

## ORIGINAL ARTICLE

# Clinical spectrum and management outcomes of suprarenal masses in infants: a 17-year tertiary center experience

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## Summary

**Introduction:** The detection of suprarenal masses (SRM) in neonates and infants has increased due to widespread prenatal and postnatal ultrasonography. While surgery was historically the standard treatment, a conservative approach is now advocated for small, asymptomatic masses. This study aimed to analyze the management and clinical outcomes of SRM at a single tertiary care center over the last two decades.

**Material and Methods:** A retrospective analysis of 39 patients diagnosed with SRM between 2006 and 2023 was conducted. Clinical, radiological (US, CT, MRI), and laboratory data (urinary VMA/HVA, NSE) were evaluated. The follow-up protocol consisted of ultrasonography every 2 weeks during the first 3 months of life, followed by monthly or quarterly evaluations until complete resolution, with a median follow-up of 16.6 months (range: 1.9–89). Patients were managed via upfront surgery or a conservative protocol.

**Results:** SRM larger than 5 cm was identified in 18% of patients (7/39), of whom 5 underwent surgery and confirmed neuroblastoma (NBL), and in the remaining 2 patients, spontaneous resolution of the mass occurred. For the 32 patients with masses smaller than 5 cm, a conservative approach was initially adopted. Eight of these patients (25%) eventually required surgery due to elevated urinary catecholamines, which proved to be a reliable indicator of NBL. Complete regression was observed in all other cases managed conservatively.

**Conclusion:** Close observation of small SRM is safe in carefully selected patients and effectively reduces unnecessary surgical interventions. Urinary catecholamine metabolites remain a valuable tool for identifying high-risk patients requiring surgical treatment.

**Keywords:** suprarenal mass, neuroblastoma, infant, neonate, conservative management

## INTRODUCTION

Increased use of ultrasonography (US), both routine prenatal and postnatal, and a higher level of suspicion among clinicians have led to a greater number of diagnosed suprarenal masses (SRM) (1,2). Fetal SRM is usually detected in the last trimester of pregnancy during routine obstetric examination (1). Incidental findings of SRM in the first year of life are most often reported when children are referred to a radiologist for other medical conditions (e.g., urinary tract infections, constipation) or for routine hip dysplasia screening (3).

The differential diagnosis of SRM in the newborn and infants includes non-neoplastic benign lesions (adrenal hemorrhage, extralobar pulmonary sequestration, gastric duplication cyst, splenic cyst, etc.) or neoplastic malignant tumors, with neuroblastoma being the most frequent (3,4). Neuroblastoma at this age has a very good prognosis, as it often shows spontaneous regression and usually has favorable biological characteristics (5,6).

However, clinical management has been controversial, since upfront surgical removal of the tumor has been used routinely in the past. Over the last two decades, studies have evaluated a more conservative approach (7). It has been shown that small SRM can be safely observed with close clinical and radiological monitoring without negative impact on survival (7-9). This approach has enabled clinicians to withhold surgical resection in most cases without jeopardizing favorable outcomes in these patients (9).

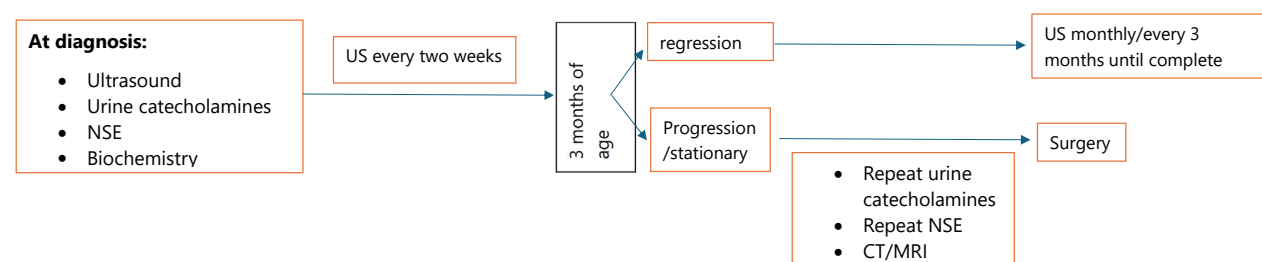
In selected patient groups, surgery and histopathological confirmation are necessary. These patients can be identified through close monitoring, MIBG scintigraphy, analysis of catecholamine metabolites in urine, and, in some cases, plasma MYCN amplification (10-12). Our study aims to analyze the approach and management of SRM at a tertiary care hospital in the last two decades.

