REFACS

**Original Article**
**Rev. Fam., Ciclos Vida Saúde Contexto Soc.**
*http://seer.uftm.edu.br/revistaeletronica/index.php/refacs/index*
**ISSN**: 2318-8413 DOI: 10.18554/refacs.v14i00.8482

# Precocious adrenarche in children under five years old with adrenal adenocarcinoma

***Adrenarca precoce em crianças menores de cinco anos com adenocarcinoma adrenal***

***Adrenarquia precoz en niños menores de cinco años con adenocarcinoma suprarrenal***

**Received:** 19/05/2025 **Accepted:** 03/12/2025 **Published:** 10/01/2026

**José Manoel Santos Júnior[1], Heloisa Marcelina da Cunha Palhares[1], Beatriz Hallal Jorge Lara[2] Flávia Alves Ribeiro[2], Maria de Fátima Borges[2]**

**Abstract:**
**Objective**: describe the main laboratory, imaging and histopathological findings in pediatric patients with adrenal adenocarcinoma, as well as the clinical progression of the analyzed cases. **Methods**: descriptive study was conducted by reviewing medical records of children seen at the Endocrinology and Metabolism Department from a tertiary hospital in the Brazil, from October 1999 to March 2024. **Results**: four cases with ages at diagnosis ranging from six months to two years and six months, female and with precocious adrenarche. During the follow-up, only one patient developed recurrent metastases and subsequently died. Three have shown good progress to date. **Conclusion**: early diagnosis and active postoperative surveillance are crucial for a favorable prognosis and survival of patients with adrenal adenocarcinoma.
**Keywords**: Adrenal gland neoplasms; Adrenal gland diseases; Adrenocortical carcinoma.

**Resumo**:
**Objetivo:** descrever os principais achados laboratoriais, de imagem e histopatológicos em pacientes pediátricos com adenocarcinoma adrenal, bem como a evolução clínica dos casos analisados. **Método:** estudo descritivo realizado através de prontuários de crianças atendidas no Departamento de Endocrinologia e Metabolismo de um hospital terciário no Brasil, considerando o período de outubro de 1999 a março de 2024. **Resultados:** detectou-se quatro casos com idades ao diagnóstico variando de seis meses a dois anos e seis meses, do sexo feminino e com adrenarca precoce. Durante o acompanhamento, apenas uma paciente apresentou recidiva metastática e posteriormente óbito. Três pacientes apresentaram boa evolução até o momento. **Conclusão:** o diagnóstico precoce e o acompanhamento pós-operatório ativo são cruciais para um prognóstico favorável e sobrevida de pacientes com adenocarcinoma adrenal.
**Palavras-chave**: Neoplasias das glândulas suprarrenais; Doenças das glândulas suprarrenais; Carcinoma Adrenocortical.

**Resumen**:
**Objetivo**: describir los principales hallazgos de laboratorio, imagenológicos e histopatológicos en pacientes pediátricos con adenocarcinoma suprarrenal, así como la progresión clínica de los casos analizados. **Métodos**: se realizó un estudio descriptivo mediante la revisión de los registros médicos de los niños atendidos en el Departamento de Endocrinología y Metabolismo de un hospital terciario de Brasil, entre octubre de 1999 y marzo de 2024. **Resultados**: cuatro casos con edades en el momento del diagnóstico que oscilaban entre meses y dos años y seis meses, de sexo femenino y con adrenarquia precoz. Durante el seguimiento, solo un paciente desarrolló metástasis recurrentes y posteriormente falleció. Tres han mostrado una buena evolución hasta la fecha. **Conclusión**: el diagnóstico precoz y la vigilancia postoperatoria activa son fundamentales para un pronóstico favorable y la supervivencia de los pacientes con adenocarcinoma suprarrenal.
**Palabras clave**: Neoplasias de las glándulas suprarrenales; Enfermedades de las glándulas suprarrenales; Carcinoma corticosuprarrenal.

**Corresponding Author:** Flávia Alves Ribeiro – flaviaalvesribeiro@yahoo.com.b

1. Hospital de Clínicas, Universidade Federal do Triângulo Mineiro, Uberaba/MG, Brazil
2. Departamento de Endocrinologia, Hospital de Clínicas, Universidade Federal do Triângulo Mineiro, Uberaba/MG, Brazil

## INTRODUCTION

Adrenal adenocarcinoma is a rare disease with a low global incidence. It has a bimodal age distribution, with peak incidence in children under 5 years of age and in adults between the 4th and 5th decades of life, with a higher prevalence in females[1-4].

