Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/19522
DOI URL: http://dx.doi.org/10.21474/IJAR01/19522

RESEARCH ARTICLE

NEONATAL ADRENAL HEMORRHAGE

S. Rahmouni[1] K. SkalliHoussaini[2], El. D. Oukachou[2], El.Ouanouche[4,5], S. Stati[3] and F. Hmami[1,2]

[1]Faculty of Medicine and Pharmacy, Moulay Abdellah University, Fez, Morocco.
[2]Department of Neonatology and Neonatal Resuscitation Unit, University Hospital Hassan II, Fes, Morocco.
[3]Psychiatric Emergency Department, Arrazi Psychiatric University Hospital, Salé-Morocco.
[4]Higher Institute of Nursing and Health Technology of Tanger- Morocco.
[5]Biology and Health Department. Faculty of Science. Ibn Tofail University Kenitra-Morocco.

Manuscript Info

Manuscript History
Received: 25 July 2024
Final Accepted: 27 August 2024
Published: September 2024

Key words:-
Adrenal Hemorrhage, Newborn, Renal Ultrasound

Abstract

Introduction: Adrenal hemorrhage is a rare condition in the neonatal period. The significant size of the adrenal gland and its particular hypervascularization are predisposing factors for bleeding, especially in cases of trauma or vascular thrombosis (of the renal vessels or the inferior vena cava). The aim of this study is to analyze the medical records to perform a descriptive study of neonates hospitalized in the Neonatology and Neonatal Resuscitation Department of CHU Hassan II in Fez.

Method: The cross-sectional study included all cases of neonates diagnosed with adrenal hemorrhage based on renal ultrasounds performed at the Neonatology and Neonatal Resuscitation Department of CHU Hassan II in Fez, between January 2016 and December 2023.

Result: Sixteen cases of adrenal hemorrhage were identified. The incidence of adrenal hemorrhage during the study period within the department was 2 per 1,000 hospitalizations. Both sexes are equally affected, with a male predominance of 62.5%. The two main reasons for hospitalization in our series were perinatal asphyxia and jaundice. Uterine expression was reported in 87.5% of cases. The most common clinical signs, in order of frequency, are: jaundice (56.25%), abdominal mass (50%), skin and mucous membrane pallor (31.25%), fever (31.25%), respiratory distress (31.25%), and fractures in 6.25% of cases. Severe hyperbilirubinemia was found in 3 patients, accounting for 18.75%. Anemia was found in 6 patients, or 37.5%. Adrenal insufficiency was observed in 3 cases, or 18.75%. Abdominal ultrasound was performed on all patients, revealing right adrenal hemorrhage in 8 cases, left in 5 cases, and bilateral in 3 cases. The outcome was favorable in 81.25% of cases, while 18.75% of patients died.

Conclusion: Adrenal hematoma is a rare condition in the neonatal period but can be severe, which justifies systematically searching for it in the presence of risk factors. Abdominal ultrasound is the key diagnostic test. The condition typically resolves spontaneously after several weeks.

Corresponding Author:-S.Rahmouni
ADDRESS:Faculty of Medicine and Pharmacy, Moulay Abdellah University, Fez, Morocco.

Introduction:-

Adrenal hemorrhage is a rare condition in the neonatal period but can be severe, which justifies systematically searching for it in the presence of risk factors(1).

It can be of traumatic or non-traumatic origin(2).

The traumatic origin is related to difficulties during delivery and the practice of uterine expression(3).

In cases of non-traumatic adrenal hemorrhage, the factors identified include perinatal asphyxia, maternal-fetal infection, high birth weigh(4,5)t, and pre- or postnatal thrombosis of the renal vein or inferior vena cava(6).

The hypervascularization of the adrenal glands during the neonatal period makes adrenal hemorrhage particularly more common during this stage of life.

Ultrasound is the preferred method for diagnosing adrenal hemorrhage and for ensuring the subsequent follow-up of patients(7).