## MATERIALS AND METHODS

A retrospective study was conducted from 2006 to 2023 at the Department of Hematology and Oncology at the University Children's Hospital. Data were collected from

patients' electronic medical records, with appropriate approval from the Ethics Committee of the University Children's Hospital (approval number 16/78/2026). Patient consent was waived due to the study's retrospective design. The inclusion criterion was a confirmed SRM on abdominal US in newborns and infants. Diagnosis of SRM was established prenatally or postnatally using standardized radiological methods, including ultrasound (US), computed tomography (CT), or magnetic resonance (MR) imaging. Patients with SRM greater than 5 cm in diameter on US were immediately referred for MRI or CT of the abdomen, followed by surgery. Patients with a mass smaller than 5 cm were eligible for further follow-up according to local protocol (Figure 1). Details regarding the affected side, the size of the mass, its structure, and echogenicity were noted. The date of diagnosis was the date of initial SRM detection by US for postnatally diagnosed children and the date of birth for those that were diagnosed prenatally. Standard demographic parameters were noted, as well as all relevant clinical information, including, but not limited to, data about pregnancy, childbirth, anthropometric parameters at birth, physical findings, complete blood count, biochemical tests, ferritin, neuron-specific enolase (NSE), urine catecholamines (VMA/HVA), and chest X-ray. NSE was considered positive if the value was 2 times the upper normal limit. Urinary catecholamine levels (VMA/HVA) were analyzed as a binary variable and considered elevated if values were at least 1.5 times above the upper normal limit. MIBG scintigraphy was performed only if the diagnosis of neuroblastoma was confirmed. MYCN status was evaluated in tumor tissue only; thus, it was not used to evaluate the need for surgery.

A favorable clinical outcome was defined as complete regression of the lesion or remission of the disease, while all other outcomes were considered less favorable. Patients were classified as having neuroblastoma only if the diagnosis was histologically confirmed, whereas patients managed conservatively with complete regression were considered non-neuroblastoma. Tumor morphology was categorized based on ultrasound findings as cystic, solid, mixed, or undefined. Tumors were categorized as small (<5 cm) or large ( $\geq 5$  cm) according to maximal diameter at diagnosis. Conservative management was defined as close clinical and ultrasound follow-up without



**Figure 1.** Management protocol

Legend: NSE – neuron-specific enolase; US – ultrasound; CT – computed tomography; MRI – magnetic resonance imaging

immediate surgical intervention. Time to surgery was defined as the interval between initial diagnosis and surgical treatment. In contrast, follow-up duration was defined as the period from diagnosis until the last clinical or imaging evaluation.

Statistical analysis was performed using the SPSS Statistics software (version 26). Variables were expressed as absolute numbers and percentages, mean  $\pm$  standard deviation, or median with interquartile range, depending on the type of variable. Data distribution normality was assessed using the Kolmogorov-Smirnov test. To compare the diameters of suprarenal masses between the neuroblastoma and regression groups, the Student's t-test or the Mann-Whitney U test was used, depending on the distribution. Differences in categorical proportions, including comparisons of prenatal detection rates between our cohort and international studies, were analyzed using the Chi-square test or Fisher's exact test, as appropriate. In all analyses, a p-value of  $<0.05$  was considered statistically significant.

## RESULTS

From November 2006 to November 2023, 39 patients met the inclusion criteria. The study group consisted of 20 newborns and 19 infants, with a slight predominance of females (54%). The median age at diagnosis was 0.7 months (21 days), ranging from birth to 12 months. The mean initial tumor diameter on postnatal ultrasound was 3.8 (range 1.5–8.7 cm).