In Brazil, the incidence of adrenal tumors in the pediatric population has increased, and it is 15 times more frequent than the global average. This is attributed to the inheritance of a specific pathogenic heterozygous germline mutation at codon 337 of the TP53 gene (R337H), which is prevalent in certain regions of the country, and leads to loss of the native allele in tumor tissue. The TP53 gene is a tumor suppressor gene located on chromosome 17p13.1[1,3,5-7].

Adrenal adenocarcinomas are classified as functioning and non-functioning tumors, with the majority (60%) associated with excessive hormonal production. In the general population, the most common clinical manifestation is Cushing's syndrome due to cortisol production; followed by androgen production with virilizing syndrome, characterized by acne, hirsutism and oligomenorrhea; and, more rarely, estrogen production leading to feminization in men (gynecomastia, loss of libido and testicular atrophy). In non-functioning tumors, clinical manifestations are typically related to mass effects, such as abdominal discomfort, back pain, or nonspecific malignancy symptoms such as fever, weight loss, or general malaise[3,8].

In children with adrenocortical tumors, symptoms often include signs of precocious puberty, particularly precocious adrenarche and virilizing syndrome. Cushing's syndrome may also be present due to mixed secretion with hypercortisolism[1,3,5].

Initial laboratory investigation aims to identify hormonal secretion and exclude differential diagnoses of adrenal lesions. Hypercortisolims should be assessed using tests such as the dexamethasone suppression test at a dose of 20 mcg/kg, 24-hour free urinary cortisol, and measurements of basal cortisol and adrenocorticotropic hormone (ACTH). In cases of suspected mineralocorticoids excess, potassium levels should be measured and the aldosterone-renin ratio calculated, but only in patients with hypertension and/or hypokalemia. Evaluations of sex steroids, excess includes measurement of dehydroepiandrosterone (DHEA), 17-OH progesterone, androstenedione. and testosterone levels. Pheochromocytoma should be excluded through assessment of fractionated metanephrines in a 24-hour urine collection or free plasma metanephrines[3,8-9].

Adrenal tumors are typically large, heterogeneous masses that are often initially identified on abdominal ultrasound. However, further evaluation requires more accurate imaging studies. On CT scans, adrenocortical carcinomas show pre-contrast densities greater

than 10 Hounsfield units, indicating low lipid content and contrast washout between 40 and 50%. CT and MRI have similar efficacy in evaluating the lesion. Positron emission tomography (PET) using 18F-fluorodeoxyglucose (FDG-PET) can also be useful, as malignant lesions typically exhibit high metabolic activity leading to high FDG uptake. unlike adrenal adenomas. However, false-ósitive results may occur, as pheochromocytomas, adrenal metastases, and some adenomas can also demonstrate increased metabolic activity[5,8-9].

Histopathological evaluation is a crucial step in diagnosing and monitoring these tumors. This assessment includes macroscopic criteria such as tumor size and weight, capsule integrity, and presence of hemorrhage or necrosis; and microscopic criteria[4-5]. In 1984, Weiss proposed a scoring system based on 9 microscopic criteria to predict distinguish malignant from benign tumors, following a multicenter review of 43 cases[10].

Once malignancy is confirmed histopathologically, tumor staging is important for treatment planning, prognosis estimation and postoperative follow-up. The European Network for the Study of Adrenal Tumors (ENSAT) staging system is the most widely used[1,5,11-13].

Tumor staging is the most important prognostic factor in adrenal adenocarcinomas. Additionally, other factors associated with worse prognosis are highlighted in the S-GRAS scale, which included tumor grade (Weiss >6 and/or Ki67 >20%); surgical status (incomplete resection of the primary tumor); age (>50 years); and presence of symptoms related to the tumor or hormonal secretion, with mixed secretion of androgens and cortisol [4-5,12-14].

Complete surgical resection of the lesion with open adrenalectomy remains the treatment of choice and should be performed by an experienced surgeon[6,8,12]. After surgical resection, long-term active surveillance should be implemented[15].

This study aims to describe the main laboratory, imaging and histopathological findings in pediatric patients with adrenal adenocarcinoma, as well as the clinical progression of the analyzed cases.