The risk of severe hyperbilirubinemia and acute adrenal insufficiency, especially in cases of bilateral hemorrhage, constitutes serious complications(2,4,9). However, few studies have been published on this subject in Morocco.

The objective of our study is to describe the clinical characteristics, ultrasound findings, laboratory results, identified risk factors, therapeutic measures, and outcome profile of newborns diagnosed with adrenal hemorrhage.

Method:-

This study was conducted in the Neonatology and Neonatal Intensive Care Unit of the Hassan II University Hospital in Fes, a tertiary care center located on the third floor of the Mother and Child Hospital. The unit receives newborns primarily referred from the maternity ward of Hassan II University Hospital, provincial hospitals, clinics in Fes and surrounding regions. The service includes a day hospital and two hospitalization units: a neonatal intensive care unit and a premature infant unit.

This was a retrospective, descriptive study, including all records of newborns diagnosed with adrenal hemorrhage based on renal ultrasounds performed in the Neonatology and Neonatal Intensive Care Unit at Hassan II University Hospital in Fes, covering a period of six years from January 1, 2016, to December 31, 2023.

All newborns who underwent renal ultrasound in the Neonatology and Neonatal Intensive Care Unit at Hassan II University Hospital in Fes, which revealed adrenal hemorrhage regardless of the reason for hospitalization, were included.

Data were collected from the service registers, clinical records, and ultrasound reports. A data sheet was created for each newborn to facilitate the collection and analysis of various clinical and paraclinical parameters.

Statistical analyses were performed using JAMOVI software for Windows 2016. Qualitative variables were presented as frequencies and percentages, while quantitative variables were presented as mean standard deviation (SD) or median (interquartile range, IQR).

Result:-

During the period of our study spanning 6 years (January 1, 2016, to December 31, 2023), 7,610 newborns were hospitalized in our service. During this period, 16 newborns had adrenal hemorrhage. Therefore, the incidence of adrenal hemorrhage during the study period within the service was 2 per 1,000 hospitalizations.

The majority of our patients were admitted within 24 to 72 hours of life. Both sexes are equally affected, with a male predominance of 62.5%.

Parental consanguinity was found in 2 cases in our series, representing a frequency of 12.5%.

One mother was monitored for preeclampsia with Aldomet, and another was monitored for ulcerative colitis with Pentasa during pregnancy. The newborn of the latter was born with renal thrombosis extending to the inferior vena cava, complicated by adrenal hemorrhage.

The two main reasons for hospitalization in our series were perinatal asphyxia and jaundice, each present in 5 newborns, or 31.25%. Other reasons included fever in 3 patients, or 18.75%, maternal-fetal infection in 2 patients, or 12.5%, and malformative uropathy in 1 case, or 6.25%.

Vaginal delivery was the most common route (69.39%), and uterine expression was reported in 87.5% of cases. The duration of labor ranged from 1 hour to 2 days, with an average of 13 hours.

Eleven newborns showed good adaptation to extrauterine life, representing a frequency of 68.75%, while 5 cases, or 31.25%, showed poor adaptation to extrauterine life and required resuscitation measures initially undertaken in the delivery room and continued in the service after hospitalization.

The weight of the hospitalized newborns at admission ranged from 2,600 g to 4,100 g, with an average of 3454.5 g.

The most frequent clinical signs, in order of importance, are: jaundice (56.25%), abdominal mass (50%), skin and mucous membrane pallor (31.25%), fever (31.25%), and respiratory distress (31.25%).

Table 1:-ClinicalExamination Data.

Clinical Signs	Number of Cases	Percentage
Jaundice	9	56.25%
Skin and mucous membrane pallor	5	31.25%
Abdominal mass	8	50%
Hypotonia	9	56.25%
Fever	5	31.25%
Feedingdifficulties	6	37.5%
Respiratorydistress	5	31.25%
Fracture	1	6.25%
Scrotal hematoma	1	6.25%

Severe hyperbilirubinemia was found in 3 patients, representing 18.75%. Anemia was found in 6 patients, or 37.5%, and adrenal insufficiency was found in 3 cases, or 18.75%.

