Short communications

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The possible role of uric acid in renal hyper-echogenicity in neonatal hypoxic acute shock

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1 Introduction

Perinatal asphyxia frequently causes renal injury [9]. Normally, rather than being hypo-echogenic, the echogenicity of the cortex of the neonatal kidney is equal to that of the liver and spleen. In contrast, the medullary pyramids are normally hypo-echogenic and prominent [4, 5, 7]. Hyper-echogenicity of the renal cortex, and especially of the renal pyramids is a well-known phenomenon. It is common in newborns with anatomical abnormalities (e.g.: polycystic kidneys) [12], however, opinions vary about its importance in cases without any underlying anatomical abnormality. In a report from Germany it was considered to be a physiologic sign of adaptation [10], while in an Italian study of a larger population of neonates with hyper-echogenic renal pyramids, patients with no anatomical abnormality were found to have had fetal asphyxia [12].

In this paper we describe a number of newborns with hypoxic episodes of different etiology and severity. Ultrasonographic examination was performed and the pathophysiologic background was investigated.

2 Patients and methods

2.1 Patients

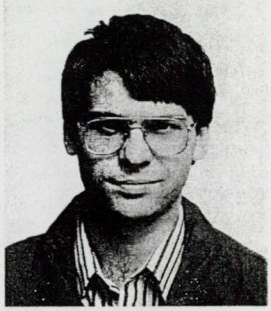
Four newborns were examined after perinatal asphyxia. Three of them were mature and one of them was immature. In every case the following criteria were fulfilled: Apgar score (1. minute) < 4, umbilical artery pH < 7.2 and $paO_2 < 50$ mmHg. Patients were observed in the Neonatal Intensive Care Unit (NICU).

2.2 Methods

The kidneys were examined ultrasonographically using a Hitachi EUB-450 real-time equipment and its 5 MHz transducer within the first 24 hours after the hypoxia was noted, and examinations were continued for 14 days.

Blood samples were collected immediately right after arrival of the baby at the NICU. Determination of uric acid (UA) and hypoxanthine (HX)

Curriculum vitae



GYULA TÁLOSI, *M.D., was born in 1969 in Nagykanizsa, Hungary. During his university training he spent three months in the Department of Physiology of the Free University of Amsterdam. In 1993 he graduated with "summa cum laude" at the Albert Szent-Györgyi University Medical School, Szeged. In the same year he started his residential training at the Pediatric Clinic of the university.*
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were performed with High Pressure Liquid Chromatography using a method elaborated by HARKNESS et al. [6]. Other parameters were determined using conventional laboratory techniques.

Urine output was measured and urine calcium/creatinine (creat.) and UA/creat. ratios [15] were calculated.

3 Case report

Case 1: Male infant born at 40 weeks gestation weighing 4100 g. Apgar scores at 1, 5 and 10 minutes were 2, 6 and 8 respectively. Meconium aspiration syndrome (MAS) was present. After successful resuscitation nasal Continuous Positive Airway Pressure (CPAP) was started using 60% oxygen. Arterial pO_2 was 48 mmHg, pH was 7.18 at the age of 12 hours (tables I + II). Sonographic examination of the kidneys was performed on the first day of life. Hyper-echogenicity was detected in the apices of the medullary pyramids of the right kidney. This was no longer visible from day 3.

Case 2: Female infant born at 28 weeks gestation weighing 2950 g. Apgar scores at 1, 5 and 10 minutes were 4, 7 and 9 respectively. At 17 hours, the baby unexpectedly collapsed with "near miss" Sudden Infant Death Syndrome. Resuscitation was partially successful. She was having repeated convulsions and was intubated and ventilator treatment was started. The hypoxic state lasted three hours (tables I ÷ II). On day 2 reflectivity of the renal cortices was increased. Increased reflectivity could also be confirmed to be present in the pyramids of both kidneys. By day 3 no hyper-echogenicity of the cortices nor of the medulla could be detected any more. This patient died at the age of 10 days (figure 1).

Case 3: Female infant born at 36 weeks gestation weighing 3680 g. The clinical diagnoses were fetal distress and diabetic fetopathy. Comprehensive resuscitation was required because asphyxia was severe, with Apgar scores of 0, 1 and 1 at 1, 5 and 10 minutes. After intubation ventilation was commenced. Her oxygen requirement was 55% (tables I + II). At the age of 4 days marked echogenicity was found to be present in the medulla of both kidneys. By day 14 the renal medullary hyper-reflectivity had disappeared.

Case 4: Female infant born at 27 weeks gestation weighing 720 g. Apgar scores were 1, 1 and 3 at 1, 5 and 10 minutes. and she was intubated and

Table I. Purine metabolites and renal hyper-echogenicity in neonatal hypoxic acute shock

Case	Birth weight (g)	Gest. age (week)	Apgar score	paO_2 mmHg	Uric acid (mmol/l)	Hypo-xanthine (mmol/l)	UA Creat. in urine (mg mg)	Renal sonography
1	4100	40	2/6/8	48.0	337.0	8.4	2.7	Pathologic on lifeday 1.
2	2950	38	4/7/9	39.0	570.0	81.4	2.9	Pathologic on lifeday 2.
3	3850	36	0/1/1	50.0	645.0	64.4	6.2	Definitely pathologic on lifeday 4.
4	720	27	1/1/3	44.0	688.0	20.1	2.1	Pathologic on lifeday 1.

Table II. Blood and urine values in neonatal hypoxic acute shock on the 1st day after birth

Case	Sex	Diagnosis	pH	BUN (mmol/l)	Creatinine (mmol/l)	Ca (mmol/l)	Quantity of urine (ml/kg h)	Osmolality of urine (mosm/kg)	Ca/Creat. in urine (mg/mg)
1	M	MAS	7.18	9.9	142.5	1.68	0.3	366	0.11
2	F	SIDS	7.12	7.0	110.0	2.20	1.4	392	0.06
3	F	Fetal Distress	7.17	11.4	154.0	1.82	0.2	286	0.40
4	F	IRDS	7.2	19.5	173.0	1.06	0.6	175	0.22

transported to our hospital immediately because of extreme prematurity and IRDS. Respirator treatment was started immediately after her arrival (tables I + II). At 1 day of age, increased echogenicity of the renal parenchyma was found. This very immature infant died of intraventricular hemorrhage on the fourth day of life.

4 Discussion

In our previous animal experiment, UA nephropathy due to acute shock could be induced, and sonographic examination showed hyper-echogenicity of the renal medulla [14]. According to these experimental results a study protocol was designed for hypoxic neonates. So far we have examined 4 cases, who fulfilled all the criteria of our protocol. UA level was 560 ± 156.4 μmol/l (x ± SD), which was about 3.5 times higher than the normal neonatal concentration found in our laboratory (160 μmol/l). HX level in our asphyxia patients was 43.6 ± 34.9 μmol/l (x ± SD), while the normal level found in our laboratory is < 5 μmol/l. Very high HX levels predict a bad prognosis [13], which was also shown in two of our patients, who died at the age of 4 and 10 days. BUN concentration was 12.0 ± 5.3 mmol/l (x ± SD), which was slightly elevated (normal: 2−9 mmol/l). Creat. level was 145.0 ± 26.4 μmol/l (x ± SD), when the normal level is 10−70 μmol/l. Case 4, the immature newborn with a birthweight of 720 g had the highest values (BUN 19.5 mmol/l, creat. 172 μmol/l). 3 of the 4 patients had oliguria of various degrees, and osmolality of the urine was increased. There was no hypercalcemia in any of the patients. Although furosemide was given to every patient, the low urine Ca/creat. ratio (maximum 0.4 mg/mg, normal = 0.32−0.78 mg/mg) practically excludes the possibility of nephrocalcinosis. On the other hand, all newborns were hyper-uricosuric (normal range: 0.79 mg/mg, patients data in the tables).

Hyper-echogenicity of the medulla was found of different grades in all of the cases. In two cases the entire parenchyma was hyper-reflective. The increased renal parenchymal echogenicity was transient in all of the cases.