## METHODS

The cases were obtained from the archives of the Endocrinology and Metabolism Department archive of Hospital de Clínicas of Universidade Federal do Triângulo Mineiro (HC/UFTM) and through a retrospective review of medical records of pediatric patients seen in this department over the past 25 years, from October 1999 to March 2024, in a retrospective case series study. Data collection was carried out from May 2024 to November 2024.

Children diagnosed between six months and two years and six months of age who underwent surgical resection of adrenal lesions with histopathological diagnosis of

adenocarcinoma were included. Patients without the corresponding diagnosis and out of the age range were excluded.

Among the laboratory tests, we analyzed values of LH (luteinizing hormone), FSH , estradiol, DHEAS (dehydroepiandrosterone sulfate), 17-hydroxyprogesterone, testosterone, cortisol and cortisol after suppression with dexamethasone, using chemiluminescence methods in both pre- and postoperative settings.

Patients were classified according to the criteria proposed by Weiss. The analyzed criteria include: high nuclear grade, mitotic rate greater than 5/50 high-power fields, atypical mitoses, less than 25% clear cells, diffuse architecture, microscopic necrosis and invasion of venous, sinusoidal and capsular structures[10].

Tumor staging was performed using the ENSAT system, which classifies tumors into four stages. Stages I and II are confined to the adrenal gland, with Stage I being less than five cm and Stage II being greater than five cm. Stage III corresponds to tumors with invasion of adjacent tissues or metastasis to regional lymph nodes. Stage IV is determined by the presence of distant metastases[5,11,13].

This study was submitted to the Ethics and Research Committee of HC-UFTM and authorized under number 6.811.758.

## RESULTS

Four cases of adrenal adenocarcinoma diagnosed between October 1999 and July 2020 were analyzed. Among them, three cases were investigated and the patients underwent surgical treatment at the study center, while one case was investigated and managed at an external facility but with immediate postoperative follow-up at the Endocrinology outpatient clinic of HC-UFTM. Clinical, laboratory and histopathological data are summarized in Chart 1.

All patients were female, from the southeastern region of Brazil. The median age at diagnosis was 16.5 months. In all cases studied, the patients initially exhibited virilizing syndrome with precocious pubarche due to precocious adrenarche; in one case, it was also associated with cortisol hypersecretion (Cushing's syndrome). Although pubarche was present in all analyzed cases, one patient initially sought our service due to abdominal pain (mass effect) rather than virilizing syndrome. Clinical findings are shown in Figure 1.

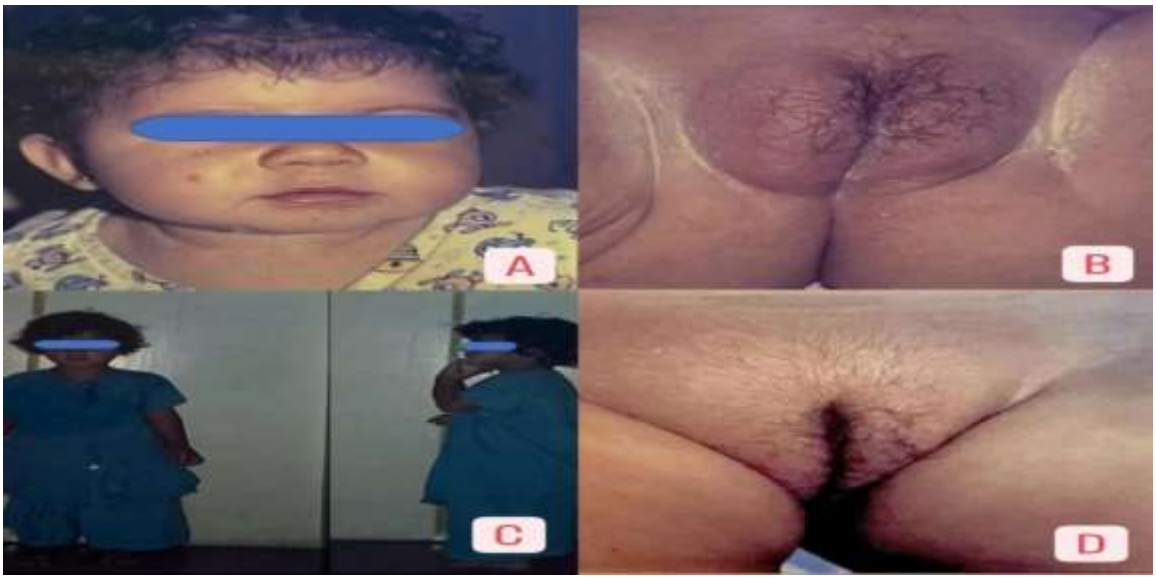
**Chart 1**. Clinical, laboratory and histopathological data of patients with adrenal adenocarcinoma treated at the Endocrinology and Metabolism Department of the Hospital de Clínicas of UFTM from October 1999 to March 2024. Uberaba/MG, Brazil, 2025.