Abdominal ultrasound was performed on all patients, revealing right adrenal hemorrhage in 8 cases, left in 5 cases, and bilateral in 3 cases. The size of the lesions ranged from 17 to 50 mm.

Treatment is primarily symptomatic, including management of jaundice and anemia as well as addressing the underlying etiology and adrenal insufficiency. All patients in our series were initially placed on combined antibiotic therapy (third-generation cephalosporins and aminoglycosides). Fivepatients received phototherapy, representing 31.25%. One patient received a blood transfusion, or 6.25%. Three patients were treated with phenobarbital (Gardenal), or 18.75%. Two patients underwent exchange transfusion, or 12.5%. Three patients were given hydrocortisone, or 18.75%. Three patients received hypokalemic measures with intravenous NaCl, hyperhydration, and glucose supplementation.

The duration of hospitalization ranged from 3 to 20 days, with an average of 6 days. The outcome was favorable for the majority of our patients; in fact, 13 cases, or 81.25% of the total, showed good progression. However, 3 patients, or 18.75%, died, 2 of whom had bilateral adrenal hemorrhage. The duration of hydrocortisone treatment was 4 weeks for the only survivor among the 3 with bilateral adrenal hemorrhage and adrenal insufficiency. Follow-up ultrasound showed complete resolution of the hematomas after 27 days to 2 months and 11 days, with an average of 55 days.

Discussion:-

Adrenal hemorrhage in the neonatal period is rare. The relatively large size and extensive vascularization of the gland contribute to its vulnerability to trauma and asphyxial injuries(10). The incidence of adrenal hemorrhage during our study period within the service was 0.21%, compared to 0.28% and 1.9% in the series by Zita Gyurkovits(11) and Zlata Felc(10)., respectively. The relatively high number of cases found in the studies by Zita Gyurkovits and Zlata Felc may be explained by the systematic use of abdominal ultrasound for all hospitalized newborns during their study periods, allowing for the incidental detection of even asymptomatic adrenal hemorrhage.

The male predominance observed in our series is also noted in the series by Zita Gyurkovits(11), Mehmet Mutlu(4), Wei Yao(12), and Zlata Felc(10).

Table 2:-Comparison of Series by Sex.

Series	Number of Cases	Frequency of Males	Frequency of Females
Mehmet Mutlu	13	10	3
Wei Yao	28	17	11
Zita Gyurkovits	74	45	29
ZlataFelc	16	10	6
Our Series	16	10	6

In our series, all newborns were born at term, representing 100% of the cases, which is consistent with the study by Alabsi SY(13) . Indeed, adrenal hemorrhage primarily affects term newborns rather than preterm ones.

Most of the newborns in our study, as well as in other studies, were delivered vaginally. Vaginal delivery predisposes to the occurrence of adrenal hemorrhage, although its pathophysiology remains uncertain. However, the most widely accepted theory is as follows: The progression of the fetus through the vaginal canal causes adrenal compression, leading to an ischemia-reperfusion phenomenon, which in turn triggers increased secretion of adrenocorticotropic hormone (ACTH) bythe pituitary gland. ACTH, in turn, causes venous spasm, compromising venous return, and increases adrenal arterial flow. The resulting venous stasis leads to adrenal hemorrhage(11).

Some authors assert that the incidence of adrenal hemorrhage is higher in macrosomic newborns compared to those with normal weight for gestational age(14,15) . In our series, most of the newborns were of normal weight for gestational age.

The practice of uterine expression is, according to experts, commonly used, but its actual frequency is unknown. There is no validated indication for uterine expression, which is "neither taught, codified, nor evaluated." This maneuver is "normalized and very rarely documented in the patient's medical record." However, it can be a source of maternal and fetal trauma.In our series, we observed that the use of uterine expression during childbirth is a risk factor for the occurrence of adrenal hemorrhage in newborns. Indeed, 14 cases in our series involved uterine expression during delivery, representing a frequency of 87.5%. A similar observation was reported by the team at the Casablanca University Hospital(1), who documented 3 cases of adrenal hemorrhage, 2 of which occurred in mothers who had undergone uterine expression during childbirth.