UA was considered to be a possible cause of transient renal insufficiency of the neonate as early as the 70/s [1], however, hyper-reflectivity of the kidneys could not be diagnosed at that time. With the introduction of ultrasonography echogenicity of the kidneys during the first days of life is often found to be increased [2, 3, 4]. In a study from Italy [2], 90 newborn infants out of 103 had med-

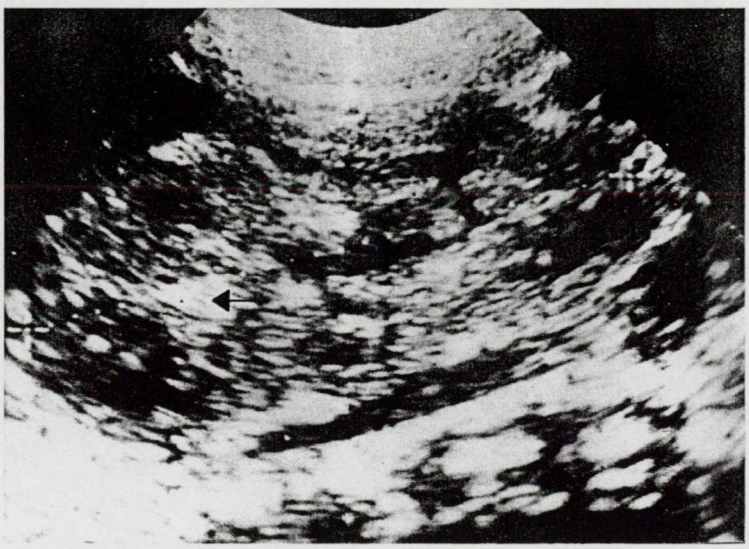

Figure 1. On the 2nd day of life, increased reflectivity of both kidneys occurred, either in the cortical, or in the medullary parenchyma.

ullary hyper-echogenicity secondary to perinatal asphyxia, however parameters of renal function and pathophysiology are not discussed in this article. Alteration in medullary hyper-echogenicity is often thought to explain the presence of Tamm-Horsfall protein [10, 11], a mucoprotein, excreted by the distal tubulus [8]. Opinions in the literature are, however divided as to whether this protein causes transient renal failure or just physiological hyper-echogenicity of the pyramids. In two of our cases, we found hyper-echogenicity of either the cortices or the medulla, which cannot be explained by deposition of Tamm-Horsfall protein.

In our opinion medullary hyper-echogenicity of the neonatal kidney seems to be a pathological phenomenon. In addition, we consider that sonographic examination of the kidneys and measurement of hypoxanthine and uric acid levels should be used as sensitive indicators in the diagnosis and grading of hypoxic injury in the neonate.

Abstract

Sonographic examinations as well as blood and urine chemistry tests were carried out in 4 neonates (3 mature, 1 premature) with transient renal failure, who were suffering from the effects of neonatal asphyxia of varying etiology. The first ultrasound examinations of the kidneys were performed within 24 hours after the hypoxic event. Simultaneously, blood and urine tests for parameters of renal function and purine metabolites were also carried out. Transient insufficiency of renal function could be detected in all cases with hyper-uricemia and hyper-uricosuria with no hypercalciuria. Ultrasonographic examinations showed hyper-echogenicity of the renal pyramids in all of the cases and hyper-reflectivity of the renal cortex in cases 2 and 4. In 3 cases, hyper-echogenicity appeared within 24 hours and disappeared in a short time, while in case 3 it could be detected from day 4 until day 14. These findings demonstrate, that the neonatal kidney is very sensitive to hypoxia and that hypoxic renal failure is accompanied by hyper-echogenicity of the kidneys. Uric acid is a possible cause of the renal hyper-echogenicity.

Keywords: Hypoxia, neonate, renal hyper-echogenicity, uric acid.

Zusammenfassung

Die mögliche Rolle von Harnsäure bei renaler Hyper-Echogenität bei neonatalem akutem hypoxischem Schock

Sonographische Untersuchungen sowie chemische Blut- und Urinuntersuchungen wurden an vier Neugeborenen (3 ausgetragene, 1 nicht-ausgetragenes) mit vorübergehender Niereninsuffizienz vorgenommen, die unter den Auswirkungen von Asphyxia neonatorum unterschiedlicher Ätiologie litten. Die ersten Ultraschalluntersuchungen der Nieren wurden innerhalb von 24 Stunden nach dem hypoxichen Ereignis vorgenommen. Gleichzeitig wurden Blut- und Urintests auf Parameter der Nierenfunktion und Purinmetabolite ebenfalls durchgeführt. Eine vorübergehende Insuffizienz der Nierenfunktion konnte in allen Fällen mit Hyperurikämie und Hyperurikosurie ohne Hyperkalziurie festgestellt werden. Die Ultraschalluntersuchungen zeigten eine Hyper-Echogenität der Nierenpyramiden in allen Fällen und ein Hyper-Reflexionsvermögen der Nierenrinde in den Fällen 2 und 4. In drei Fällen trat die Hyper-Echogenität innerhalb von 24 Stunden auf und verschwand in kurzer Zeit, während sie im Fall 3 vom Tag 4 bis zum Tag 14 festgestellt werden konnte. Diese Befunde zeigen, daß die neonatale Niere sehr empfindlich gegenüber Hypoxie ist, und daß das hypoxische Nierenversagen von einer Hyper-Echogenität der Nieren begleitet wird. Harnsäure ist eine mögliche Ursache der renalen Hyper-Echogenität.

Schlüsselwörter: Harnsäure, Hypoxie, Neugeborenes, renale Hyper-Echogenität.

Résumé

Rein hyper-échogénique et rôle possible de l'acide urique dans le choc hypoxique néonatale aigu

Nous avons effectué les examens échographiques, les examens chimiques du sang et de l'urine sur 4 nouveaunés (3 matures, 1 immature) présentant une altération du passage rénal et souffrant des séquelles d'une asphyxie néonatale d'étiologie diverse. Le premier examen échographique a été réalisé dans les 24 heures suivant l'événement hypoxique. Nous avons effectué dans le même temps les examens du sang et de l'urine pour établir

les paramètres de la fonction rénale et les métabolites puriques. Nous avons détecté sur tous une insuffisance de passage de la fonction rénale avec hyperuricémie et hyperuricurie mais sans hypercalciurie. Les examens échographiques ont révéle un rein hyper-échogénique au niveau des pyramides rénales dans tous les cas et une hyper-réflectivité du cortex rénal dans les cas 2 et 4. Dans 3 cas, le rein hyper-échogénique est apparu dans les 24 heures mais a disparu rapidement alors que dans le cas 3, il a été détecté du jour 4 au jour 14. Ces résultats montrent que le rein néonatal est extrêmement sensible à l'hypoxie et que l'hypoxie rénale s'accompagne d'un rein huper-échogénique. Il est possible que l'acide urique soit à l'origine de ce rein huper-échogénique.

Mots-clés: Acide urique, hypoxie, nouveau-né, rein hyper-échogénique.

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Fetal renal hyperechogenicity in pathological pregnancies

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1 Introduction

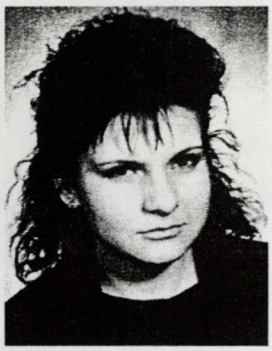
ESTROFF et al. examined the fetal and neonatal hyperechogenicity. Neonatal renal hyperechogenicity is a characteristic feature in chronic or acute perinatal hypoxia [2, 18]. The cause of fetal renal hyperechogenicity in hypoxic cases is presumed to be the accumulation of ATP depletion products.