| | CASE 1 | CASE 2 | CASE 3 | CASE 4 |
|---|---|---|---|---|
| **Age at Diagnosis** | 6 months | 2 years and 6 months | 2 years and 1 month | 8 months |
| **Clinical Presentation** | Pubarche + clitoromegaly + Cushing's Syndrome; M1P3, SDH: +1.78, SDW: +2.68; BA: 2.6 years | Palpable mass in the abdomen in PS + Pubarche for 3 months; M1P2; SDH: -0.24 SDW: -0.27; BA: 2 years | Pubarche for 8 months; M1P3 SDH: +0.2; SDW: +0.8 BA: 5 years | Pubarche for 8 month; M1P2; SDH: -2,32 SDW: -0,45 BA: 12 months |
| **DHEAS (mcg/dL)** | Pre-op 252 Post-op <30 | Pre-op 7580 Post-op 1 | Pre-op 2940 Post-op <30 | Pre-op >1000 Post-op 7 |
| **17 OHP (ng/mL)** | 1,08 | Pre-op 20 Post-op 0,8 | Pre-op 10,3 | Post-op 10 |
| **Testosterone (nd/dL)** | Pre-op 430 Post-op 45 | Pre-op 150 Post-op < 20 | Pre-op 70,1 Post-op 20 | Pre-op 956 Post-op < 7 |
| **Cortisol (mcg/dL)** | 9,3 | 21,7 | 21,20 | 22,68 |
| **Cortisol Post-Dexamethasone (mcg/dL)** | Pre-op 23,8 Post-op <1 | Pre-op 14,6 Post-op <1 | Pre-op11,8 Post-op <1 | Not done |
| **Anatomopathological** | LA; Weight 102 g; Dimensions 7.0 x 6.0 x 3.5 cm; | RA; Weight 405 g; Dimensions 12.0 x 9.0 x 7.0 cm; | RA; Weight 32 g; Dimensions 4.5 x 3.5 x 2.5 cm; | RA; Weight 145 g; Dimensions 8 cm in the largest axis; |
| **Histopathological Analysis** | ACA; Weiss: 8/9; ENSAT III T3N0M0 | ACA; Weiss 4/9; ENSAT III T3N0M0; p53 -; high cellular proliferation | ACA; Weiss 3/9; ENSAT II T2N0M0; p53-; low cellular proliferation | ACA; Weiss 5/9; ENSAT II T2N0M0; p53+; high cellular proliferation |

*** SDH** - Standard deviation of height; **SDW** - Standard deviation of weight; **BA** - bone age; **LA** - Left adrenalectomy; **RA** - Right adrenalectomy; **ACA** - Adrenal adenocarcinoma.

The figure 1 present the images. In image (A) you can see full moon facies (Cushing's syndrome) in patient with a tumor that co-secretes androgens and cortisol. In image (B) early pubarche and clitoromegaly. In the image (C) and (D) respectively facies and early pubarche of patient.

**Figure 1**. Image of patients Endocrinology Service Archive of Hospital de Clínicas of UFTM from October 1999 to March 2024. Uberaba/MG, Brazil, 2025.




In all patients analyzed, FSH, LH and estradiol levels were within normal levels for age. In contrast, all patients demonstrated a significant increase in DHEAS and testosterone levels, with normalization of these levels postoperatively. Three of the analyzed patients had post-dexamethasone cortisol assessed, with only one patient showing values suggestive of hypercortisolism (and associated with Cushing's syndrome due to hormonal co-secretion). Cortisol suppression testing was not performed in one patient, who nevertheless exhibited no clinical signs of hypercortisolism.

