Published in: Pediatric Nephrology: Journal of the International Pediatric Nephrology Association (2001), vol. 16, iss. 7, pp. 575-580
Status: Postprint (Author's version)

Fetal renal hyperechogenicity in intrauterine growth retardation: importance and outcome

A. Surányi
Department of Pediatrics, University of Szeged, Szeged, Hungary
C. Retz, J. Rigo, J.R Schaaps, J.M. Foidart
Department of Obstetrics and Gynecology, University of Liège, C.H.R. de la Citadelle, Liège, Belgium

Abstract

The object of the study was to investigate the outcome in growth-retarded newborns who were diagnosed with fetal renal hyperechogenicity without anatomical abnormality during any stage of pregnancy. Depending on the fetal renal ultrasonography result, the cases were divided into two study groups. There was an intrauterine growth-retarded group with fetal renal medullary hyperechogenicity and another group without fetal renal medullary hyperechogenicity. The renal parenchyma was observed after birth, within the first 5 days of life, and several times until the 14th postpartum day in positive cases. Hyperechogenic renal medullae were detected in 25 of 90 cases with intrauterine growth retardation during the 8-month study period. This may be an in utero cause of subsequent intrauterine and neonatal complications, such as cesarean section because of fetal distress (36%), perinatal infection (24%), treatment in a neonatal intensive care unit (52%), or increased perinatal mortality (8%). The results demonstrate that fetuses with hyperechoic medullae had 1.5 times the risk of an abnormal outcome compared with fetuses with normal echoic kidneys and intrauterine growth retardation. Detailed ultrasound examinations of renal parenchyma appear to be useful for the prenatal diagnosis of intrauterine hypoxia, allowing the detection of possible pathological fetal conditions in utero.

Keywords Intrauterine growth retardation · Neonatal outcome · Renal hyperechogenicity · Ultrasonography

Introduction

The fetal and neonatal renal medulla is hypoechogenic in its normal state, so medullary hyperechogenicity is a characteristic and striking feature on ultrasound examination [1, 2, 3]. Hyperechogenicity can also be found in other diseases. According to the recent literature [4, 5, 6, 7], hyperechogenic kidneys are due to urinary tract obstruction, polycystic and glomerulocystic kidney disease, obstructive nephrological disease, and nephrocalcinosis. In about 20% of cases with fetal renal hyperechogenicity the mechanism and diagnosis are unclear [2].

A possible connection between intrauterine growth retardation and fetal renal medullary hyperechogenicity has not been examined to date. Hyperechogenicity of the renal cortex and especially of the renal pyramids is a well-known phenomenon; however, its importance in cases with no anatomical alteration (e.g., polycystic kidney) is controversial [2, 3, 4, 5, 7].

During our examinations, fetal medullary hyperechogenicity was investigated as a possible indicator of the fetal hypoxic state [8]. The aim of the present study was to establish a correlation between fetal renal medullary hyperechogenicity without anatomical alterations and postnatal clinical outcome in cases with intrauterine growth retardation.

Materials and methods

Ninety cases of intrauterine growth retardation among pregnant women undergoing routine scans were included in our prospective study. The study period lasted for 8 months. Both normal and pathological cases were investigated during routine scans, so the stages of the pregnancies were the first, second, and third trimesters. The gestational age was calculated according to Naegele's rule and the first trimester ultrasonography examination. Intrauterine growth retardation was established by Hadlock's weight estimation, based on biparietal diameter, abdominal circumference, and femur length. We used international standards defining pathological conditions of pregnancy (e.g., amniotic fluid) [9].

Besides the routine scan we investigated fetal medullary echogenicity and the size of the kidneys. Renal ultrasound studies were carried out using an ATL Ultramark-9 and ATL-3000 machine using 3- to 5-MHz transabdominal transducers during pregnancy and an ATL-3000 machine fitted with 7.5-MHz linear and sectorial transducers during postnatal life.