Neonatal hyperechogenic kidneys have been reported in connection with urinary tract obstruction, polycystic and glomerulocystic kidney disease, obstructive nephrological disease and nephrocalcinosis [5, 9, 11, 17]. In about 20% of cases of fetal renal hyperechogenicity, the cause is unknown [7]. The possibility of a connection between intrauterine growth retardation and hyperechogenicity has not been examined so far. Hyperechogenic kidney is diagnosed when the fetal kidney displays an echogenicity higher than that of the liver or the spleen [6]. Hyperechogenicity of the renal cortex and especially the renal pyramids is a well-known phenomenon, but opinions differ appreciably as to its importance in cases involving no anatomical alterations. CHIARA et al. examined a large population of neonates with hyperechogenic pyramids, but no anatomical abnormality was ever found to accompany fetal asphyxia [2].

We have investigated the echogenicity of the fetal kidneys during the last period of intrauterine life in normal and pathological pregnancies, focusing on pregnancies complicated by chronic fetal hypoxia (pregnancy-induced hypertension and preeclampsia). Pregnancy-induced hypertension does not always involve intrauterine hypoxia, but in our cases this was the case.

These fetal examinations were designed to screen for medullary hyperechogenicity, and to examine whether there is a connection between the hyperechogenicity of the fetal kidney and the presence of an intrauterine hypoxic state (figures 1 + 2).

Curriculum vitae



ANDREA SURÁNYI *M.D., graduated from Albert Szent-Györgyi Medical University in 1994, since when she has been a postgraduate student at Albert Szent-Györgyi Medical University. She is currently working on fetal ultrasound examinations of pathological pregnancies.*

2 Patients and methods

Onehundred and twenty pregnancies were investigated between the 28th and 36th weeks of gestation. All these women had toxemia, as defined by the Fédération Internationale de Gynecologie et d'Obstetrique (FIGO); EPH gestation has edema, proteinuria and hypertension. The gestation age was calculated according to NAEGELE's rule and the first trimester ultrasound examination. In the positive group (15 cases), fetal renal hyperechogenicity was diagnosed, without other fetal ana-

tomical abnormalities. The control group comprised of the other 105 cases of the 120 pathological pregnancies.

The maternal liver and kidneys and the fetal brain, heart, bowel, liver and renal parenchyma were screened by ultrasound. The blood flows of the fetal renal artery and the umbilical artery were measured by Doppler. Examinations were performed using Hitachi EUB-450 ultrasound equipment fitted with a 3.5 MHz transducer. Hyperechogenic kidney was diagnosed when the fetal renal medulla or cortex displayed an echogenicity similar to that of the surrounding bone, but higher than that of the liver or spleen (figures 1 + 2). The pathological waveforms of the renal arteries include diastolic zero flow, reverse flow, postsystolic incisura or higher flow parameters than those of the normal field [18].

Between the 28th and 36th weeks of gestation, at the same time as the ultrasound examinations, blood was taken from the mothers for determination of electrolytes (Na, K, Ca, Cl) and kidney (creatinine, urea-N, uric acid, triglyceride, cholesterol) and liver (SGOT, SGPT, GGT, bilirubin) functions. Blood was also collected after the delivery, from the pulsating umbilical artery and from the cubital vein of the mothers for the same reasons. Blood was collected from the non-pulsating umbilical artery within the first 15 minutes of life for determination of acid-base parameters (pH, st. bicarb., pCO_2, pO_2, O_2 saturation) as a usual investigation. Blood samples were examined by standard laboratory techniques.

The liver and kidneys of the neonates were screened with Hitachi EUB-450 ultrasound equipment fitted with a 3.5 MHz transducer during the first 5 days after birth.

The results were analysed by the chi-square test with the Yates correction.

3 Results

Fitfteen out of 120 pathological pregnancies involved fetal renal hyperechogenicity without any other fetal anatomical abnormalities. In the control group, 21 of the 105 cases displayed some pathological fetal and neonatal states, but no fetal renal hyperechogenicity. The pregnant women in the hyperechogenic group developed toxemia after the 28th week of gestation. Serious hypertension was detected in 9 mothers. The pregnant women had normal electrolyte levels. The kidney function was abnormal in 3 mothers. In 2 cases there were abnormal urea-N levels and in 3 cases abnormal creatinine levels. Two women had pathological urea-N and creatinine levels, and one had abnormal uric acid, urea-N and creatinine levels. A pathological uric acid level was observed in 4 cases. All of the investigated maternal cases exhibited increased liver enzyme levels.

Table I lists the umbilical artery serum parameters at delivery. The 15 newborns had hyperuricemia, especially the first and the fourth case. In 4 cases, there was an elevated creatinine level and in 7 cases a high urea-N level. In the control group, there were no kidney function abnormalities. Similarly, no abnormalities were found in the blood samples taken for determination of acid-base parameters within the first 15 minutes in the two groups of newborns. In the postnatal period, ultrasonography revealed a pathological renal morphology (renal hypoplasia) in 1 case and transitory renal hyperechogenicity in 6 cases, but there were no renal lesions in the other cases in the hyperechogenic group. In the control group, 3 polycystic kidneys were identified in the intrauterine state. In the hyperechogenic group, there were 6 cases of IUGR (40%), whereas in the control group there were only 3 cases (3%). The mode of delivery was Cesarean section in 7 cases in the hyperechogenic group (46%), and in 6 cases in the control group (6%).

The results were evaluated statistically by the chi-square test with the Yates correction (χ^2 test 9.16, $p < 0.01$), sensitivity: 93%, specificity: 30%, positive predictive value: 60%, negative predictive value: 80%, validation: 77%.

4 Discussion

Fetal and neonatal renal hyperechogenicity was first examined by ESTROFF et al. [6]. Fetal and neonatal renal hyperechogenicity has different causes from those in pediatric and adult patients. CHIARA et al. identified different types of neonatal hyperechogenicity [2]. Diffuse renal hyperechogenicity is caused by polycystic kidney, renal

candidiasis, dysplastic kidney and thrombosis of the renal vein. They observed an increased cortical echogenicity in a neonate with hemolytic-uremic syndrome. Medullary hyperechogenicity was found in renal disease secondary to perinatal asphyxia [2, 18]. Neonatal renal hyperechogenicity may have different causes, but the cause is unknown in 20%. We investigated this group in both the intrauterine and postnatal states. It is our opinion that increased medullary echogenicity is an early sign of intrauterine hypoxia, if there are no other anatomical disorders. This is not a nor-

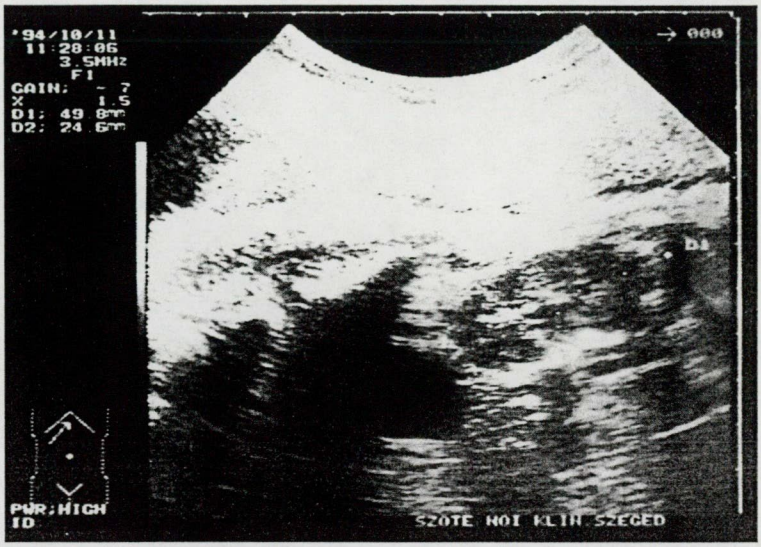


Figure 1. Longitudinal ultrasound view of a normal-sized hyperechogenic fetal kidney in the third trimester. Renal pyramids are hyperechogenic.