The clinical presentation of adrenal hemorrhage is highly variable, ranging from a completely asymptomatic situation to specific signs. Abdominal mass and prolonged jaundice are the most common clinical presentations(4). Jaundice is a consequence of post-hemorrhagic hemolysis and is characterized by a rather late onset and prolonged course, often requiring phototherapy. When faced with an unusually presenting jaundice, it is important to consider the possibility of an adrenal hematoma and perform an abdominal ultrasound(7).

Pallor is related to blood loss associated with adrenal hemorrhage.

An abdominal mass with lumbar contact is usually common. However, clinical assessment depends on the examiner's experience. Once detected, this sign should prompt consideration of adrenal hemorrhage, especially in the presence of other signs such as jaundice and pallor.

Adrenal hemorrhage can be associated with a scrotal hematoma due to blood leakage into the intra-peritoneal or retro-peritoneal spaces. The blood then enters the scrotum through the peritoneo-vaginal canal, forming a scrotal hematoma that can be clinically identified (11,16).

Table 3:- Distribution of clinical signs in newborns according to studies.

Signs	Jaundice	Pallor	RespiratoryDistress	Abdominal Mass	Scrotal Hematoma
Zita Gyurkovits(11)	8.1%	8%			
Mehmet Mutlu(4)	85%	38.4%	23.07%	38%	15%
Wei Yao(12)	28.57%		10.71%	7.14%	7.14%
ZlataFelc(10)	75%	31.3%	6.25%		
Our Series	56.25%	37.5%	31.25%	50%	6.25%

Acute adrenal insufficiency is rarely reported in cases of adrenal hemorrhage because the hemorrhage is primarily subcapsular, and hormonal insufficiency does not occur until there is more than 90% involvement of the adrenal tissue(7). Additionally, the adrenal gland has a significant capacity for regeneration, which explains why most adrenal hematomas are not associated with significant adrenal insufficiency(4). The occurrence of adrenal insufficiency in these patients may be secondary to the combination of adrenal hemorrhage with other underlying risk factors such as prematurity, septicemia, disseminated intravascular coagulation, perinatal hypoxia, or intraventricular hemorrhage. In our series, adrenal insufficiency was observed in newborns with bilateral adrenal hemorrhage.

Table 4:- Frequency of Adrenal Insufficiency.

Study	Frequency of AdrenalInsufficiency
Zita Gyurkovits(11)	1.3%
Mehmet Mutlu(4)	30.76%
Wei Yao (12)	0%
ZlataFelc(10)	6.25%
Our Series	18.75%

Abdominal ultrasound is the cornerstone for diagnosing adrenal hematoma. It not only confirms the diagnosis but also determines the location, laterality, and extent of the hematoma, measurements, other hemorrhagic sites, and diagnoses of renal thrombosis or inferior vena cava thrombosis. It also allows for ongoing monitoring until complete resolution of the adrenal hematoma (7).

CT scan is reserved for doubtful cases or when adrenal hemorrhage is associated with other lesions, particularly thrombotic ones. As observed in other studies(12,16), the right-sided adrenal hematoma remains the most common in our series. This right-sided predominance is explained by the positioning of the adrenal gland, which is situated between the liver and the spine. Additionally, the venous drainage of the right adrenal gland occurs directly into the inferior vena cava, while the left adrenal vein drains into the renal vein before joining the inferior vena cava. This makes the right adrenal gland more sensitive to changes in central venous pressure, which is transmitted directly to the gland(17).

Table 5:- Location of Adrenal Hematoma According to Studies.