Hyperechogenic medullae were diagnosed when the fetal renal medullae displayed an echogenicity similar to that of the surrounding bone, but higher than that of the liver or spleen [10].

Intrauterine growth-retarded fetuses were divided into two groups: cases with (group I) and without (group II) fetal medullary hyperechogenicity. The 25 fetuses with renal medullary hyperechogenicity were compared with the remaining intrauterine growth-retarded cases (65 cases) as a control group. The clinical outcome was followed very carefully for 14 days after delivery. The results were analyzed using the odds ratio.

Fig. 1 *Longitudinal view of a normal-sized hyperechogenic fetal kidney (33rd gestational week). The kidney gives pattern B [15]*

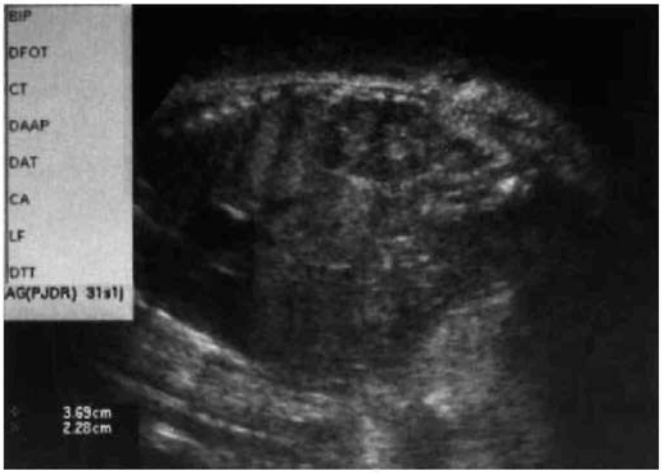
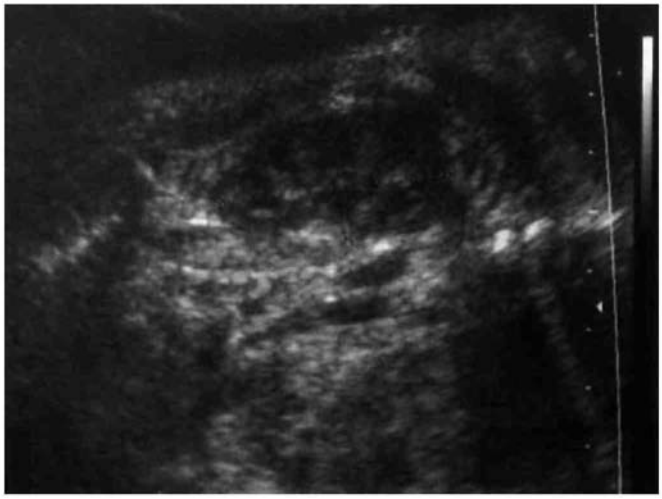


Fig. 2 *Normal fetal kidney (33rd gestational week)*



Published in: Pediatric Nephrology: Journal of the International Pediatric Nephrology Association (2001), vol. 16, iss. 7, pp. 575-580
Status: Postprint (Author's version)

Table 1 *Cases of fetal renal hyperechogenicity with intrauterine growth retardation (IUGR) (NICU neonatal intensive care unit, HELLP-sy hemolysis elevated liver enzymes and low platelet syndrome)*