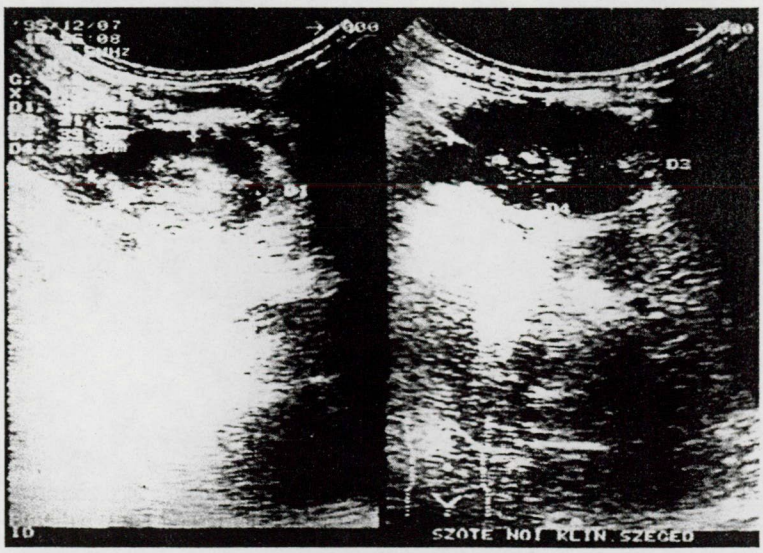


Figure 2. Longitudinal ultrasound view of the left and right kidneys in a 2-day-old infant. The left kidney gives pattern C, and the right kidney pattern D of hyperechogenic pyramids [13].

Table I. Characterization of cases when fetal renal hyperechogenicity was present

Case number	Delivery age [weeks]	Delivery weight (grams)	Apgar score (1' 5' 10')	Acid-base parameters pH-st. bicarb-CO_2-O_2	Uric acid (mmol/l)	CN (mmol/l)	Creatinine (umol/l)	Notes
1	35	1600	4, 7, 9	7,32–24,2–44,3–60,1	419	4,9	148	sectio c., IUGR, uricosuria, azotemia, anuria, postnatal renal hyperechogenicity
2	32	3600	7, 9, 9	7,34–21,3–43,6–64,4	242	2,8	56	sectio c., WAC
3	36	2200	7, 8, 10	7,26–19,3–45,2–67,3	269	3,4	75	PVN, IUGR
4	31	1460	2, 4, 7	7,24–21,7–39,2–47,1	399	8,2	153	sectio c., PRH, renal hypoplasia on right side, NEC
5	39	2980	10, 10, 10	7,36–21,0–42,2–71,3	174	3	67	PVN, WAC
6	39	2750	10, 10, 10	7,37–17,2–30,6–43,9	259	3,4	66	PVN, IUGR, PRH on left side
7	38	3740	9, 10, 10	7,30–22,3–46,1–33,0	210	3,2	79	PVN, WAC
8	31	1500	5, 7, 8	7,33–24,1–46,9–63,8	372	4,1	101	sectio c., IRDS
9	38	3010	9, 10, 10	7,20–22,1–48,8–30,0	357	8,9	119	PVN, WAC
10	38	2940	10, 10, 10	7,39–18,4–31,3–79,3	401	5,2	123	PVN, WAC
11	40	3170	10, 10, 10	7,31–20,3–41,5–38,3	376	3,7	92	sectio c., IUGR, PRH
12	38	2870	10, 10, 10	7,14–13,4–40,1–35,3	324	4,2	97	PVN, WAC
13	28	1130	7, 9, 10	7,36–25,0–45,7–27,1	240	2,7	56	sectio c., part. praemat., IRDS, PRH
14	40	2180	10, 10, 10	7,43–23,2–35,7–66,4	224	2,9	57	PVN, IUGR, part. praemat.
15	32	1440	2, 8, 9	7,21–21,6–56,0–57,0	365	3,6	69	sectio c., IUGR, part. praemat., IRDS, PRH

PRH = postnatal renal hyperechogenicity
PVN = per vias naturales
IUGR = intrauterine growth retardation
IRDS = idiopathic respiratory distress syndrome
sectio c. = sectio caesarea
part. praemat. = partus praematurus
NEC = necrotic enterocolitis
WAC = without any complication

mal variant, because it is associated with an intrauterine hypoxia.

Our results, in accord with literature findings, indicate that there are indirect signs of an intrauterine hypoxic state [3, 4, 16, 19]. These are decreased flow parameters in the umbilical artery and the renal artery, oligohydramnion and IUGR [1, 12, 14]. The pathological renal artery and/or umbilical artery flow should induce the retarded growth development [3, 15]. In 6 of the 15 renal hyperechogenic cases, IUGR was found (40%), whereas there were only 3 cases in the control group (2.8%).

Besides the ultrasound signs (echogenicity and flow parameters) we also examined blood samples from the cubital vein of the pregnant women for electrolytes and for kidney and liver functions. These investigations revealed a pathological kidney function in the mothers. This suggests an abnormal purine metabolism, which is an indirect sign of intrauterine hypoxemia.

The measured blood parameters of the 15 fetal renal hyperechogenic cases suggest a pathological renal function connected with a chronic hypoxic state in the fetuses. We found the following alterations in the newborns: high urea-N, pathological creatinine and increased uric acid levels. The fetal liver enzyme levels were normal. ESTROFF et al. observed a slightly increased serum creatinine level, 1 week after birth [6]. Regional prolonged hypoperfusion results in a hyperechogenic kidney. However, the chronically hypoxic state is balanced by a brain-sparing effect [8, 10]. This relationship is a feature of the redistribution of the cardiac output that has been reported in hypoxic human fetuses. It has been noted in IUGR fetuses, presumably as a result of the associated hyperechogenicity. It occurs in 40% of the cases of fetal hyperechogenic kidneys. It is an early and subtle sign of mesenteric vasoconstriction secondary to a hemodynamic redistribution [7]. Growth-retarded fetuses have been demonstrated to have an increased incidence of Cesarean section because of the fetal distress. In our study, Cesarean section for fetal distress was performed in 6 cases (40%).

The statistical approach demonstrates a significant relation between fetal renal hyperechogenicity and a pathological postnatal clinical outcome ($p < 0.01$). The statistical results suggest a good relation between the diagnostic method and the clinical outcome. The specificity is low, because we investigated only simple fetal renal hyperechogenicity with no anatomical disorders.

Fetal renal hyperechogenicity appears to be a good predictive sign of intrauterine hypoxia. The clinical outcome support this.

Attention is drawn to the importance of examining the fetal renal echogenicity. We consider that ultrasound investigation of fetal renal echogenicity is necessary during the routine scan. It is important to direct pregnant women to the perinatal intensive care unit to detect this pathological fetal state in time.

Abstract

A relationship was sought between renal hyperechogenicity and the hypoxic state of fetuses.
120 pathological pregnancies were examined between the 28th and 36th week. All of these women exhibited moderately increased levels of hepatic enzymes, 3 of them had a pathological kidney function, and 4 of them displayed hyperuricemia during the examination period. The echogenicity of the fetal kidneys was examined with Hitachi EUB-450 ultrasound equipment with a 3.5 MHz transducer. The kidney (creatinine, urea-N, uric acid, triglyceride, cholsterin) and liver (SGOT, SGPT, GGT, bilirubin) functions and plasma electrolytes (Na, K, Ca, Cl) of the mothers were also examined and blood was collected from the pulsating umbilical artery for determination of the same parameters. After delivery, the physical condition of the neonates was followed and their kidneys were examined with the same ultrasound equipment within the first 5 days.
There was a significant correlation between a pathological neonatal clinical outcome and the frequency of fetal and hyperechogenicity (chi-square test with Yates correction, $p < 0.01$).
The results demonstrate that fetuses exhibiting renal hyperechogenicity in pathological pregnancies require particularly careful obstetric control and neonatological consultation. It is important that hyperechogenic cases be admitted to a perinatal intensive care unit. Fetal renal hyperechogenicity is considered to be associated with an enhanced risk of an adverse perinatal outcome.

Keywords: Fetus, renal hyperechogenicity, ultrasound.

