, in July 2022, including the inpatient ward (IW), emergency department (ED), outpatient clinic (OC), and neonatal and pediatric intensive care unit (NPICU).

Data collection

A survey was developed and divided into the following fields: "demographic and professional data"; "theoretical knowledge evaluation: myths on pain management in children"; "pain assessment and evaluation"; "non-pharmacological interventions"; and "pharmacological interventions and sedoanalgesia". The survey included 14 closed questions (one true or false, seven multiple-choice, and six ranking questions), and three open-ended questions. It was filled in voluntarily and anonymously by all participants.

Statistical analysis

Descriptive analysis was carried out. Data from the six ranking questions was presented using five-point Likert scale charts (Figs. 1 and 3). A chi-square test, Fisher's exact probability test, and T-test were used to study relationships between independent variables while Mann-Whitney and Kruskal-Wallis tests analyzed dependent variables. If samples had a dimension higher than 30, a normal distribution was accepted according to the central limit theorem. Homogeneity of variances was analyzed with Levene's test.

The statistical significance was analyzed concerning the type of career (doctors versus nurses) and several variables: scores achieved in the theoretical knowledge evaluation; number of non-pharmacological interventions mentioned (student's t-distribution); perspective on pain recognition and treatment in their department; levels of confidence using sedoanalgesia drugs (Mann-Whitney U test); choice of method to evaluate pain; and practices concerning a eutectic mixture of local anesthetics - lidocaine/prilocaine (EMLA®) (chi-square test, Fisher's exact probability test). The same variables were also studied regarding the years of experience of both doctors and nurses, separately: scores achieved in the theoretical knowledge evaluation; perspective on pain recognition and treatment in the department; number of non-pharmacological interventions mentioned; levels of confidence managing sedoanalgesia drugs (Kruskal Wallis tests and Mann-Whitney U test); choice of method to evaluate pain; and EMLA® practices (chi-square test, Fisher's test). P values of < 0.05 were considered statistically significant.

All the analysis was done using the *Statistical Package for the Social Sciences* (SPSS) 28®.

Study definitions

Pain assessment scales: valid tools recognized to be effective in assessing acute pain. All share a common numeric scale relying on the clinical observation of a child (physiological and behavior scales) or on children's self-report, according to age and cognitive development[11].

Non-pharmacological interventions: actions used as a complement to analgesic drugs to reduce pain perception and anxiety associated with painful procedures[17-19].

Pharmacological interventions: analgesics that can be administered in mild, moderate, or severe pain.

Sedoanalgesia: integration of both analgesics and sedatives to achieve a reduction in severe pain and a decrease in the level of consciousness and perception, maintaining stable vital signs and a patent airway[17-19].

Results

Demographic data and professional experience

Eighty-one (81/122; 66%) answers were obtained anonymously from doctors and nurses of a pediatric department in a secondary hospital. Among them, 42%

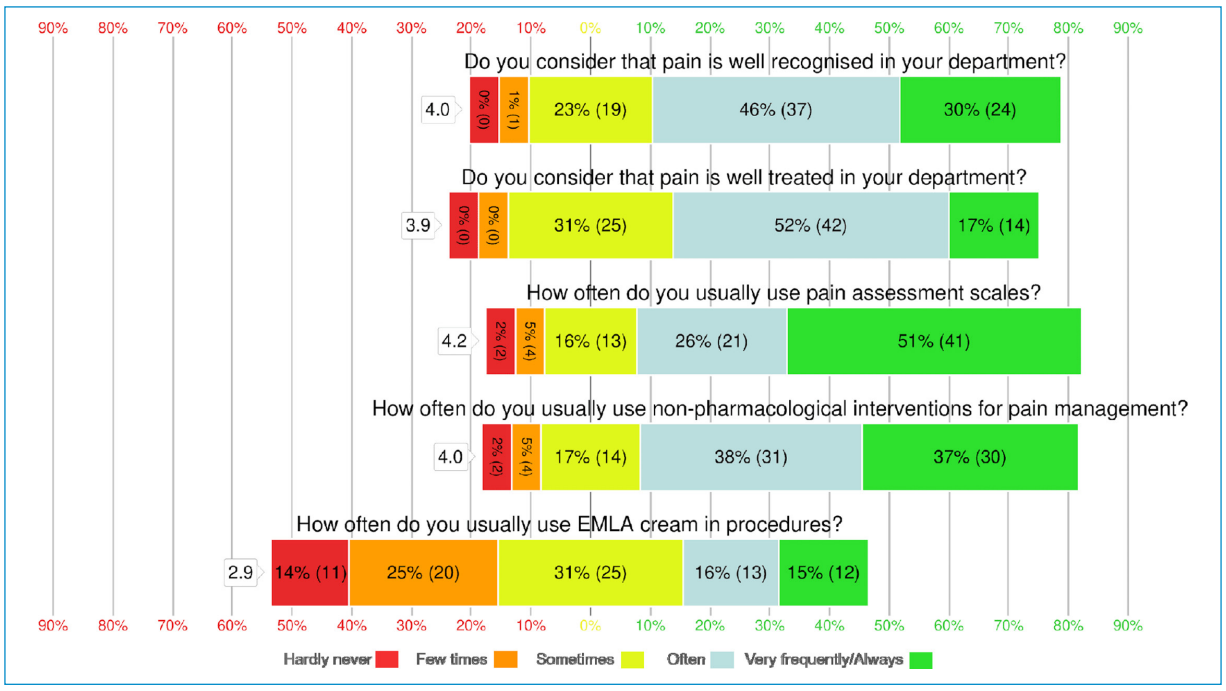

Figure 1. Healthcare workers' perspective on pediatric pain recognition, assessment, and management in day-to-day routines. Five-point Likert scale (1: Hardly ever; 2: Rarely; 3: Sometimes; 4: Often; 5: Very frequently/Always) chart showing the opinion of healthcare workers on the effectiveness of pain recognition and treatment in their workplace, as well as how frequently pain assessment scales are used to quantify pain, non-pharmacological interventions, and EMLA® cream in day-to-day work routines.

were doctors and 58% were nurses, with a female:male ratio of 7:1. They were distributed across several departments and most of them worked in more than one department: 48% in the ED (either as a permanent team or working ED shifts); 40% in the IW; 30% in the OC; and 24% in the NPICU. Regarding their professional experience, 44% had more than 20 years of service and a quarter had started their professional activity in the last five years. Specifically, 62% of the nurses had more than 20 years of professional experience, but 41% of the doctors were junior doctors (< 5 years) (Table 1).

Theory knowledge evaluation

The survey contained one true or false question, with 14 statements, to evaluate basic theoretical knowledge in pediatric pain management. The median of correct answers was 12 out of 14 (86%) with a minimum score of 8/14 (57%) and a maximum of 14/14 (100%). The percentages of respondents who classified each statement correctly can be seen in table 2. All participants correctly classified phrase number six as false (*"Infants feel less pain compared to adolescents"*). The sentences with the least correct answers were numbers eight, 10 and 11, all concerning the features of opioid drugs. Among these, the statement with the lowest percentage of correct answers (54%) was number eight. *("Fentanyl is 100 times more potent than morphine").* Concerning the final scores, no statistical differences were found either between doctors and nurses, or across the years of professional experience ($p > 0.05$).

Pain recognition, assessment, and evaluation in children

Healthcare workers were first questioned about their perspective on the current pathway in pediatric pain management followed in their department. As seen in figure 1, 76% believed that pain was "often" or "always" well recognized and 69% believed it was "often" or "always" well treated, in their workplace. Almost one third of the surveyed professionals considered pain to be "sometimes" well treated. Tendentially, pain was therefore considered to be better recognized than treated. On statistical analysis, this tendency was predominantly observed amongst doctors, when compared to nurses, although with no statistical significance ($p > 0.05$). Among doctors, it was statistically significant that doctors with more than five years of experience considered pain to be well recognized more often than

Table 1. Demographic data and professional experience

Variables	Doctors n (%)	Nurses n (%)	Total n (%)
	34 (42%)	47 (58%)	81 (100%)
Gender			
Female	28 (82%)	43 (91%)	71 (88%)
Male	6 (18%)	4 (9%)	10 (12%)
Professional experience (years)			
< 5	14 (41%)	5 (11%)	19 (23%)
5-10	8 (23%)	3 (6%)	11 (13%)
10-20	5 (15%)	10 (21%)	15 (19%)
> 20	7 (21%)	29 (62%)	36 (44%)
Pediatric department division*			
ED	23 (68%)	16 (34%)	39 (48%)
NPICU	8 (24%	23 (68%)	19 (24%)
OC	20 (59%)	7 (15%)	27 (33%)
IW	27 (50%)	15 (32%)	32 (40%)

*The total value is more than 81 (100%) as several worked in more than one department section.
ED: emergency department; IW: inpatient ward; NPICU: neonatal and pediatric intensive care unit; OC: outpatient clinic.

Table 2. True or false questions on theoretical knowledge and respective scores per statement

Questions	Scores (%)
1. Pain is felt with less intensity by premature infants due to their immature pain processing pathways. (F)	99
2. Pain assessment scales are useful even in emergency situations. (T)	95
3. Repeated exposure to painful procedures promotes tolerability. (F)	98
4. Drugs should be administered via the least invasive route. (T)	85
5. If analgesic medication is used, non-pharmacological interventions are not needed. (F)	98
6. Infants feel less pain compared to adolescents. (F)	100
7. Midazolam is an analgesic drug. (F)	98
8. Fentanyl is 100 times more potent than morphine. (T)	54
9. Opioids should be avoided due to the risk of drug dependence. (F)	84
10. Respiratory depression associated with morphine is a rare side effect. (T)	67
11. Neuropathic pain has a good response to opioids. (F)	58
12. EMONO is recommended for use in mild to moderate painful short procedures. (T)	91
13. Analgesics should not be taken regularly and in fixed intervals. (F)	94
14. Psychosocial and cultural factors affect the efficacy of non-pharmacological interventions. (T)	91

EMONO: 50%-50% equimolar mixture of oxygen and nitrous oxide; F: false; T: true.

junior doctors ($p = 0.015$). No statistical differences were found among nurses ($p > 0.05$).

Regarding pain assessment, 77% reported using pain assessment scales "often" or "always" in their day-to-day clinical evaluation (Fig. 1).

Focusing on different patient ages and the presence of cognitive impairment, doctors and nurses were questioned about which method they usually used to quantify pain for each category (Fig. 2).

"Clinical observation/examination" was the most commonly chosen method (74%) to evaluate pain in newborns. In the other groups, pain assessment scales were considered the preferred approach, ranging from 73% for children with cognitive impairment to 91% for children aged over six. Doctors and nurses very commonly chose more than one method, and "asking parents" was an option chosen by 46 to 59% of the respondents across all categories.

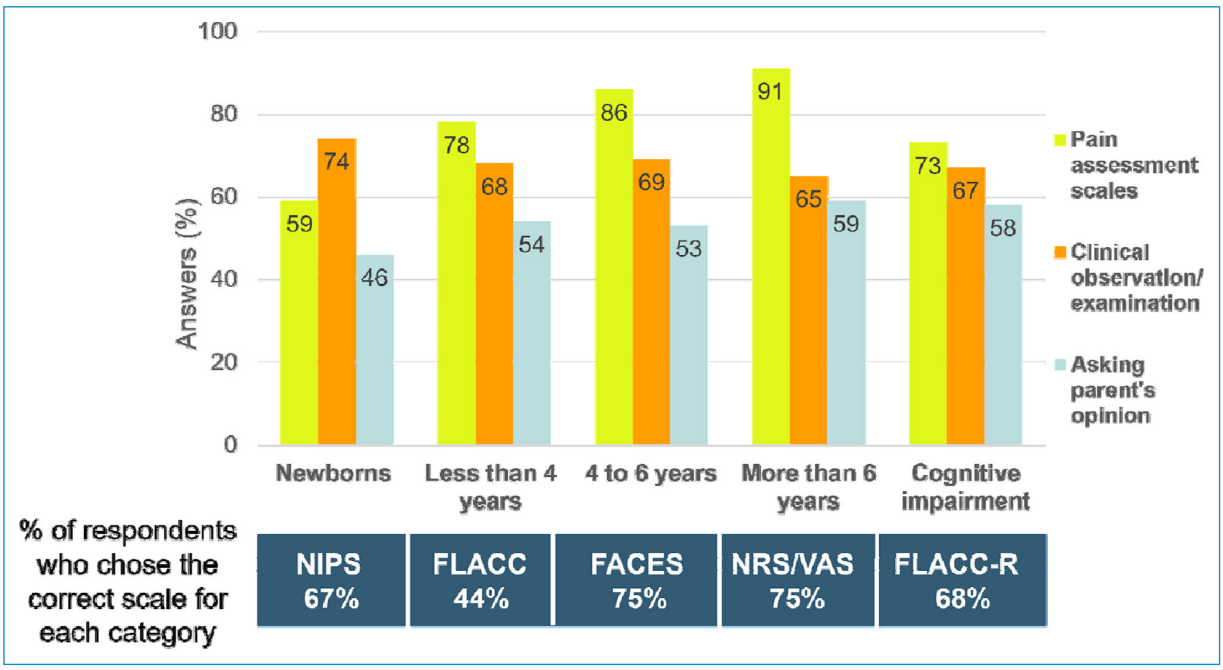

Figure 2. Methods for evaluating or quantifying pain in daily clinical practice. Healthcare workers were questioned about the method they used most in their daily routine to assess pain in children, according to their age and neurocognitive development. Below the graph, among those who chose to use pain assessment scales for each category, we analyzed how many chose the correct scale. FACES: facial clinimetric evaluation scale; FLACC: face, legs, activity, cry and consolability scale; FLACC-R: revised face, legs, activity, cry and consolability scale; NIPS: neonatal infant pain scale; NRS/VAS: numerical rating scale/visual analogic scale.

Finally, we analyzed who selected the most suitable pain assessment scale for each group, among those who stated that they used specific scales for each category. For the "children aged four to six years old" and "over six years old" sets, a correct answer for the proper scale was obtained in 75%. On the other hand, smaller percentages of correct answers were observed concerning the appropriate pain scale for "newborns" (67%) and "children aged under four years old" (44%) (Fig. 2).

Across all five categories of patients, it was statistically significant that nurses used pain assessment scales more often, while doctors relied more on clinical examination and parents' opinions ($p < 0.05$). No differences were found between professionals with differing years of experience ($p > 0.05$).

Non-pharmacological interventions in pediatric pain management

Three quarters of the participants answered that they "often" or "always" used non-pharmacological interventions in their approach to pain (Fig. 2). In an open-ended question, overall, 24 different interventions were described by doctors and nurses and 83% wrote at least three. The most commonly mentioned interventions were "non-nutritive and nutritive suction" (56%), "positioning and handling" (49%), "distraction" (46%), "music therapy" (40%), and "glucose 30%" (36%). It was statistically significant ($p = 0.01$) that nurses cited a higher number of interventions compared to doctors. No differences were found between years of experience ($p > 0.05$).

Pharmacological interventions and sedoanalgesia procedures

Firstly, the participants were questioned about the usefulness of EMLA® topical cream. In two closed questions (Yes/No), 96% considered EMLA® cream to be an important approach in acute medical procedures in the emergency department and 91% were of the opinion that it must be included in protocols for painful invasive procedures. No differences were found between types of career and years of experience regarding these two questions ($p > 0.05$). The frequency of use of EMLA® cream was also analyzed (Fig. 1).

Regarding routes for drug administration, an open-ended question was used to enquire about which drugs could be used intranasally for sedoanalgesia procedures

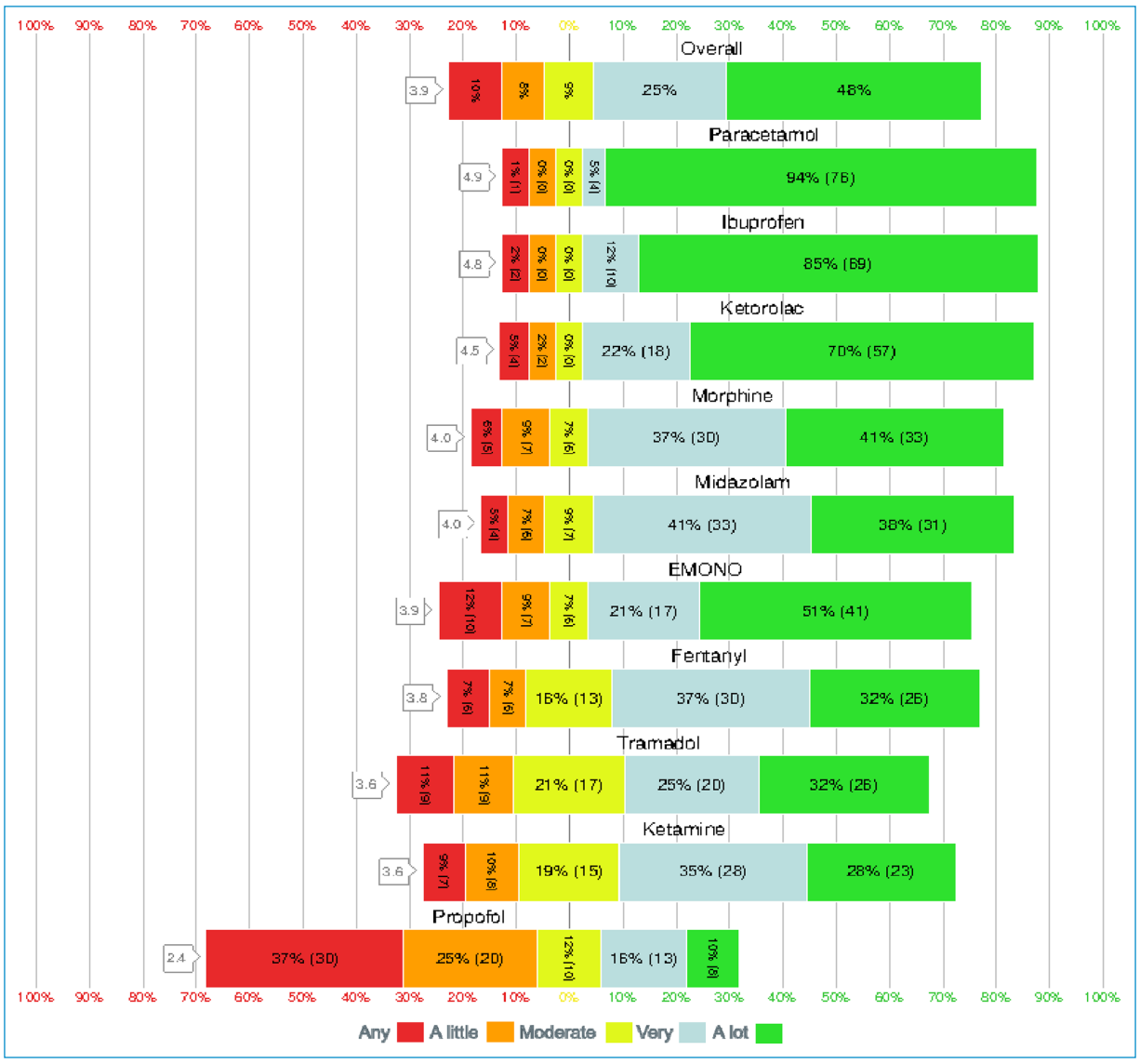

Figure 3. Healthcare workers' levels of confidence using drugs in sedo analgesia procedures. Levels of confidence in managing several medications used in sedoanalgesia were rated by doctors and nurses. Data was displayed as a five-point Likert scale chart (Levels of confidence: 1 = Not confident; 2 = Somewhat confident; 3 = Moderately confident; 4 = Quite confident; 5 = Very confident). EMONO: 50%-50% equimolar mixture of oxygen and nitrous oxide.

(analgesic and sedatives). Most participants answered midazolam (93%) and/or fentanyl (72%); another drug cited was ketamine (15%).

Confidence levels and the professionals' experience in sedoanalgesia were evaluated. Overall, high levels of confidence were observed (Fig. 3). More specifically, paracetamol, ibuprofen, and ketorolac were drugs that 90% of participants felt "quite" or "very" confident in using. Other drugs, including midazolam (79%), morphine (78%), and a 50%-50% equimolar mixture of oxygen and nitrous oxide (EMONO) (72%) were also observed to be associated with high levels of confidence ("quite"/"very"), followed by fentanyl (69%) and ketamine (63%). Propofol was the drug with the lowest rates of confidence, with 62% answering as being "not confident" or "somewhat confident".

It was statistically significant that higher levels of confidence were found in nurses compared to doctors, while managing propofol ($p = 0.002$), tramadol ($p = 0.024$), morphine ($p = 0.003$), and midazolam ($p = 0.048$). Furthermore, it was statistically significant that doctors with more than five years of professional experience were more confident compared to junior doctors in regard to using most drugs, namely: tramadol, morphine, midazolam ($p = 0.001$); fentanyl, propofol ($p = 0.002$); and ketamine ($p = 0.011$). No statistical differences,

regarding professional experience and confidence levels, were found among nurses ($p > 0.05$).

Finally, the last open-ended question, exclusively directed at the medical team, asked which were the most appropriate analgesics to control mild, moderate, and severe pain. Doctors (n = 34) chose paracetamol (n = 33; 97%), ibuprofen (n = 32; 94%), and ketorolac (n = 1; 3%) to manage mild pain; ketorolac (n = 34; 100%), tramadol (n = 20; 59%), and opioids (n = 3; 9%) to handle moderate pain; and morphine (n = 32; 94%), fentanyl (n = 27; 79%), ketamine (n = 16; 47%), ketorolac (n = 8; 24%), and tramadol (n = 7; 21%) to treat severe pain.

Discussion

A significant percentage of professionals answered the survey. Also, a considerable fraction of these takes care of patients in acute and urgent conditions, in ED or NPICU, managing acute pain every day (Table 1). This is a substantial representation of the state of the art of pain assessment and management in this pediatric department.

On theoretical evaluation (Table 2), the questions were more difficult compared to the survey conducted 15 years ago in the same department (*data not shown*), and higher scores were obtained in the present survey. Furthermore, in the present survey, almost no one agreed with the following statements: "*infants feel less pain than adolescents", "analgesics should not be taken regularly", and "midazolam is an analgesic drug*". These statements are major myths regarding pediatric pain, and we can affirm that they are no longer current beliefs, compared to other series[28-32].