Case	Pregnancy	Sex	Weight (g)	Gestational age (weeks)	Apgar score (1 min)	Apgar score (5 min)	When renal hyperechogenicity was detected (weeks)	Notes	NICU
1	IUGR	F	2,170	40	9	10	35	Without any problem	+
2	Hypertension	F	3,035	40	8	9	35	Perinatal infection, tachycardia	+
3	Hypertension	F	3,030	39	8	9	37	Without any problem	-
4	Normal	F	3,600	40	9	10	37	Perinatal infection	+
5	Normal	M	3,320	39	9	10	26	Perinatal infection	+
6	Hypertension	M	3,100	38	8	9	34	Cesarean section	-
7	IUGR, toxicoman	M	2,030	35	9	10	34	Cesarean section	+
8	Renal malformation	M	3,260	38	7	8	18	Multicystic kidney	+
9	IUGR	F	2,020	38	8	9	36	Fetal infection?	+
10	IUGR, hypertension	M	950	31	1	6	30	Cesarean section, bradycardia, apnea, metabolic acidosis, cataract, intraventricular hemorrhage, death on 2nd day	+
11	Hypertension	F	3,260	41	5	7	37	Without any problem	-
12	Hypertension	F	1,690	37	9	9	34	Gemini "A", cesarean section	+
13	Hypertension	F	1,870	37	4	8	34	Gemini "B", cesarean section	+
14	IUGR, HELLP-sy	F	1,580	33	7	9	32	Cesarean section	+
15	IUGR, intrauterine parvovirus infection, hydrops fetalis	F	2,260	33	4	8	31	Cesarean section, reanimation, meconium in amniotic fluid	+
16	Hypertension	F	3,455	39	7	9	24	Cesarean section	+
17	Normal	F	3,800	40	8	9	36	Without any problem	+
18	Normal	F	2,860	37	9	9	35	Cesarean section	-
19	Normal	M	2,910	38	9	10	36	Without any problem	-
20	Normal	F	3,720	39	8	8	32	Perinatal infection	+
21	Hypertension	F	2,460	36	8	9	33	Without any problem	-
22	IUGR, hypertension, oligohydramnios	F	2,260	38	7	9	37	Perinatal infection?	+
23	Normal	F	3,600	39	9	9	35	Cesarean section	-
24	Hypertension	F	3,190	41	9	10	32	Without any problem	-
25	IUGR	M	420	31	0	0	27	Stillborn	No transfer
	Mean		2,634.0	37.5	7.2	8.5	32.7		
	SD		741.1	2.2	1.8	1.2	3.4		

Table 2 *Comparison of two groups of prenatally diagnosed IUGR cases: with or without renal medullary hyperechoge-nicity*

	Group I IUGR with renal medullary hyperechogenicity (25 cases)	**Group II IUGR without renal medullary hyperechogenicity (65 cases)**
Gestational age at delivery (weeks)	37.5±2.2	33.6±2.7
Birth weight (g)	2,634±741	1,945±681
Delivery by cesarean section	9 (36%)	13 (20%)
Fetal distress	9 (36%)	7 (10%)
Renal malformation	No	2 (3%)
Pathological amniotic fluid	1 (4%)	9 (14%)
Perinatal infection	6 (24%)	4 (6%)
Meconium-stained amniotic fluid	1 (4%)	No
Brain malformations	No	3 (4.6%)
Facial malformation	No	1 (1.5%)
Spina bifida	No	1 (1.5%)
Gastrointestinal tract malformations	No	2 (3%)
Single umbilical artery	No	1 (1.5%)

Table 3 *Differences in the outcome of two groups of prenatally diagnosed IUGR cases: with or without renal medullary hyperechogenicity*

	IUGR with renal medullary hyperechogenicity (25 cases)	**IUGR without renal medullary hyperechogenicity (65 cases)**	**Rate (hyperechoic to normoechoic)**
Neonatal mortality	2 (8%)	3 (4.6%)	1.7
Neonatal morbidity	17 (68%)	30 (42%)	1.6
NICU stay	16 (64%)	38 (55%)	1.2

Results

In our study we found intrauterine growth retardation in 90 cases among the routinely scanned fetuses. We detected 25 cases with fetal medullary hyperechogenicity (Fig. 1) and 65 cases without fetal medullary hyperechogenicity (group II) (Fig. 2).

Table 1 shows data of the 25 newborns (18 girls and 7 boys) with fetal medullary hyperechogenicity (group I). The mean (±SD) duration of gestation at birth was 37.5±2.2 weeks and the mean (±SD) birth weight was 2,634±741 g. The Apgar scores were 7.2±1.8 (mean±SD) at 1 min and 8.5±1.2 (mean±tSD) at 5 min. We compare the two study groups in Table 2 and present the clinical outcome in Table 3.