All patients underwent open adrenalectomy. Histopathological analysis revealed a wide variation in weight among the surgical specimens, ranging from 32 to 405 grams. During the surgical procedure, there was no capsule rupture in any of the analyzed cases.

Subsequently, patients underwent histopathological evaluation and were classified according to Weiss criteria. One patient, with a Weiss score of 8/9, experienced disease recurrence. After recurrence, this patient received adjuvant therapy with mitotane followed by cytotoxic chemotherapy but died due to disease progression. Another patient, diagnosed more recently (July 2020), remains under active follow-up at our service. The remaining cases, after a mean follow-up period of 154 months, opted for external follow-up and there are reports from their doctors indicating no recurrence in adulthood.

Mutation in the p53 gene was tested in three patients and was positive in only one. One case was not tested for this mutation.

## DISCUSSION

This article describes pediatric cases treated at the endocrinology department of a tertiary hospital. The age of diagnosis and sex are in accordance to the studies, which describe adrenal adenocarcinoma as a a rare condition with a bimodal incidence pattern, affecting both children and adults in their 4th or 5th decade of life, with a higher prevalence in females[1-4].

The cases analyzed are from the southeastern region of Brazil, a regions known to have an incidence of pediatric adrenal adenocarcinoma up to 15 times higher than the global average due to inherited mutations in the p53 gene found in individuals from this region[1,3,5-6]. Despite this, in this series of cases, a p53 mutation was found in only one of the cases (25%).

The most common clinical presentation found in our study was virilizing syndrome, with the presence of pubarche due to early adrenarche in all cases analyzed and one case also had associated hypersecretion of cortisol (Cushing's syndrome). These findings align with the data reported in the literature for the pediatric age group[1,3,5].

Among the laboratory tests analyzed, DHEAS and testosterone were highlighted as markers of disease activity, showing rapid normalization after tumor resection. This finding is consistent with previous reports, as all cases presented with virilizing syndrome (hypersecretion of androgens) and these markers served as early indicators for disease recurrence[3,8-9].

The standard treatmentof adrenal adenocarcinoma is surgical resection of the lesion via open adrenalectomy performed by an experienced surgeon. Given the high rate of recurrence, adjuvant therapy may be indicated. Evidence suggests that combining mitotane (an adrenolytic agent) with surgery reduces recurrence and mortality. Radiotherapy may be considered for patients with incomplete tumor resection or uncertain resection status. In selected cases of advanced tumors, mitotane may be combined with chemotherapeutics such as etoposide[7-8,12-13,16].

In all the presented cases, the patients underwent adrenalectomy for both therapeutic and diagnostic purposes. Tumor weight ranged from 32 to 405 grams. Despite the significant variation in weight, patients with heavier surgical specimens did not have a worse prognosis in this case series. Capsule integrity was preserved in all described cases.

After surgery, all patients underwent histopathological analysis, with Weiss's scores greater than 3. Of the cases analyzed, only one showed disease recurrence during follow-up and had eight of the nine malignancy predictors proposed by Weiss (Weiss >6 is considered a predictor of poor prognosis[10]) and exhibited early elevation of DHEAS during post-surgery

follow-up. This case resulted in death due to disease recurrence, refractory to adjuvant treatment with mitotane and cytotoxic chemotherapy.

Long-term active surveillance after surgival resection is essential for early detection and timely intervention in case of recurrence. It is recommended to conduct laboratory tests and imaging studies (chest CT and abdominal MRI) every three months during the first year; every four months in the second year; every six months in the third year; annually in the fourth and fifth years; and from the sixth year post-surgery, only annual laboratory tests and bone age evaluation may be performed[15].

Active surveillance was conducted in all cases with laboratory tests and imaging studies. Only one case presented recurrence, progressing to death, and DHEAS demonstrated good sensitivity in detecting active disease. Two cases have a mean follow-up time of 154 months without intercurrences. One case was diagnosed more recently and till now, no recurrence was seen.

## CONCLUSION

The main limitation of this study is the small sample size, which reflects the rarity of adrenal adenocarcinomas. There is a need for multicentric studies with systematic review and analysis of a larger number of cases.

Early recognition of adrenal adenocarcinoma is crucial for prompt intervention and improved prognosis. The main clinical marker was the presence of early adrenarche accompanied by significant elevations in DHEA-S concentrations.