Overall, the median of corrected answers (86%) was satisfactory and higher than previous surveys in literature[31-36], although it is difficult to compare due to the heterogeneity of the surveys. As seen in various series[15,31-33,35], opioid-related questions had a lower percentage of correct answers. Training in opioid management must be a priority, in relation to drug characteristics, adverse effects, and equivalence dosing across different types[31,35].

Regarding the professionals' perspective on pain management in their departments (Fig. 1), they were more likely to consider pain to be well recognized than well treated. This perspective was more prevalent among nurses and junior doctors, in contrast with senior doctors. This might be explained by the fact that the former are more closely involved in daily, direct, patient care, highlighting the need for more consistent/frequent follow-up on the effectiveness of pain relief prescriptions for any given patient, thus guaranteeing the pairing of recognition to treatment[22,23].

On assessment (Fig. 2), the use of scales was very frequent (77%) and higher than in other cohorts[37]. However, when asked to choose the appropriate scale for each category, the lowest rates of correct answers were seen for children under four years old, including neonates, as stated by Moutte, et al.[37]. Most children going to the ED are in this age group[38]. As they are in the preverbal stage of development or still have difficulty voicing their feelings, they completely rely on the caregiving team and their parents for the interpretation of their discomfort. Therefore, this subjective information (also highly used by our professionals, as seen in the analysis) is crucial, but it must be structured and converted into an objective assessment using accurately validated item-based scales of pain assessment, such as NIPS or FLACC[10,11].

Physicians are less trained in this structured assessment[37], compared to nurses, as observed in our results, which is a concern considering therapeutic regimens are mainly this group's responsibility.

Focusing on treatment, non-pharmacological measures are already highly widespread in the department (Fig. 1), differing from other hospitals[32]. However, they must be included in doctors' daily practices as they are in nurses' routines. Several studies showed the major role of these measures on promoting a synergic effect with the analgesics and in reducing the levels of anxiety compared to the simple and harsh restraint of a child[32,39,40].

Topical analgesia was considered by the respondents to be a very important measure to be included in protocols of acute procedures in ED, but, overall, the frequency of using EMLA® (Fig. 1) was much lower than what we expected, and in lower rates compared to what is proposed in protocols[21,22]. This might be explained by the fact that, in urgent procedures, it can be difficult to guarantee its placement within the time needed to ensure effectiveness. However, whenever possible, the need for EMLA® should be predicted and anticipated in a timely manner.

The intranasal route was shown to be widely known by our respondents, in line with the most recent literature which states that the most efficient treatment should be administered by the least invasive route[16,21].

High levels of confidence in managing sedoanalgesia drugs were seen across departments (Fig. 3), except for propofol, which is understandable as it is more commonly used in NPICU procedures. However, we cannot disregard that this is subjective data and that professionals in several other series stated they feel a

lack of experience in managing these drugs[32,41]. Our results also highlighted the relevance of training, as junior doctors had lower rates of confidence, which is also supported by a few other studies[31,34].

On the other hand, the high levels of confidence, even with opioids and ketamine, might positively reflect the team's concern to provide training and to update practices according to the most recently established protocols.

Professionals also reported high confidence levels in managing EMONO, a commonly used analgesic for short-term procedures with minimal adverse effects[42]. This confidence likely reflects the ease of administration with a non-intravenous route, which is particularly appealing for pediatric care[42,43]. The well-established effectiveness and safety profile of EMONO could support its adoption as a standardized practice in pediatric medical institutions[43].

Nurses demonstrated higher confidence levels in their responsibilities related to sedoanalgesia compared to doctors. However, a direct comparison may be challenging since each professional has different responsibilities within the procedure. Nurses primarily focus on the technique and the route of administration, whereas the medical team is mainly responsible for assessing indications, monitoring efficacy, dosing, interactions, and adverse effects.

Finally, regarding the last question in the survey, addressed specifically to the medical team, the drugs chosen for the treatment of mild, moderate, and severe pain were in accordance with recent international and national guidelines[16-23], endorsing updated practices.

The main limitation of this study is that it is a single-center cross-sectional study. Also, as the survey was designed specifically for this department, it is difficult to compare it with other series. Finally, although an effort was made to make the survey as simple and objective as possible, we are analyzing data that depends on the healthcare professionals themselves, which may induce bias due to individual perspectives.

Conclusions

This study represents one of the first surveys regarding pediatric pain management and assessment, directed at both nurses and doctors, to have ever been conducted in Portugal. Overall, our series showed a good level of knowledge and experience in this topic, which is a major difference in comparison with several other series, as previously discussed. However, we concluded that: constant training on opioid management and sedoanalgesia is needed to guarantee high levels of experience with all drug classes; non-pharmacological and topical interventions should be regularly included in protocols and urgent procedures; and more guidance is needed on the use of structured pain assessment scales to elicit an objective assessment of pain, especially for younger children, aged under four years old. Pain should be managed in multidisciplinary teams, with doctors and nurses working together, to ensure adequate recognition, treatment, and reassessment of pain, thus guaranteeing the best quality of care for our children.

Previous presentations

This research was presented at the National Pediatric Meeting (Congresso Nacional de Pediatria), in Porto, Portugal, as an oral presentation organized by the Portuguese Pediatric Society on the October 28, 2022.

Author contributions

B. Saraiva, I. Gomes: Conception and design of the study, report, review or other type of work or paper; Acquisition of data either from patients, research studies, or literature; Analysis or interpretation of data either from patients, research studies, or literature; Drafting the article; Critical review of the article for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work. All the other authors: Conception and design of the study, report, review or other type of work or paper; Acquisition of data either from patients, research studies, or literature; Critical review of the article for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work.

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None.

Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients,

and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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ORIGINAL ARTICLE

Obstructive sleep-related breathing disorders in overweight and obese adolescents

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Abstract

Introduction and Objectives: The causes behind obstructive sleep-related breathing disorders (OSRBD) are multifactorial, with obesity playing a significant role. Approximately 60% of obese children experience OSRBD. This study aims to characterize the severity of OSRBD in overweight or obese adolescents undergoing polysomnography (PSG) in a tertiary-level hospital. **Methods:** This retrospective descriptive study analyzed clinical records and PSG parameters of overweight or obese adolescents referred for PSG between 2016 and 2021. Adolescents with neuromuscular, genetic, or syndromic pathologies were excluded. **Results**: Sixty-seven overweight/obese adolescents were included, with 67% being males. Clinical manifestations of OSRBD included snoring in 94%, apneas in 70%, and daytime symptoms (excessive somnolence, headaches, and low school performance) in 76%. The median age at PSG was 14 years old. OSRBD was found in 75% of adolescents, with 16% experiencing moderate to severe obstructive sleep apnea syndrome. Notably, three of these adolescents were asymptomatic. Approximately 27% of the adolescents studied had an indication for non-invasive ventilation (NIV). Out of those who were followed up for at least twelve months after starting NIV (9/18), 56% exhibited good adherence. **Discussion:** In our study, the prevalence of OSRBD was higher than described in the literature, albeit in a selected sample. The presence of OSRBD in three asymptomatic adolescents underscores the necessity of PSG, even in asymptomatic patients. NIV is a frequently chosen treatment, with challenges regarding long-term adherence in these patients.

Keywords: Adolescent obesity. Non-invasive ventilation. Obstructive sleep apnea syndrome.

Distúrbios obstrutivos do sono relacionados com a respiração em adolescentes com sobrepeso e obesos

Resumo

Introdução e Objetivos: A Perturbação Respiratória Obstrutiva do Sono (PROS) tem causas multifatoriais, com a obesidade a desempenhar um papel crescente. Cerca de 60% das crianças obesas tem PROS. Pretende-se caracterizar a gravidade da PROS em adolescentes com excesso de peso ou obesos referenciados para polissonografia (PSG) num hospital terciário. **Métodos:** Este estudo retrospetivo descritivo analisou os processos clínicos e parâmetros das PSG de adolescentes com excesso de peso ou obesos referenciados para PSG, entre 2016 e 2021. Foram excluídos adolescentes com patologias neuromusculares, genéticas ou sindrómicas. **Resultados**: Foram incluídos 67 adolescentes com excesso de peso ou obesidade,

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sendo 67% do sexo masculino. As manifestações clínicas de PROS incluíram ressonar em 94%, apneias em 70% e sintomas diurnos (sonolência diurna excessiva, cefaleias, baixo rendimento escolar) em 76%. A média de idade na realização da PSG foi 14 anos. Identificou-se PROS em 75% dos adolescentes, sendo em 16% Síndrome de Apneia Obstrutiva do Sono moderada a grave. De referir que três dos adolescentes com PROS eram assintomáticos. Cerca de 27% dos adolescentes estudados iniciaram ventilação não invasiva (VNI). Naqueles com pelo menos doze meses de follow-up (9/18), verificou-se boa adesão em 56%. **Discussão:** No nosso estudo, a prevalência de PROS foi mais elevada do que o descrito na literatura, mas esta era uma população selecionada. Três adolescentes assintomáticos apresentaram PROS, reforçando a necessidade de PSG mesmo em pacientes assintomáticos. A VNI é muitas vezes o tratamento de escolha, com problemas de adesão a longo prazo nestes doentes.

Palavras-chave: Obesidade na adolescência. Ventilação não-invasiva. Síndrome de apneia obstrutiva do sono.

Keypoints

What is known
- Obesity is associated with obstructive sleep-related breathing disorders, especially obstructive sleep apnea syndrome
- Non-invasive ventilation is key for treatment along with weight loss

What is added
- Obese or overweight adolescents should be evaluated with PSG even when asymptomatic

Introduction

Obstructive sleep-related breathing disorders (OSRBD) are more prevalent in the pediatric population, particularly among obese children and adolescents. Approximately 59 to 66% of obese children have OSRBD[1-4]. The etiology of OSRBD is multifactorial, involving factors such as adenotonsillar hypertrophy, craniofacial morphology, obesity, and genetic predisposition[1,5,6]. The significance of obesity as a risk factor for pediatric OSRBD is growing, mirroring the rising prevalence of obesity in this population[1-4]. The pathophysiology is characterized by the obstruction and collapse of the upper airway during sleep, along with decreased pulmonary compliance and impaired responses to hypoxemia and hypercapnia[1,5-8].

Characteristic symptoms of OSRBD, such as snoring, apnea, and daytime sleepiness, often go undervalued or underdiagnosed due to their normalization in the general population. However, it is essential to note that snoring is not synonymous of OSRBD, and OSRBD can manifest without snoring[1,6,7,9,10-12]. Polysomnography (PSG) is therefore considered the gold standard for diagnosis[6,11,13,14]. Nonetheless, there are significant limitations in performing PSG, as it is a demanding examination, requiring technical and human resources[6,13].

The identification of overweight or obese adolescents with OSRBD is crucial due to their consequences, particularly in elevating cardiovascular and metabolic risks. In OSRBD, hypoxemia, hypercapnia, and microarousals contribute to increased sympathetic activity, oxidative stress, inflammatory cytokines, as well as endothelial and platelet dysfunction[1,5,10,11].

The primary approach to treating OSRBD in overweight and obese patients is weight control. However, in some cases, non-invasive ventilation (NIV) may be necessary[15]. Long-term adherence in adolescents is often challenging and inconsistent[2,15].

The objective of this study is to characterize the severity of OSRBD in adolescents referred for PSG due to their obesity, with or without symptomatology.

Methods

Study sample

This study includes patients referred for PSG between 2016 and 2021, aged 10 years and older, with a body mass index (BMI) ≥ +2 z-score (obesity[1]) or with a BMI ≥ +1 z-score (overweight[1]) and symptoms of OSRBD.

In our hospital, obese or overweight adolescents with OSRBD symptoms, with a BMI > 35 kg/m^2 or a z-score ≥ 3, or with other cardiovascular or metabolic comorbidities, are typically referred for PSG. Patients with other independent risk pathologies for OSRBD (neuromuscular, genetic, or syndromic diseases) were excluded.

Study location

The adolescents included were evaluated beforehand in General Pediatric, Pediatric Obesity, or Pediatric Pneumology outpatient appointments at a tertiary-level hospital. PSG was performed in our hospital Sleep Laboratory.

Study design

The PSG tests conducted in the Sleep Laboratory were filtered according to the study criteria. Examination reports and patient electronic records were analyzed, and relevant data was collected.

All PSG tests were performed with the Alice 5 Respironics System®, under the supervision of trained sleep technicians. Various parameters were recorded, including an electroencephalogram (C3M2, C4M1, O1M2, O2M1, F3M2, F4M1), bilateral electrooculogram, submental electromyogram, right and left tibial electromyogram, electrocardiogram (DII), respiratory flow with nasal cannula and oronasal thermistor, thoracic and abdominal movements, peripheral oxygen saturation, transcutaneous carbon dioxide, respiratory noise, body position, and an audio-visual record. American Academy of Sleep Medicine rules were applied for sleep and respiratory scoring[16]. The following definitions were used: upper airway resistance syndrome (UARS) if respiratory effort-related arousals (RERA) were > 1/hour; obstructive sleep apnea syndrome (OSAS) according to the obstructive apnea-hypopnea index (AHI) (mild if AHI is 1 to 5, moderate if 5-10 and severe if ≥ 10); and obstructive sleep hypoventilation (OSH) if transcutaneous CO_2 ($TcCO_2$) > 50 mmHg in > 25% of the total sleep time (TST)[16,17].

Adherence to non-invasive ventilation was considered "good" if the percentage of nights on NIV was more than 80%, and the mean duration on NIV was at least six hours per night.

Dyslipidemia was considered if the total cholesterol was > 170 mg/dL, or triglycerides were > 150 mg/dL, or LDL cholesterol was > 130 mg/dL or HDL cholesterol was < 35 mg/dL, (blood tests collected with a minimum 12-hour fasting period)[18]. Insulin-resistance was considered to be positive if a fasting homeostasis model assessment of insulin resistance was > 2 in more than one evaluation with a minimum 12-hour fasting period[19]. Hypertension was taken into consideration if the adolescent's blood pressure (systolic or diastolic blood pressure) was over the 95th percentile for age, sex, and height, in multiple evaluations.

Data collection methods

Demographic and clinical information was collected, including gender, age, previous ear, nose, and throat (ENT) surgery, allergic rhinitis, co-morbidities with increased cardiovascular and metabolic risk, and parents' obesity and NIV use. In terms of symptomatology, we evaluated snoring, apnea, and daytime symptoms such as excessive daytime somnolence, headaches, or low school performance. Anthropometric data at the PGS was recorded and the BMI z-score was calculated.

The PSG results analyzed were efficiency, obstructive AHI, RERAs, minimum blood oxygen level, time spent with $TcCO_2$ above 50 mmHg, and PSG conclusion. For those adolescents who started NIV, adherence was evaluated at the 12-month follow-up.

Data analysis methods

Descriptive and univariate analyses were performed using independent t-tests for continuous variables and a Chi-square test for categorical ones. The non-parametric Mann-Whitney test was used for variables with a non-normal distribution. Results were expressed as mean ± standard deviation for normally distributed variables and as median [minimum – maximum values] for non-normally distributed variables. The significance level was set at $p < 0.05$. The statistical analysis was made using the Statistical Package for Social Sciences (SPSS®) for Windows®, version 29.0.

Ethics

The study complies with national legislation and the Helsinki Declaration.

Results

Sixty-seven adolescents were included, with 67% being males. PSG for these patients accounted for 8% of the total PSG tests performed in the Sleep Laboratory during the study period. Patients' demographic and clinical data are summarized in table 1. Most of the patients were referred from outpatient consultations in our hospital, and 24% were referred from level II hospitals in the Central Region of Portugal. The median age at referral for PSG was 14 (10-18) years old. Snoring was the most frequent symptom (94%), nocturnal apneas were identified in 70% of the patients, and 76% exhibited diurnal symptoms (excessive daytime somnolence, headaches, or low school performance). Four adolescents were referred without any symptoms, and they had a mean BMI z-score of +4.2 ± 0.59. About 24% had undergone previous ENT surgery for OSAS (adenotonsillectomy), and 45% were undergoing medical treatment for allergic rhinitis. The mean BMI z-score at the PSG was +3.2 ± 0.88 kg/m^2. The prevalence of other cardiovascular or metabolic risk factors was as follows: insulin-resistance in 44%, dyslipidemia in 18%, and hypertension in 11%. At least one parent was

Table 1. Demographic and clinical information

Variables	n = 67
Gender (male)	45 (67%)
Adolescent's age at PSG (years old)	14 (10-18)
Symptomatology	
Snoring	63 (94%)
Apneas	47 (70%)
Diurnal symptoms	51 (76%)
ENT surgery	15 (24%)
Allergic rhinitis	30 (45%)
BMI z-score at PSG	+3.2 ± 0.9
Cardiovascular or metabolic co-morbidities	
Insulin resistance	22 (44%)
Dyslipidemia	9 (18%)
Hypertension	6 (11%)
Parents	
Obesity	23 (42%)
NIV use	7 (13%)

BMI: body mass index; ENT surgery: ear, nose, and throat surgery; NIV: non-invasive ventilation.

Table 2. PSG data

Variables	n = 67
PSG data	
Median efficiency, n (%)	77 (27-92)
Obstructive AHI (per hour)	0 (0-22)
RERA index (per hour)	11 (0-52)
Minimum blood oxygen level, n (%)	93 (83-98)
% of total sleep time with $TcCO_2$ > 50 mmHg, n (%)	0 (0-100)
PSG conclusion	
No respiratory compromise	17 (25%)
UARS	22 (33%)
Mild OSAS	14 (21%)
Moderate OSAS	6 (9%)
Severe OSAS	5 (8%)
OSH	3 (4%)

AHI: apnea hypopnea index; OSAS: obstructive sleep apnea syndrome; OSH: obstructive sleep hypoventilation; RERA: respiratory effort-related arousals; TcCO2: transcutaneous CO2; UARS: upper airway resistance.

obese in 42% adolescents, and 13% of parents had OSAS treated with NIV.

The data from the PSG tests is summarized in table 2. OSRBD were identified in 75% of the obese adolescents (50/67 patients): 33% had UARS, 21% had mild OSAS, 9% had moderate OSAS, 8% had severe OSAS, and 4% had OSH. Adolescents with an abnormal PSG were older and had a higher BMI z-score at the time of referral for PSG than those with a normal PSG, though with no statistical significance. Three obese adolescents with OSRBD (one with moderate OSAS and two with mild OSAS) were asymptomatic

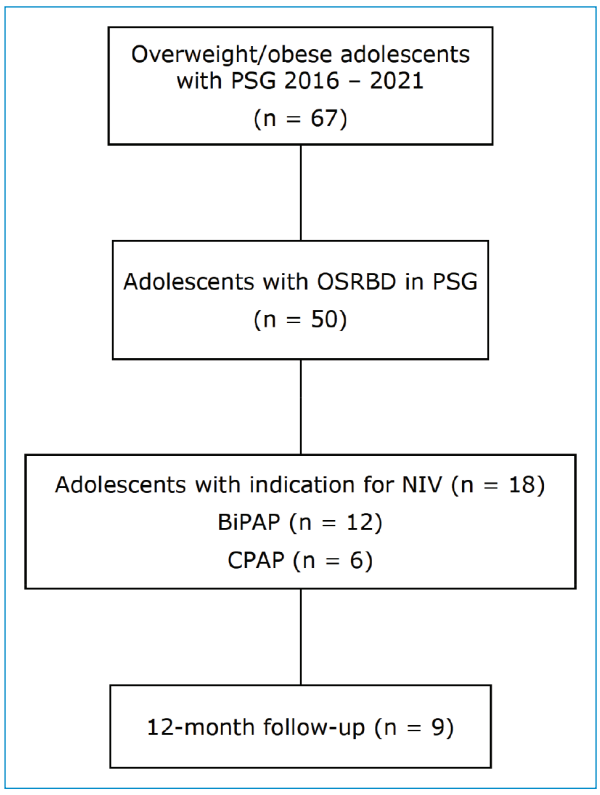

Figure 1. Sample description.

and were referred for PSG due to a high BMI (median BMI 39 kg/m^2 and a median BMI z-score of +4.3). When analyzing adolescents with OSAS, nocturnal apnea was more frequent in mild and moderate cases than in severe ones, without statistical significance (79% vs. 67% vs. 40%, p = 0.283).

Approximately 36% of those with any OSRBD in the PSG (18/50) had an indication for NIV, corresponding to 27% of the total sample (Fig. 1). All adolescents with an indication for NIV had higher BMI z-scores than others with OSRBD but without this indication, without statistical significance (+3.6 ± 1.1 vs. +3.1 ± 0.9, p = 0.055). All patients with severe OSAS and OSH initiated NIV. Among those with moderate OSAS (five), four initiated NIV, and one showed significant weight control after one year, leading to an improvement in OSRBD. Five patients with mild OSAS or UARS initiated NIV due to significant diurnal symptoms. BiPAP was the ventilation mode used in all patients with severe OSAS, OSH, and in most patients (three out of five) with moderate OSAS. In the other cases, CPAP or auto-CPAP was used.

One of the asymptomatic patients with OSRBD started NIV. He was referred for PSG due to a BMI of 39 kg/m^2 (BMI z-score of +4.9), and his PGS showed moderate OSAS.

Out of all the patients on NIV (18/67), nine were followed up for at least twelve months. Overall adherence to NIV was good in five, corresponding to 56% of this group.

Discussion

Pediatric obesity has become an increasingly prevalent health issue in recent decades, leading to a rise in pathologies where obesity serves as a risk factor. Consequently, pediatric OSRBD are on the rise, especially among overweight and obese children and adolescents[1-4].

Our hospital, the only one in the Central Region of Portugal with a Pediatric Sleep Laboratory, faces limited availability for PSG, requiring careful consideration and structuring indications. Throughout the study period, approximately 8% of all the PSG tests conducted were for obese adolescents, either with or without significant OSRBD symptoms, or overweight adolescents with concerning OSRBD symptoms. The mean BMI at the time of referral for PSG was 33.5 ± 6.6 kg/m^2 (BMI z-score of +3.2 ± 1.0), indicating a selection of more severe cases for this evaluation. Most patients were referred from our hospital's outpatient consultations, possibly indicating a lack of awareness about the incidence of OSRBD and the need for PSG in obese patients among pediatricians in other centers.

OSRBD prevalence was 75%, unsurprisingly higher than in other studies involving obese adolescents due to the selected sample in our study. Males were more frequently affected, in line with the literature, which reports a higher incidence of identifiable respiratory compromise in PSG among males[14,20-22].