Postnatally diagnosed patients were diagnosed at a median age of 0.5 months (range 1 day to 12 months). The mean tumor diameter in this group was similar to that observed in the overall cohort (3.8 cm) (Table 1).

Prenatal US led to diagnosis in only 5 patients (12.8%) at a median gestational age of 35 weeks (range 31–37). Diameters of SRM on prenatal US and details of US findings were unavailable for this group of patients. In patients diagnosed prenatally, the mean tumor diameter was 4.4 cm (2.8–8.0 cm).

In patients with masses  $<5$  cm, the mean diameter was 3.1 cm; in those with masses  $\geq 5$  cm, it was 6.8 cm.

In five of seven patients with a mass larger than 5 cm, CT/MR imaging was performed, followed by surgery. Diagnosis of NBL has been confirmed in all of them. In the remaining two patients, follow-up US confirmed regression of the mass, which progressed to complete resolution.

Surgery has been performed in 13 patients. The reasons for surgery were a large initial SRM diameter ( $>5$  cm) in five patients (38.5%), urine VMA/HVA positivity in six patients (46.1%), and progression of the mass in one patient (7.7%). Another patient was referred to our department after upfront surgery had already been performed at another department (Figure 2). Diagnosis of

neuroblastoma was confirmed in all 13 patients. The mean time from diagnosis to surgery was 52 days (range 0–165 days).

**Table 1.** Patients' characteristics

|                                         | N° (%)      |                         |
|-----------------------------------------|-------------|-------------------------|
| <b>Total</b>                            | 39          |                         |
| Male                                    | 18 (46)     |                         |
| Female                                  | 21 (54)     |                         |
| <b>Timing of diagnosis</b>              | N° (%)      |                         |
| Prenatal                                | 5 (12.8)    |                         |
| Postnatal                               | 34 (87.2)   |                         |
| <b>Median age at diagnosis</b>          |             |                         |
| Prenatal (gestation age in weeks)       | 35 (31–37)* |                         |
| Postnatal (months)                      | 0.5 (0–12)* |                         |
| <b>NSE</b>                              | N° (%)      |                         |
| Elevated                                | 9 (23)      |                         |
| Normal                                  | 22 (76)     |                         |
| Not done                                | 8 (21)      |                         |
| <b>Urine catecholamines</b>             | N° (%)      |                         |
| Elevated                                | 13 (33)     |                         |
| Normal                                  | 17 (44)     |                         |
| Not done                                | 9 (23)      |                         |
| <b>US structure of mass</b>             | N° (%)      |                         |
| Cystic                                  | 11 (28)     |                         |
| Solid                                   | 7 (18)      |                         |
| Mixed                                   | 11 (28)     |                         |
| Not defined                             | 10 (26)     |                         |
| <b>Mass diameter on US (cm)</b>         | N° (%)      |                         |
| Overall                                 | 39 (100)    | 3.8 $\pm$ 1.7 (1.5–8.7) |
| $\geq 5$                                | 7 (18)      | 6.8 $\pm$ 1.4 (5–8.7)   |
| $< 5$                                   | 32 (82)     | 3.1 $\pm$ 0.7 (1.5–4.6) |
| Prenatal diagnosis                      | 5 (12.8)    | 4.4 $\pm$ 2.1 (2.8–8.0) |
| Postnatal diagnosis                     | 34 (87.2)   | 3.8 $\pm$ 1.7 (1.5–8.7) |
| <b>Location of mass on US</b>           | N° (%)      |                         |
| Left                                    | 8 (21)      |                         |
| Right                                   | 28 (72)     |                         |
| Bilateral                               | 3 (7)       |                         |
| <b>Number of postnatal US performed</b> |             | 6.6 $\pm$ 5.1 (1–26)    |
| <b>Follow-up duration (months)</b>      |             | 16.6 (1.9–89)*          |
| <b>Surgery</b>                          | N° (%)      |                         |
| Yes                                     | 13 (33)     |                         |
| No                                      | 26 (67)     |                         |
| <b>Time to surgery (days)</b>           |             | 52 $\pm$ 52 (0–165)     |

Legend: NSE – neuron-specific enolase; US – ultrasound;

\* - Values are presented as median (range). All other continuous variables are presented as mean  $\pm$  standard deviation (range).