Understanding the epidemiology, main associated clinical syndromes and key laboratory and imaging findings is essential for ensuring the detection of suspicion and proceeding with further investigation.

Surgical intervention, in addition to being therapeutic, is crucial for histopathological analysis, disease staging, defining prognostic factors and evaluating the need for adjuvant therapy.

Long-term active surveillance, serial laboratory markers and imaging studies are fundamental components of postoperative care for the early detection and intervention in case of recurrences.

Thus, the study and discussion of adrenal adenocarcinoma in the pediatric population provide a basis for early recognition of the condition and improvements in clinical practice. Although rare, it is important not neglecting the disease and the need for broader studies with a larger number of cases, given that, our study is a series of cases, it has a descriptive character.

## REFERENCES

1. Bachega FS, Suartz CV, Almeida MQ, Brondani VB, Charchar HLS, Lacombe AMF, et al. Retrospective analysis of prognostic factors in pediatric patients with adrenocortical tumor from unique tertiary center with long-term follow-up. J Clin Med. [Internet]. 2022 [cited in 12 Oct 2024]; 11(22):6641. DOI: https://doi.org/10.3390/jcm11226641

2. Kumar S, Tiwari P, Das RK, Kundu AK. Virilizing adrenal carcinoma in a 3-year-old boy: a rarity. Indian J Med Paediatr Oncol. [Internet]. 2010 [cited in 12 May 2024]; 31(1):30-2. DOI: https://doi.org/10.4103/0971-5851.68851

3. Antonini SR, Leal LF, Cavalcanti MM. Pediatric adrenocortical tumors: diagnosis, management and advancements in the understanding of the genetic basis and therapeutic implications. Expert Rev Endocrinol Metab. [Internet]. 2014 [cited in 12 July 2024]; 9(5):445-64. DOI: https://doi.org/10.1586/17446651.2014.941813

4. Zambaiti E, Duci M, De Corti F, Gamba P, Dall'Igna P, Ghidini F, et al. Clinical prognostic factors in pediatric adrenocortical tumors: a meta-analysis. Pediatr Blood Cancer [Internet]. 2021 [cited in 12 June 2024]; 68(3):e28836. DOI: https://doi.org/10.1002/pbc.28836

5. Almeida MQ, Bezerra-Neto JE, Mendonça BB, Latronico AC, Fragoso MCBV. Primary malignant tumors of the adrenal glands. Clinics (Sao Paulo) [Internet]. 2018 [cited in 12 July 2024]; 73(Suppl 1):e756s. DOI: https://doi.org/10.6061/clinics/2018/e756s

6. Monteiro NML, Rodrigues KES, Vidigal PVT, Oliveira BM. Adrenal carcinoma in children: longitudinal study in Minas Gerais, Brazil. Rev Paul Pediatr. [Internet]. 2019 [cited in 12 June 2024]; 37(1):20-6. DOI: https://doi.org/10.1590/1984-0462/;2019;37;1;00002

7. Srougi V, Bancos I, Daher M, Lee JE, Graham PH, Karam JA, et al. Cytoreductive surgery of the primary tumor in metastatic adrenocortical carcinoma: impact on patients' survival. J Clin Endocrinol Metab. [Internet]. 2022 [cited in 12 Oct 2024]; 107(4):964-71. DOI: https://doi.org/10.1210/clinem/dgab865

8. Fassnacht M, Libé R, Kroiss M, Allolio B. Adrenocortical carcinoma: a clinician's update. Nat Rev Endocrinol. [Internet]. 2011 [cited in 12 Oct 2024]; 7(6):323-35. DOI: https://doi.org/10.1038/nrendo.2010.235

9. Fassnacht M, Tsagarakis S, Terzolo M, Tabarin A, Sahdev A, Newell-Price J, et al. European Society of Endocrinology clinical practice guidelines on the management of adrenal incidentalomas, in collaboration with the European Network for the Study of Adrenal Tumors. Eur J Endocrinol. [Internet]. 2023 [cited in 12 Oct 2024]; 189(1):G1-G42. DOI: https://doi.org/10.1093/ejendo/lvad066

10. Weiss LM. Comparative histologic study of 43 metastasizing and nonmetastasizing adrenocortical tumors. Am J Surg Pathol. [Internet]. 1984 [cited in 14 June 2024]; 8(3):163-9. DOI: https://doi.org/10.1097/00000478-198403000-00001