Symptoms were as frequent as in other studies[1,13,22] and did not predict the presence of OSRBD in PSG. In our study, three obese asymptomatic adolescents had OSAS in PSG, with one of them requiring NIV. This underscores the importance of assessing OSRBD in all obese adolescents and conducting PSG if there are risk factors (BMI > 35 kg/m^2 or BMI z-score ≥ +2 or co-morbidities with cardiovascular and metabolic risks), even in the absence of symptoms[11,13].

Approximately 27% (18/67) of the obese adolescents studied met the criteria for NIV. BiPAP was the preferred ventilation mode when OSAS was moderate to severe or in OSH situations. This choice was linked to the severity of the upper airway collapse and the need for higher pressures to reduce AHI. It is also associated with the impact of restriction and decreased pulmonary compliance due to obesity. NIV was initiated for all adolescents during an inpatient period, with the collaboration of nurses and pediatricians experienced in NIV adaptation. Regular outpatient consultations (first month and every six months) were conducted. Among patients completing twelve months of follow-up, only 56% exhibit good NIV adherence. This difficulty in the adolescent population is well-described in literature (related to defiance of authority and difficulties in therapeutic compliance, common in this age and present in other chronic pathologies). This is verified even when adherence is defined with less ambitious criteria (at least four hours per night in 50-70% of nights)[23,24].

The main limitations in this study include the small sample size and the fact that it involved a selected population. Consequently, the prevalence of OSRBD and its various subtypes cannot be generalized.

However, our study points out that the importance of conducting at least one PSG test during the follow-up of even apparently asymptomatic obese adolescents. OSRBD may be present and could be severe enough to start non-invasive ventilation. This brings attention to the reality of limited PSG availability, primarily due to inadequate human and technical resources. There is a need to readapt and establish protocols for diagnosing and managing obese adolescents, given the increasing prevalence of this health problem. Furthermore, it is crucial to enhance treatment approaches, focusing not only on NIV, but especially on strategies with a genuine impact on weight control.

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Author contributions

M. Lopes Costa: Conception and design of the study, report, review or other type of work or paper; Acquisition of data either from patients, research studies, or literature; Analysis or interpretation of data either from patients, research studies, or literature; Drafting the article; Critical review of the article for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work. S. Ferreira, R. Soares: Critical review of the article for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work.

N. Madureira: Conception and design of the study; Analysis or interpretation of data either from patients, research

studies, or literature; Critical review of the article for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work.

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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PORTUGUESE JOURNAL OF PEDIATRICS

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ORIGINAL ARTICLE

Impact of diet and body composition on donor human milk: a cross-sectional pilot study

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Abstract

Introduction and Objectives: Donor human milk is recommended in Neonatal Intensive Care Units when maternal breast milk is unavailable. This study aimed to explore the association between the eating habits, body mass index, and body composition of human milk donors with the nutritional composition of their donor milk. **Methods:** A cross-sectional observational study involved 65 human milk donors. Sociodemographic, lifestyle, and clinical data were collected by questionnaires administered through interviews. Height, weight, and fat mass were measured and body mass index was calculated. Eating habits were assessed using a Food Frequency Questionnaire. Donor human milk samples were analyzed before and after pasteurization using the Miris Human Milk Analyzer™. **Results:** Thirty-three (50.8%) human milk donors were overweight, with a median fat mass of 33.2%. No significant associations were found between body mass index or fat mass and the nutritional composition of donated milk. However, infants' gestational age showed a positive correlation with the protein content after the donated milk had been pasteurized. The energy of donor human milk before pasteurization was positively associated with carbohydrate intake ($r = 0.272$, $p = 0.029$). The consumption of carbohydrate sources was positively correlated with the energy of donor human milk before ($r = 0.271$, $p = 0.029$) and after pasteurization ($r = 0.248$, $p = 0.046$). Potato intake showed a positive correlation with fat content in donor human milk before ($r = 0.474$, $p < 0.001$) and after the milk had been pasteurized ($r = 0.443$, $p < 0.001$). **Discussion:** These results highlight the importance of monitoring human milk donors' nutrition to optimize their nutritional status and donated milk composition.

Keywords: Body mass index. Donor human milk. Eating habits. Human milk donors. Nutritional composition.

Impacto da dieta e da composição corporal no leite humano doado: um estudo piloto transversal

Resumo

Introdução e Objetivos: O leite humano de dadora é recomendado nas Unidades de Cuidados Intensivos Neonatais quando o leite materno está indisponível. Este estudo explorou a associação entre hábitos alimentares, índice de massa corporal e

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composição corporal de dadoras de leite humano com a composição nutricional de leite doado. **Métodos:** Estudo transversal com 65 dadoras de leite humano. Obtiveram-se dados sociodemográficos, clínicos e de estilo de vida via questionários. Mediu-se a altura, o peso e massa gorda e calculou-se o índice de massa corporal. Avaliaram-se hábitos alimentares pelo Questionário de Frequência Alimentar. Analisaram-se amostras de leite humano de dadora, antes e após pasteurização, pelo *Miris Human Milk Analyzer*™. **Resultados:** Trinta e três (50,8%) dadoras de leite humano apresentavam excesso de peso e mediana de massa gorda de 33,2%. Não foram encontradas associações significativas entre índice de massa corporal e massa gorda das dadoras de leite humano com a composição nutricional do leite doado. A idade gestacional dos recém-nascidos associou-se positivamente ao teor proteico após pasteurização do leite doado. Antes da pasteurização, o valor energético do leite associou-se positivamente à ingestão diária de hidratos de carbono ($r = 0,272$; $p = 0,029$). O consumo de fontes de hidratos de carbono correlacionou-se positivamente com a energia antes ($r = 0,271$; $p = 0,029$) e após pasteurização ($r = 0,248$; $p = 0,046$) do leite doado. A ingestão de batatas associou-se positivamente à gordura antes ($r = 0,474$; $p < 0,001$) e após pasteurização ($r = 0.443$, $p < 0.001$) do leite. **Discussão:** O acompanhamento nutricional das dadoras de leite humano é crucial para otimizar o seu estado nutricional e a composição do leite doado.

Palavras-chave: Composição nutricional. Dadoras de leite humano. Hábitos alimentares. Índice de massa corporal. Leite humano de dadora.

Keypoints

What is known
- Breastfeeding is often a challenge in Neonatal Intensive Care Units.
- Donor human milk is recommended for preterm and infants with a low birth weight, offering protection against health issues.
- Eating habits and body composition can lead to fluctuations in the nutritional composition of human milk.

What is added
- Body mass index and fat mass do not appear to impact the nutritional composition of donated human milk.
- Greater carbohydrate consumption is linked to higher energy in donated milk, crucial for meeting premature infants' high energy needs.
- Ensuring proper nutrition during breastfeeding is crucial, especially when considering the donation of human milk.

Introduction

Maternal breast milk is a natural and adequate food that helps to meet the energy and nutritional needs of any newborn. Today, the beneficial impact of breastfeeding on the health of both infants and mothers is widely recognized[1,2]. Literature has associated breastfeeding with a lower risk of morbidity and mortality, as well as improvements in infants' neurodevelopment. Breastfeeding has also been associated with a lower incidence of breast and ovarian cancer in women[1,3].

The World Health Organization (WHO) currently recommends that infants be exclusively breastfed during the first six months of life and should continue breastfeeding for two years alongside food diversification[4]. However, there may be circumstances where mother's own milk (MOM) is not available or is insufficient to meet infants' needs, which is a common challenge in Neonatal Intensive Care Units[5]. In these cases, the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) suggests donor human milk (DHM) as a viable alternative due to the superiority of human milk (HM) characteristics compared to commercial formulas[6]. Using DHM from Human Milk Banks is particularly important for preterm or newborns with a low birth weight, when MOM cannot be used[7].

According to previously randomized clinical trials[8], feeding infants with DHM instead of commercial formulas has several advantages such as the higher protection conferred against necrotizing enterocolitis, bronchopulmonary dysplasia, and different types of infections[9]. Although HM has the nutrients needed for the healthy development of infants up to six months of age, literature suggests that several factors such as the mother's diet and maternal body composition can cause variations in the concentration of certain nutrients[3,10]. In fact, it has been increasingly suggested that maternal overweight may be associated with nutritional composition changes in HM, particularly in terms of fat and lactose levels[11]. However, the impact

Table 1. Characteristics of human milk donors and their infants (n = 65)

Characteristics of human milk donors	
Age, years, median (p25, p75)	33.0 (30.0, 36.0)
School level, n (%) Lower secondary level Secondary level Advanced qualification	 1 (1.5) 13 (20.0) 51 (78.5)
Health professional, n (%)	21 (32.3)
First pregnancy, n (%)	31 (47.7)
Cesarean delivery, n (%)	28 (43.1)
Smoking (at least once during their lifetime), n (%)	16 (24.6)
Regular physical activity, n (%)	27 (41.5)
Sleep hours, h, median (p25, p75)	7.0 (6.0, 8.0)
BMI, kg/m^2*, median (p25, p75) With pre-obesity (25.0-29.9 kg/m^2), n (%) With obesity (≥ 30.0 kg/m^2), n (%)	25.1 (20.8, 27.6) 26 (40.0) 7 (10.8)
Fat mass†, %, median (p25, p75), n = 56	33.2 (27.5, 37.5)
Characteristics of human milk donors' infants	
Male sex, n (%)	29 (44.6)
Preterm infant (< 37 weeks), n (%)	7 (10.8)
Gestational age, weeks, median (p25, p75)	39.0 (38.0, 40.0)
Birth weight, g, median (p25, p75)	3320.0 (2867.5, 3662.5)

**According to WHO classification: World Health Organization. Obesity: preventing and managing the global epidemic. Report on a consultative meeting. Geneva, Switzerland: Author; 1997.*
†Body fat percentage. [website]. Tanita; 2012 – 2022. [cited on: 23 Jun 18]. Available at: https://tanita.eu/understanding-your-measurements/body-fat-percentage.
p25: 25th percentile; p75: 75th percentile; h: hours; BMI: body mass index; kg/m^2: kilogram per square meter; g: grams; %: percentage.

of a mother's diet on her own milk's composition is not well understood, as available information is limited and often inconsistent, primarily due to the small number of studies on this topic and variations in study methodologies[12,13].

As mentioned above, DHM is a highly beneficial choice for preterm infants or newborns with a low birth weight. It is therefore crucial that we further increase our understanding about the factors associated with its nutritional composition in order to promote the optimization of DHM in alignment with the specific nutritional needs of its main recipients[2]. In Portugal, there is a rising interest in personalized fortification of DHM. Studies have already assessed the influence of DHM's nutritional composition on the growth of recipient infants[14]. However, the potential impact of human milk donors' (HMDs') diet on the composition of DHM has not yet been investigated. Also, given the high prevalence of Portuguese women in reproductive age with obesity[15], understanding the possible implications of their eating habits, body mass index (BMI), and body composition on the nutritional composition of DHM is a matter of urgency.

This paper aimed to study the association between the eating habits, BMI, and body composition of HMDs' and the nutritional composition of their donor milk, and to understand if this relationship differs before and after pasteurizing the DHM.

Methods

Study design and sampling

A cross-sectional observational study was conducted between March 2023 and March 2024 at (institution name) in HMDs'. To become an HMDs', women have to follow specific pre-established criteria such as (a) being a healthy lactating woman who, despite exclusively breastfeeding her child, has excess milk, (b) being the mother of an infant under six months old, (c) not smoking or consuming alcoholic drinks or beverages with a high caffeine content and (d) not testing positive for HIV 1 or 2, Hepatitis B or C, Human T-cell Lymphotropic Virus I or II, or Syphilis. A complete description of the inclusion criteria is described elsewhere[16]. Also, all participants must be over 18 years old and cannot have any special dietary needs. At the start of the study, 26 HMDs' were active, and a further 52 were later recruited, resulting in a total of 78 HMDs'. Of these, 65 were included in this study (participation proportion = 83.3%).

Data collection

For the purpose of the study, a questionnaire with sociodemographic, lifestyle, and clinical data was created and applied through an interview during a clinical appointment at (institution name). The nutritional composition of each participant's milk samples was analyzed and recorded at (institution name).

Sociodemographic data included the participants' age as well as their education level, with 11 options ranging from "no formal education" to "doctorate". We further categorized this into three groups: lower secondary level (< 12 years of schooling), secondary level (12 years of schooling), and an advanced qualification (> 12 years of schooling). Profession was asked as an open question and subsequently categorized as either healthcare or non-healthcare professional.

Table 2. Impact of pasteurization on the nutritional composition of donor human milk (n = 65)

Variables	Before pasteurization*	After pasteurization*	Difference (after – before)	p†	Delta%‡
	Median (p25, p75)				
Energy, kcal/100 ml	69.0 (61.5, 75.1)	65.4 (59.5, 71,2)	–3.0 (–4.9, –1.2)	**< 0.001**	–4.5 (–7.0, –1.9)
True protein, g/100 ml	0.8 (0.7, 0.9)	0.8 (0.7, 0.9)	0.0 (–0.1, 0.0)	**0.003**	0.0 (–11.1, 0.0)
Crude protein, g/100 ml	1.0 (0.9, 1.2)	1.0 (0.9, 1.1)	–0.1 (–0.1, 0.0)	**0.002**	–7.1 (–10.0, 0.0)
Fat, g/100 ml	3.5 (2.8, 4.1)	3.1 (2.6, 3.9)	–0.3 (–0.5, –0.1)	**< 0.001**	–8.3 (–12.7, –3.5)
Carbohydrate, g/100 ml	8.1 (8.0, 8.2)	8.0 (7.9, 8.2)	–0.1 (–0.1, 0.0)	**0.005**	–1.2 (–1.3, 0.0)

*Using the Miris HMA™ (Human Milk Analyzer, Miris AB, Uppsala, Sweden).
†Wilcoxon test.
‡The percentage reduction (Delta %) in energy and macronutrients for DHM was calculated using the ratio for the difference in energy and macronutrients before and after pasteurization and the value of energy and macronutrients before pasteurization.
The statistically significant values (with $p < 0.05$) are highlighted in bold.
p25: 25th percentile; p75: 75th percentile; kcal: kilocalories; g: grams; ml: milliliters.

Lifestyle data related to smoking and physical activity were collected with dichotomous questions (yes/no). The participants answered 'yes' if they had ever smoked in their life, and if they regularly do physical activity. Regarding sleeping habits, they were asked about the number of hours of sleep each day during the week and at weekends. The average of these two periods was then used. Eating habits over the previous year were assessed, by interview, through a semi-quantitative Food Frequency Questionnaire (FFQ) validated for the Portuguese adult population[17,18]. Food frequency was indicated by the participants according to nine categories from "never or less than once a month" to "more than six times a day". For each food item, the amount ingested was registered according to the comparison with pre-established average portions. The consumption of each food, in grams, was calculated by multiplying the frequency of consumption by the portion size reported by the participants and, if appropriable, by a seasonal variation factor. The Food Processor Plus software (ESHA Research, Salem, Oregon) was used to convert FFQ items into nutrient intakes expressed in grams[17,18].

Anthropometric measurements were collected according to standard procedures[19]. Height was measured in centimeters (with 0.1 cm of resolution) using a SECA 213 measuring station or, failing that, it was obtained from the height recorded on the citizen's identity card. Body weight, in kilograms (kg), and fat mass (FM), in percentage (%), were determined using the TANITA® TBF-300 bioimpedance scale. BMI was calculated and categorized according to WHO criteria: underweight (< 18.5 kg/m^2), normal weight (18.5-24.9 kg/m^2), pre-obesity (25.0-29.9 kg/m^2), and obesity (≥ 30.0 kg/m^2)[20].

The HMDs' obstetric history was evaluated. They were asked about the number of pregnancies and the type of delivery, as well as the birth weight and gestational age of the infant which had resulted from their last pregnancy. Infants were classified as preterm if their gestational age was less than 37 weeks[21].

The nutritional composition of DHM samples was analyzed, before and after pasteurization, using the Miris Human Milk Analyzer™ (Miris AB, Uppsala, Sweden), an analytical innovative technique based on mid-infrared transmission spectroscopy principles[22]. The samples of raw DHM were collected by HMDs' in their own homes after they were instructed on good practices for extracting and cold-storing milk. When the raw DHM arrived at the Human Milk Bank, conformity parameters were checked in the samples (for example, organoleptic characteristics, bottle condition, and the storage temperature range of the raw DHM at the HMD's home). The Miris Human Milk Analyzer™ measured milk samples' true protein, crude protein, fat, and carbohydrate contents, in grams (g) per 100 milliliters (ml), and its energy, in kilocalories (kcal) per 100 ml, using a 3 ml sample of DHM. Prior to analysis, the device was calibrated by the calibration solution Miris Calibration Control Kit™ (Miris AB, Uppsala, Sweden), and the samples were homogenized using the Miris Ultrasonic Processor™ (Miris AB, Uppsala, Sweden) and warmed according to the respective protocol[22].

Statistical analysis

The collected data was compiled in a database using the IBM SPSS® program (Statistical Package for Social Sciences), version 28.0, for the respective statistical analysis. The normality of each quantitative variable

Table 3. Comparison between the gold standard of mature human milk and donor human milk composition before and after pasteurization (n = 65)

Variables	Gold standard mature HM‡	Before pasteurization*	p†	After pasteurization*	p†
		Median (p25, p75)		Median (p25, p75)	
Energy, kcal/100 ml	66	69.0 (61.5, 75.1)	**0.036**	65.4 (59.5, 71.2)	0.604
Crude protein, g/100 ml	1.0	1.0 (0.9, 1.2)	**0.040**	1.0 (0.9, 1.1)	0.629
Fat, g/100 ml	3.8	3.5 (2.8, 4.1)	**< 0.001**	3.1 (2.6, 3.9)	**0.015**
Carbohydrate, g/100 ml	7.0	8.1 (8.0, 8.2)	**< 0.001**	8.0 (7.9, 8.2)	**< 0.001**

*Using the Miris HMA™ (Human Milk Analyzer, Miris AB, Uppsala, Sweden).
†One-sample Wilcoxon signed rank test.
‡According to Rêgo et al.[23]
The statistically significant values (with $p < 0.05$) are highlighted in bold.
HM: human milk; p25: 25th percentile; p75: 75th percentile; kcal: kilocalories; g: grams; ml: milliliters.

was tested using the Kolmogorov-Smirnov test. To streamline the analysis, the median, 25th percentile (p25), and 75th percentile (p75) were used, as certain variables did not follow a normal distribution. Categorical variables were expressed as absolute and relative frequencies.

A comparison between the nutritional composition of the DHM before and after pasteurization was conducted using the Wilcoxon test. The percentual impact (Delta %) of each DHM's component analyzed was calculated by the ratio, in percentage, between the difference of each component before and after pasteurization and the respective value before pasteurization. The energy and macronutrient contents of DHM before and after pasteurization were compared to the gold standard mature HM[23] described in literature, using a one-sample Wilcoxon signed rank test.

Correlations between the DHM's nutritional composition before or after pasteurization and age, sleep hours, BMI, and FM of HMDs, and birth weight and gestational age of their infants were determined using Spearman's correlation coefficients. An identical approach was used to identify the correlations between the HMDs' dietary habits and respective energy and macronutrient intake with the nutritional composition of DHM before and after pasteurization. An alpha level of < 0.05 was set for all analyses.

Ethics

This research was approved by the Ethics Committee of the Centro Hospitalar Universitário de São João/Faculdade de Medicina da Universidade do Porto (report number 78/2023) and all the ethical principles of the Declaration of Helsinki, Portuguese Law, and the Good Clinical Practice Guidelines were followed. Informed consents were obtained from each participant, authorizing their participation in the study, after presenting all the necessary information and the respective rights regarding their collaboration in this research.

Results

The median age of this sample was 33.0, ranging from 21.0 to 43.0 years old. Fifty-one (78.5%) had an advanced qualification, 47.7% (n = 31) were pregnant for the first time, 43.1% (n = 28) had a cesarean section, and 41.5% (n = 27) practiced regular physical activity and slept a median of 7.0 hours per day. Also, 50.8% (n = 33) were overweight with a median FM value of 33.2% (Table 1). Table 1 also presents the descriptive characteristics of the HMDs' infants.

Table 2 represents the impact of pasteurization on the nutritional composition of DHM. Pasteurization significantly affected the energy and all the macronutrients of DHM ($p < 0.05$). There was an increased percentage impact on the energy, crude protein, and fat content of DHM (Delta %: −4.5, −7.1, and −8.3, respectively). In table 3, statistically significant differences were observed for energy and all the macronutrients of DHM before pasteurization when compared to the gold standard value[23] for mature human milk ($p < 0.05$). Additionally, significant differences were noted in both

Table 4. Spearman's correlation between the characteristics of human milk donors and their infants and the nutritional composition of donor human milk (n = 65)

	Donor human milk composition before pasteurization*										Donor human milk composition after pasteurization*									
	Energy (kcal/100 ml)		True protein (g/100 ml)		Crude protein (g/100 ml)		Fat (g/100 ml)		Carbohydrate (g/100 ml)		Energy (kcal/100 ml)		True protein (g/100 ml)		Crude protein (g/100 ml)		Fat (g/100 ml)		Carbohydrate (g/100 ml)	
	R	p	R	p	R	p	R	p	R	p	R	p	R	p	R	p	R	p	R	p
Characteristics of HMDs'																				
Age, years (n = 65)	0.079	0.531	0.114	0.364	0.075	0.552	0.056	0.660	–0.095	0.453	0.038	0.761	0.070	0.580	0.047	0.709	0.030	0.815	–0.046	0.718
Sleep hours, h (n = 65)	0.207	0.098	0.099	0.432	0.109	0.387	0.226	0.070	–0.189	0.131	0.214	0.087	0.143	0.257	0.132	0.294	0.218	0.081	–0.156	0.215
BMI, kg/m^2 (n = 65)	0.033	0.796	0.088	0.488	0.089	0.483	0.023	0.858	–0.013	0.916	–0.003	0.981	0.042	0.739	0.026	0.836	0.014	0.914	–0.185	0.140
Fat mass, % (n = 56)	0.139	0.306	0.191	0.158	0.187	0.167	0.110	0.418	0.022	0.874	0.128	0.348	0.176	0.195	0.165	0.225	0.130	0.341	–0.155	0.253
Characteristics of infants																				
Gestational age, weeks (n = 65)	–0.139	0.269	0.230	0.065	0.210	0.094	–0.130	0.301	–0.115	0.362	–0.138	0.272	**0.260**	**0.036**	0.211	0.092	-0.136	0.281	–0.174	0.166
Birth weight, g (n = 65)	0.166	0.185	–0.009	0.942	–0.018	0.888	0.159	0.206	0.022	0.864	0.106	0.399	–0.064	0.613	–0.087	0.492	0.124	0.324	–0.002	0.990

*Using the Miris HMA™ (Human Milk Analyzer, Miris AB, Uppsala, Sweden).
The values in bold represent statistically significant correlations, with $p < 0.05$.
HMDs': human milk donors; BMI: body mass index; kcal: kilocalories; g: grams; ml: milliliters; h: hours; kg/m^2: kilogram per square meter; %: percentage.