Cesarean section was performed in 9 cases in the hyperechogenic group (36%) and in 13 in the control group (20%). Sixteen newborns (64%) with hyperechoic medullae were transferred to the neonatal intensive care unit, while 38 cases (55%) in group II were transferred to the unit. The causes of transfer were immaturity of anatomical structures or physiological and biochemical functions, leading to inability to maintain body temperature and problems with breathing, nutrition, metabolism, immunological function, and detoxification. These pathological conditions are defined as respiratory distress syndrome, asphyxia, bradycardia, congenital malformations, repeated apnea, necrotizing enterocolitis, resuscitation, etc. [11].

We would like to emphasize serious complications in 2 cases (Table 1, case no.10 and no.25) in group I (cases with fetal medullary hyperechogenicity). One infant was stillborn (case no.25) at the 31st week of gestation (birth weight 420 g). One postnatal death was observed on postnatal day 2 after a cesarean section (case no.10). The intervention was indicated by pre-eclampsia, bilateral notch on the flowmetry of the uterine artery, and a pathological cardiotocography test. The newborn was premature, hypotrophic, bradycardic, and suffered from apnea, metabolic acidosis, cataract, and intraventricular hemorrhage (birth weight 950 g at the 31st week of gestation).

In group II serious complications were observed in 3 pregnancies (4.6%). One was a twin pregnancy, in which one of the fetuses died because of a heart malformation, as a result of a rubella infection. The twin sibling exhibited retarded growth only, but the clinical outcome was good. The other stillbirth in the control group was due to left ventricular hypoplasia. The third fetus with a heart malformation was born alive.

One case of multicystic kidney was diagnosed in utero in the hyperechoic group. Renal hyperechogenicity was first detected at the 18th week of gestation. Serial examinations were started, but later a different etiology was identified (Table 1, case no.8).

Fig. 3 *Longitudinal view of a normal-sized hyperechogenic neonatal kidney (1st day of life). The kidney gives pattern D [15]*

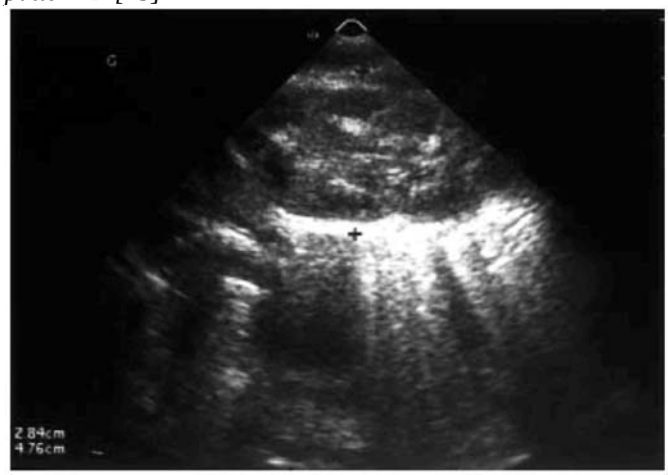


Fig. 4 *Normal neonatal kidney (1st day of life)*

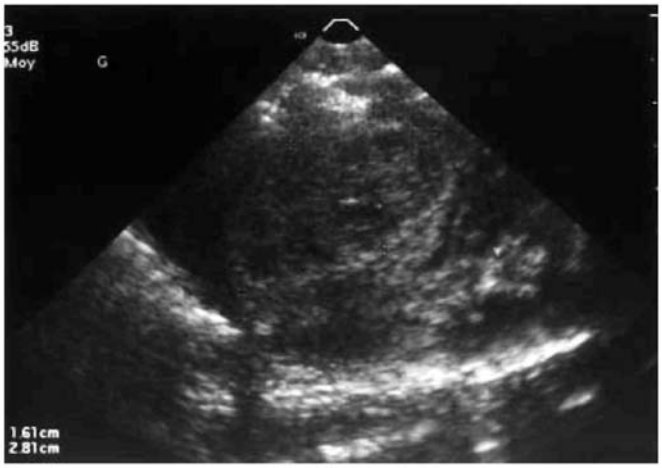


Fig. 5 *Intrauterine non-diagnosed intrauterine growth retardation (IUGR) cases (n=65)*