Signs	Right AdrenalHematoma	LeftAdrenalHematoma	BilateralAdrenalHematoma
Zita Gyurkovits(11)	48.7%	45.9%	5.4%
Mehmet Mutlu(4)	53.8%	7.69%	38.4%
Wei Yao (12)	82.8%	17.8%	0%
ZlataFelc(10)	81.26%	12.5%	6.25%
Our Series	50%	31.25%	18.75%

Risk factors for adrenal hemorrhage are multiple and include perinatal asphyxia or hypoxia during delivery, maternal-fetal infection, prolonged labor, difficult extraction, septicemia, coagulation disorders, high birth weight, thrombocytopenia(14,15,18), renal vein thrombosis, trauma during or shortly after delivery(6) , and necrotizing enterocolitis. However, in some cases, no identifiable risk factors can be found. In our series, obstetric trauma with

the practice of uterine expression was the primary risk factor (87.5%). Other factors included perinatal asphyxia in 31.5%, maternal-fetal infection in 12.5%, and the presence of renal vein or inferior vena cava thrombosis in 12.5%.

While the diagnosis of adrenal hematoma is relatively straightforward when the clinical context is suggestive and the lesions are bilateral, it can be more challenging when the lesion is echogenic, unilateral, and does not change rapidly over time. In such cases, the differential diagnosis includes neonatal neuroblastoma, especially in its cystic form(19). The diagnosis is based on imaging (CT scan) and urinary catecholamine assays: vanillylmandelic acid and homovanillic acid. Currently, it is possible to differentiate adrenal hemorrhage from neuroblastoma, particularly with ultrasound. Neuroblastoma appears on ultrasound as a solid, echogenic, and homogeneous mass, whereas adrenal hemorrhage may initially appear homogeneous but will evolve into a cystic mass over time(13).

Urinary catecholamines were requested for 3 patients in our series and came back negative.

Treatment is primarily symptomatic, addressing jaundice and anemia. Blood transfusions should be administered in cases of poorly tolerated anemia, and electrolyte imbalances should be corrected. Phototherapy should be considered for jaundice, and antibiotic therapy for infection. Treatment of the underlying etiology and adrenal insufficiency, if present, is also an essential part of management. Glucocorticoid supplementation is always necessary in cases of decompensated adrenal insufficiency(1). The child should be monitored and considered at risk for adrenal insufficiency during stress (fever, trauma, surgical intervention), which justifies treatment with hydrocortisone until the resolution of adrenal hemorrhage and normalization of hormonal levels(7).

Table 6:- Treatments Administered According to Studies.

Signs	Phototherapy	Transfusion	AntibioticTherapy	Hydrocortisone
Zita Gyurkovits(11)	50%			1.3%
Mehmet Mutlu(4)			30.76%	
Wei Yao (12)			0%	
ZlataFelc(10)	75%	31.25%	18.75%	6.25%
Our Series	31.25%	6.25%	100%	18.25%

The evolution should be monitored with iterative ultrasounds. Regular ultrasound monitoring every two weeks is essential to track changes in the size and echostructure of the lesion. Resolution of adrenal hematoma typically occurs within 3 weeks to 6 months(19). In our series, the duration of resolution of adrenal hemorrhage ranged from 4 to 8 weeks.

Conclusion:-

Adrenal hematoma is a rare but potentially serious condition in the neonatal period, which justifies its systematic investigation in the presence of risk factors(20).

Adrenal hemorrhages more commonly affect the right adrenal gland.

The clinical manifestations of adrenal hemorrhage vary depending on the extent of the hemorrhage, the involvement of the adrenal cortex, and whether the hemorrhage is unilateral or bilateral(7).

Jaundice, anemia, and lumbar contact remain the classic triad to look for, especially in the absence of an obvious explanation for unusually intense or prolonged jaundice in a term newborn.

Abdominal ultrasound is the key diagnostic examination.

The condition may progress to spontaneous recovery after several weeks or to the development of adrenal calcifications, sometimes leading to chronic adrenal insufficiency that requires ongoing monitoring and potentially long-term substitution therapy.

Reference:-

1. Fadil FZ, Lehlimi M, Chemsi M, Habzi A, Benomar S. [Neonatal adrenal hematoma: various modes of presentation]. Arch Pediatr. sept 2014;21(9):990-4.