Table 5. Spearman's correlation between human milk donors' energy and macronutrient intake and the nutritional composition of donor human milk (n = 65)

		Donor human milk composition before pasteurization*										Donor human milk composition after pasteurization*									
	Median (p25, p75)	Energy (kcal/100 ml)		True protein (g/100 ml)		Crude protein (g/100 ml)		Fat (g/100 ml)		Carbohydrate (g/100 ml)		Energy (kcal/100 ml)		True protein (g/100 ml)		Crude protein (g/100 ml)		Fat (g/100 ml)		Carbohydrate (g/100 ml)	
		R	p	R	p	R	p	R	p	R	p	R	p	R	p	R	p	R	p	R	p
Energy and macronutrient intake																					
Energy, kcal/day	2147.4 (1554.0, 2514.7)	0.243	0.052	0.128	0.311	0.127	0.315	0.206	0.100	0.068	0.590	0.180	0.152	0.022	0.861	-0.008	0.949	0.192	0.126	–0.093	0.462
Protein, g/day	103.8 (81.7, 131.6)	0.141	0.262	0.009	0.941	0.002	0.989	0.107	0.396	0.113	0.371	0.047	0.710	–0.082	0.518	–0.123	0.331	0.064	0.615	–0.053	0.673
Fat, g/day	81.8 (58.0, 104.1)	0.171	0.173	0.082	0.515	0.064	0.613	0.139	0.270	0.073	0.563	0.105	0.406	–0.064	0.614	–0.102	0.420	0.127	0.313	–0.100	0.428
CHO, g/day	243.2 (182.5, 313.4)	**0.272**	**0.029**	0.177	0.160	0.192	0.126	0.240	0.054	0.026	0.836	0.240	0.054	0.116	0.359	0.102	0.418	0.240	0.054	–0.082	0.514

*Using the Miris HMA™ (Human Milk Analyzer, Miris AB, Uppsala, Sweden).
The values in bold represent statistically significant correlations, with $p < 0.05$.
p25: 25th percentile; p75: 75th percentile; kcal: kilocalories; Kcal/ day: kilocalories per day; g: grams; g/day: grams per day; ml: milliliters; CHO: carbohydrates.

Table 6. Spearman's correlation between human milk donors' eating habits and the nutritional composition of donor human milk (n = 65)

	Donor human milk composition before pasteurization*											Donor human milk composition after pasteurization*									
	Median (p25, p75)	Energy (kcal/100 ml)		True protein (g/100 ml)		Crude protein (g/100 ml)		Fat (g/100 ml)		Carbohydrate (g/100 ml)		Energy (kcal/100 ml)		True protein (g/100 ml)		Crude protein (g/100 ml)		Fat (g/100 ml)		Carbohydrate (g/100 ml)	
Food group intake, g/day		R	p	R	p	R	p	R	p	R	p	R	p	R	p	R	p	R	p	R	p
Dairy[†]	255.7 (65.6, 508.5)	0.038	0.764	−0.029	0.818	−0.073	0.564	0.033	0.793	0.049	0.699	0.036	0.774	0.014	0.914	0.031	0.806	0.028	0.825	0.081	0.520
Meat, fish, and eggs	200.9 (151.9, 259.0)	0.013	0.920	−0.093	0.459	−0.078	0.535	−0.018	0.885	0.182	0.146	−0.102	0.420	−0.171	0.174	−0.230	0.065	−0.090	0.475	0.012	0.922
Eggs	22.2 (14.8, 44.4)	−0.037	0.769	−0.146	0.244	−0.085	0.503	−0.065	0.606	**0.304**	**0.014**	−0.035	0.782	−0.119	0.347	−0.152	0.227	−0.065	0.605	0.205	0.102
Meat[‡]	110.9 (76.6, 132.6)	0.001	0.995	−0.019	0.879	−0.046	0.714	−0.017	0.895	−0.037	0.771	−0.105	0.407	−0.050	0.695	−0.084	0.506	−0.077	0.544	−0.181	0.149
Fish and seafood[§]	61.7 (33.2, 92.9)	0.047	0.712	−0.085	0.501	−0.048	0.705	0.023	0.855	**0.267**	**0.032**	−0.038	0.761	−0.218	0.080	**−0.273**	**0.028**	−0.039	0.758	0.180	0.151
Fruits[¶]	313.3 (204.1, 451.8)	0.088	0.486	0.121	0.337	0.152	0.228	0.089	0.483	−0.186	0.138	0.099	0.433	0.022	0.863	0.005	0.971	0.121	0.337	−0.173	0.168
Vegetables[**]	179.8 (111.2, 271.8)	0.073	0.561	−0.033	0.793	−0.030	0.814	0.065	0.608	0.013	0.920	0.047	0.711	−0.106	0.399	−0.126	0.318	0.055	0.663	0.032	0.797
Nuts[††]	10.2 (2.5, 30.5)	0.020	0.874	0.164	0.192	0.150	0.234	0.006	0.961	−0.031	0.805	0.020	0.873	0.054	0.667	0.017	0.896	0.036	0.779	−0.111	0.379
Bread, rice, pasta, and potatoes	191.9 (154.8, 259.3)	**0.271**	**0.029**	0.221	0.077	0.192	0.126	0.231	0.064	0.148	0.240	**0.248**	**0.046**	0.177	0.159	0.176	0.161	0.219	0.080	0.047	0.711
Bread[‡‡]	50.3 (33.6,75.7)	−0.012	0.926	0.244	0.050	0.209	0.094	−0.054	0.669	0.008	0.947	−0.050	0.692	0.234	0.061	0.202	0.107	−0.072	0.566	−0.017	0.894
Rice and pasta	85.7 (60.7, 142.9)	0.173	0.168	0.113	0.372	0.107	0.396	0.148	0.238	0.154	0.219	0.155	0.217	0.068	0.590	0.070	0.580	0.128	0.311	0.082	0.517
Potatoes[§§]	50.0 (23.8, 76.2)	**0.474**	**< 0.001**	0.212	0.090	0.168	0.181	**0.443**	**< 0.001**	0.129	0.306	**0.476**	**< 0.001**	0.176	0.160	0.201	0.109	0.462	**< 0.001**	−0.005	0.971
Fats	10.5 (4.7, 16.9)	0.053	0.675	0.021	0.870	−0.015	0.906	0.037	0.771	0.018	0.889	0.014	0.914	−0.119	0.344	−0.129	0.304	0.030	0.811	−0.024	0.852
Saturated fat[¶¶]	1.0 (0.0, 4.7)	0.208	0.096	0.064	0.615	0.027	0.833	0.183	0.144	0.097	0.441	0.148	0.239	0.007	0.959	−0.027	0.833	0.143	0.256	0.014	0.914
Unsaturated fats[***]	5.8 (2.9, 13.5)	−0.017	0.893	−0.001	0.997	−0.025	0.844	−0.025	0.842	−0.015	0.903	−0.037	0.769	−0.127	0.313	−0.126	0.317	−0.018	0.886	−0.029	0.816

*Using the Miris HMA™ (Human Milk Analyzer, Miris AB, Uppsala, Sweden).
[†]Whole milk, semi-skimmed milk, skimmed milk, yogurt, and cheese.
[‡]Chicken, turkey, rabbit meat, beef, pork, and lamb.
[§]Fatty, lean and canned fish, cod fish, squid, octopus, and shellfish.
[¶]Apples, pears, oranges, tangerines, bananas, kiwis, strawberries, cherries, peaches, plums, melon, watermelon, persimmons, figs, loquats, and grapes.
[**]White or savoy cabbage, bunch, kale, broccoli, cauliflower, brussels sprouts, turnip greens, spinach, green beans, lettuce, watercress, onion, carrot, turnip, tomato, pepper, and cucumber.
[††]Almonds, hazelnuts, walnuts, pistachios, and peanuts.
[‡‡]White or wholemeal bread, toast, and cornbread.
[§§]Fried, boiled, roasted, stewed, and mashed potatoes.
[¶¶]Butter.
[***]Olive oil, oil, and margarine.
p25: 25th percentile; p75: 75th percentile; kcal: kilocalories; g: grams; g/day: grams per day; ml: milliliters.
The values in bold represent statistically significant correlations, with $p < 0.05$.

fat (3.1 vs. 3.8 g/100 ml) and carbohydrate contents (8.0 vs. 7.0 g/100 ml) after pasteurization.

Regarding the relationship between demographic, lifestyle, and anthropometric data of HMDs or their infants and the composition of DHM before and after pasteurization, only gestational age was positively associated with the true protein content of pasteurized DHM ($r = 0.260$, $p = 0.036$), as indicated in table 4.

Table 5 characterizes the energy and nutritional profile of the HMDs' diet, indicating the following median intake values: 2147.4 kcal/day, 103.8 g/day, 81.8 g/day, and 243.2 g/day of energy, protein, fat, and carbohydrate intake, respectively. By analyzing the nutritional composition of the DHM, the energy of DHM before pasteurization was positively correlated with daily carbohydrate intake, in grams ($r = 0.272$, $p = 0.029$).

Table 6 describes their eating habits by food group over the last year. A higher consumption of meat was observed compared to fish and seafood (110.9 vs. 61.7 g/day). Daily fruit intake was higher than vegetable consumption (313.3 vs. 179.8 g/day). Rice and pasta were considered the primary sources of carbohydrates, while bread and potatoes were consumed in smaller quantities (85.7 vs. 50.3 and 50.0 g/day, respectively). There was also a higher intake of unsaturated fats compared to saturated fats (5.8 vs. 1.0 g/day, respectively). In terms of correlations between the dietary habits of HMDs and the nutritional composition of DHM before pasteurization, both eggs and fish and seafood consumption showed a positive association with the carbohydrate content of DHM ($r = 0.304$, $p = 0.014$ and $r = 0.267$, $p = 0.032$, respectively). The consumption of carbohydrate sources was positively associated with the energy of DHM ($r = 0.271$, $p = 0.029$). Potato intake showed a positive correlation with both energy and fat DHM content ($r = 0.474$, $p < 0.001$ and $r = 0.443$, $p < 0.001$, respectively). After pasteurization, similar associations were observed for the intake of carbohydrate sources. Fish and seafood consumption had a negative correlation with DHM's crude protein content ($r = -0.273$, $p = 0.028$).

Discussion

In this cross-sectional study, it was found that Holder pasteurization has an impact on the nutritional composition of DHM. Significant differences were observed, particularly in the energy and fat content of DHM, with a higher percentage reduction in energy, fat, and protein, which aligns with previous research findings[24]. The percentage impact on these macronutrients differs from the findings of Quitadamo et al., (energy: −4.5% vs −8.1%; fat: −8.3% vs −14.9%; crude protein: −7.1% vs 2.7%, respectively)[24]. However, it is evident that fat is consistently the macronutrient that is most significantly affected in both studies. These results have practical implications in clinical settings, especially for the individualized fortification of DHM provided to premature newborns or infants with a very low birth weight, who are the primary recipients of DHM[14]. It was also observed that the macronutrient with the greatest deviation from the gold standard for mature HM was carbohydrates, both before and after pasteurization. Notably, carbohydrates appear to be one of the macronutrients least impacted by pasteurization in percentage terms, which is a key point, given their role as essential energy sources, particularly for DHM-fed newborns with heightened energy needs[25]. It is vital to understand that DHM undergoes a pasteurization process before it is distributed to recipient infants. Therefore, when interpreting the relationship between the eating habits of HMDs' and the composition of DHM, it is essential to consider the nutritional implications of this processing step.

In this sample, 50.8% of participants were overweight, which is greater than the prevalence observed in a recent study with Portuguese women at reproductive age[26] (35%) and lower than the prevalence found in Portuguese women according to the *National Food, Nutrition, and Physical Activity Survey 2015-2016* (55%)[15]. Furthermore, the median FM value (33.2%) of our sample exceeded the recommended range for adult women aged from 20 to 39 years (21.0-33.0%)[27]. Generally, no associations were found between the nutritional composition of DHM and HMDs' body composition in this study, but only with HMDs' eating habits.

In this paper, factors such as age and the number of hours of sleep in HMDs', as well as their infants' birth weight, also do not seem to affect the nutritional composition of DHM. Dritsakou et al., revealed a positive relationship between maternal age and HM fat content, while the gestational age and birth weight of their infants exhibited a negative association with the energy, fat, and protein content of HM[28]. The highest levels of carbohydrates were also observed in mature milk from preterm deliveries. One possible explanation for this study not showing associations with these variables may be the small size of the sample and the fact that it only includes mature DHM samples (> two weeks postpartum) while Dritsakou et al., included HM samples from different stages of lactation[28].

Gestational age seems to be positively correlated with the protein content of DHM after pasteurization in this study. However, it is noteworthy that most of the

infants were born at more than 37 weeks. As highlighted by Agostoni et al., it is well-established that the nutritional composition of HM differs between preterm and full-term births[25] but, according to previous research conducted by Gidrewicz et al., this disparity decreases as lactation progresses[29]. Also, a longitudinal study[30] that exclusively analyzed DHM samples from HMDs' with full-term deliveries did not find any association between gestational age and the nutritional composition of DHM. It is important to mention that all of these studies only considered samples of raw milk, so the statistically significant association found could be attributed to the effect of pasteurization on protein in DHM. Therefore, more studies are needed to understand the role of these variables in the nutritional composition of DHM.

The literature suggested that lactating women who are overweight or have a higher percentage of FM may produce milk with a higher fat content[11]. In this study, neither BMI nor FM exhibited any association with the nutritional composition of DHM. Therefore, further research is needed to validate our findings, considering the limited number of participants in this study.

Our specific results revealed that increased carbohydrate intake in HMDs' was associated with the energy content of raw DHM. This impact lost statistical significance after DHM pasteurization, likely due to its susceptibility to the pasteurization process. These findings are supported by Binder et al., who also observed that higher dietary macronutrient intake was reflected in higher levels of respective macronutrients in DHM[21], although this paper did not confirm those results. Binder et al. used a 24-hour recall method to assess participants' eating habits, whereas our study utilized an FFQ, which limits the validity of direct comparisons between the two studies.

In a study conducted on Portuguese pregnant women[26], a lower consumption of fish compared to meat was also observed, while vegetable intake exceeded that of fruit, which is contrary to our findings. It is worth noting that this previous study did not distinguish between carbohydrate sources or different types of fats. Thus, our study can contribute to advancing knowledge in this specific field.

This paper indicated an expected positive association between the consumption of carbohydrate sources and DHM's energy both before and after pasteurization. It is of relevance that the association between dietary intake and DHM's energy content may hold relevant implications for the nutrition of preterm infants, who have higher energy and nutritional requirements compared to full-term infants[31]. Surprisingly, a higher intake of potatoes appears to be associated with higher fat content in DHM. However more research is required to fully comprehend this observation. Also, in this study, we found that the consumption of protein sources (meat, fish, and eggs) was inversely associated with the protein content of DHM, with statistical significance observed only for fish and seafood, after pasteurization. A previous study conducted on lactating women in China investigated the association between maternal dietary patterns during lactation and HM macronutrient composition. The authors found a negative correlation between protein content in colostrum and the "high-in-animal-sourced-foods pattern", characterized by high consumption of oils, vegetables, meat/poultry, grains, beans, dairy, and seafood[32]. This same study[32] claimed that, in mature milk, a positive association was observed between the "high-in-animal-sourced-foods pattern" and the carbohydrate concentration of DHM. Interestingly, our results also revealed a positive association between eggs, fish, and seafood consumption and the carbohydrate content of DHM. However, more studies are needed to provide a comprehensive understanding of this topic.

In general, there is a lack of evidence regarding the relationship between HMDs' food intake and the nutritional composition of DHM, making further studies in this area necessary to better understand all of these results.

There are some limitations in this study that should be noted. The first limitation is the small sample size, which may have impacted the ability to detect significant associations. Additionally, being a cross-sectional study makes it impossible to establish a causal relationship. On the other hand, in this study, a validated FFQ for the Portuguese adult population was used and this was the first study of its kind conducted in a Portuguese Human Milk Bank.

Our findings reinforce the importance of nutritional monitoring during the lactation period, particularly in the context of HM donation. It can also contribute to the development of public policies aimed at improving the dietary habits of HMDs', thereby adjusting the nutritional composition of DHM to meet the specific nutritional needs of recipient infants. Based on the high percentage of overweight HMDs and the potential associations between diet and the nutritional composition of DHM demonstrated in this study, we recommend that HMDs receive nutritional guidance and food education. We also propose increasing awareness about the importance of donating HM to premature infants and those with high-risk conditions.

In conclusion, no relationship was found between the BMI or FM of HMDs' and the nutritional composition of their DHM. Carbohydrate intake was positively associated with the energy of DHM. Further research is needed to confirm findings, considering major covariates and larger sample sizes.

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Author contributions

S. Lopes da Silva: Acquisition of data either from patients, research studies, or literature; Analysis or interpretation of data from patients, research results, or literature search; Drafting the article; Critical review of the manuscript for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work. B. Teixeira: Conception and design of the study, report, review or other type of work or paper; Analysis or interpretation of data from patients, research results, or literature search; Drafting the article; Critical review of the manuscript for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work. S. Pissarra: Acquisition of data either from patients, research studies, or literature; Critical review of the manuscript for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work. S. Fraga: Acquisition of data either from patients, research studies, or literature; Critical review of the manuscript for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work. R. Moita: Acquisition of data either from patients, research studies, or literature; Critical review of the manuscript for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work. H. Soares: Critical review of the manuscript for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work. C. Martins: Critical review of the manuscript for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work. C. C. Dias: Analysis or interpretation of data from patients, research results, or literature search; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work. D. e Silva: Conception and design of the study, report, review or other type of work or paper; Acquisition of data either from patients, research studies, or literature; Critical review of the manuscript for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work.

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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ORIGINAL ARTICLE

Pediatric death: perceptions and experience of healthcare professionals

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Abstract

Introduction and Objectives: As a result of its particular nature, pediatric death presents healthcare workers with personal and professional challenges that are complex to manage. The objective of this study was to characterize the experience of healthcare workers in a level II pediatric department, focusing on grief and the impact of death in a professional setting. **Methods:** A cross-sectional study was conducted in 2023. A paper-based questionnaire was used, with questions divided into three areas: biopsychosocial characterization, impact of death, and potential insecurities. **Results:** A total of 97 questionnaires were distributed, with 74 (76.3%) responses collected, mostly from nurses (47.3%) and doctors (39.2%). The experience of pediatric death was reported by 61 (82.4%) professionals, mostly in emergency situations (62.3%). The emotions most frequently mentioned were sadness (93.4%) and compassion (63.9%), with no differences between professional subgroups or experience ($p > 0.05$). Regarding the impact of death, professionals reported more difficulty falling asleep, particularly those with fewer years of experience ($p = 0.014$). Doctors were more likely to question the appropriateness of their professional practices ($p = 0.048$). When evaluating insecurities about a future event, professionals with less experience reported greater concern about scientific preparedness ($p = 0.031$), while professionals without children expressed more concern about delivering the news to caregivers ($p = 0.002$). **Discussion:** Pediatric death causes changes to the routines and behaviors of professionals in our department, which highlights the importance of finding tailored strategies to support grieving. The impact and concerns are heterogeneous, varying with professional experience and family background, indicating that interventions should be adapted to the specific concerns of each subgroup.

Keywords: Pediatric death. Healthcare worker. Grief. Emergency department.

Morte pediátrica: perceções e experiência dos profissionais de saúde

Resumo

Introdução e Objetivos: A morte em idade pediátrica representa desafios pessoais e profissionais complexos para os profissionais de saúde. O objetivo foi caracterizar a experiência dos profissionais de um serviço de pediatria, relativamente ao luto e ao impacto da morte em contexto laboral. **Métodos:** Foi conduzido um estudo transversal em 2023, utilizando um questionário com perguntas divididas em três áreas: caraterização biopsicossocial, impacto da morte e potenciais inseguranças.

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Resultados: Foram distribuídos 97 questionários, obtendo-se 74 (76,3%) respostas, a maioria de enfermeiros (47,3%) e médicos (39,2%). A experiência de morte pediátrica foi relatada por 61 (82,4%) profissionais, principalmente em emergências (62,3%). As emoções mais sentidas foram tristeza (93,4%) e compaixão (63,9%), sem diferenças entre subgrupos profissionais ou experiência ($p > 0.05$). Relativamente ao impacto da morte, os profissionais relataram maior dificuldade em adormecer, em particular aqueles com menos anos de experiência ($p = 0.014$). Os médicos questionaram-se mais se as suas práticas profissionais eram adequadas ($p = 0.048$). Ao avaliar as inseguranças face a um futuro evento de morte, os profissionais com menos experiência relataram maior preocupação com a preparação científica ($p = 0.031$), enquanto os profissionais sem filhos revelaram maior preocupação em comunicar a notícia aos cuidadores ($p = 0.002$). **Discussão:** A morte em idade pediátrica provoca alterações nas rotinas e nos comportamentos dos profissionais, sublinhando a importância de encontrar estratégias ajustadas para apoiar o luto. O impacto e as preocupações são heterogéneas, variando com a experiência profissional e o contexto familiar, o que indica que as intervenções devem ser adaptadas às preocupações específicas de cada subgrupo.

Palavras-chave: Morte pediátrica. Profissional de saúde. Luto. Serviço de urgência.

Keypoints

What is known
- The impact of pediatric death in the workplace is well documented in contexts where it is more frequent, such as Pediatric Oncology and Intensive Care.
- Even though pediatric emergency situations pose a range of complexities in terms of management, workers rarely feel helplessness due to a greater sense of effective effort in attempting to prevent death compared to chronic untreatable diseases.
- Younger professionals may experience greater feelings of guilt and anxiety, with the incidence of post-traumatic stress reaching up to 81%.