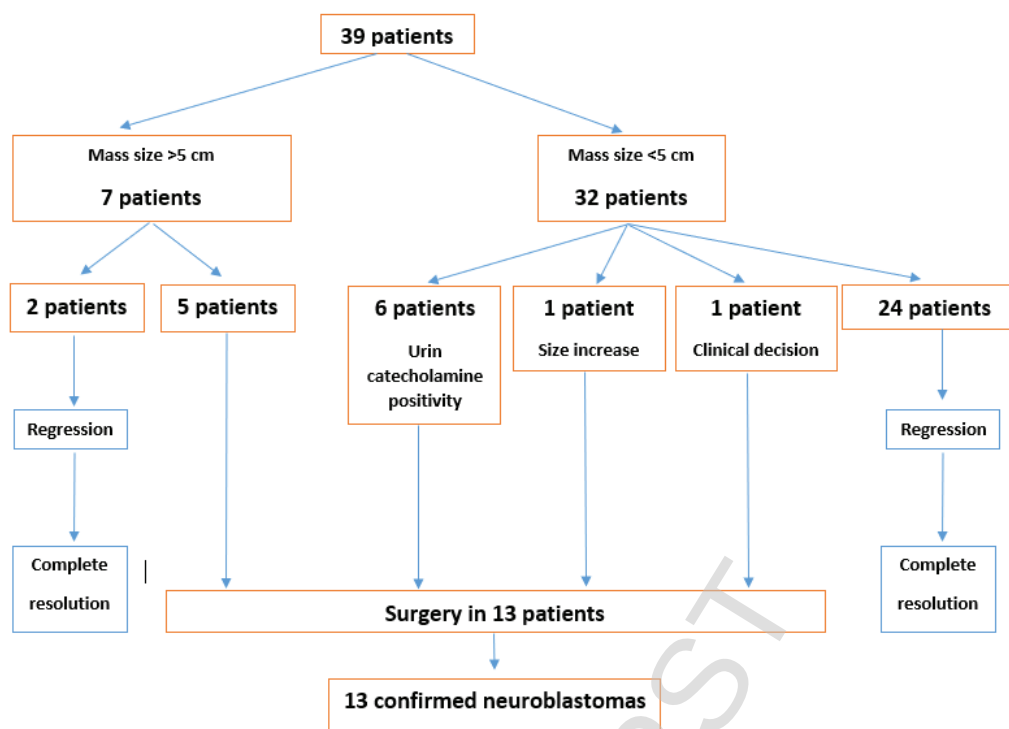


Figure 2. Management of patients

The mean tumor diameter was significantly larger in patients with neuroblastoma (6.8 vs 3.1 cm,  $p < 0.05$ ) (Table 2).

The distribution of US tumor morphology differed between patients with and without neuroblastoma. Solid lesions were more frequently associated with confirmed neuroblastoma, with 5 out of 7 patients (71.4%) having histologically verified disease. In contrast, cystic lesions were rarely associated with neuroblastoma (2 out of 12 patients, 16.7%). However, this association did not reach statistical significance ( $\chi^2 = 5.9$ ,  $p = 0.116$ ), likely due to the limited sample size (Table 2).

No statistically significant association was found between tumor morphology and clinical outcome ( $\chi^2 = 0.96$ ,  $p = 0.389$ ). However, all patients with solid tumors had a favorable outcome (100%), while favorable outcomes were also observed in the majority of cystic (66.7%) and mixed lesions (70%).

Patients with favorable outcomes were slightly older at the time of diagnosis compared to those with less favorable outcomes ( $1.9 \pm 3.0$  vs  $1.0 \pm 1.5$  months); however, this difference did not reach statistical significance ( $p = 0.235$ ) (Table 2).

