Coll. Antropol. **28** (2004) 2: 817–823
UDC 612.466.2-008.87:616.61-053.31
Original scientific paper

Clinical Importance of Significant Asimptomatic Bacteriuria in Newborns and Infants During Early Postnatal Period

Vesna Milas[1], Josip Milas[2], Silvija Pušeljić[1], Jasna Gardašanić[1], Dubravka Vuković[2] and Jasminka Milas[1]

[1] University Hospital Osijek, Osijek, Croatia
[2] Public Health Institute Osijek-Baranja County, Osijek, Croatia

A B S T R A C T

The aim of the study was to detect newborns at risk for developing renal impairment, and to point out the importance of significant asimptomatic bacteriuria in perinatal period and early infancy. Severe urinary tract anomalies are very often accompanied only by asimptomatic bacteriuria in perinatal period. Three urinalysis ware done after delivery. 212 newborns with significant asimptomatic bacteriuria underwent ultrasound examination, and were followed up to three months. Those with normal findings and with passing bacteriuria in the first 2 months were excluded. Group of 52 newborns underwent radioisotope examination. Frequency of urinary tract anomalies in newborns was 34.6%. Increased risk for renal impairment had children with urinary tract anomalies in close family, urinary tract infection or bacteriuria, EPH gestosis and prepartal symptoms of febrile infection in mother, children with IUGR, strangulated umbilical cord, prolonged jaundice and attacks of peripheral cyanosis in perinatal period.

Key words: *asimptomatic bacteriuria, newborns, urinary tract anomalies, perinatal period, infants*

Introduction

Children with severe congenital urinary tract anomalies (UTA) are believed to be at risk for ongoing renal damage with subsequent impairment of renal function leading to considerable invalidity. Chronic renal failure in children is caused by unrecognised or untreated vesicoureteral reflux (VUR) in 7% of cases, and by un-

Received for publication October 9, 2003

treated or unrecognised obstructive uropathy in 16% of cases[1,2]. Children with urinary tract infections (UTI) are at risk to develop renal damage. Early onset of UTI implicates more severe urinary tract anomaly. Therefore, it is important to exclude urinary tract abnormalities in children with persistent asimptomatic bacteriuria[3].

The aim of our study was to elucidate importance of significant asimptomatic bacteriuria in newborn and infants during early neonatal period and to define one of the risk groups for renal damage in the early childhood. Based on family history, course of pregnancy and delivery, and neonatal clinical features after delivery, we selected group of infants to screen for severe UTA (that do not necessary present by UTI).

Patients and Methods

1200 newborns were examined at neonatal department and neonatology intensive care unit (NICU), Clinical Hospital Osijek. Urinalysis was taken from all newborns with collecting bags. If the first urine culture showed significant bacteriuria (10^5 or more Gram negative, or 10^4 or more Gram positive bacteria in 1ml of urine), additional two were taken. In children with 3 positive findings, urinalysis, red blood cell (RBC), white blood cell (WBC) count, platelets, C-reactive protein and total bilirubin (if child had jaundice) were examined. By analysing three subsequent urine cultures we obtained result specificity of 95%[4]. Newborns with asimptomatic bacteriuria but no laboratory tests implying UTI (normal urinanalysis, WBC and C-reactive protein) were followed-up to 3 months. Their mothers were questioned about family history, complications during pregnancy, and their urine cultures were examined. Children with temporary bacteriuria that vanished in the first 2 months were excluded.

The patient group consisted of 52 newborns. Urine culture, urinanalysis and abdominal ultrasound were examined once a month. At the end of the follow-up period, using radioisotope methods performed additional urinary tract evaluation: direct radionuclide cystigraphy (DRC), ^{99m}technetium-dimerkapto-succinic acid (DMSA) perfusion, and ^{99m}technetium-MAG3 dynamic scanning. Intravenous urography was done only exceptionally in children requiring surgery. The control group included randomly selected 77 newborn infants with negative urine cultures. Their mothers were also included and analysed.

Data on risk factors in newborns were taken from medical records of mother and child, and based upon mother's questioning. Using standard microbiologic methods, while standard biochemical methods cultured urine specimens performed urinanalysis and peripheral blood laboratory tests. Statistical analysis was performed using χ^2 test, and statistical significance was set at $p<0.05$.

Results

Family risk factors, risk factors during pregnancy and delivery

Asimptomatic bacteriuria was detected in 212 infants (10.7% of examined newborns) after the delivery. It was persistent during 3 months in 52 infants (25% of children with asimptomatic bacteriuria), or in 4.3% of examined newborns.

Bacteriuria (after delivery) during pregnancy was found in 29% of mothers of infants with bacteriuria. In control group only 10% of mothers had this complication, $\chi^2 = 6.01$, $p<0.05$.