What is added
- Even though death is less frequent in level II units, its impact on the lives of professionals is the same, and in some areas even greater than in other settings where death is more common.
- The feelings experienced by professionals do not depend on their years of experience or the specific responsibilities of each role, and include sadness and compassion.
- Younger professionals are more likely to feel an impact on their sleep quality after a death event.

Introduction

Death in pediatric age is a rare event and is associated with complex challenges on the emotional, cultural, procedural, and legal levels. In Portugal, the mortality rate for those under 19 years of age has substantially decreased due to improvements in healthcare and the population's quality of life, representing 0.4% of all deaths in 2023 compared to 6.9% in 1980. This decrease translates into pediatric professionals being less exposed to death events[1]. In the pediatric age, in European countries, the causes of death are shifting, with increasing prominence of prematurity and its consequences, trauma and accidents, neoplasms, and adolescent suicide, while the influence of infectious diseases and congenital malformations on pediatric mortality rates is progressively declining[2].

For healthcare professionals, the responsibility in situations that result in a patient's death is two-fold: on one hand, applying clinical and scientific expertise to prevent the fatal outcome; on the other, coordinating and leading multidisciplinary teams to ensure comprehensive and compassionate care throughout the process. Studies show that healthcare professionals may repress or delay grief due to professional responsibilities and self-expectations, which is linked to a high rate of secondary traumatic stress[3]. Other studies indicate that up to two-thirds of professionals experience high levels of psychological stress when caring for children who eventually pass away[4-5]. The social repression of grief, which positions the caregiver as the primary mourner, combined with the demand to maintain professional performance regardless of personal feelings, contributes to the phenomenon of the "forgotten mourner"[6]. In particular, professionals working in settings where death is less frequent may have different experiences in dealing with grief compared to professionals in palliative care, pediatric oncology, and intensive care, whose grief has been well characterized in the literature[7-9].

The objective of this study was to characterize the experience of healthcare professionals in a pediatric department regarding grief over deaths in a professional context. The study aimed to classify and characterize preceding clinical events, interpersonal difficulties, team management problems, and the

event's impact on personal and professional life in the weeks following the death. This study also aims to identify the strengths and vulnerabilities of professionals monitoring such events, in a department that lacks a defined local protocol for case analysis and review, as well as specific training in the area. The goal is to establish initial indicators that will guide the development and implementation of interventions.

Methods

A quantitative cross-sectional and correlational study was conducted in December 2023 in the Pediatric Department of a level II Portuguese hospital.

Participants were selected based on their workplace, covering all healthcare professionals (doctors, nurses, and assistants) working in the Pediatric Emergency Department (PED) and the Special Care Unit for Newborns (SCUN). The team consists of 97 professionals: 39 doctors, 41 nurses (20 in the PED and 21 in the SCUN), and 17 operational assistants (10 in the PED and seven in the SCUN). The PED is an emergency department with an average of approximately 20,000 admissions annually, providing healthcare to all those up to 17 years and 364 days who were admitted on their own initiative or referred by primary healthcare services, the SNS24 hotline, or through the National Institute of Medical Emergencies. The SCUN admits all newborns from its referral area with a gestational age of over 32 weeks who require special care, with an average of 340 admissions annually. The Pediatric Department also includes a pediatric palliative care team that provides support in the outpatient and inpatient settings. There is no specific, permanent team working or providing consultations at the Emergency Department.

In terms of death events in pediatrics within the department, occupational health provides informal support if needed, upon request or through self-referral by the healthcare professional. There is no established local protocol for conducting debriefings or annual mortality review meetings.

The instrument used in this study was a paper questionnaire, divided into three parts. The first part included closed-ended, single or multiple-choice questions about the participant's biopsychosocial characteristics. The second part (personal experience with death in Pediatrics) was to be completed only by professionals who had witnessed a pediatric death during their work and included closed-ended questions and five-point Likert scale questions about the circumstances of the death and how they coped with the situation. The third part (professional training), which applied to all participants, set out to assess knowledge about technical procedures after death, to classify factors triggering fear or insecurity in the face of a potential death, and to evaluate the number of professionals with training in palliative care. The questionnaire was completed by doctors and nurses in full, and a version excluding clinical questions was completed by assistants. To preserve participant confidentiality, questionnaires with non-anonymized content were excluded from the analysis. Before digitizing each document, a random code was assigned, separating the questionnaires into two parts: the biopsychosocial questions (part 1) and the questions included in parts 2 and 3.

Categorical variables were expressed as absolute and relative values, and continuous variables were expressed as measures of central tendency and dispersion according to their distribution type. Hypothesis tests were applied between categorical variables using the chi-square test or Fisher's exact test (for expected frequencies of below five), and differences in the distribution of continuous variables across categorical variable subgroups were assessed using non-parametric tests. To analyze factors with potential confounders described in the literature, logistic regression was used to adjust for the identified variables. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS), software version 26.0.

This study was approved by the Hospital Ethics Committee in September 2023.

Results

A total of 97 questionnaires were distributed and 74 (76.3%) responses were obtained, 66 (89.2%) of which were from female participants. Regarding the professional category, most respondents were nurses (n = 35; 47.9%), followed by doctors (n = 29; 39.7%), then assistants (n = 9; 12.3%). One participant did not identify their professional group. Fourteen professionals worked exclusively in the SCUN. The most common age group among healthcare professionals was between 40 and 50 years old (n = 21; 28.4%), and 42 (56.8%) had 15 or fewer years of professional experience in pediatrics. Previous training in palliative care was reported by 31.1% of professionals, 26.1% of whom felt that this training was sufficient to deal with death.

The experience of witnessing a pediatric death was reported by 61 (82.4%) professionals, and it was significantly more common among professionals with more years of experience ($p < 0.001$). When adjusted for years of experience, no difference was found

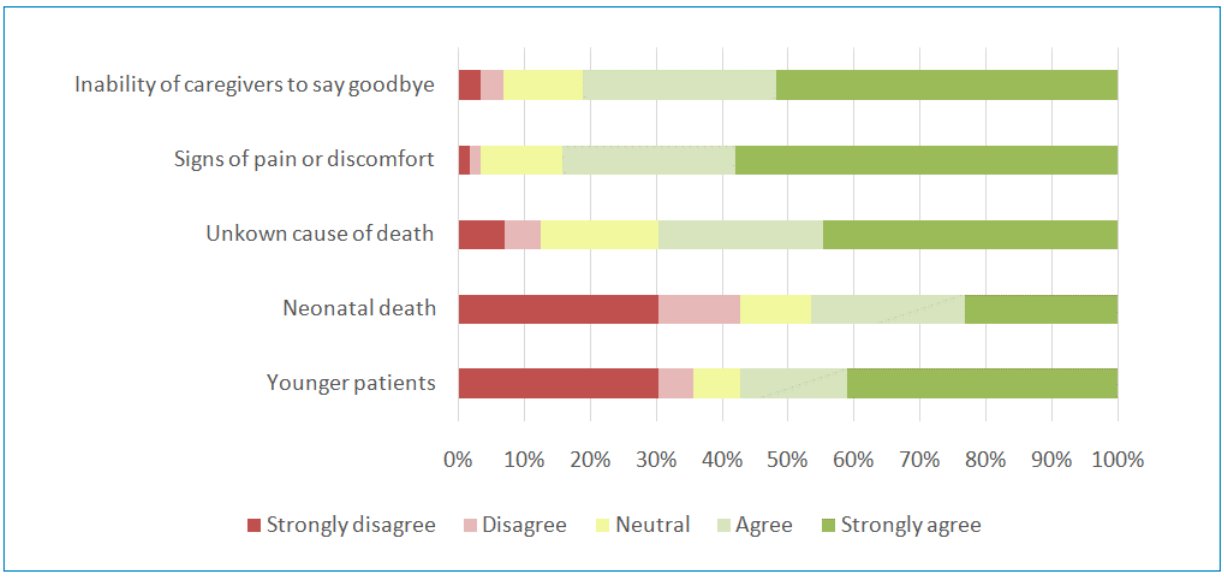

Figure 1. Agreement of healthcare workers about clinical factors that contributed to a more difficult management of death.

between the age of the healthcare professional (p = 0.575) or professional group (p = 0.268) and whether or not they had witnessed a pediatric death. In terms of the number of deaths, 32 (52.5%) had witnessed fewer than five deaths and 11 (14.9%) had seen more than 10. Twenty-two (36.1%) professionals witnessed their most recent death less than a year ago. The most frequent clinical context of death was pediatric emergency situations (n = 38; 62.3%), followed by neonatal emergencies, then chronic illnesses with a predictable clinical outcome (both n = 18; 29.5%) and chronic illnesses with an unpredictable clinical outcome (n = 1; 1.6%).

The emotions most commonly experienced by healthcare professionals were sadness (n = 57; 93.4%) and compassion (n = 39; 63.9%). Less common emotions were anger (26.2%), guilt (14.8%), and indifference (0.0%). No differences were found in the distribution of emotions experienced across professional groups or years of experience. None of the professionals reported feelings of indifference.

Most professionals (n = 50; 82.0%) talked to someone about how they felt, most often with colleagues (n = 47; 94.0%), spouses (n = 28; 56.0%), family members, or friends (both n = 17; 34.0%). No one shared their concerns with occupational health services. Among the group of professionals who did not talk about their feelings (n = 11; 18.0%), the reported reasons were: difficulty in expressing feelings, insecurity, lack of support from the institution, and respect for the patient's family.

The agreement with various clinical or social factors that contributed to making a death more difficult to manage is shown in figure 1. No differences were found in the agreement between the statements and the healthcare professional's age, years of experience, professional category, or the number of deaths witnessed.

Professionals also reported the frequency of a set of personal or professional situations and actions that occurred during the week following the death event they witnessed (Fig. 2).

Difficulty falling asleep was more frequent among assistants (p = 0.048) and professionals with fewer years of experience (p = 0.014). Doctors were more likely to question the appropriateness of their practices (p = 0.048). Professionals with children were more inclined to seek contact with close family members (p = 0.049). Professionals working exclusively in the SCUN reported less difficulty falling asleep (p = 0.003), less difficulty controlling their emotions (p = 0.009), and less introspection about their professional practices (p = 0.019). Difficulty falling asleep was more prevalent in the group of professionals who experienced anxiety (p = 0.001), fear (p = 0.021), or guilt (p = 0.001) when dealing with death, but it was not observed in those who reacted with anger (p = 0.960), sadness (p = 0.922), or pity (p = 0.438).

When asked if they had learned to cope better with death over time, 34 (55.7%) responded affirmatively, which was significantly more frequent in the group of professionals dedicated exclusively to the SCUN

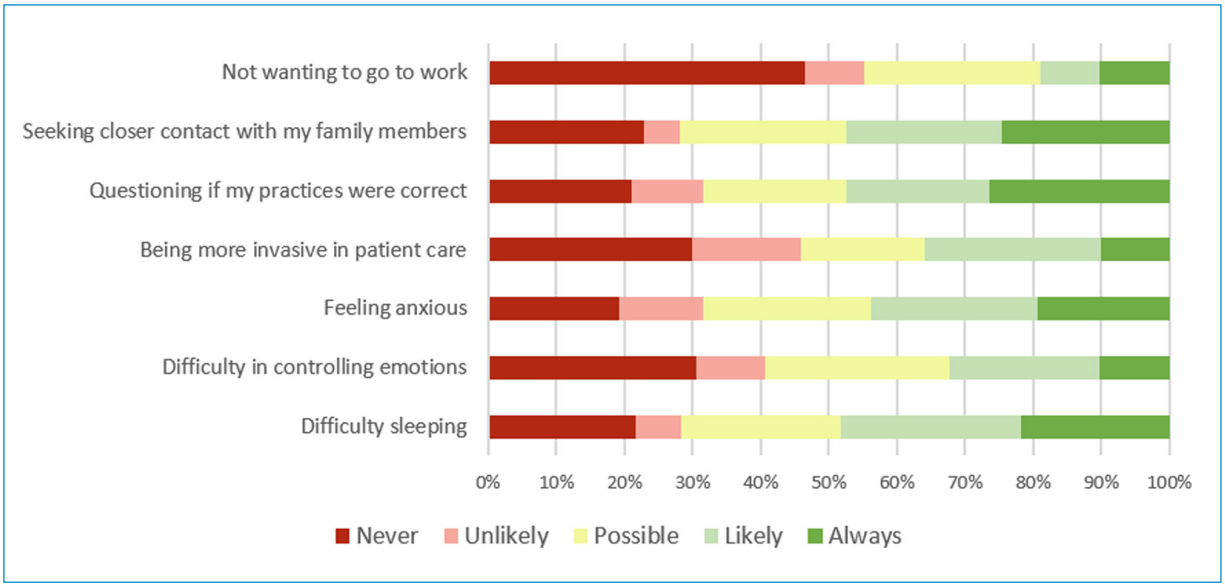

Figure 2. Frequency of situations and personal actions in the week following the pediatric death event.

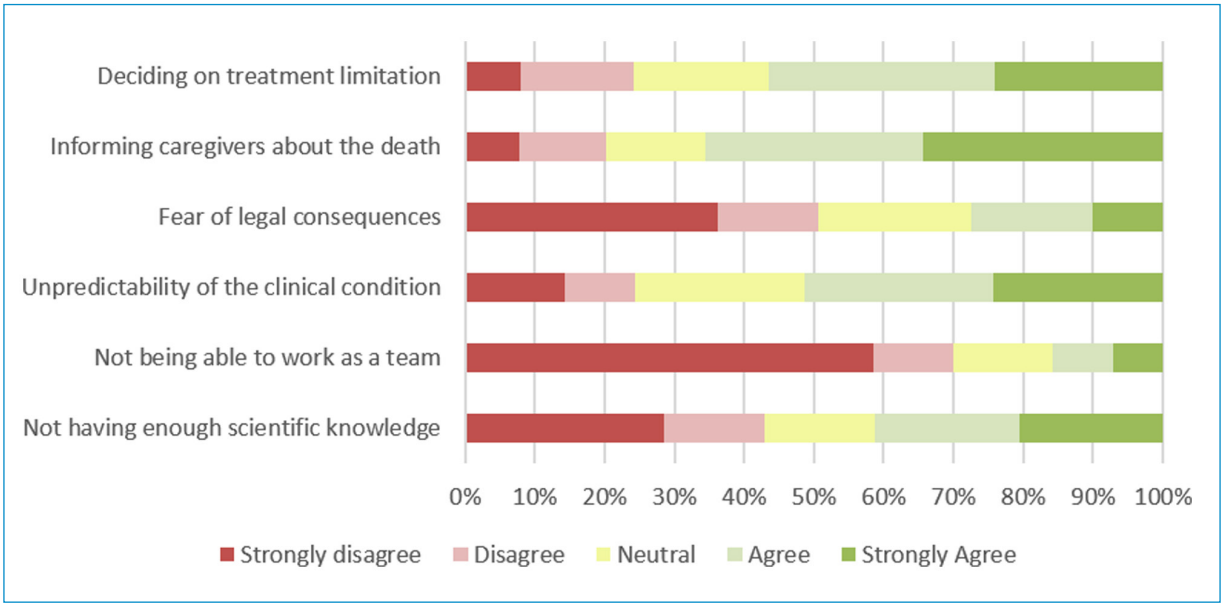

Figure 3. Fears and insecurities about dealing with a future pediatric death event.

($p = 0.048$), but with no differences between subgroups of professional experience.

The overall perception of healthcare professionals, including those who have never witnessed a pediatric death, regarding factors that may contribute to insecurity or fear in dealing with pediatric death, is represented in figure 3. Professionals with fewer years of experience more frequently reported concern about their scientific preparation, while professionals without children found it more difficult to deliver the news to caregivers.

Discussion

The perception and experience of healthcare professionals in situations involving pediatric death remains a complex subject. Although the incidence of pediatric death in our center is relatively low, each occurrence represents a profoundly disruptive event that significantly impacts the lives of healthcare professionals. The emotional weight of a child's death extends beyond the clinical context, often influencing both the personal and professional dimensions of a caregiver's life.

The response rate (76.3%) to our questionnaire was higher than that reported in the literature for studies with a similar methodology, which may indicate genuine interest among the professionals in the department regarding this topic[10].

In the department where the study was conducted, between 1997 and 2023, there were 71 deaths, with a median age of 2.5 years, 41 of which occurred in the Emergency Department and two in the SCUN. In the Pediatric Emergency Department, 83.8% of the deaths occurred within the first hour after admission[11]. Most of the healthcare professionals who responded to the questionnaire work in the Emergency Department, which corresponds to the subgroup of professionals most likely to have witnessed a death in the department. This aligns with our results, where the most frequent clinical context of death was pediatric emergency situations (62.3%). Studies in the same field report that the death of a child or adolescent in emergency care is a globally rare event, leading to few doctors feeling like specialists in managing these situations. However, most have some knowledge and experience that can be enhanced through collaboration with other healthcare professionals[12].

One important consideration is the wide range of clinical presentations seen when a child dies in the Emergency Department. This includes complex challenges such as determining when to stop resuscitation efforts, recognizing and managing signs of discomfort, communicating with and supporting families, meeting forensic obligations, withdrawing or withholding treatment in chronically ill children, and coping with the emotional toll of returning to work afterward. In our study, the most commonly reported challenges were breaking the news to caregivers, making decisions about therapeutic limitations, and dealing with clinical unpredictability and signs of suffering – findings that align with existing literature[12-13]. Additional factors known to influence the experience of a child's death include the child's age and the cause of death[5]. In our department, however, the cause of death played a more significant role than age in shaping how these situations were managed.

Emotionally, the feelings reported by teams often include anger, sadness, inadequacy, or guilt. In our department, sadness was the most common emotion (93.4%), which is consistent with the literature. Compared to other studies, guilt was a relatively uncommon feeling in our context. Research more frequently associates feelings of guilt with situations where the resuscitation chain of events was not effectively implemented or therapeutic limitations were decided upon[13]. In our department, however, most deaths occurred in previously healthy children, in emergency settings where efforts are typically exhaustive and unrestricted, which may contribute to a sense of inevitability following the team's maximal efforts.

Compared to another study conducted at the same institution, professionals in the delivery room dealt with gestational loss with a lower rate of sadness (45%), with the feeling of helplessness being more frequent (80%)[14]. In the literature, helplessness is less often associated with pediatric emergency contexts compared to perinatal death, due to the multitude of procedures and therapies used in resuscitation, contributing to a greater sense of effective effort in attempting to prevent death. Even in healthcare settings where death is more frequent, such as pediatric intensive care units, up to 46% of doctors perceive death as a professional failure, and 92% would like to receive training on how to manage these situations[15].

Younger professionals in the department, in particular, have different concerns from the more experienced subgroup, which is consistent with other studies identifying that interns report more self-doubt, reflecting their inexperience. Some even report that 67% of interns who witnessed a death had no training on the topic and 81% showed one or more symptoms of post-traumatic stress[16-17]. In our study, less experienced professionals more frequently experienced anxiety-related behaviors, such as difficulty falling asleep ($p = 0.014$), and greater concern about their scientific preparedness.

The concern over delivering the news to the family was a source of insecurity or fear (65%), particularly among professionals without children. This factor has generated scientific interest in methods for handling such situations, including taking some time to prepare emotionally and establishing in advance what to say[13]. In cases where the family is present during resuscitation, it can be helpful for the team leader to periodically summarize the resuscitation efforts and the clinical response, as well as to provide guidance on the short-term ongoing care of the patient[12].

A large proportion of our professionals showed changes in their routine and behavior during the week following the death event, particularly with changes in sleep patterns, personal introspection, and seeking to maintain closer contact with family members. Some of these changes may serve as coping mechanisms in the grieving process, but others may signal difficulty in dealing with emotions or signs of pathological stress. Some studies suggest coping strategies such as emotional regulation (social support or religion), helping with problem-solving (support

for bereaved families), cognitive restructuring (making a difference and investing in research), and distraction (breaks, physical activities, entertainment, and time with one's children)[18]. The lack of institutional support was considered a negative aspect in our institution, similar to other studies, highlighting the need for improvement in recognizing the role of healthcare professionals in the deaths of the patients they care for[19].

Overall, professionals facing pediatric death deserve measures addressing their concerns, including team management, communication with caregivers, and scientific preparation for these events. Some interventions in education have been proposed, including incorporating this topic into the Pediatric Advanced Life Support (PALS) course, which 79% of participants in this modality found very useful[20].

Implementing targeted supportive interventions for healthcare professionals who manage pediatric deaths is essential to promote emotional well-being, resilience, and professional sustainability. Regular discussion groups provide a structured space for team members to share experiences, process grief collectively, and foster mutual support, helping to mitigate feelings of isolation and emotional exhaustion. Individual supervision offers a more personalized approach, allowing professionals to explore their emotional responses, ethical dilemmas, and coping strategies in a confidential setting[21,22,23]. Studies highlight the importance of debriefing meetings after such events, discussing how the team worked, what could be improved, and how everyone felt, potentially reducing burnout and traumatic stress and improving compassion satisfaction[24]. Another potentially useful resource is performing a closure ritual. These rituals can include a brief statement by the leading element of the team, taking the time to thank everyone for their effort and acknowledging the feelings of losing the patient. Other types of rituals can include one minute of silence[25].

Palliative care training also equips staff with the necessary skills to deliver compassionate, patient-centered care, while simultaneously enhancing their ability to navigate complex conversations, manage symptoms effectively, and support families through end-of-life situations[26]. Combined, these interventions create a more supportive work environment, reduce burnout, and ultimately improve the quality of care delivered during profoundly difficult moments.

Incorporating death and mourning into the training curricula of health professionals is a crucial step toward preparing them for the emotional and clinical complexities of end-of-life care. Despite its inevitability in medical practice, death is often underrepresented in formal education, leaving professionals unprepared to cope with the emotional toll and interpersonal challenges it presents. A comprehensive approach should include both theoretical and practical components: theoretical instruction can provide an understanding of grief models, cultural variations in mourning, ethical considerations, and communication strategies, while practical training, such as role-playing, simulation exercises, and supervised clinical experiences, can build confidence in managing real-life situations[27,28]. By normalizing discussions about death during training, future professionals are more likely to approach these moments with empathy, clarity, and competence, ultimately improving care for patients and support for their families[27,28].

This study has several limitations that should be acknowledged. As a cross-sectional design was used, it is not possible to establish causal relationships between the identified factors and the experiences of healthcare professionals. A longitudinal approach would be more suitable for assessing how professionals' emotional responses and coping mechanisms evolve. Additionally, the study was conducted in a single pediatric department, which may limit the generalizability of the findings to other healthcare settings or cultural contexts.