MIBG scan was performed in nine patients after diagnosis of neuroblastoma had been confirmed, and it was positive in eight of them (88%).

Elevated urinary catecholamines (VMA/HVA) were strongly associated with histologically confirmed neuroblastoma, as all patients with elevated values who underwent surgery were diagnosed with neuroblastoma. No statistically significant association was found between urinary catecholamine levels and clinical outcome ( $\chi^2 = 0.04$ ,  $p = 0.832$ ). Favorable outcomes were observed in the majority of patients with both normal (83.3%) and elevated catecholamine levels (72.7%). A weak positive

Table 2. Comparison between patients with neuroblastoma and patients with spontaneous regression

| Variable*                 | Neuroblastoma | Spontaneous regression | p-value |
|---------------------------|---------------|------------------------|---------|
| Tumor size (cm)           | 6.8 ± 1.4     | 3.1 ± 0.7              | <0.05   |
| Tumor morphology          |               |                        | 0.116   |
| Solid                     | 5 (38.5)      | 2 (7.7)                |         |
| Mixed                     | 3 (23.1)      | 7 (26.9)               |         |
| Cystic                    | 2 (15.4)      | 10 (38.5)              |         |
| Other/Undefined           | 3 (23.1)      | 7 (26.9)               |         |
| Urine catecholamines      |               |                        |         |
| elevated                  | 13 (100)      | 0 (0)                  | <0.001  |
| Age at diagnosis (months) | 1.0 ± 1.5     | 1.9 ± 3.0              | 0.235   |

\*Continuous variables are presented as mean ± standard deviation. Categorical variables are presented as No (%)

correlation was observed between tumor size and elevated urinary catecholamine levels (Spearman  $\rho = 0.30$ ); however, this association did not reach statistical significance ( $p > 0.05$ ) (Table 2).

Twenty-six patients experienced spontaneous regression. Conservative follow-up was initiated in 24 patients with lesions  $<5$  cm, while two additional patients with lesions  $>5$  cm also demonstrated spontaneous regression. At initial diagnosis, all patients underwent US, along with urine VMA/HVA, NSE, and routine blood tests. Neither one of them had positive VMA/HVA or NSE. All patients had US controls every two weeks. Only one patient had an MIBG scan performed; it was positive, but the mass regressed and then resolved completely. The mean number of postnatal ultrasound follow-up examinations was  $6.6 \pm 5.1$  (range 1–26), and the median follow-up duration was 16.6 months. The median age at complete resolution was 29.8 weeks (range, 3.6–180.8 weeks), and the median duration from diagnosis to complete resolution was 27.8 weeks.

In 28 patients, SRM was located on the right side, and in 8 on the left. Three patients had bilateral masses. Five of 13 neuroblastoma patients had a left-sided mass, and the remaining eight patients had a right-sided one.

Overall, none of the analyzed clinical or imaging parameters showed a statistically significant association with clinical outcome.

## DISCUSSION

The etiology of suprarenal masses (SRM) in the fetal, neonatal, and infant period is diverse, ranging from benign non-neoplastic conditions to malignant tumors, with neuroblastoma (NBL) being the most clinically significant entity (13). In this context, the primary clinical challenge is to distinguish patients who require surgical intervention from those who can be safely managed with close observation (2).

Compared to large multicenter studies, such as those conducted by the SIOPEN group, our study showed a lower rate of prenatal diagnosis. This difference is likely attributable to variability in prenatal screening practices and access to high-resolution ultrasound technology. Nevertheless, the clinical outcomes in our cohort were comparable, further supporting the general applicability of a conservative management approach (8).

Tumor size emerged as a key parameter in clinical decision-making. Larger masses ( $\geq 5$  cm) were significantly associated with histologically confirmed neuroblastoma and were more likely to require surgical intervention. This finding is consistent with previously published reports that emphasize tumor size as an important predictor of malignancy and a practical criterion for early, aggressive management (7,14). However, it should be noted that two patients with initially large masses showed

regression during follow-up, suggesting that size alone should not be used as an absolute indication for surgery.