Pyelonephritis during pregnancy was five times more frequent in mothers of infants with bacteriuria compared to mothers in control group, $\chi^2 = 10.46$, $p<0.01$.

EPH gestosis was more then 8 times more often during pregnancy in mothers of infants with bacteriuria, $\chi^2 = 4.50$, $p<0.05$ (Table 1).

Every fourth child with bacteriuria had intrauterine growth retardation (IUGR), compared to every tenth child in control group, $\chi^2 = 5.80$, $p<0.05$.

Umbilical cord encirclement was nine times more frequent complication during delivery in children with asimptomatic bacteriuria compared to controls, $\chi^2 = 8.06$, $p<0.01$.

Premature rupture of membranes (premature velamentous rupture) was more often in control group, and it was not related to neonatal bacteriuria (Table 2).

Urinary tract anomalies in close relatives of children with bacteriuria (21,2% in examined children compared with 1.3% in controls) were 17 times more often compared to controls, $\chi^2 = 9.84$, $p<0.01$.

Clinical signs, ultrasound findings and congenital anomaly of the urinary tract in children with asimptomatic bacteriuria

Infants with asimptomatic bacteriuria had jaundice twice as much as controls, $\chi^2 = 7.31$, $p<0.01$. Periodic attacks of peripheral cyanosis were present in every fifth infant with bacteriuria, while it was not found in control group, $\chi^2 = 7.22$, $p<0.01$ (Table 3).

The most frequent ultrasound finding among newborns was mild dilatation of the pyelon with or without thickening of the wall of the urinary bladder. Follows dilatation of the pyelon more than 10

TABLE 1
MATERNAL COMPLICATIONS DURING PREGNANCY

Maternal complications	Mothers of newborns with bacteriuria		Mothers of newborns without bacteriuria	
	Number	%	Number	%
Bacteriuria	15	28.8	8	10.4
UTI	4	26.9	4	5.2
EPH gestosis	6	11.5	1	1.3
Without complication	17	32.7	64	83.1
Total	52		77	

TABLE 2
OBSTETRIC RELATED COMPLICATIONS IN NEWBORNS WITH ASIMPTOMATIC BACTERIURIA AND CONTROLS

Obstetric complications	Newborns with bacteriuria		Healthy newborns	
	Number	%	Number	%
Strangulated umbilical cord	17	32.7	3	3.9
IUGR	13	25.0	6	7.8
Premature velamentous rupture	4	7.7	7	9.1
Without complication	18	34.6	61	79.2
Total	52		77	

TABLE 3
CLINICAL POSTNATAL SYMPTOMS OF NEWBORNS WITH ASIMPTOMATIC BACTERIURIA AND CONTROLS

Symptoms in newborns	Newborns with bacteriuria		Healthy newborns	
	Number	%	Number	%
Jaundice	18	34.6	10	13.0
Peripheral cyanosis	10	19.2	–	–
Without symptoms	24	46.2	67	87
Total	52		77	

TABLE 4
RESULTS OF ULTRASOUND EXAMINATION IN NEWBORNS WITH ASIMPTOMATIC BACTERIURIA

	Number	%
Width of the pyelon form 7 to 10 mm	18	34.6
Hydronephrosis (pyelectasia more than 10 mm)	9	17.3
Thickened wall of the urinary bladder (4 and more mm)	6	11.5
Hydronephrosis with megaurether	3	5.8
Horse-shoe kidney	1	1.9
Hyperechogenicity of the parenchyma without clear differentiation between cortex and medulla of the kidney	1	1.9
Hypotrophic kidneys	1	1.9
Without any changes	13	25.0
Total:	52	100.0

mm. A quarter of newborns were without ultrasound findings (Table 4).

Urinary tract abnormalities were detected in 18 children with asimptomatic bacteriuria (33.4% of examined newborns), of whom 12 were boys (66.7%) and 6 girls (33.3%) (Table 5).

Discussion

According to paediatric literature, neonatal asimptomatic bacteriuria has no clinical significance, as it disappears spontaneously during the first month of life[5]. In majority of children without urinary tract abnormality, bacteriuria usually vanishes. In perinatal period, 212 of newborns had asimptomatic bacteriuria, and it persisted in only 25% of children. More than 1/3 of those children had urinary tract anomaly. Therefore, it means that 8.4% of newborns with significant bacteriuria during perinatal period have UTA that, if unrecognised, can severely damage kidneys.

Pregnant women are more susceptible to UTI due to pressure of enlarged uterus on urinary tract. Close contact with mother's excretions enables transfer of bacteria into newborn during delivery[6]. Some countries routinely perform screening of pregnant women for bacteriuria as UTI can endanger child during pregnancy[6]. In view of the fact that in our country this is not yet practice, it is very important to recognize and select children with UTA.