11. Fassnacht M, Johanssen S, Quinkler M, Bucsky P, Willenberg HS, Beuschlein F, et al. Limited prognostic value of the 2004 International Union Against Cancer staging classification for adrenocortical carcinoma: proposal for a Revised TNM Classification. Cancer [Internet]. 2009 [cited in 23 June 2024]; 115(2):243-50. DOI: https://doi.org/10.1002/cncr.24030

12. Lin W, Dai J, Xie J, Liu J, Sun F, Huang X, et al. S-GRAS score performs better than a model from SEER for patients with adrenocortical carcinoma. Endocr Connect. [Internet]. 2022 [cited in 12 June 2024]; 11(6):e220114. DOI: https://doi.org/10.1530/EC-22-0114

13. Elhassan YS, Altieri B, Berhane S, Cosentini D, Calabrese A, Haissaguerre M, et al. S-GRAS score for prognostic classification of adrenocortical carcinoma: an international, multicenter ENSAT study. Eur J Endocrinol. [Internet]. 2021 [cited in 12 June 2024]; 186(1):25-36. DOI: https://doi.org/10.1530/EJE-21-0510

14. Riedmeier M, Agarwal S, Antonini S, Costa TEIJB, Diclehan O, Fassnacht M, et al. Assessment of prognostic factors in pediatric adrenocortical tumors: the modified pediatric S-GRAS score in an international multicenter cohort-a work from the ENSAT-PACT working group. Eur J Endocrinol. [Internet]. 2024 [cited in 12 Oct 2024]; 191(1):64-74. DOI: https://doi.org/10.1093/ejendo/lvae079

15. Brondani VB, Fragoso MCBV. Pediatric adrenocortical tumor - review and management update. Curr Opin Endocrinol Diabetes Obes. [Internet]. 2020 [cited in 12 Aug 2024]; 27(3):177-86. DOI: https://doi.org/10.1097/MED.0000000000000540

16. Riedmeier M, Antonini SRR, Brandalise S, Costa TEJB, Daiggi CM, Figueiredo BC, et al. International consensus on mitotane treatment in pediatric patients with adrenal cortical tumors: indications, therapy, and management of adverse effects. Eur J Endocrinol. [Internet]. 2024 [cited in 12 Aug 2024]; 190(4):G15-G24. DOI: https://doi.org/10.1093/ejendo/lvae038

**Associated Publisher**: Rafael Gomes Ditterich

**Conflict of Interests**: the authors declared no conflict of interests

**Financing**: none

**Contributions**:
Concept – Borges MF, Lara BHJ, Palhares HMC, Ribeiro FA, Santos Júnior JM
Investigation – Borges MF, Santos Júnior JM
Writing – first draft – Borges MF, Santos Júnior JM
Writing – revision and editing – Borges MF, Lara BHJ, Palhares HMC, Ribeiro FA, JM

**How to cite this article (Vancouver)**
Santos Júnior JM, Palhares HMC, Lara BHJ, Ribeiro FA, Borges MF. Precocious Adrenarche in Children Under 5 Years Old with Adrenal Adenocarcinoma. Rev Fam, Ciclos Vida Saúde Contexto Soc. [Internet]. 2026 [cited in *insert day, month and year of access*]; 14:e026003. DOI: https://doi.org/10.18554/refacs.v14i00.8482

**How to cite this article (ABNT)**
SANTOS JÚNIOR, J. M.; PALHARES, H. M. da C.; LARA, B. H. J.; RIBEIRO, F. A.; BORGES, M. de F. Precocious Adrenarche in Children Under 5 Years Old with Adrenal Adenocarcinoma. **Revista Família, Ciclos de Vida e Saúde no Contexto Social**, Uberaba, MG, v. 14, e026003, 2026. DOI: https://doi.org/10.18554/refacs.v14i00.8482. Access in: *insert day, month and year of access*.

**How to cite this article (APA)**
Santos Júnior, J. M., Palhares, H. M. C., Lara, B. H. J., Ribeiro, F. A., & Borges, M. F. (2026). Precocious Adrenarche in Children Under 5 Years Old with Adrenal Adenocarcinoma. Rev. Fam., Ciclos Vida Saúde Contexto Soc., 14, e026003. Retrieved in *insert day, month and year of access* from https://doi.org/10.18554/refacs.v14i00.8482