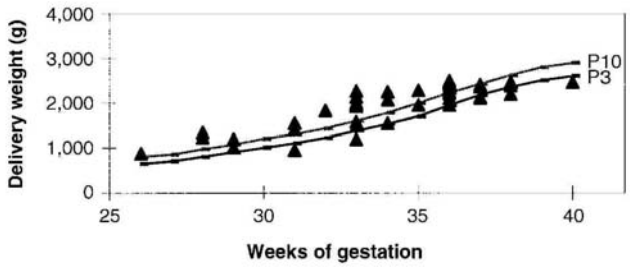
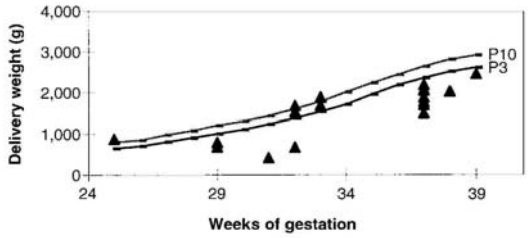


Fig. 6 *Intrauterine diagnosed IUGR cases (n=25)*



Examinations involved measurement of the kidneys. The size of the organs were in the normal range and adequate for gestational age. During fetal life the normal range for the fetal kidney varies with weeks of gestation, therefore we did not average the size of fetal kidneys.

The results were evaluated statistically using the odds ratio. Newborns with hyperechoic medullae (Fig. 3) had 1.5 times the risk by the odds ratio of an abnormal postnatal outcome compared with newborns with normal kidneys (Fig. 4) with intrauterine growth retardation: the odds ratio was 1.5 (1.00; 2.26); confidence interval 95%.

We used the chi-squared test for statistical analysis of birth weight abnormalities, because we expected the data to lie in a standardized range, not a fixed one (Figs. 5 and 6).

The result of chi-squared test was χ^2=3.76 (P<0.05) in intrauterine growth-retarded cases with fetal renal hyperechogenicity. The difference is significant.

Discussion

Fetal and neonatal renal hyperechogenicity can be due to causes different from those in pediatric and adult patients. The possible cause of fetal and neonatal renal hyperechogenicity was first described by Estroff et al. [12], who identified that the hyperechoic renal parenchyma in the fetus was associated with sonographic or functional abnormalities in 74% of surviving cases.

Chiara et al. [13] described the types of neonatal hyperechogenicity, i.e., diffuse, cortical, and medullary. Diffuse renal hyperechogenicity was found in cases of polycystic kidney, renal candidiasis, dysplastic kidney, and renal venous thrombosis. They observed increased cortical echogenicity in neonates with hemolytic uremic syndrome. Medullary hyperechogenicity occurred in cases of renal disease secondary to perinatal asphyxia [1, 13,14].

Shulman [4] summarized the possible causes of neonatal hyperechogenicity in an editorial letter. Calcium deposition, precipitation of Tamm-Horsfall proteins, crystalloids, and precipitation of other proteins or uric acid, papillary necrosis, vascular congestion, sickle cell anemia, medullary fibrosis, lymphocellular infiltration, dehydration, intrarenal reflux, and renal venous thrombosis could all have the sonographic appearance of renal hyperechogenicity [4, 14, 15].

Neonatal medullary hyperechogenicity occurs in asphyxia, therefore we investigated this group of neonates experiencing chronic hypoxic conditions in the intrauterine and postnatal periods. We detected 25 cases of fetal renal medullary hyperechogenicity by examining 90 complicated pregnancies with intrauterine growth retardation.