In conclusion, the death of a pediatric patient, though infrequent, has a profound impact on healthcare professionals, affecting them both personally and professionally. Recognizing this reality underscores the importance of targeted training, emotional support strategies, and institutional policies that promote resilience and compassionate care.

Author contributions

I. Silva Costa: Conceptualization; Study design; Data collection; Data analysis; Drafting manuscript; Revision of manuscript; Final approval of manuscript. I. Melo: Data collection; Drafting manuscript; final approval of manuscript. C. Moutinho: Conceptualization; Revision of manuscript; Final approval of manuscript. S. Reis: Conceptualization; Study design; Revision of manuscript; Final approval of manuscript. L.M. Ferreira: Conceptualization; Study design; Revision of manuscript; Final approval of manuscript. C. Baptista: Conceptualization; Study design; Revision of manuscript; Final approval of manuscript.

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Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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CASE REPORT

Neuroleptic malignant syndrome in an adolescent with the GNAO1 mutation movement disorder phenotype: a challenging diagnosis

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Abstract

Introduction: Neuroleptic malignant syndrome (NMS) is a rare and life-threatening condition resulting from exposure to dopamine-blocking agents. GNAO1 mutations are a neurodevelopmental disorder associated with a hyperkinetic movement disorder, usually treated with dopamine-blocking agents. **Case report:** A 16-year-old adolescent, previously diagnosed with a GNAO1 dyskinetic movement disorder, and prescribed tetrabenazine, chlorpromazine and clonidine, was admitted during the summer due to nausea, fever and a slight worsening of dyskinesias. Initially, a heat stroke was assumed. A few days later, the patient manifested generalized dyskinesias, refractory hyperthermia, diaphoresis and progressive worsening of consciousness, suggesting neuroleptic malignant syndrome. Neuroleptic treatment was stopped, and the patient was started on dantrolene and admitted to the pediatric intensive care unit. The patient eventually recovered over the subsequent two months, symptomatic treatment for dyskinesias was slowly introduced, except chlorpromazine, and he was admitted to a rehabilitation center. **Discussion:** This case illustrates the diagnostic challenge of malignant neuroleptic syndrome in children and adolescents, particularly in patients with previous dyskinetic movement disorders treated with dopamine antagonists.

Síndrome neuroléptica maligna em um adolescente com fenótipo de transtorno do movimento por mutação GNAO1: um diagnóstico desafiador

Resumo

Introdução: O síndrome maligno dos neurolépticos é uma entidade grave, associada ao uso de agentes antidopaminérgicos. Mutações no gene GNAO1 podem manifestarse por doenças do movimento hipercinéticas, frequentemente tratadas com agentes antidopaminérgicos. **Relato do caso:** Um adolescente de 16 anos, com antecedentes de doença do movimento associada a mutação no gene GNAO1, tratado com tetrabenazina, clorpromazina e clodina, foi admitido no verão por náusea, febre e agravamento de discinesias. Inicialmente, foi assumido o diagnóstico de golpe de calor. Dias depois, apresentou discinesias generalizadas, hipertermia refratária, diaforese e agravamento progressivo do estado de consciência, sugerindo um síndrome maligno dos neurolépticos. Os fármacos neurolépticos foram suspensos, foi iniciado dantroleno e o doente foi

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transferido para a unidade de cuidados intensivos pediátricos. Verificou-se recuperação progressiva em dois meses, e a medicação de ambulatório foi lentamente introduzida, exceto a clorpromazina. **Discussão:** Este caso ilustra o desafio do diagnóstico de síndrome maligno dos neurolépticos em idade pediátrica, particularmente em doentes com antecedentes de doenças do movimento hipercinéticas tratadas com antagonistas dopaminérgicos.

Palavras-chave: Síndrome maligno dos neurolépticos. Mutação GNAO1. Doença do movimento.

Keypoints

What is known
- Neuroleptic malignant syndrome is a rare and life-threatening condition associated with exposure to dopamine-blocking agents.
- It manifests itself with severe extrapyramidal symptoms, an altered level of consciousness, fever, dysautonomia, rhabdomyolysis and potential multiple organ failure.
- Early diagnosis and treatment are crucial to improve prognosis.

What is new
- Patients on dopamine-blocking agents are more susceptible to both heat stroke and NMS.
- In patients with a previous history of movement disorders and pre-existing extrapyramidal symptoms, a high level of suspicion is required to diagnose NMS.

Introduction

Neuroleptic malignant syndrome (NMS) is a rare, yet life-threatening condition. It was first defined in the late 1950s[1], and the term was originally used to describe potentially severe extrapyramidal symptoms as side effects of first-generation antipsychotic drugs. It is now known that even atypical dopamine antagonists and the withdrawal of dopamine agonists and mood stabilizers are alternative causes. The main risk factor for developing NMS is the initiation or increase in the dosage of dopamine-blocking agents[2].

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) includes exposure to dopamine-blocking agents, severe muscle rigidity and fever as major diagnostic criteria. Other features are an altered level of consciousness, tremor, dysphagia, dysautonomia, leukocytosis and elevated creatine phosphokinase[3]. Complications include rhabdomyolysis, renal and respiratory failure, sepsis and death (mortality rate 5.6%). Emergency treatment is required, with the prompt cessation of causative agents and the initiation of supportive therapy and benzodiazepines. Globally, the prevalence of NMS is now lower (0.01 – 0.02%) as a result of attention to the prescription and titration of these drugs[4].

We report the occurrence of NMS in a male adolescent diagnosed with GNAO1 mutation with a hyperkinetic movement disorder. This is a challenging diagnosis in children with movement disorders given the low incidence and the pre-existence of extrapyramidal symptoms.

Case report

On a hot August afternoon, a 16-year-old adolescent was admitted to the emergency department due to feeling unwell, nauseated and refusing to eat after being at the beach with his family during the day. He had been diagnosed with GNAO1 encephalopathy at the age of 12 (confirmed by genetic testing), presenting with global development delay, dystonia and chorea since his first year of life. The brain magnetic resonance imaging (MRI) and metabolic testing were normal. Following several episodes of status dystonicus requiring hospital admission in the ICU, he was submitted to bilateral deep brain stimulation of the internal globus pallidus (GPi DBS) when he was 13 years old, with significant improvement. Before the event in question, the patient was partially dependent for daily routine activities, but capable of autonomous gait. He had dysarthric but fluent speech, and had oral, trunk and limb dystonia, controlled with tetrabenazine 18.75 mg daily (TID), chlorpromazine 37.5 mg daily (TID) and clonidine 0.33 mg daily (TID). There had been no recent changes to medication.

When the patient first arrived at the hospital, his temperature was 40.7 °C, while other vital signs and his blood glucose levels were normal. Besides a slight worsening of upper limp dyskinesias controlled with diazepam, the neurological examination presented no additional remarks. Blood tests in the first 12 hours of admission showed significant leukocytosis (35400 x 10^9 cells/L), elevated creatine phosphokinase (CK) (87250 U/L), and acute renal failure (creatinine 1.61 mg/dL). The

patient was admitted to the Pediatric Neurology department with the hypothesis of a heat stroke and secondary rhabdomyolysis and acute renal failure. Aggressive hydration was started, as well as diuresis monitoring through bladder catheterization.

In the first five days of hospital admission, he was apyretic and showed a significant clinical recovery. His renal function was normal and CK levels were consistently decreasing (21747 U/L). Fever and dysuria then ensued, with elevated inflammatory parameters, suggesting a urinary tract infection in the context of recent bladder catheterization. He was started on empiric antibiotic therapy with amoxicillin and clavulanic acid. The next day, severe generalized dyskinesia followed, and symptomatic treatment with oral and intravenous diazepam 5 mg and intravenous chlorpromazine 25 mg was administered. However, at the end of the day he deteriorated to the point of refractory hyperthermia, tachycardia, diaphoresis and a progressive decline in consciousness (Glasgow Coma Scale 9 – O2V2M5). His blood pressure and cardiac rhythm were normal and he showed no muscle rigidity. Deep brain stimulation (DBS) was functioning correctly. At this point, CK levels were rising again (80550 U/L) and neuroleptic malignant syndrome was suspected. Chlorpromazine and tetrabenazine were immediately stopped, hydration therapy was intensified, diazepam was continued and he was started on dantrolene 140 mg.

The patient was admitted to the pediatric intensive care unit (ICU) given the systemic multiple organ failure and distributive shock. His CK levels reached over 600000 U/L during his admission to the ICU, where he stayed for 26 days. The patient needed respiratory support through mechanical ventilation for 13 days, kidney function support through ultrafiltration for 18 days and cardiac support with vasoactive drugs during his initial days of admission. On the 20th day, following an acute decline in consciousness, the brain MRI showed bilateral occipital parenchymal hemorrhage suggestive of posterior reversible encephalopathy syndrome (Fig. 1) because of uncontrolled hypertension (probably the consequence of acute renal failure), which was then treated with labetalol and minoxidil. Concomitant respiratory infections were also diagnosed and treated.

After one month in the ICU, cardiac, respiratory and renal function returned to normal, as did his CK levels. Following progressive improvement in consciousness, the dyskinesias worsened. In the acute setting, dyskinesias were first controlled by adjusting sedative therapy (midazolam, fentanyl and ketamine). Clonidine was then restarted (first intravenously, max. 2 mcg/kg/h and then orally, max. 300 mcg every four hours). Other drugs were needed during the subacute phase to control dyskinesias, namely diazepam (max. 10 mg, TID), topiramate (max. 50 mg, BID), baclofen (max. 20 mg, TID) and trihexyphenidyl (max. 1 mg, TID). DBS parameters were also adjusted.

Two months later, the patient was discharged after an adjustment to his medication, communicating through mime and simple words. He had left-sided homonymous hemianopsia, generalized muscle atrophy and moderate tetraparesis, and also sporadic oral dyskinesias and left hand dystonia. Tetrabenazine was then slowly introduced in the clinic to better control dystonia, but chlorpromazine was not restarted. One year later, he recovered independent gait and speech, and the patient is now stable under tetrabenazine 37.5 mg per day, clonidine 1.8 mg per day (QID) and DBS stimulation.

Discussion

We present a challenging diagnosis of neuroleptic malignant syndrome. The first episode that brought the patient to the emergency room makes us wonder whether this was already the insidious start of NMS or in fact a heat stroke. These two entities share common features, such as hyperthermia, central nervous system dysfunction, dysautonomia, rhabdomyolysis and a potentially poor prognosis with intensive care admission. Heat stroke may also be facilitated in patients taking antipsychotic drugs, as the blockage of hypothalamic thermoregulatory pathways inhibits heat dissipation[5,6]. Another possibility to be considered, given the previous history of status dystonicus, would be a dystonic storm in the event of sudden DBS failure[7]. However, DBS was confirmed to be functioning correctly.

This episode occurred during a very hot summer day, during which the patient refused to eat and drink, leading to dehydration. There had been no changes to his antipsychotic medication in the last few months, and the patient improved after hydration alone and a slight increase in the benzodiazepine dosage on demand, without the need to stop regular medication. This suggests that the first episode was a heat stroke. Although there is no widely accepted definition for this, Bouchama's definition describes exposure to environmental heat, a core body temperature of > 40 °C and organ dysfunction (central nervous system, liver, renal, cardiovascular or respiratory).

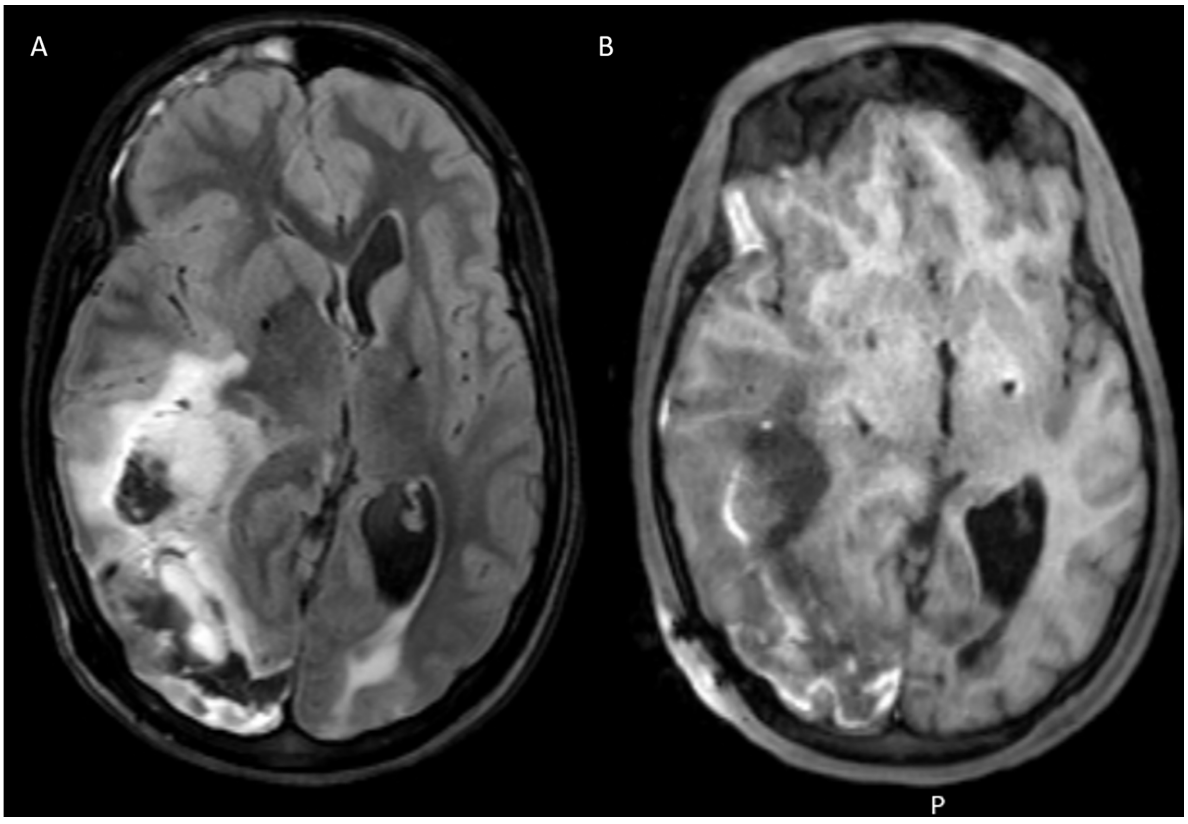

Figure 1. Brain magnetic resonance imaging showing (**A**) bilateral occipital T2 FLAIR subcortical hyperintensities, particularly on the right, (**B**) with T1 peripheral gadolinium enhancement and hemorrhage, causing subfalcine herniation, compatible with posterior reversible encephalopathy syndrome.

After a transient clinical improvement, fever and dysuria ensued in the context of a post-catheterization bladder infection. The baseline dyskinesia became more frequent, and the symptomatic medication dosage was increased (benzodiazepine and chlorpromazine). We hypothesized that this was the moment NMS ensued, as it most frequently occurs within two weeks after drug initiation or an increase in the dosage[1]. However, NMS is ultimately an idiosyncratic reaction and has been known to occur in patients who have been stable on medication for years[8]. Besides chlorpromazine, the patient was also medicated with tetrabenazine, which has also been associated with NMS[9].

Movement disorders are known to be a feature of NMS. However, in this case, they were first interpreted as neurological worsening secondary to heat stroke, dehydration and infection. In this particular subgroup of movement disorders, a high level of suspicion is needed to detect NMS. Pediatric patients are also more susceptible to side effects related to antipsychotic drugs, even in lower doses[10].

Nonetheless, few studies exist regarding NMS in children and adolescents. A recent review of case reports[1] identified 57 pediatric patients diagnosed with NMS between 2000 and 2018. The mean age was 14 years, most patients were male and 49/57 had psychiatric comorbidities requiring antipsychotic treatment. The most common symptoms were muscle rigidity, autonomic instability and fever. Abnormal involuntary movements were more frequently associated with classical antipsychotic drugs, such as chlorpromazine.

In these patients, after managing the acute period, long-term treatment also presents a challenge, as chorea may become refractory after stopping the worst-offending drugs. In our case, even with DBS parameter adjustments, dyskinesia became very frequent while sedation was decreased. Clonidine was the first drug to be reintroduced since it was less likely to cause NMS and more likely to have a beneficial effect in controlling the dysautonomia in this syndrome. Tetrabenazine was later introduced during clinical follow-up, but chlorpromazine was not restarted given its stronger association

with NMS. A case report in the literature describes a woman with a GNAO1 mutation who developed NMS induced by tiapride and haloperidol[11], who was then successfully treated with topiramate as a safe alternative. In the subacute/rehabilitation phase, diazepam, topiramate, baclofen and trihexyphenidyl were needed to achieve symptomatic control.

In conclusion, our case highlights the difficulty of diagnosing malignant neuroleptic syndrome in an adolescent with previous movement disorder diagnosis. It also illustrates the overlap between heat stroke and NMS in these patients. Close monitoring by a multidisciplinary team consisting of a neurologist, pediatrician and intensivist is essential to avoid unfavorable outcomes. Although rare, the use of clinical protocols and algorithms when NMS is suspected, could be helpful in the therapeutic management of these patients.

Author contributions

M. Santos: Writing – Original Draft, Investigation. T. Proença dos Santos: Resources, Investigation, Writing – Review & Editing. S. Almeida: Resources, Investigation, Writing – Review & Editing. M. Coelho: Resources, Investigation, Writing - Review & Editing. A. Levy: Writing – Review & Editing, Supervision.

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Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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CASE REPORT

Multiple and giant Becker's nevus. Case report

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Abstract

Introduction: Becker's nevus is a rare condition presenting benign skin lesions characterized by skin hyperpigmentation. **Case report:** We present an atypical case of a 17-year-old male adolescent with lumbosacral scoliosis, right breast hypoplasia, and three large hyperpigmented macules, with irregular extension between the bilateral scapular region and the knees bilaterally, with associated hypertrichosis. The histological analysis confirmed the diagnosis of Becker's nevus, and a watchful waiting approach was adopted. The association of Becker's nevus, unilateral breast hypoplasia, and scoliosis falls within the spectrum of Becker's nevus syndrome. **Discussion:** Given the atypical nature of this presentation, this case report holds significant relevance.

Keywords: Case report. Adolescent. Hyperpigmentation. Hypertrichosis. Nevus.

Nevo de Becker múltiplo e gigante. Relato de caso

Resumo

Introdução: Os nevos de Becker são lesões cutâneas raras e benignas, que cursam com hiperpigmentação da pele. **Relato de caso:** Apresentamos um caso atípico de um adolescente de 17 anos, do sexo masculino com escoliose lombo-sagrada, hipoplasia mamaria direita e três máculas hiperpigmentadas de grandes dimensões, com extensão irregular entre a região escapular bilateral e os joelhos bilateralmente, com hipertricose associada. A análise histológica confirmou o diagnóstico de nevo de Becker, e foi adotada uma atitude expectante. A associação de nevo de Becker, hipoplasia mamária unilateral e escoliose enquadra-se na síndrome do nevo de Becker. **Discussão:** Dada a natureza atípica da apresentação da doença, este relato do caso possui relevância significativa.

Palavras-chave: Caso clínico. Adolescente. Hiperpigmentação. Hipertricose. Nevo.

Keypoints

What is known

- Becker's nevus is a rare condition presenting benign skin lesions characterized by hyperpigmentation.
- The typical presentation of Becker's nevus consists of unilateral macular lesions.
- These lesions typically manifest during adolescence and are more prevalent in males.

What is new

- There are few reports of giant, bilateral Becker's nevi in the pediatric age group.
- A case of Becker's nevus syndrome characterized by multiple, giant, bilateral Becker's nevi, unilateral breast hypoplasia, and lumbosacral scoliosis.

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Introduction

Becker's nevus is a rare, benign condition presenting hyperpigmented skin lesions, more frequently identified from the first two decades of life and rarely present at birth[1,2]. The exact pathophysiology is still poorly understood, but it has been suggested that androgenic stimulation plays a role[3].

The lesions, usually unilateral, are characterized by hyperpigmented macules with irregular borders, associated with hypertrichosis. They grow gradually and usually present as a single lesion with an irregular contour or as multiple macules arranged along a single border[1]. Becker's nevi are initially light in color and become progressively hyperpigmented with exposure to sunlight[4]. Hypertrichosis usually appears during puberty, after the development of hyperpigmentation[4].

The condition is primarily isolated and unilateral, but concomitant ipsilateral anomalies such as other skin lesions, musculoskeletal changes, and breast hypoplasia were detected in 5% of cases and few cases of giant, multiple Becker's nevi have been reported[1].

The Becker's nevus syndrome or hairy epidermal nevus syndrome was described for the first time by Happle in 1995, as an association of Becker's nevi with unilateral breast hypoplasia and muscle, skin and/or skeletal abnormalities[5,6].

We present a rare clinical case of Becker nevus syndrome in an adolescent with multiple, giant, bilateral Becker's nevi, unilateral breast hypoplasia, and lumbosacral scoliosis.

Case report

A 17-year-old male adolescent with a history of lumbosacral scoliosis (Cobb angle > 10), who was diagnosed at the age of 11 and managed conservatively, presented with flat, asymptomatic, brownish lesions characterized by irregular borders (Fig. 1). These lesions first appeared at the age of 15 and exhibited a progressive darkening and increase in size. Cutaneous examination revealed tree hyperpigmented macules with irregular edges. The first macule was located bilaterally in the scapular region, displaying a symmetrical distribution that extended to the shoulders, forearms, and upper chest on both sides. Hypertrichosis was notably present, predominantly on the left shoulder (Fig. 2). The second macule extended from the entire right abdomen and right lumbosacral region to the level of the knees on both sides, with hypertrichosis evident solely in the left lower limb. The third macule was the smallest of the three; it was unilateral and limited to the left lumbar region.

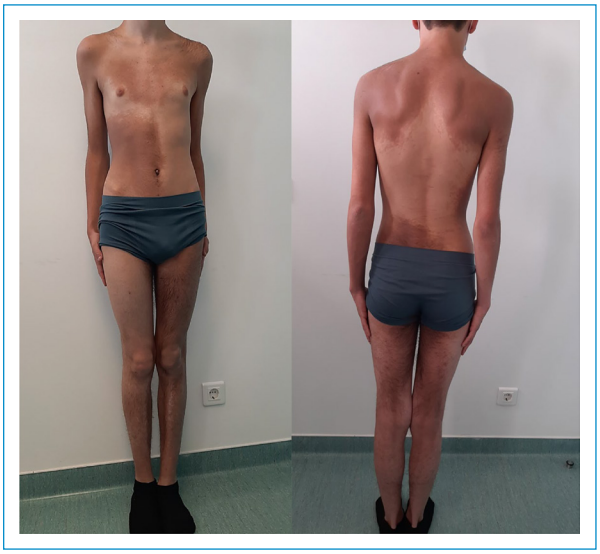

Figure 1. Multiple giant Becker's nevi and scoliosis.