In our cohort, the majority of SRMs were smaller than 5 cm in diameter. Most of these lesions regressed spontaneously during follow-up, supporting the safety and effectiveness of a conservative “watch and wait” strategy in carefully selected patients. These findings are consistent with previous studies indicating that small SRMs in infants often represent biologically favorable lesions with a high potential for spontaneous regression (8).

One quarter of these patients underwent surgery in the third month of age. The decision to perform surgery was based on positive urinary catecholamine metabolites in six patients (75%) and on the increasing size of the SRM in only one patient. In contrast, findings from the SIOPEN study indicate that the most frequent trigger for surgical intervention was an increase in tumor size (69%), followed by metastases (progression to stage MS) in the remaining patients (31%). For small suprarenal masses that were MIBG-positive, with or without elevated catecholamines, a conservative approach with monthly ultrasound follow-up up to 48 weeks has been recommended (15). In our cohort, three patients with small suprarenal masses and elevated catecholamines underwent surgery despite stable tumor size during follow-up, after a mean observation period of 5.8 weeks. In these cases, patient age played an important role in decision-making. While one patient was close to three months of age at diagnosis and could have been considered for continued observation, the remaining two were older infants (4.8 and 12 months, respectively). Whether the “watch and wait” strategy can be safely extended to infants older than three months remains unclear and warrants further investigation (16).

The wide variability in time to surgery reflects heterogeneity in clinical presentation and individualized decision-making, with some patients requiring immediate intervention. In contrast, others were managed expectantly for a prolonged period.

Although urinary catecholamines are reported to be unreliable for screening and diagnosing NBL (13,15), they were assessed in most patients in our cohort. In all cases where surgery was performed based on elevated catecholamine levels, the diagnosis of neuroblastoma was confirmed. In our cohort, urinary catecholamine elevation was strongly associated with histologically confirmed NBL and may represent an important decision-supportive parameter. However, interpretation of this association should be made with caution, as elevated catecholamines were among the key factors prompting surgical exploration and histological confirmation.

In the remaining patients with small SRMs, a conservative approach was continued, and in all, complete resolution of SRM was observed. Complete resolution of SRMs was observed in those without elevated values of urinary catecholamines and NSE, so the diagnosis of

adrenal hemorrhage was assumed. Similar data are provided by a study that found regression of adrenal hemorrhage may take up to 90 days (13).

Although larger tumors were more frequently associated with elevated catecholamine levels, tumor size alone was not a reliable predictor of biochemical activity. This finding highlights the heterogeneity of suprarenal masses and suggests that combined clinical, biochemical, and imaging assessment is necessary.

Tumor morphology on US did not demonstrate a statistically significant association with clinical outcome. Although solid and mixed lesions were more frequently observed in patients with NBL, some solid masses resolved completely, while certain cystic lesions were ultimately diagnosed as NBL. This observation highlights the biological heterogeneity of SRMs and indicates that imaging characteristics alone cannot reliably distinguish benign from malignant lesions, consistent with other studies (2,15). Although tumor morphology was associated with the higher likelihood of neuroblastoma diagnosis, it did not predict clinical outcome. This finding suggests that biological tumor behavior and molecular characteristics may be more important determinants of prognosis than imaging appearance alone.

MIBG scan was not performed in any of our patients in the follow-up group. It has been performed only in patients who underwent surgery and in whom the diagnosis of NBL was confirmed. The decision not to perform MIBG scans for all patients was based on potential risks of radionuclide exposure in small infants, risks of other MIBG-related procedures (sedation or anesthesia, thyroid blockade), and, to some extent, on the availability of MIBG. The SIOPEN study recommends performing an MIBG scan after 90 days of follow-up, and if there is no mass regression (8). While MIBG remains an important tool for staging and risk stratification, our experience suggests that careful clinical and biochemical monitoring may allow safe initial observation in selected patients.

**Study Limitations:** The primary limitations of this study are its retrospective design and the relatively small sample size, which are common in single-center studies of rare conditions in very young children. In addition, not all diagnostic modalities, such as MIBG scintigraphy, were uniformly applied to all patients. Despite these

limitations, our study provides valuable real-world data on the management of SRMs in a tertiary care setting.