In intrauterine growth-retarded fetuses there is a relationship between hypoxia and redistribution of cardiac output [9, 11]. This relationship is the part of the brain-sparing effect that has been reported in hypoxic human fetuses to induce intrauterine growth retardation. This mechanism may result in transient renal insufficiency, usually a benign disease [14]. By applying ultrasound examination, modified echogenic medullae can also be observed during the short postnatal oliguric period [1. 10].

The renal medullary hyperechogenicity due to fetal hypoxia develops in the second or third trimester of pregnancy [8]; in our cases between the 24th and 37th weeks of gestation. Our results show that the fetal circulation can compensate for the hypoxic state for rather a long time. This relationship is a feature of the redistribution of the cardiac output that has been reported in hypoxic human fetuses [9]. It has been noted in intrauterine growth-retarded fetuses, presumably as a result of the associated hyperechogenicity. In transient hyperechogenic cases, the cause is transient renal insufficiency [3, 10, 16, 17]. Increased echogenicity may

represent a tubular blockage caused by Tamm-Horsfall protein precipitation [18]. Consistent evidence supports the idea that the transient renal insufficiency is accompanied by Tamm-Horsfall proteinuria in the postnatal period [18].

The complication is benign if it is a transitory condition. Therefore, renal failure does not always yield tubular necrosis. The etiology and the clinical condition of acute necrosis and acute blockage of the tubules are the same. They are differentiated by the degree and the course of the disease [19, 20, 21].

In our cases the fetal medullary echogenicity could be explained by the same mechanism, which started in intrauterine life. The Tamm-Horsfall protein blockage and increased medullary echogenicity disappears with the start of urinary production after birth [2].

Intrauterine pathological states have ultrasonographic signs, such as oligohydramnios, decreased umbilical artery flow, etc. [22, 23]. Our study assumed that the fetal medullary hyperechogenicity was a pathological sign of an in utero hypoxic state. The medulla of the kidney is very sensitive to hypoxia and hypoxic renal failure is accompanied by hyperechogenicity of the kidneys [14]. In addition, we found that intrauterine growth retardation complicated with renal medullary hyperechogenicity suggests a more-serious pathological state.

The statistical results suggest a good relationship between this diagnostic method and the pathological clinical outcome. The odds ratio was used to analyze the association between prenatal pathological renal medullary echogenicity and pathological postnatal clinical outcome. In intrauterine growth retardation, the risk was revealed by an odds ratio of 1.5 times the normal.

We extended the ultrasonographic study over the intrauterine period and observed other consequences of chronic intrauterine hypoxia, such as retarded growth and cesarean section as the mode of delivery. There were higher rates of cesarean section because of fetal distress (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 newborns 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 rates are much lower in the normal population.

These ultrasound signs disappear quickly after the first postnatal urinary production. In our investigations, the hyperechoic features disappeared by day 2 in 51% of cases and by the end of the 2nd week in 73% of 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.

Fetal renal hyperechogenicity appears to be a good predictive sign of intrauterine hypoxia. The clinical outcome supports this idea. The detection of fetal renal medullary hyperechogenicity involves a simple examination, and could therefore be performed during a routine scan. For this reason, we suggest the detection of renal echogenicity as an early sign of an intrauterine hypoxic state, since it is important to direct pregnant women to a perinatal intensive care center in order to follow the possible pathological fetal state.

It is hoped, that new means of studying fetal hypoxia - such as fetal kidney ultrasonographic investigation - will enhance our understanding of the complex issue of normal and abnormal development during pregnancy.