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ORIGINAL ARTICLE

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Fetal renal artery flow and renal echogenicity in the chronically hypoxic state

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Abstract The object of this study was to investigate the fetal renal arterial blood flow in normal and hyperechogenic kidneys during the third trimester of gestation. The pregnancies screened were all chronically hypoxic. Depending on the etiology of the intrauterine chronic hypoxia, the cases were divided into two study groups. Group I comprised 120 pregnant women with pregnancy-associated hypertension and/or proteinuria. Group II consisted of 87 pregnancies with intrauterine growth retardation. Both study groups included pregnant women from the third trimester. Hyperechogenic medullae were detected in 15 out of 120 cases with pregnancy-associated hypertension and/or proteinuria, and in 22 fetuses of the 87 pregnancies involving intrauterine growth retardation. Fetal renal hyperechogenicity appears to be an indicator of fetal arterial circulatory depression, correlated with pathological changes in the resistance index for the fetal renal arteries. The fetal renal arterial blood flow resistance index was significantly lower in hyperechogenic cases. This may also be an in utero indication of subsequent intrauterine and neonatal complications, such as cesarean section because of fetal distress (43%), treatment in a neonatal intensive care unit (51%) or increased perinatal mortality (5.4%, as compared with 0.8–1.0% in the normal population). Detailed ultrasound and Doppler examinations of renal parenchyma and arteries appear to be useful methods in the prenatal diagnosis of reduced renal perfusion and of intrauterine hypoxia to detect possible pathological fetal conditions in utero.

Key words Fetus · Renal hyperechogenicity · Renal artery · Ultrasound · Vascular resistance

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Introduction

The fetal and neonatal renal medulla is normally hypoechogenic on ultrasonic examination and hence hyperechogenicity is a characteristic and striking sonographic feature [1–3]. Hyperechogenicity occurs in different diseases, which may have a clear diagnosis. However, in 20% of the cases of fetal renal hyperechogenicity, the pathomechanism is unclear [4]. Hyperechogenicity of both the renal cortex and the pyramids is a well-known phenomenon, but the importance of hyperechogenicity in cases with no anatomical alterations is controversial.

Flow velocity waveforms from branches of the abdominal aorta including the renal arteries potentially provide a more sensitive method to predict the adequacy of fetal oxygenation than an examination of aortic flow [5]. Investigation of multiple fetal vessels improves the validity of blood flow parameters [6, 7]. Fetal renal arterial resistance index decreases moderately during the third trimester of pregnancy, possibly related to the increased blood flow of the renal circulation.

In the fetus, the high vascular resistance observed in the lower extremities during the third trimester cannot explain the reduced renal vascular resistance of advancing gestation, since this increased lower extremity vascular resistance is associated with a decreased umbilical arterial vascular resistance [8].

The aim of the present study was to establish a correlation between abnormal renal arterial blood flow and the clinical outcome in fetuses with hyperechogenic renal medullae to discern if these probes are useful in the early detection of chronically hypoxic state in the fetal life.

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Material and methods

Fetal kidney ultrasound examinations were performed. Renal blood flow and echogenicity studies were carried out with two ATL ultrasound machines (Ultramark-9 and 3000), using the Combison 530 Kretz technique with a 3–5 MHz abdominal transducer, and EUB-450 ultrasound equipment with a 3.5 MHz transducer.

Umbilical artery examination

The umbilical cord was localized and the umbilical artery identified: the Doppler gate was placed in the lumen of the vessel and recordings were made on a strip-chart recorder. Signals were recorded with the fetus in a quiet state and during apnea.

Renal artery examination

An axial view of the fetus was obtained at the level of the kidneys. The Doppler gate was placed at the renal hilus, so that the maximum signal from the renal artery was obtained. The abdominal aorta gives a significantly different signal, which helps in differentiating between the two waveforms. There is no significant difference between the two sides of the renal artery [5], thus fetal renal arterial blood flow was determined on only one side.

Flow measurements were interpreted with respect to the normal ranges for the umbilical and renal arteries. The normal range was defined by regression lines and confidence values: the mean (a regression line in the middle) ± standard deviation (SD; two lines below and above the mean line). The normal field was taken from literature data on the umbilical artery [9] and the renal artery [5, 10, 11]. We employed the international standard.

Measurements were made during the absence of fetal breathing movements, since fetal breathing movements are known to exert marked effects on blood flow. The most uniform frozen waveform was used for calculation of the resistance index, defined as the difference between the peak systolic and end-diastolic frequency shifts divided by the peak systolic frequency shift [12]. The mean and the SD of the resistance index were calculated for both fetal vessels, a normal distribution being assumed [13].

The study group consisted of 207 pregnancies complicated by chronic hypoxia in the third trimester. Pregnancies were investigated between 24 and 39 weeks of gestation. The gestational age was calculated according to Naegele's rule and a first trimester ultrasound examination.The clinical outcome of the neonates was investigated until 14 days after birth.

Depending on the etiology of intrauterine chronic hypoxia, the pregnancies were divided into two study groups. Group I comprised those cases with pregnancy-associated hypertension and/or proteinuria (120 cases). This group was further subdivided into a positive group (15 cases) and a control group, those cases in which fetal renal hyperechogenicity was detected without any fetal anatomical abnormalities (105 cases).

Pregnancy-associated hypertension and/or proteinuria was defined according to the guidelines of the Committee of the American Obstetricians and Gynecologists [14], which recommend that a total protein concentration of 300 mg or more per liter in a 24-h urine collection should be regarded as abnormal; hypertension in pregnancy was defined as two consecutive measurements of diastolic blood pressure of 90 mmHg or more 4 h or more apart. The finding of edema and weight gain in pregnancy as a sign of preeclampsia is a matter of dispute, and although edema and excess weight gain may be valuable signs in particular clinical circumstances, they are unsuitable signs for classification purposes [14].

Group II comprised pregnancies involving intrauterine growth retardation (87 cases). Intrauterine growth retardation was established by the Hadlock weight estimation, based on biparietal diameter, abdominal circumference and femur length. The 22 positive cases were compared with the remaining intrauterine growth-retarded neonates (65 cases).

Hyperechoic pyramids were detected by comparison with the renal cortex, liver or spleen since normal medullary pyramids are hypoechogenic in the fetus and in newborns. The sonographic finding of hyperechogenicity is, thus, noteworthy [15].

The abnormal waveforms of the renal arteries that were detected were decreased systolic flow, diastolic zero flow, reverse flow, postsystolic ischemia or higher flow parameters than those of the normal field [3].

The umbilical artery and renal artery blood flow resistance indices were analyzed statistically to compare the cases with and without fetal renal hyperechogenicity. The results were analyzed by the Chi-square test. The method was analyzed via the odds ratio.

Results

For this study, 217 fetuses in 207 pregnancies were examined for hyperechogenicity of the renal medulla: these included 120 pregnancies (120 babies) with pregnancy-associated hypertension and/or proteinuria (group I), and 87 pregnancies (97 babies) with intrauterine growth retardation (group II).

In group I (58%), the 120 pregnancies with pregnancy-associated hypertension and/or proteinuria included 15 cases with fetal renal hyperechogenicity. Table 1 shows the data and clinical outcome of these 15 babies (6 girls and 9 boys). The mean (± SD) duration of gestation at birth was 35.7±3.3 weeks and the mean (± SD) birth weight was 2438±741 g. The Apgar scores were 7.5±2.5 at the 1st min and 8.9±1.3 at the 5th min. In the postnatal period, ultrasonography revealed renal hypoplasia in 1 case (6.6%) and transitory renal hyperechogenicity in 6 cases (40%), but there were no other renal lesions in the hyperechogenic group. In the control group (babies without medullary hyperechogenicity, whose mothers had pregnancy-associated hypertension and/or proteinuria), 3 polycystic kidneys were identified in the mothers in the intrauterine period. The mode of delivery was cesarean section in 7 cases in the hyperechogenic group (46%), and in 6 cases in the control group (6%). Babies with hyperechoic medullae were transferred to the neonatal intensive care unit in 6 cases (40%). In the postnatal period, respiratory distress developed in 3 cases (13.6%) and necrotizing enterocolitis in 1 case (4.5%) in the positive group, while there were no instances in the control group. Babies with hyperechoic medullae have six times the risk (analyzed by the odds ratio) of a pathological clinical outcome compared to babies with a normal echoic kidney in pregnancy-associated hypertension and/or proteinuria: the odds ratio was 6.22 (95% confidence limits: 2.84, 13.62).