2. Duman N, Oren H, Gülcan H, Kumral A, Olguner M, Ozkan H. Scrotal hematoma due to neonatal adrenal hemorrhage. Pediatr Int. juin 2004;46(3):360-2.
3. Black J, Williams DI. Natural history of adrenal haemorrhage in the newborn. Arch Dis Child. mars 1973;48(3):183-90.
4. Mutlu M, Karagüzel G, Aslan Y, Cansu A, Okten A. Adrenal hemorrhage in newborns: a retrospective study. World J Pediatr. nov 2011;7(4):355-7.
5. Perl S, Kotz L, Keil M, Patronas NJ, Stratakis CA. Calcified adrenals associated with perinatal adrenal hemorrhage and adrenal insufficiency. J Clin Endocrinol Metab. mars 2007;92(3):754.
6. Abdu AT, Kriss VM, Bada HS, Reynolds EW. Adrenal hemorrhage in a newborn. Am J Perinatol. sept 2009;26(8):553-7.
7. Oulmaati A, Hays S, Mory-Thomas N, Bretones P, Bensaid M, Jordan I, et al. [Neonatal adrenal hemorrhage revealed by jaundice: a case report]. Arch Pediatr. avr 2012;19(4):429-31.
8. Gunlemez A, Karadag A, Degirmencioglu H, Uras N, Turkay S. Management of severe hyperbilirubinemia in the newborn: adrenal hematoma revisited. J Perinatol. déc 2005;25(12):803-4.
9. Watterberg KL. Adrenal insufficiency and cardiac dysfunction in the preterm infant. Pediatr Res. avr 2002;51(4):422-4.
10. Felc Z. Ultrasound in screening for neonatal adrenal hemorrhage. Am J Perinatol. sept 1995;12(5):363-6.
11. Gyurkovits Z, Maróti Á, Rénes L, Németh G, Pál A, Orvos H. Adrenal haemorrhage in term neonates: a retrospective study from the period 2001-2013. J Matern Fetal Neonatal Med. 2015;28(17):2062-5.
12. Yao W, Li K, Xiao X, Zheng S, Chen L. Neonatal suprarenal mass: differential diagnosis and treatment. J Cancer Res Clin Oncol. févr 2013;139(2):281-6.
13. Alabsi SY, Layland T. Adrenal Hemorrhage in Neonates: Unusual Presentation. Neonatal Netw. 2015;34(4):220-6.
14. Henriksen T. The macrosomic fetus: a challenge in current obstetrics. Acta ObstetGynecol Scand. 2008;87(2):134-45.
15. Orün E, Yildirim M, Yilmaz AE, Tufan N. Is routine abdominal ultrasonography necessary in macrosomic newborns with difficult delivery? J Matern Fetal Neonatal Med. juill 2012;25(7):1195-6.
16. Yarci E, Arayici S, Sari FN, Canpolat FE, Uras N, Dilmen U. Adrenal hemorrhage presenting as a scrotal hematoma in the newborn: A case report. Arch Argent Pediatr. juin 2015;113(3):e161-163.
17. Velaphi SC, Perlman JM. Neonatal adrenal hemorrhage: clinical and abdominal sonographic findings. Clin Pediatr (Phila). oct 2001;40(10):545-8.
18. O'Neill JMD, Hendry GMA, MacKinlay GA. An unusual presentation of neonatal adrenal hemorrhage. Eur J Ultrasound. févr 2003;16(3):261-4.
19. Rumińska M, Welc-Dobies J, Lange M, Maciejewska J, Pyrzak B, Brzewski M. [Adrenal haemorrhage in neonates: risk factors and diagnostic and clinical procedure]. Med WiekuRozwoj. 2008;12(1):457-62.
20. Katar S, Oztürkmen-Akay H, Devecioğlu C, Taşkesen M. A rare cause of hyperbilirubinemia in a newborn: bilateral adrenal hematoma. Turk J Pediatr. 2008;50(5):485-7.