## CONCLUSION

In recent years, the “watch and wait” strategy has been advocated for small SRMs, demonstrating no negative impact on patient outcomes (7,8). This approach relies on strictly defined, non-invasive clinical and radiological monitoring. Our study confirms that close observation of patients with small SRMs can significantly reduce or delay the need for surgery in the majority of cases without adverse outcomes during follow-up. Beyond ultrasonography and other cross-sectional imaging (CT, MRI), our findings suggest that urinary catecholamines remain highly valuable for identifying patients at higher risk of neuroblastoma, potentially serving as a reliable indicator for surgical intervention in selected cases. This study emphasizes the importance of careful clinical monitoring and individualized decision-making in the management of suprarenal masses in early childhood. However, further prospective studies are needed to identify reliable prognostic markers and optimize patient selection for conservative management.

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**Author Contributions:** Conception or design of the manuscript: GM, OI, PR; acquisition, analysis, or interpretation of data: OI, JS, JK, TR, DjP; drafting or revising manuscript critically: GM, OI, NK, JK, JL, SJ; final approval of the version to be published: GM, OI, JL, SJ, NK, JK, JS, JK, TR, DjP, PR.

**Ethical approval:** This study was approved by the Institutional Ethical Board of the University Children's Hospital (approval number and date: 16/78, date: 12.3.2026).

**Informed consent:** Patient consent was waived due to the study's retrospective design.

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## KLINIČKI SPEKTAR I ISHOD ZBRINJAVANJA SUPRARENALNIH MASA KOD ODOJČADI: 17-GODIŠNJE ISKUSTVO TERCIJARNOG CENTRA

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### Sažetak

**Uvod:** Učestalost suprarenalnih masa (SRM) kod novorođenčadi i odojčadi je u značajnom porastu, najviše zahvaljujući rutinskoj prenatalnoj i postnatalnoj ultrazvučnoj dijagnostici. Iako je hirurško lečenje u prošlosti bilo standard terapije, danas se kod malih, asimptomatskih masa zagovara konzervativni pristup. Cilj ove studije je analiza pristupa i ishoda SRM u tercijarnom centru tokom poslednje dve decenije.

**Materijal i metode:** Retrospektivnom studijom je obuhvaćeno 39 pacijenata sa dijagnozom SRM u periodu od 2006. do 2023. godine. Evaluirani su klinički, radiološki (UZ, CT, MR) i laboratorijski podaci (VMA/HVA u urinu, NSE). Protokol praćenja podrazumevao je ultrazvučne preglede jednom u dve nedelje tokom prva tri meseca života, a nakon toga mesečne ili tromesečne kontrole do potpune rezolucije promene, uz medijanu praćenja od 16,6 meseci (opseg 1,9–89).

**Ključne reči:** suprarenalna masa, neuroblastom, odojče, novorođenče, konzervativno lečenje

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**Rezultati:** SRM veće od 5 cm identifikovane su kod 18% pacijenata (7/39). Kod pet od ovih sedam pacijenata, učinjena je hirurška intervencija i potvrđena je dijagnoza neuroblastoma (NBL). Kod preostala dva pacijenta došlo je do spontane regresije mase. Kod 32 pacijenta sa masama manjim od 5 cm, inicijalno je primenjen konzervativni pristup. Osam pacijenata iz ove grupe (25%) je na kraju operisano, zbog povišenih vrednosti kateholamina u urinu, što se pokazalo kao pouzdan indikator NBL u našoj kohorti. Potpuna regresija zabeležena je kod ostalih pacijenata koji su lečeni konzervativno.

**Zaključak:** Minuciozno praćenje malih SRM je bezbedno kod selektovanih pacijenata i smanjuje broj nepotrebnih hirurških intervencija bez ugrožavanja ishoda lečenja. Metaboliti kateholamina u urinu ostaju dragoceno sredstvo za identifikaciju visokorizičnih pacijenata kojima je neophodno hirurško lečenje.