In group II (42%), 87 pregnancies with intrauterine growth retardation involved 22 cases with fetal renal hyperechogenicity. Table 2 contains data on these 22 babies (16 girls and 6 boys). The mean duration of gestation at birth was 37.6±2.4 weeks and the mean birth weight was 2683±727 g. The Apgar scores were 7.2±1.8 at the 1st min and 8.5±1.4 at the 5th min. In this group there were no anatomical abnormalities in the kidneys. In the control group there were 2 renal malformations (2.6%): 1 multi-

Table 1 Characterization of neonates with hyperechogenic medullae in pregnancy-associated hypertension and/or proteinuria (*NICU* neonatal intensive care unit)

Case no.	Sex	Delivery weight (g)	Delivery age (weeks)	Apgar score (1st min)	Postnatal clinical outcome (5th min)	Transfer to NICU	
1	M	1600	35	4	7	Cesarean section, uricosuria, azotemia, anuria, postnatal renal hyperechogenicity	+
2	M	3600	32	7	9	Cesarean section, without any problem	–
3	M	2200	36	7	9	Without any problem	–
4	M	1460	31	2	4	Cesarean section, postnatal renal hyperechogenicity, renal hypoplasia on right side, necrotizing enterocolitis	+
5	F	2980	39	10	10	Without any problem	–
6	M	2750	39	10	10	Postnatal renal hyperechogenicity	–
7	F	3740	38	9	10	Without any problem	–
8	F	1500	31	5	7	Cesarean section, respiratory distress syndrome	+
9	M	3010	38	9	10	Without any problem	–
10	M	2940	38	10	10	Without any problem	–
11	M	3170	40	10	10	Cesarean section, postnatal renal hyperechogenicity	–
12	F	2870	38	10	10	Without any problem	–
13	F	1130	28	7	9	Cesarean section, prematurity labor, respiratory distress syndrome, postnatal renal hyperechogenicity	+
14	F	2180	40	10	10	Prematurity labor, cesarean section, prematurity labor, respiratory distress	+
15	M	1440	32	2	8	Syndrome, postnatal renal hyperechogenicity	+
Mean		2438.00	35.67	7.47	8.87		
SD		740.8	3.33	2.44	1.26		

Table 2 Characterization of neonates with hyperechogenic medullae in intrauterine growth retardation

Case no.	Sex	Delivery weight (g)	Delivery age (weeks)	Apgar score (1st min)	Postnatal clinical outcome (5th min)	Transfer to NICU	
1	F	2170	40	9	10	Without any problem	+
2	F	3035	40	8	9	Perinatal infection, fetal tachycardia	+
3	F	3030	39	8	9	Without any problem	–
4	F	3600	40	9	10	Perinatal infection	+
5	M	3320	39	9	10	Perinatal infection	+
6	M	3100	38	8	9	Cesarean section	–
7	M	2030	35.5	9	10	Toxicoman mother, cesarean section	+
8	F	2020	38	8	9	Fetal infection?	+
9	M	950	31	1	6	Bradycardia, apnea, metabolic acidosis, cataract, intraventricular hemorrhage, death on 2nd day	+
10	F	3260	41	5	7	Without any problem	–
11	F	1580	33	7	9	HELLP syndrome, cesarean section	+
12	F	2260	33	4	8	Intrauterine parvovirus infection, hydrops fetalis, meconial amniotic fluid, cesarean section, reanimation	+
13	F	3455	39.5	7	8	Cesarean section	+
14	F	3800	40	8	9	Without any problem	+
15	F	2860	37	9	9	Cesarean section	–
16	M	2910	38	9	10	Without any problem	–
17	F	3720	39	8	8	Perinatal infection	+
18	F	2460	36	8	9	Without any problem	–
19	F	2260	38	7	9	Oligohydramnios, perinatal infection?	+
20	F	3600	39	9	9	Cesarean section	–
21	F	3190	41	9	10	Without any problem	–
22 transfer	M	420	31	0	0	Stillborn	no
Mean		2683.18	37.55	7.23	8.50		
SD		727.15	2.43	1.78	1.27		

HELLP hemolysis, elevated liver enzymes, low platelets

cystic kidney, and 1 hydronephrosis. Pathological fluid was observed in only 1 case (4.5%) among the babies with hyperechoic medullae, as compared with 1 case with polyhydramnios (0.9%) and 8 with oligohydramnionos (7.6%) in the control group. Five babies had a perinatal infection (23%) (unconfirmed in 1 case). Two babies had an intrauterine parvovirus infection and in 1 case there was a suspicion of this, but the origin was unclear (9%). Overall, the infection rate was 32%. In the control group, infection was observed in 4 babies (5.2%). Two of them were twins, whose mother was HIV positive; the others 2 involved cytomegalovirus infections.

Cesarean sections were performed in 9 infants in the hyperechogenic group (40.9%), and in 13 of the control group (17%). Babies with hyperechoic medullae were transferred to the neonatal intensive care unit in 13 cases (59%).

There were very serious complications in 2 cases (9%). One baby died in utero. One newborn died on the 2nd day of life with bradycardia, apnea, metabolic acidosis, cataract and intraventricular hemorrhage.

In the control group there were serious complications in 3 pregnancies (3.9%). One was a twin pregnancy, where the baby died because of a heart malformation, the result of a rubella infection. The twin sibling exhibited only retarded growth, but the clinical outcome was good. The other stillbirth in the control group was due to left ventricular hypoplasia. A third baby with a heart malformation was born alive.

In case 12 (Table 2), meconial amniotical fluid was noted and the newborn was resuscitated. Intrauterine parvovirus infection and fetal hydrops had been recognized before the birth.

In the control group of intrauterine growth-retarded pregnancies, the following pathological cases were found: hydrocephalus (1 case), microcephalia (1 case), agenesia of the corpus callosum (1 case), facial malformation (1 case), spina bifida (1 case), oesophageal atresia (1 case), gastoschisis (1 case) and single umbilical artery (1 case) (comprising 10.4% of the control group).

There was pathological amniotic fluid in 1 baby with hyperechogenic medullae (4.6%), versus 9 cases (11.8%) in the control group. Babies with hyperechoic medullae had 1.5 times the risk by the odds ratio of an abnormal postnatal outcome compared with babies with normal echoic kidneys in intrauterine growth retardation: the odds ratio was 1.5 (95% confidence limits: 1.00, 2.26).

Doppler flow studies of umbilical arterial blood flow velocity did not reveal any significant differences in any case. This applies to groups I and II without fetal renal hyperechogenicity [χ^2=2.049 (P<0.05) in pregnancy-associated hypertension and/or proteinuria cases and χ^2=0.075 (P<0.05) in intrauterine growth-retarded cases] (Figs. 1, 2).