TABLE 5
URINARY TRACT ANOMALIES IN NEWBORNS WITH ASIMPTOMATIC BACTERIURIA

Urinary tract anomalies	Number	%
Ureteropelvic junction obstruction	7	13.5
Vesicoureteral reflux (VUR)	6	11.5
Megaurether	3	5.8
Horse-shoe kidney	1	1.9
Hypotrophic non-functional kidney	1	1.9
Without anomalies	34	65.4
Total	52	

IUGR was more frequent in children with asimptomatic bacteriuria compared to controls. IUGR by itself is important risk factor for renal impairment[7]; however, underlying UTA can cause it. 26.4% newborns with obstructive UTA have IUGR[8]. Inadequate transplacental perfusion during last trimester leads to enhance intrauterine growth retardation. Finally, hypo perfusion can cause cell hypoxia, hypoglycaemia, hypoaminoacidemia, and decreased production of growth hormones (thyroxin, insulin). Immune system is also affected leading to impaired immune competence of newborn child. EPH gestosis is one of the most important factors for IUGR.

EPH gestosis was 6 times more often in mothers of children with asimptomatic bacteriuria compared to controls. It appears that unidentified renal impairment could become evident during pregnancy. The gestosis weakens immune competence and resistance to infection in pregnant women as well as in child[9,10]. Usually, there are decreased immunoglobuline levels, as well as diminished suppressor T lymphocyte number and function[11,12]. Furthermore, changes in beta2 micro globulin concentration in pregnant women with EPH gestosis leads to further renal impairment[13]. UTA in close relatives was more often in newborns with asimptomatic bacteriuria and similar results were reported in literature[14].

Umbilical cord encirclement was more frequent in newborns with asimptomatic bacteriuria compared to control group. Foetal hypoxia due to EPH gestosis or maternal UTI could lead to excessive foetal movements, and subsequently to formation of umbilical cord node or umbilical cord strangulation around child's neck.

Clinical symptoms were apparent in 53.8% of children in perinatal period. Jaundice was the most common[15]. It may be consequence of IUGR (hemoconcentration and subsequent haemolysis), EPH gestosis or maternal infection. In this study, periodical attacks of peripheral cyanosis appeared only in children with UTI, although they can be also present in healthy newborns. Sometimes, cyanosis ensued only in the first few minutes after delivery, reflecting poor adaptation to extra uterine conditions. This symptom is usually consequence of hypoxia and hemoconcentration. It can be accompanied by dyspnoea, but not necessarily[7]. Newborns with asimptomatic bacteriuria have been born very often with intrauterine growth retardation[16,17]. Most frequent ultrasound findings among examined children were mild dilatation of the pyelon. Findings were comparable with the literature[18]. Obstruction of pyeloureteric

junction was the most commonly UTA detected by ultrasound[19,20]. Three quarters of newborns have had some pathologic ultrasound findings. Congenital anomaly of the urinary tract was present in less than a half of them. It means that examination by means of ultrasound is very sensitive, but not enough specific in putting suspicious on urinary tract anomalies. Incidence of urinary tract anomalies among children with persistent asimptomatic bacteriuria was 34,6%. Goldman et al. point out the incidence of 50% among male newborns with urinary tract infection[19]. Diagnosis was confirmed by static and dynamic ^{99m}Tc MAG3 scintigraphy. VUR was diagnosed in 6 newborns by DCR. Megaureter was found in 3 newborns, and in addition to radioisotope methods, IVU was also performed in those children. One child had ren arcuatus diagnosed by ultrasound. Hypoplastic, non-functional kidney was found in one child by using ultrasound and radioisotope procedures.

Conclusion

During perinatal period, some infants with bacteriuria are at risk to develop subsequently renal damage. Those are the newborns with mothers suffering UTI or bacteriuria during pregnancy, EPH gestosis, and children with UTA in close relatives. Other risk factors are low birth weight, umbilical cord strangulation, postnatal jaundice (not caused by blood groups or Rh incompatibility), and peripheral cyanosis (normal lung, heart and brain).

Therefore, urine cultures and ultrasound have to be performed in the risk group of newborns. Children with persistent bacteriuria or abnormal ultrasound should be additionally examined by radioisotope procedures.