A previous history of trauma, burns, or habitual medication was also excluded, and there was no family history of dermatological pathology. In addition to lumbosacral scoliosis and right breast hypoplasia (Fig. 2), no other changes were detected in the systemic physical assessment.

The histopathological examination of the skin biopsy taken from the second lesion on the abdomen and the left thigh revealed findings of epidermal acanthosis and elongation of the epidermal ridges, accompanied by hyperpigmentation of the basal layer. Notably, there was no evidence of melanocyte proliferation. The dermis exhibited smooth muscle tissue proliferation, while the hypodermis showed no distinctive features.

Based on the clinical history, skin examination, and histopathological evaluation, the adolescent was diagnosed with Becker nevus syndrome, characterized by multiple giant Becker's nevi, right breast hypoplasia, and lumbosacral scoliosis. It was proposed that the patient should be followed up in a dermatology consultation, adopting an expectant approach.

Discussion

Becker's nevi are hyperpigmented epidermal lesions with an approximate prevalence of 0.5%. They can manifest in various sizes and may present as isolated (typical presentation) or multiple lesions (as in this case)[7]. They can also exhibit varying degrees of hypertrichosis and other skin changes like acne[8]. In some cases, non-cutaneous abnormalities may be associated[7,8].

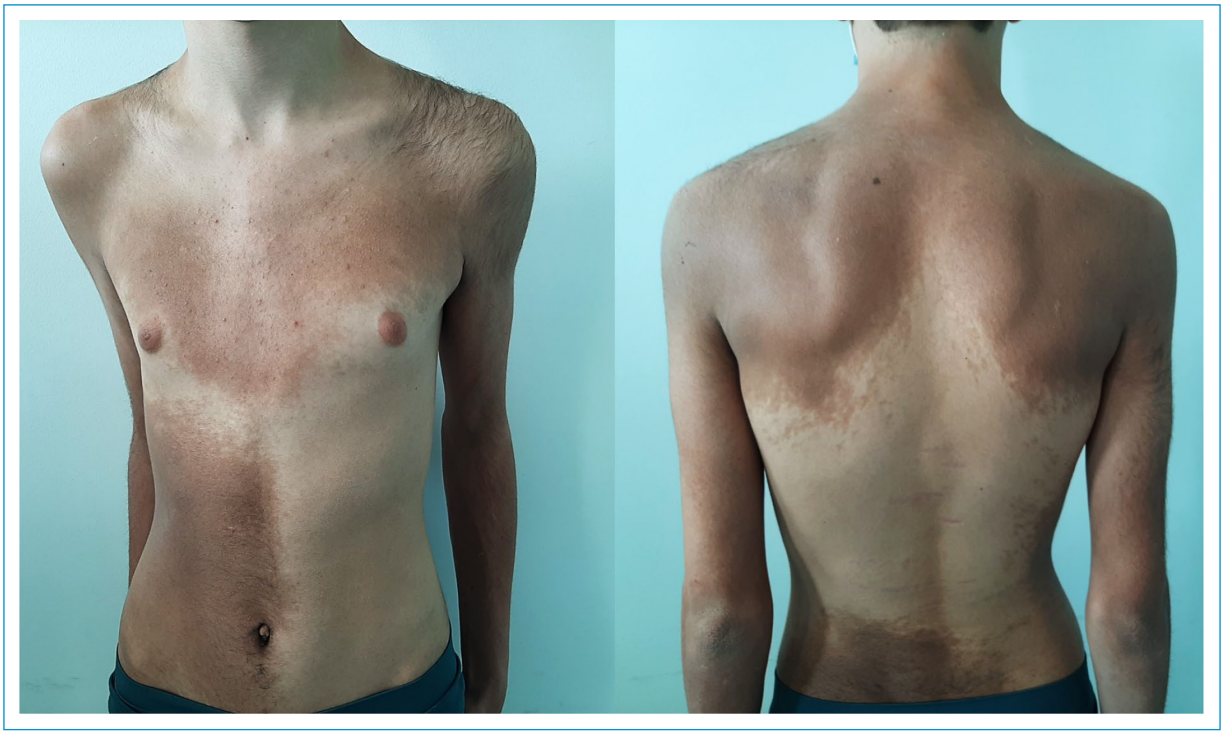

Figure 2. Hypertrichosis on both shoulders, predominantly on the left, and right breast hypoplasia.

Typically, they present as unilateral macular lesions with well-delimited borders and a geographic shape[8].

They are more prevalent in men (5:1 male-to-female ratio), with androgen stimulation believed to play a role in their pathophysiology[3,9]. This is supported by the clinical characteristics often associated with androgens, such as acne, acanthosis, and hypertrichosis. Notably, Becker's nevus tends to exhibit less hypertrichosis and hyperpigmentation when present in women[9,10]. A significantly higher expression of androgen receptors was also observed in the epidermis of Becker's nevi[10].

It has also been suggested that postzygotic mutations in beta-actin are associated with Becker's nevi[2].

Becker's nevi can simulate and make a differential diagnosis with other hyperpigmented lesions such as Albright's syndrome or congenital melanocytic nevi. The presence of hypertrichosis can make the diagnosis less challenging, but histological examination remains essential[3].

Although no standard treatment has been defined, therapy with pigment-specific lasers for cosmetic purposes can be considered[11,12].

For the diagnosis of Becker nevus syndrome or hairy epidermal nevus syndrome, the presence of Becker's nevus is fundamental in characterizing the syndrome. However, its association with breast hypoplasia or other skin, muscle, and/or skeletal disorders is also necessary. Typically, these disorders affect the same side of the body, although they may be bilateral. It is important to note that breast hypogenesis, scoliosis, or any other findings alone are insufficient to establish a diagnosis of the syndrome[5,6].

Our patient presented with lumbosacral scoliosis and right breast hypoplasia associated with the presence of multiple, giant, bilateral Becker's nevi. Given the unusual nature of this presentation within a rare disease and the scarcity of published cases in the pediatric age group, it is crucial to share related clinical cases for broader awareness.

Author contributions

C. Couto: Acquisition and interpretation of patient data and the literature; Writing of the article; Critical revision of the article for important intellectual content. F. Sutre: Acquisition and interpretation of patient data and the literature; Writing of the article. J. Onofre: Acquisition and interpretation of patient data and the literature; Critical revision of the article for important intellectual content; Final approval of the version to be published. M. João Silva: Acquisition and interpretation of patient data and literature; Critical revision of the article for important intellectual content; Final approval of the version to be published. A. Lopes: Critical revision of the article for important intellectual content; Final approval of the version to be published.

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Conflicts of interest

The authors declare no conflicts of interest in drafting this paper.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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CASE REPORT

Acute cerebellar ataxia in a patient with maple syrup urine disease: a case report

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Abstract

Introduction: Maple syrup urine disease (MSUD) is an inborn error of amino acid metabolism, potentially resulting in metabolic intoxication crises accompanied by neurological manifestations. **Case report:** This article reports a case involving a six-year-old boy with MSUD who developed a post-infectious neurological disorder following COVID-19. Initially presenting with fever, cough, and ataxia, he was diagnosed with a metabolic crisis due to COVID-19. Despite an initial recovery, the patient experienced a relapse characterized by ataxia, tremor, and dysarthria, necessitating readmission. A subsequent investigation ruled out an MSUD crisis. A lumbar puncture and MRI failed to rule out a demyelinating acute disorder. Methylprednisolone treatment yielded no improvement, prompting the initiation of intravenous immunoglobulin, which led to improvement after 14 days. **Discussion:** The case posed challenges due to the overlapping symptoms between MSUD crises and post-infectious neurological conditions. This highlights the complexity of managing these patients, particularly due to the potential for more vigorous manifestations and slower recovery.

Keywords: MSUD. PINS. COVID-19. Ataxia.

Ataxia cerebelar aguda num doente com leucinose: relato de caso

Resumo

Introdução: A leucinose é uma doença hereditária do metabolismo dos aminoácidos que pode levar a crises de intoxicação metabólica com manifestações neurológicas. **Relato de caso:** Este artigo relata um caso de distúrbio neurológico pós-infeccioso numa criança de 6 anos com leucinose após infeção por SARS-CoV-2. Inicialmente apresentou-se com febre, tosse e ataxia, testou positivo para SARS-CoV-2 e foi diagnosticado com uma crise metabólica. Após a recuperação, apresentou um quadro de ataxia, tremores e disartria, levando a um reinternamento. Após a exclusão de intoxicação metabólica, realizou punção lombar e ressonância magnética, não sendo possível excluir uma alteração desmielinizante. Sem melhoria sob

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metilprednisolona, foi tratado com imunoglobulina intravenosa, observando-se recuperação ao fim de 14 dias. **Discussão:** Este caso revelou-se desafiante devido à sobreposição de sintomas entre crises de leucinose e condições neurológicas pós-infecciosas. Destaca-se a complexidade da abordagem destes doentes particularmente por poderem apresentar manifestações mais exuberantes e uma recuperação mais lenta.

Palavras-chave: MSUD. PINS. COVID-19. Ataxia.

Keypoints

What is known
- Patients with MSUD are susceptible to metabolic decompensation crises featuring neurological symptoms during episodes of catabolism.
- Post-infectious neurological syndromes (PINS) have been linked to several viruses, including coronaviruses.
- Distinguishing between decompensation crises and PINS can be challenging in individuals with chronic neurological or metabolic disorders.

What is added
- The overlapping symptoms between MSUD crises and PINS pose a diagnostic, and thus therapeutic, challenge.
- Including prior imaging in these patients could provide valuable insights, aiding in the differentiation between acute neurological post-infectious inflammation and chronic manifestations of MSUD.

Introduction

Maple syrup urine disease (MSUD) is an amino acid catabolic disorder that results in the inability to break down branched-chain ketoacids due to the absence of the appropriate enzyme (branched-chain ketoacid dehydrogenase). Branched-chain amino acids (valine, leucine, and isoleucine) and branched-chain ketoacids therefore accumulate. This accumulation interferes with the cerebral amino acid transport system and myelin formation. The accumulation of ketoacids may also lead to metabolic encephalopathy and cerebral edema[1]. During periods of catabolism, such as infection, surgery, exercise, or fasting, individuals with MSUD may present with metabolic intoxication crises, which are mainly managed with nutritional interventions. These crises may present clinically as refusal to feed and vomiting and are accompanied by neurological signs such as ataxia, dystonia, hyperactivity, somnolence, or stupor. In these patients, viral infections, such as SARS-CoV-2, may trigger metabolic crises.

Symptoms such as fever, cough, and anosmia are commonly reported in SARS-CoV-2 infection. However, the literature has also described rare neurological symptoms and post-infectious syndromes, which pose new challenges to our clinical reasoning. In patients with pre-existing neurological or metabolic disorders, differentiating between decompensation crises and acute or post-infectious neurological symptoms can be challenging.

Post-infectious neurological syndromes (PINS) are rare heterogeneous entities with a post- or para-infectious onset. Typically, they manifest after viral or bacterial infections[2]. Numerous pathogens, including SARS-CoV-2, have been associated with these clinical entities. One example is acute post-infectious cerebellar ataxia (APCA), which usually manifests a few days to three weeks after a febrile illness[3]. It typically presents with rapid onset and progressive symptoms including gait disturbance, fine motor control problems, nystagmus, vomiting, and dysarthria. Several other neurological autoimmune disorders are believed to occur through post-infectious mechanisms. Acute disseminated encephalomyelitis (ADEM) is a rare demyelinating disease of the central nervous system (CNS) and typically appears four to 13 days after a febrile illness[4]. It presents with encephalopathy, multifocal neurological deficits, pyramidal signs, cerebellar ataxia, cranial neuropathies, myelopathy, and seizures[5,6].

With this article, the authors intend to report the first case described in the literature of PINS in a six-year-old boy with MSUD, after a SARS-CoV-2 infection.

Case report

A six-year-old boy of Roma consanguineous descent with a neonatal diagnosis of a classic, severe phenotype of MSUD (homozygous c.117delC (p.R40fs*23) was seen at the Emergency Room (ER). The boy had been diagnosed in the neonatal period (leucine at the time of diagnosis (six days): 2400 μM/L), presenting with a poor general state, hypoglycemia, hypoactivity, failure to thrive, and seizures in the first week of life. He received renal replacement therapy during this first admission. He also presented with bradypnea, requiring non-invasive ventilation followed by a period

Table 1. Amino acid chromatography

	MSUD acute decompensation	2 weeks later	Reference values
Valine (µM/L)	426.2	423.8	80.2-245.7
Isoleucine (µM/L)	273.3	426.6	26.7-52.6
Allo isoleucine (µM/L)	108.8	456.0	Not dosable
Leucine (µM/L)	889.9	42.9	46.5-109.0

of mechanical ventilation. After the diagnosis and before the additional episode described, the patient presented with multiple decompensation crises, with leucine values ranging from 500-1000 µM/L, mainly concurrent with infections. In these crises, he usually presented with ataxia. The crises gradually resulted in cognitive impairment and a delay in the acquisition of psychomotor developmental milestones. However, from the age of four until the episode being reported he presented an otherwise normal baseline neurological examination, with no ataxia or other movement disorders.

At the ER, he presented with two days of fever, cough, excessive sleepiness, and a slight ataxic gait. A nasopharyngeal swab, performed by reverse transcription polymerase chain reaction, confirmed SARS-CoV-2 infection. A complete blood analysis evaluation was performed, including amino acid chromatography (AAC) (Tables 1 and 2).

He was diagnosed with a metabolic decompensation (maximum leucine 889.9 µM/L) related to SARS-CoV-2 infection, initially managed at home. However, six days later he was admitted to the hospital ward. He was already afebrile but presented axial and appendicular ataxia. The rest of the neurological examination was normal. Natural protein intake was interrupted, and synthetic protein as well as isoleucine and valine supplements were increased according to the treatment protocol. He had a successful recovery both clinically and in terms of the laboratory tests and was discharged after a week.

After two uneventful weeks, he developed sudden onset ataxia, tremor (videos 1 and 2), and excessive sleepiness, prompting readmission two days after the symptoms began. Vital signs were stable, with no fever or meningeal signs. The neurological examination revealed dysarthria, appendicular ataxia with dysmetria, intention tremor, axial ataxia, and brisk osteotendinous reflexes; cranial nerves, and motor and sensory functions were normal. The rest of the physical examination was unremarkable. No findings suggested that pediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS-TS) was observed.

Blood tests and AAC were performed (Tables 1 and 2), which showed normal values a few days later. Before the AAC results came in, and despite initially receiving treatment for an MSUD crisis, the patient did not improve. The clinical and laboratory results were also not compatible with metabolic decompensation. Thus, further investigation was needed.

Magnetic resonance imaging (MRI) and a lumbar puncture (LP) were performed, yet they did not provide a clear etiology. The cerebrospinal fluid (CSF), in addition to cytochemical and culture analyses, was also tested for auto-immune encephalitis (Table 2), and an electroencephalogram was performed, revealing slow, abrupt waves, with no paroxysmal activity.

The results were consistent with both APCA with previous MSUD-related findings and ADEM. Since no previous MRI had been performed, it was difficult to completely rule out the latter hypothesis.

The patient was started on methylprednisolone 30 mg/kg/day for five days, yet no clinical improvement was observed. A second MRI was then performed, and the findings remained unchanged. He was then started on intravenous immunoglobulin (IVIG) for two days (1 g/kg/day).

After the second treatment, the patient gradually recovered and was discharged after 14 days, only experiencing headaches, a slight intention tremor, and dysmetria (video 3). Steroids were tapered off over four weeks.

Discussion and conclusions

Coronaviruses were already recognized as important human pathogens. Still, the significant number of infections on a global scale has led to an increased understanding of the manifestations of this pathogen and the associated clinical conditions[7].

SARS-CoV-2 infection has been linked to multiple neurological symptoms and syndromes. The most

Table 2. Blood and CSF analysis

	MSUD acute decompensation	2 weeks later	Recovery	Reference values
Blood test evaluation				
Hemoglobin (g/dL)	10.9	9.9	9.6	11.5-15.5
WBC (× 10^9/L) Neutrophils, n (%); Lymphocytes, n (%)	6.930 (N, 76.7; L, 18.8)	8.630 (N, 71.7; L, 22.7)	17.60 (N, 38.4; L, 55.2)	5.0-13.0 (N, 2.0-8.0; L, 1.0-5-0)
Platelets (× 10^9/L)	448	951	922	180-400
Glucose (mg/dL)	76	88	76	70-110
Urea (mg/dL)	6	20	14	16-49
Creatinine (mg/dL)	0.37	0.31	0.36	0.29-0.47
AST/ALT (U/L)	280/130	121/ 164	43/126	0-31/0-41
GGT (U/L)	248	271	127	0-60
C-reactive protein (mg/dL)	-	< 0.1	-	< 0.5
Anti-nuclear antibodies	-	-	Negative	-
Anti-LKM antibodies	-	-	Negative	-
Anti-DS-DNA antibodies	-	-	Negative	< 27
Anti-neutrophil cytoplasmic antibodies (c-ANCA/PR3)	-	-	Negative	< 20
Anti-neutrophil cytoplasmic antibodies (p-ANCA/MPO)	-	-	Negative	< 20
SARS-CoV-2 antibodies	-	44.70 U/mL	-	≥ 0.8 = Positive
CSF analysis				
Color	-	Transparent	-	-
Proteins (mg/dL)	-	14.3	-	15-45
Glucose (mg/dL)	-	64	-	40-70
Cells (/mm3)	-	1.6 (no predominance)	-	< 10
Culture	-	*Staphylococcus epidermidis* (likely contaminated)	-	-
Anti-Aquaporin-4	-	< 1/10 (negative)	-	< 1/10
Anti-MOG	-	< 1/20 (positive)*	-	< 1/10

commonly reported symptoms in various case series include headaches, myalgias, encephalopathy, and dizziness[8]. Movement disorders such as ataxia, motor and sensory deficits, and seizures are less commonly reported[7]. Several cases of autoimmune para-infectious and post-infectious neurological manifestations, such as ADEM[9,10] and APCA have also been documented[11,12].

In our patient, an initial MSUD acute decompensation was suspected due to the clinical features that were consistent with previous crises. However, this diagnosis was later ruled out based on both the AAC results and the treatment's lack of effectiveness.

Subsequently, both APCA and ADEM were considered possible diagnoses. Our patient exhibited features consistent with APCA, including ataxia, tremor, irritability, and dysarthria. ADEM presents with encephalopathy, which in our patient manifested as somnolence and attention impairment, and patients may also present irritability and ataxia. The time sequence was also consistent with both diagnoses.

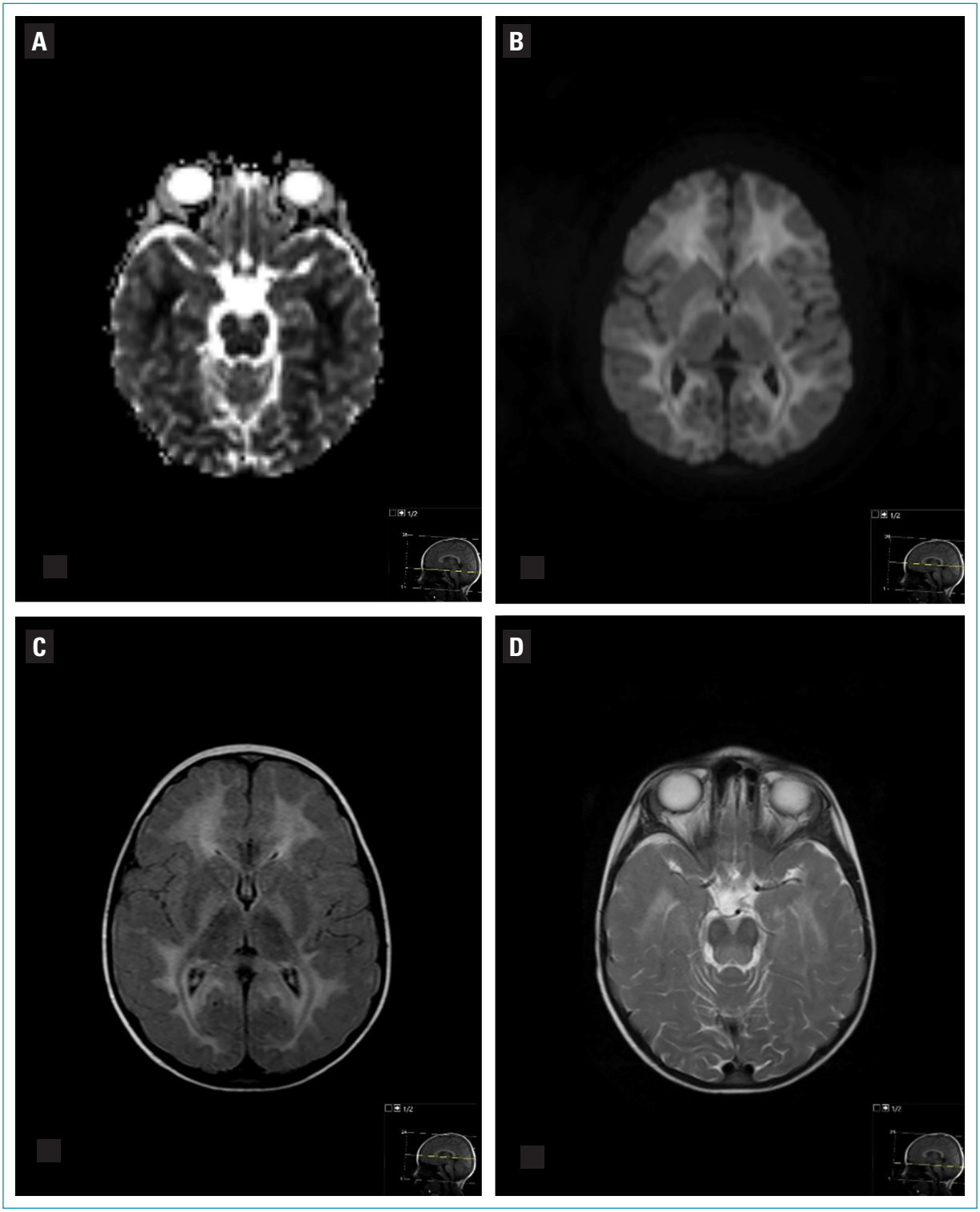

Figure 1. A-D: both MRIs showed diffuse restricted diffusion (high diffusion-weighted imaging (DWI) signal with a low apparent diffusion coefficient (ADC)) involving the bilateral cerebellar white matter, the dorsal part of the pons and brainstem, the dorsal limb of the internal capsule and the frontotemporoparietal white matter. There is also T2/FLAIR (fluid-attenuated inversion recovery) hyperintensity in the above-mentioned regions. The areas of restricted diffusion represent cytotoxic oedema. **A:** ADC, **B:** DWI, **C:** FLAIR, and **D:** T2.