Doppler ultrasonography of the renal artery revealed a significant disparity between babies with hyperechoic medullae in pregnancy-associated hypertension and/or proteinuria (Fig. 3) or intrauterine growth retardation (Fig. 4). As compared with the normal picture (Fig. 5),

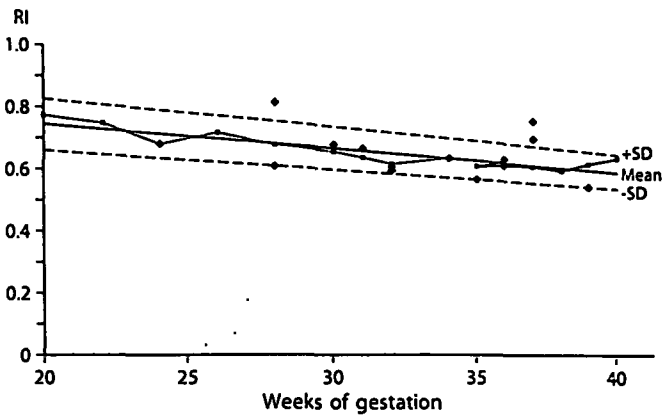

Fig. 1 Resistance index of umbilical arteries (fetuses with hyperechoic medullae in pregnancy-associated hypertension and/or proteinuria) (n=15) (*RI* resistance index)

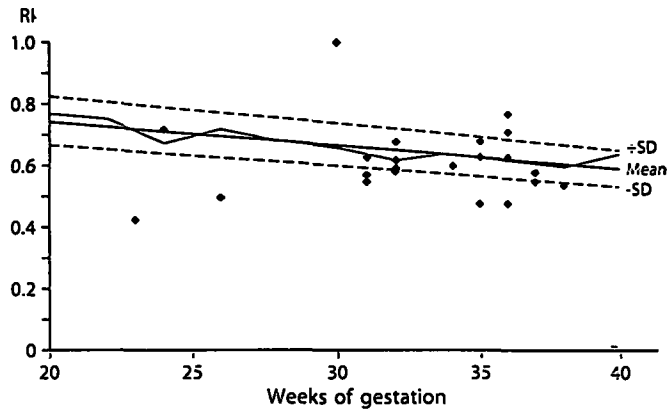

Fig. 2 Resistance index of umbilical arteries (fetuses with hyperechoic medullae with intrauterine growth retardation) (n=22)

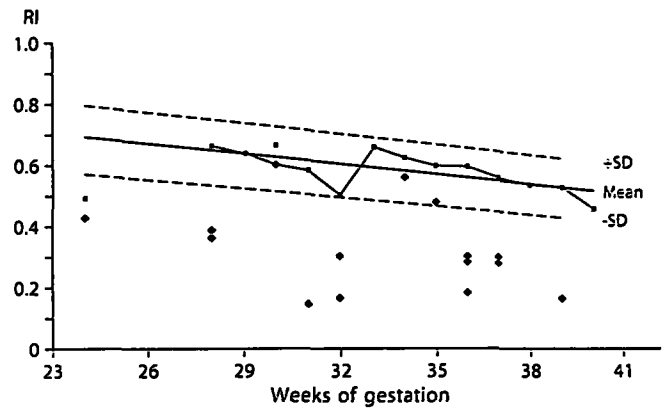

Fig. 3 Resistance index of renal arteries (fetuses with hyperechoic medullae in pregnancy-associated hypertension and/or proteinuria) (n=15)

the renal arterial blood flow velocities displayed pathological waveforms, including decreased systolic flow (Fig. 6) or postsystolic incisura (Fig. 7).

The chi-square test was applied for statistical analyses [χ^2=3.71 (P<0.05) in pregnancy-associated hypertension

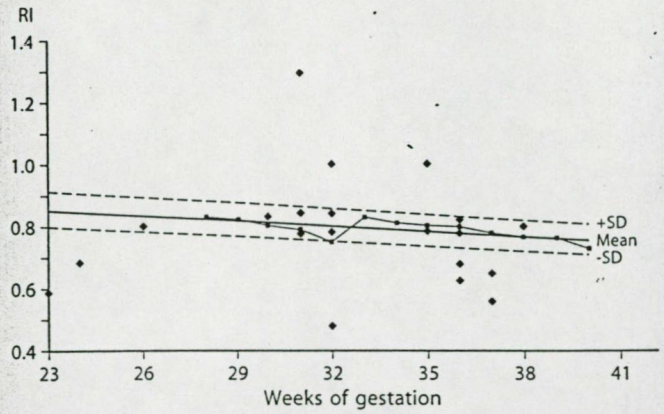

Fig. 4 Resistance index of renal arteries (fetuses with hyperechoic medullae with intrauterine growth retardation) (n=22)

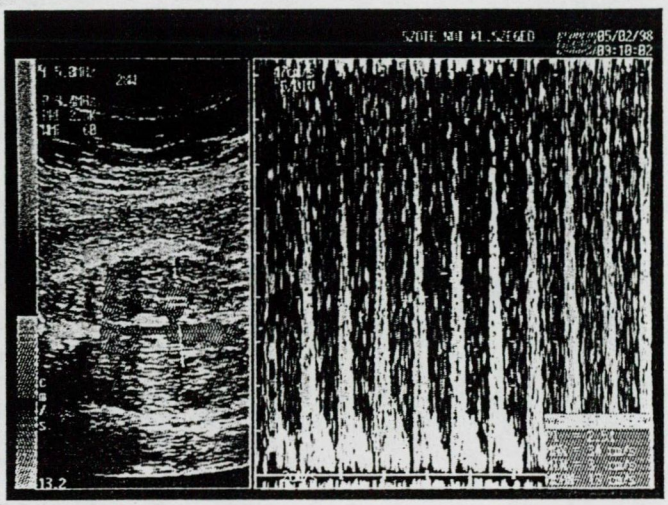

Fig. 5 Normal blood flow-velocity waveforms in the fetal renal artery at 28th week of gestation. The Doppler gate is positioned over the main renal artery

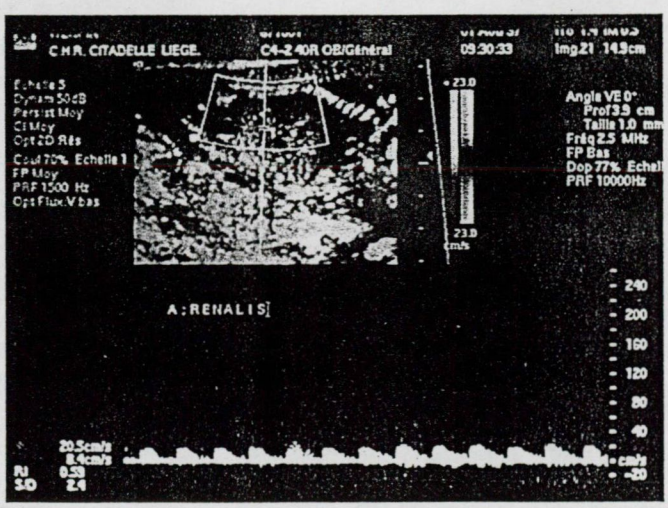

Fig. 6 Decreased blood flow-velocity waveforms in the renal artery at 32nd week of gestation. The Doppler gate is positioned over the main renal artery

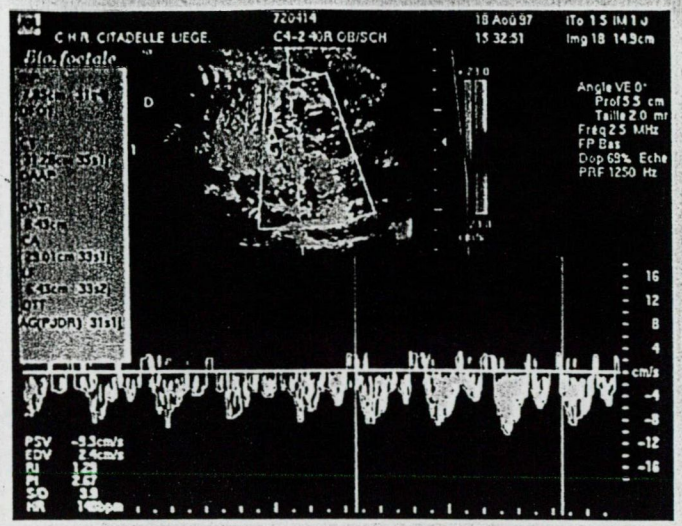

Fig. 7 Flow-velocity waveforms with postsystolic incisura in the renal artery at 31st week of gestation. The Doppler gate is positioned over the main renal artery

and/or proteinuria cases, and χ^2=3.76 (P<0.05) in intrauterine growth retarded cases]. In cases without fetal renal hyperechogenicity, there was a reduced resistance index, but differences were not significant.