References

1. Howlett DC, Greenwood KL, Jarosz JM, MacDonald LM, Saunders AJS (1997) The incidence of transient renal medullary hyperechogenicity in neonatal ultrasound examination. Br J Radiol 70:140-143

2.. Starinsky R, Vardi U, Batasch D, Goldberg M (1995) Increased medullary echogenicity in neonates. Pediatr Radiol 25:S43-S45

3. Shultz PK, Strife JL, Stife CF, McDanie JD (1991) Hyperechoic renal medullary pyramids in infants and children. Pediatr Radiol 181:163-167

4. Shulman MH (1991) Hyperechoic renal medullary pyramids in infants and children. Radiology 181:9-11

5. Diard F, Nicolau A, Bernard S (1987) Intra-renal reflux: a new cause of medullary hyperechogenicity? Pediatr Radiol 17:154-155

6. Herman TE, Siege MJ (1991) Pyramidal hyperechogenicity in autosomal recessive polycystic kidney disease resembling medullary nephrocalcinosis. Pediatr Radiol 21:270-271

7. Nayir A, Kadioglu A, Sirin A, Emre S, Tongue E, Bilge I (1995) Causes of increased renal medullary echogenicity in Turkish children. Pediatr Nephrol 9:729-733

8. Surányi A, Pál A, Streitman K, Pintér S, Kovács L (1997) Fetal renal hyperechogenicity in pathological pregnancies. J Perinat Med 25:247-279

9. Kurjak A (1992) An atlas of ultrasonography in obstetrics and gynecology (the encyclopedia of visual medicine series). The Patrhenon Publishing Group, New Jersey, USA, pp 64-67

10. Hayden CK, Santa-Cruz FR, Amparo EG, Brouhard B, Swischuk LE, Ahrendt DK (1984) Ultrasonographic evaluation of the renal parenchyma in infancy and childhood. Radiology 152:413-417

11. Behrman RE (1995) Nelson: textbook of pediatrics. Saunders, Philadelphia, pp 451-461

12. Estroff JA, Mandell J, Benacerraf BR (1991) Increased renal parenchymal echogenicity in fetus: importance and clinical outcome. Radiology 181:135-139

13. Chiara A, Chirico G, Comelli L (1990) Increased renal echogenicity in the neonate. Early Hum Dev 22:29-33

14. Talosi G, Streitman K, Suranyi A, Pinter S, Horvath I, Mulugeta Z (1996) The possible role of uric acid in renal hy-perechogenicity in neonatal hypoxic acute shock. J Perinat Med 24:693-697

15. Patriquin H, Robitaille P (1986) Renal calcium deposition in children: sonographic demonstration of the Anderson-Carr progression. AJR 146:1253-1256

16. Avni EF, Spehl-Robberecht M, Lebrun D, Gomes H, Garel L (1983) Transient acute tubular disease in the newborn: characteristic ultrasound pattern. Ann Radiol (Paris) 26:175-182

17. Avni EF, Van Sinoy ML, Hall M, Stallenberg B, Matos C (1989) Hypothesis: reduced renal mass with glomerular hyper-filtration a cause of renal hyperechogenicity in children. Pediatr Radiol 19:108-110

18. Reinhart HH, Spencer JR, Zaki NZ, Sobel ID (1992) Quantitation of urinary Tamm-Horsfall protein in children with urinary tract infection. Eur Urol 22:194-199

19. Brenner MH, Meyer TW, Hostetter TH (1982) Dietary protein intake and the progressive nature of kidney disease. N Engl J Med 307:652-659

20. Patel R, McKenzie JK, McQueen EG (1964) Tamm-Horsfall urinary mucoprotein and tubular obstruction by casts in acute renal failure. Lancet I:457-4161

21. Kensky AM, Reddish JM, Teele RL (1983) Causes of increased renal echogenicity in paediatric patients. Pediatrics 72:840-846

22. Creasy RK, Swiet M, Kahanpaa KV, Yoong WP, Rudolph AM (1973) Pathophysiological changes in the fetal lamb with growth retardation. Foetal and neonatal physiology. Cambridge University Press, Cambridge, p 641

23. Vyas S, Nicolaides KH, Campbell S (1989) Renal artery flow-velocity waveforms in normal and hypoxemic fetuses. Am J Obstet Gynecol 161:168-172