Although APCA was considered more likely, ADEM could not be ruled out, so an MRI and lumbar puncture were performed. Generally, patients with APCA may have normal imaging or show bilateral diffuse abnormalities of the cerebellar hemispheres[11,13,14]. There are no pathognomonic alterations. However, the imaging of patients with ADEM usually reveals bilateral and asymmetrical lesions in the white matter, typical of demyelination and diffusion restriction, which was present in this patient[15].

Again, the pre-existing metabolic disorder posed a confounding factor. Initially, the clinical picture was more compatible with APCA. However, since there was no prior CNS imaging results from this patient, the MRI findings could either be indicative of an acute demyelinating syndrome or reflect previous alterations from the metabolic disease. Since ADEM could not be ruled out, the patient was started on methylprednisolone and subsequently received IVIG due to the lack of clinical improvement.

As for the treatment and clinical course, APCA usually requires only supportive treatment, although some case reports of refractory illness require glucocorticoids or immunoglobulin[16,17]. Conversely, patients with ADEM should be started on immediate immune-modulating therapy, with glucocorticoids considered the first-line treatment and immunoglobulin or plasma exchange a second-line option. Regarding the clinical course, patients with APCA typically experience symptoms for 10 to 12 days and completely recover within two to three weeks[13,14]. Usually, patients with ADEM make a complete recovery over four to six weeks[18], although some may experience persistent sequelae[19].

APCA after SARS-CoV-2 infection has been reported in children[11,20,21] and also in adults[22,23] worldwide. Tomar et al.[11] reported a case of a 13-year-old who was treated with methylprednisolone and recovered over 20 days. O'Neill et al.[21] reported another case of a five-year-old who received only supportive and physical therapy and made a complete recovery after two months. These cases developed 10 and eight days after the initial COVID-19 diagnosis, respectively. Sanchéz-Morales et al.[20] reported several neurological manifestations of COVID-19, including APCA. No mention of treatment was made, and the infant made a full recovery.

ADEM after SARS-CoV-2 infection has also been reported[23,24], although it remains a rare post-infectious autoimmune complication. Most of the published cases involve adults. According to a review[24], the median time between the documentation of the SARS-CoV-2 infection and the neurological symptoms was 15.5 days. Treatment varied among the reported cases, with some patients receiving steroids, others receiving IVIG, and some reports stating that no treatment was administered.

Due to the similarity between a MSUD acute decompensation and the new onset neurological condition, our patient presented a challenge. Furthermore, the MRI findings were equivocal as it was unclear whether they were caused by the metabolic disorder or derived from an acute neurological condition. In patients with classic, severe phenotype MSUD, atypical symptoms or unusual recovery patterns may be observed. Thus, a prior MRI would have been valuable in this patient to differentiate between acute neurological post-infectious inflammation and chronic MSUD neuro-image manifestations in more severe cases.

To our knowledge, this was the first case report of acute cerebellar ataxia after SARS-CoV-2 infection in a patient with MSUD.

To conclude, SARS-CoV-2 infection and its post-infectious consequences pose new challenges, particularly in patients with severe inborn errors of metabolism that manifest with neurological symptoms. In such cases, decompensation crises may share similar symptoms. These patients may also present with more vigorous manifestations with slower recovery.

Data availability

The video materials referenced in this article are available from the corresponding author upon reasonable request.

Author contributions

C. Castro drafted the paper; P. Lipari contributed to the idea behind it, drafted part of the paper and substantively revised it; I. Carneiro drafted part of the work and contributed to the interpretation and incorporationg of the images; P. Janeiro, J. Coelho, S. Quintas and A. Gaspar made substantial contributions to the idea behind the paper and substantively revised it. F. Furtado substantively revised the work. All authors read and approved the final manuscript.

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Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

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PORTUGUESE JOURNAL OF PEDIATRICS

PERMANYER

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Neonatal heart tumor: not a bad outcome

Tumor cardíaco neonatal: nem sempre mau prognóstico

Mafalda João Pereira[1], Patrícia Mendes[1], Luísa Gaspar[2], and Graça Sousa[3]*

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Keypoints

What is known
- Cardiac tumors are rare in the pediatric population.
- Symptoms can range from heart murmurs to death.

What is added
- Echocardiograms are often performed in brief, resolved, unexplained events, but an MRI is important in the characterization of myocardial masses.
- Differentiating between benign and malignant masses through diagnostic imaging can prevent a potential heart intervention.

This article aims to present the case of a four-day-old female newborn brought to the emergency room.

The pregnancy was unremarkable. The birth was a normal delivery at 38 weeks, and she was discharged after three days.

According to the mother, before feeding the baby, she choked with secretions discharged through the mouth and nose. The mother gave sharp blows between the scapulae, but was unable to trigger crying, describing hypertonia and cyanosis. The episode resolved spontaneously, with overall improvement.

She was admitted to the Neonatal Intensive Care Unit. Her physical examination was normal, including no cutaneous alterations. A transthoracic echocardiogram was performed and found an asymmetric hypertrophic cardiomyopathy versus a single fibroma in the septum, with no other abnormalities (Figs. 1 and 2). Her electrocardiogram and 24-hour electrocardiographic monitoring revealed a sinus arrhythmia. She was then

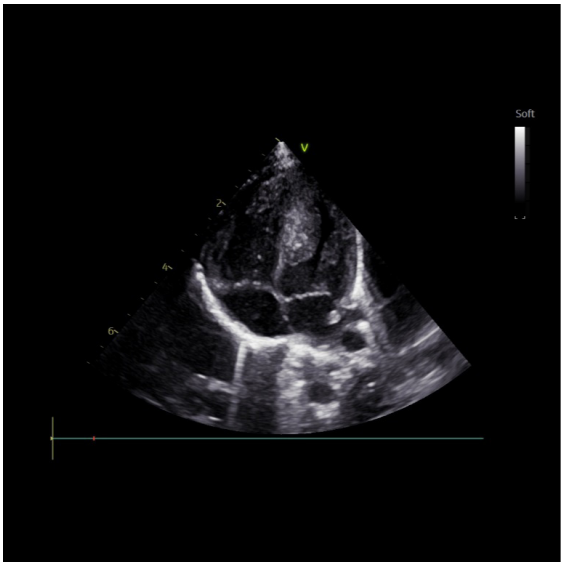

Figure 1. Apical four chamber view.

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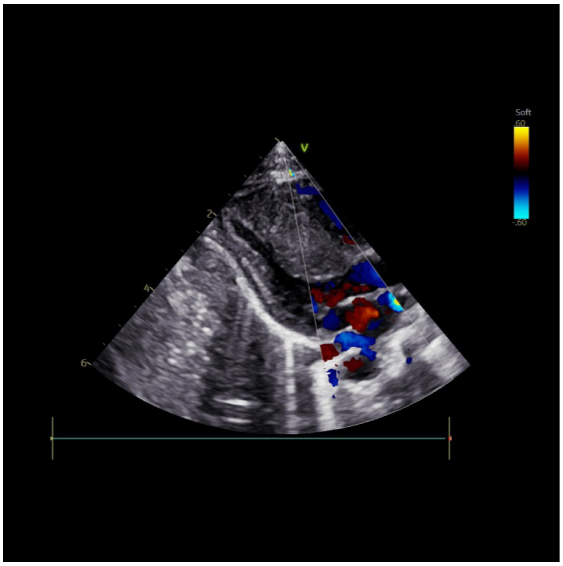

Figure 2. Parasternal long axis view.

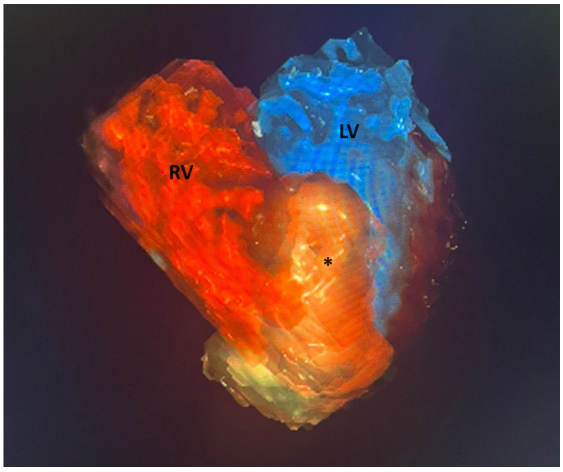

Figure 3. 3D MRI reconstruction. *Fibroma. RV: right ventricule; LV: left ventricule.

medicated with propranolol one mg/kg/dose to decrease her heart rate, increasing the duration of the diastole and reducing the ventricular outflow tract obstruction caused by the mass, as well as decreasing myocardial oxygen demand and ventricular wall stress.

The etiological study did not reveal any abnormalities, including ophthalmological examination and the hypertrophic cardiomyopathy genetic panel. Her cardiac magnetic resonance imaging confirmed a fibroma in the septum (Figs. 3 and 4).

She is currently one year old, medicated with propranolol and growing according to her percentiles. She

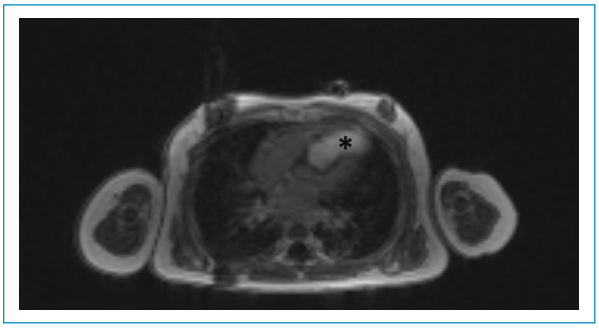

Figure 4. T1 TSE dark-fluid axial cut. *Fibroma.

is being followed up in Pediatric Cardiology, Neonatology, and Genetics outpatient consultations.

Cardiac tumors are rare in the pediatric population, most being benign[1-4]. In neonates, presenting symptoms are usually cyanosis, heart murmurs, arrhythmia, and cardiac failure[1,2].

Fibromas are the second most common type of heart tumor[1-3]. They are benign and are often found in the left ventricle or the septum[1,3]. Echocardiography may reveal a heterogeneous mass, which may condition various arrhythmias[1-3]. Cardiac masses can cause intracardiac flow obstruction, heart valve insufficiency, arrhythmia, heart failure, hydrops fetalis, or even death[1-3].

Symptomatic treatment or surgery should be considered on a case-by-case basis[1,3]. Therefore, regular echocardiograms and specialized follow-up are essential to control heart function and to determine the course of treatment[2,3].

Author contributions

M. João Pereira and L. Gaspar participated in the study conception or design. MJP participated in acquisition of data. M. João Pereira participated in the analysis or interpretation of data. M. João Pereira and L. Gaspar participated in the drafting of the manuscript. All authors participated in the critical revision of the manuscript. All authors approved the final manuscript and are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Conflicts of interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that the procedures followed complied with the ethical standards of the responsible human experimentation committee and adhered to the World Medical Association and the Declaration of Helsinki. The procedures were approved by the institutional Ethics Committee.

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Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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Beaded necklace hair: diagnosing monilethrix in a pediatric patient

Cabelo em colar de contas: diagnosticando moniletrix em um paciente pediátrico

Sara Santos do Vale[1]* *and Leandro S. Silva*[2]

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Keypoints

What is known

– Monilethrix is an inherited genodermatosis of unknown incidence, given its rarity and limited documentation.

What is added

– Due to its infrequency, it is crucial to review and share such cases, aiming to ensure diagnostic clarity and early management.

A nine-year-old female patient, with no significant medical or surgical history, was referred for limited hair growth and easy breakage since birth, resulting in permanently sparse and short hair. There was no significant family history.

On physical assessment, decreased hair density with intense hypotrichosis and small hyperkeratotic papules were observed. The hair was only a few centimeters long, with a dry and lusterless appearance (Figs. 1 and 2).

The tug test was positive, indicating hair fragility, while the pull test was negative, showing no active hair shedding. No abnormalities were observed in the nails or teeth. Trichoscopy revealed narrow areas of constriction periodically separated by elliptical nodules on the hair shaft, creating an appearance similar to a "beaded necklace/rosary beads" (Fig. 3). Based on the clinical and dermoscopic findings, the diagnosis of monilethrix was established. Topical 5% minoxidil was prescribed, to be applied twice daily.

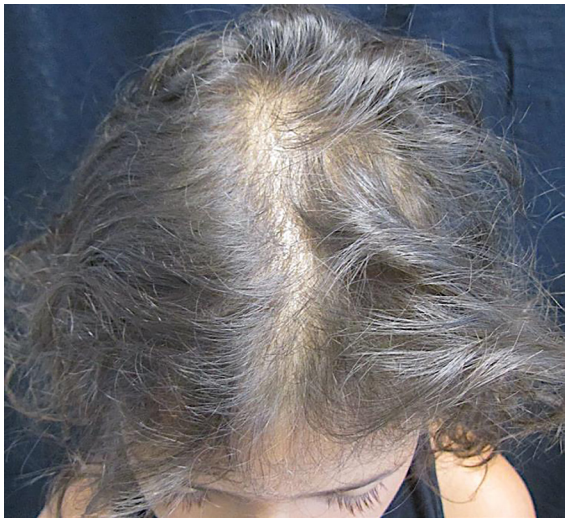

Figure 1. The scalp of a nine-year-old girl exhibits diffuse hypotrichosis with sporadic coarseness, with no impact on the eyebrows and eyelashes.

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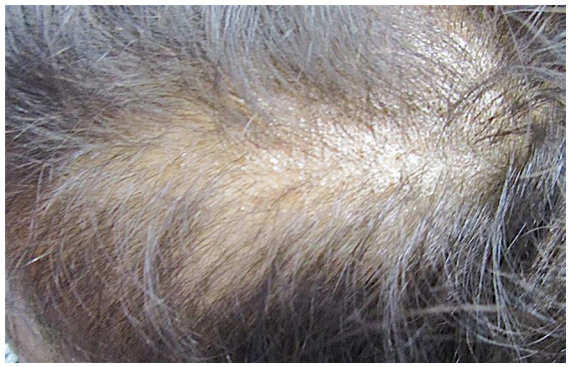

Figure 2. Hyperkeratotic follicular papules.

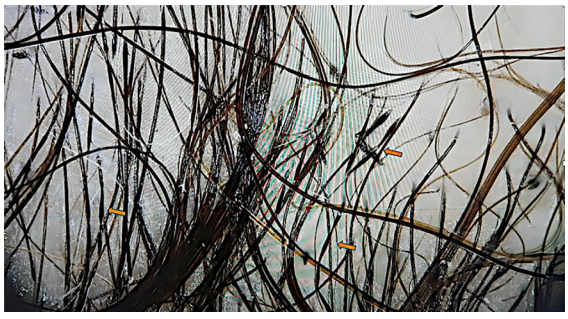

Figure 3. Trichoscopic image of the parietal scalp, showing uniform elliptical nodes, interspersed by intermittent constrictions, a pathognomonic sign of monilethrix.

Discussion

Monilethrix is a rare genodermatosis of autosomal dominant inheritance[1] that primarily affects the hair shaft and typically presents during early childhood. It is characterized by dysplasia of the hair shaft, leading to progressive hair follicle thinning and the development of fragile, short, and lackluster hair. The clinical expression of monilethrix exhibits significant variability[2] and can ultimately result in hypotrichosis due to hair fragility[2,3].

Diagnosis can be easily established by assessing the patient's clinical history and conducting trichoscopy, which can reveal intermittent constrictions along the hair shaft, resulting in a distinctive rosary bead-like appearance[3].

As of now, there is no established successful treatment for this hair condition[4]. However, topical or low-dose oral minoxidil (0.25-2.5 mg/day)[5] has shown promise as a well-tolerated and potentially effective treatment option[5].

Author contributions

S. Santos do Vale: Conception and design of the study, report, review or other type of work or paper; Acquisition of data either from patients, research studies, or literature; Drafting the article. L. Santos Silva: Conception and design of the study, report, review or other type of work or paper; Critical review of the article for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work.

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Orchitis: don't forget about immunoglobulin A vasculitis

Orquite: a não esquecer a vasculite por imunoglobulina A

Ricardo Craveiro Costa[1], Rita Marchante Pita[1], Inês Farinha[1,2], and Manuel Salgado[3]*

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Keypoints

What is known

- IgAV is the most common vasculitis in children.
- Skin involvement with the development of palpable purpuric lesions is usually the first manifestation.
- Although most cases are benign, gastrointestinal bleeding and kidney involvement are important complications to be aware of.

What is added

- Scrotal involvement as the first clinical sign in IgAV is atypical but should be kept in mind.
- It can be misdiagnosed as a testicular torsion, causing the patient to undergo unnecessary surgery, so ultrasound is important to the differential diagnosis.
- Since IgAV is usually a self-limiting condition, its accurate diagnosis is essential to avoid any unnecessary procedures.

A previously healthy seven-year-old boy presented with transient arthralgias and acute scrotal pain following treatment with amoxicillin-clavulanic acid for acute tonsillitis. Over the course of three days, he developed sudden testicular pain and swelling (Fig. 1A), prompting his hospital visit. He denied trauma, fever, gastrointestinal (GI), and urinary symptoms. Following unremarkable blood tests and imaging studies ruling out surgical emergencies, he was discharged with symptomatic treatment. However, during a subsequent evaluation, purpuric lesions appeared (Fig. 1B), leading to the diagnosis of an atypical presentation of immunoglobulin A vasculitis (IgAV). Over the course of three weeks, his clinical manifestations resolved completely without the need for pharmacological intervention.

IgAV, the most prevalent form of systemic vasculitis in children[1], often follows upper respiratory tract infections[2]. Its classic triad includes purpura, arthralgia, and abdominal pain, although renal disease, GI bleeding, and occasionally scrotal involvement can occur[1,2]. These manifestations may develop over the course of days to weeks and may vary in their order of presentation[2]. Purpura and arthralgia are usually the presenting symptoms, but this is not always the case[2]. In the absence of the classic purpuric rash, the diagnosis of IgAV may not be obvious. Rarely, orchitis may be the presenting symptom, mimicking testicular torsion since unilateral involvement is more common[1,3]. Scrotal involvement was first described by Allen et al. in 1960, with subsequent studies reporting a prevalence between 2% and 38%[3,4]. Clinical findings include pain, tenderness, and swelling of the involved testicle and/or scrotum[1,5]. The main causes of acute scrotal pain in children are testicular torsion, incarcerated inguinal hernia (both of which are surgical emergencies), torsion of the appendix testis, and epididymitis. Additional causes include trauma, IgAV, and referred pain[5]. Hence, Doppler ultrasonography is crucial, showing

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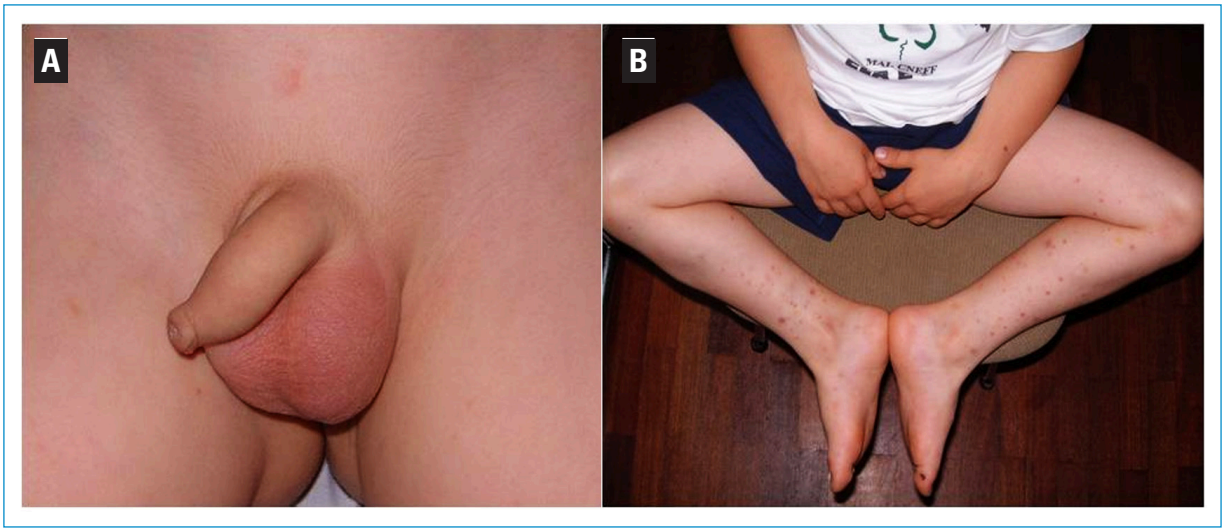

Figure 1. Findings at physical examination, depicting erythema and swelling of the scrotal wall and left testis, suggesting localized inflammatory process **(A)** and palpable purpuric skin lesions over the lower limbs, indicative of cutaneous vasculitis **(B)**.

normal results in IgAV but indicating ischemia in cases of torsion[5].

Male genital involvement as the sole initial sign of IgAV is rare, complicating the diagnostic process[3,6]. As it usually resolves on its own[6], accurate diagnosis is crucial to avoid unnecessary procedures.

Author contributions

R. Craveiro de Costa: Analyisis or interpretation of data either from patients, research studies, or literature; Final approval of the version to be published. R. Marchante Pita: Analyisis or interpretation of data either from patients, research studies, or literature; Final approval of the version to be published. I. Costa Farinha: Drafting the article; Agreement to be accountable for the accuracy or integrity of the work. M. Salgado: Critical review of the article for important intellectual content; Final approval of the version to be published; Agreement to be accountable for the accuracy or integrity of the work.

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