Discussion

Visualization of small fetal vessels such as the renal artery was described by Campbell et al. in 1988 [16]. The renal blood flow is estimated as 2–3% of the cardiac output under physiological conditions because of the very high pulsatility index (i.e., a very high resistance) in the human fetal renal artery. During hypoxemia, the renal blood flow fell by 25–50% as compared to the baseline values, but the exact mechanism of this reduction has not been elucidated [17]. This would imply that, instead of a local vasoconstriction of the renal vasculature, the fetal renal blood flow may be maintained by a combination of mechanisms including an increase in arterial pressure and the intrarenal action of various metabolites, which ultimately induce a similar hemodynamic change [18]. A direct relationship has been reported between hypoxia and the renal artery pulsatility index (e.g., resistance) [19].

Perinatal renal hyperechogenicity may have different causes, but in a considerable proportion of cases (about 20%), there was no anatomical alteration [4]. Intrauterine and/or neonatal renal hyperechogenicity has been interpreted as a sign of intrauterine hypoxia [20, 21].

We investigated intrauterine hypoxia using indirect ultrasonographic signs: renal hyperechogenicity, and decreased flow parameters in the umbilical artery and the renal artery [5, 17, 20]. The screened pregnancies were those with chronic hypoxia, caused by pregnancy-associated hypertension and/or proteinuria and intrauterine growth retardation. We selected these causes because

they are well defined and the diagnosis is possible in the prenatal period. There is similarity between these two populations in terms of the causes of the intrauterine chronic hypoxia. We examined these two types of pathological pregnancies to determine other chance differences and investigate the importance of renal hyperechogenicity in hypoxia. In this study, we investigated these parameters in parallel with the clinical outcome.

The blood flow parameters measured in 15 fetal cases with pregnancy-associated hypertension and/or proteinuria and in 22 cases with intrauterine growth retardation suggest that a pathological renal circulation is connected with the chronic hypoxic state. We found no significant deviation in the umbilical artery, despite the fact that renal artery flow parameters were significantly different.

There is good correlation between the progressive increase in renal vascular resistance and the decreased organ perfusion [22]. By Doppler methods, both fetal and uterine blood flow can be measured, thereby permitting an assessment and detection of dysfunction affecting the uteroplacental circulation. In fetuses in a chronically hypoxic state, these were significantly below the lower limits of the normal range ($P<0.05$).

The statistical results suggest a good relation between the diagnostic method and the clinical outcome. We used the chi-square test for statistical analyses of vessel flow abnormalities because we expected the blood flow data to lie in a standardized range, not a fixed one. The odds ratio was used to analyze the association between prenatal pathological renal echogenicity and postnatal clinical outcome. A 6 times higher risk of a pathological outcome was demonstrated by the odds ratio method when kidneys were hyperechoic in pregnancy-associated hypertension and/or proteinuria. In intrauterine growth retardation, the risk was 1.5 times higher than normal. This intrauterine growth retardation group is a very heterogeneous population. The cause of the retardation is not necessarily intrauterine hypoxia, but there is a very strong suspicion of it. This explains why the risk of a pathological outcome is lower than in pregnancy-associated hypertension and/or proteinuria.

We extended the ultrasonographic study over the intrauterine period and observed consequences of acute/chronicle intrauterine hypoxia such as retarded growth (birth weight below P_{10}) and cesarean section as the mode of delivery. There were higher rates of cesarean section (12 times), perinatal infection (8 times), transfer to the neonatal intensive care unit (11 times), perinatal mortality (4.5 times) and necrotizing enterocolitis (3 times) among babies with hyperechoic medullae than in the control group, where there was a suspected chronic hypoxic state with a normal echoic fetal kidney. Of course, these conditions arise with much lower rates in the normal population.

The redistribution of the fetal circulation results in abnormal renal flow. The redistribution of the blood flow is due to fetal hypoxemia. During this process, the fetal kidneys are among those organs which are sometimes compromised, leading to transient renal insufficiency, usually a benign disease [23]. In theory, fetal hypoxia triggers a discordant vasomotor reaction in the common carotid artery and descending thoracic aorta. In the descending thoracic aorta, a reduction in the mean blood velocity and an increase in the pulsatility index of flow velocity develop, while in the common carotid artery the mean blood velocity rises in parallel with a decrease in the pulsatility index in the flow velocity waveform [5]. The increased resistance index of the descending thoracic aorta could be a component of the centralization of the fetal circulation due to chronic hypoxia. The fetal renal blood flow may similarly be affected as a result of an elevated intravascular resistance, leading to a decline in renal perfusion [10].

In those neonates where there had been renal hyperechogenicity due to fetal hypoxia, this modified echogenicity of the renal medulla is usually preserved during the short postnatal oliguric period [1, 24]. These ultrasound signs disappear quickly after the first postnatal urinary evacuation. In our investigations the hyperechoic features were found to be lost by day 2 in 51% and by the end of the 2nd week in 73% of the cases. In 27%, the intrauterine renal hyperechogenicity demonstrated no ultrasonographic features. This presumed protein blockage disappeared with the start of urinary production after birth, and this was connected with the relatively rapid decrease in hyperechogenicity in the postnatal period.

In the postnatal period it is possible to identify the different etiologies of fetal renal hyperechogenicity (nephrocalcinosis, Bartter syndrome, renal tubular acidosis, etc.) [25]. The etiology is sometimes already clear during the fetal period (e.g., polycystic kidney) [26]. In contrast, renal hyperechogenicity due to fetal hypoxia develops in the last period of pregnancy, in our cases between the 25th and 39th weeks of gestation. Our results show that the fetal circulation can compensate for the hypoxic state for a rather long time. In transient hyperechogenic cases, the cause is transient renal insufficiency. The increased echogenicity may represent a tubular blockage caused by Tamm-Horsfall protein precipitation [3, 23, 27]. There is a body of evidence supporting the idea that the transient renal insufficiency is correlated with Tamm-Horsfall proteinuria in the postnatal period [23].

Renal hyperechogenicity as a complication of fetal hypoxia is benign if transitory. Fetal renal failure of hypoxic origin does not automatically lead to tubular necrosis. The etiology and clinical features of acute necrosis and acute blockage of the tubules are the same. Transitory renal failure and necrosis can, therefore, be differentiated only by the degree and the course of the disease [28, 29]. In our cases the echogenicity of the medullae could be explained by the same mechanism, which started in the final trimester of intrauterine life.

Change in the renal artery flow resistance is seen much sooner using the Doppler data than change in umbilical arterial flow. The study shows that the renal artery flow resistance already deviates significantly from the normal range, while that for the umbilical artery is in the normal field. The renal medullary hyperechogenicity and

the decrease in renal artery flow appear to be good predictive signs of serious intrauterine hypoxia.

The measurement fetal renal hyperechogenicity is a simple examination, and should, therefore, be performed during a routine scan. It is a sensitive sign, and measurement of the fetal renal artery blood flow is essential because the changes in the flow parameters are more characteristic. However, measurements on the fetal renal artery are difficult. For this reason, we suggest initial detection of renal echogenicity. Then, if hyperechogenicity is found, the blood flow can be measured with the Doppler method to detect the redistribution of the fetal circulation, as an early sign of an intrauterine hypoxic state. It is important, therefore, to direct women with such pregnancies to a perinatal intensive care center to detect the possible pathological fetal state.

It is hoped that new conception for the study of fetal hypoxia – such as fetal kidney ultrasonographic investigation – will enhance our understanding of the complex issue of normal and abnormal development of pathological pregnancies.

Our study shows that the combined use of echogenicity of the fetal renal parenchyma and Doppler flow study of the fetal renal artery can detect pathological changes in the renal artery. It may provide a better prediction of outcome in chronically hypoxic pregnancies. Thus, besides the routine scan, renal ultrasonography may be important in the diagnosis of fetal hypoxia at an early state.

Whether there is a quantitative relation between the magnitude of the hypoxia and the amplitude of the renal flow reduction reflected by hyperechogenicity of the fetal renal medulla remains to be elucidated.

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