REFERENCES

1. ANDRICH, M. P., M. MAJD, Pediatrics, 90 (1992) 436. — 2. ALEXANDER, S. R., G. S. ARBUS, K. M. H. BUTT, S. CONELY, R. N. FINE, I. GREIFER, A. B. GRUSKIN, W. E. HARMON, P. T. MCENERY, T. E. NEVIS, N. NOGUEIRA, O. SALVATIERRA, Pediatr. Nephrol., 4 (1990) 542. — 3. VLATKOVIĆ, G.: Bolesti mokraćnih organa u djece. (Školska knjiga, Zagreb, 1985). — 4. ALON, U. S., S. GANAPATHY, Clin. Pediatr.(Phila), 38 (1999) 21. — 5. KORAČ, D.: Pedijatrija. (Medicinska knjiga, Beograd – Zagreb, 1982). — 6. MACLEAN, A. B., Int. J. Antimicrob. Agents, 17 (2001) 273. — 7. HELLSTROM, M., H. HASSEL, B. JACOBSSON, U. JODAL, A. NIKLASSON, M. WENNERSTROM, A. HELLSTROM, Acta Paediatr., 90 (2001) 628. — 8. KHOURY, M. J., J. D. ERICKSON, J. F. CARDERO, B. J. MCCARTHY, Pediatrics, 82 (1988) 83. — 9. HOOTON, T. M.,. Int. J. Antimicrob. Agents, 17 (2001) 259. — 10 TIAGUNOVA, A. V., Z. V. VASILEVA, O. P. SLASTEN, I. N. BARANOVA, Klin. Lab. Diagn., 4 (1998) 38. — 11. ROSIC, B., V. SULOVIC, N. JUZNIC, B. LAZAREVIC, M. VIDANOVIC, D. MILACIC, Glas, 41 (1991) 71. — 12. LIN, Q. D., Chin. J. Obstet. Gynecol., 25 (1990) 275. — 13. TETI, G., C. PASQUINI, M. T. PANZA, B. FAVILLA, M. S. MURRU, A. STEFANELLI, M. TUONI, Ann. Ostet., Ginecol., Med. Perinat., 112 (1991) 152. — 14. AGGARWAL, V. K., K. J. VERRIER, Arch. Dis. Child., 64 (1989) 1538. — 15. GARCIA, F. J., A. L. NAGER, Pediatrics, 109 (2002) 846. — 16. AGGARWAL, V. K., K. J. VERRIER, Arch. Dis. Child., 64 (1989) 1538. — 17. CAKSEN, H., S. ARSLAN, M. ABUHANDAN, A. CELIK, H. BOZKURT, D. ODABAS, Acta Paediatr. Taiwan., 42 (2001) 338. — 18. DELLAGRAMMATICAS, H. D., N. IACOVIDOU, M. PAPADIMITRIOU, A. DASKALAKI, M. PAPADOYANNIS, Biol. Neonat., 79 (2001) 1. — 19. GOLDMAN, M., E. LAHAT, S. STRAUSS, G. REISLER, A. LIVNE, L. GORDIN, M. ALADJEM, Pediatrics, 105 (2000) 1232. — 20. ALLADI, A., S. AGRAWALA, A. K. GUPTA, C. S. BAL, D. K. MITRA, V. BHATNAGAR, Pediatr. Surg. Intl., 16 (2000) 569.

V. Milas

Neonatal Intensive Care Unit, University Hospital Osijek, Huttlerova 4, 31000 Osijek, Croatia
e-mail: josip.milas@os.htnet.hr

KLINIČKA VAŽNOST ZNAČAJNE ASIMPTOMATSKE BAKTERIURIJE KOD NOVOROĐENČADI I DOJENČADI U RANOM POSTNATALNOM PERIODU

S A Ž E T A K

Cilj je bio odrediti značenje trajne asimptomatske bakteriurije u novorođenačkoj i ranoj dojenačkoj dobi. Ranim otkrivanjem najtežih prirođenih mana mokraćnog sustava spriječilo bi se kasnije bubrežno oštećenje. Urinokultura je po porodu uzimana metodom sakupljača. 212 novorođenčadi sa značajnom bakteriurijom pregledano je ultrazvukom i praćeno tijekom tri mjeseca. Iz ispitivanja su isključena djeca u koje se bakteriurija izgubila tijekom prva 2 mjeseca, a koja su imala uredan nalaz UZV-a. Skupini od 52 dojenčadi učinjene su DRC, statička Tc99m DMSA i dinamička Tc99mMAG3 scintigrafija. Učestalost mana mokraćnog sustava je bila 34,6%. Djeca u riziku za oštećenje bubrega su ona s manama mokraćnog sustava u bližoj obitelji, čije su majke u trudnoći imale infekciju mokraćnog sustava ili bakteriuriju, EPH gestozu, simptome febrilne infekcije pred porod, odnosno djeca s intrauterinim zaostatkom u rastu, pupkovinom oko vrata, s produljenom žuticom i napadima periferne cijanoze u perinatalnoj dobi. Dojenčad s trajnom asimptomatskom bakteriurijom tijekom prvih mjeseci života, bez obzira na nepostojanje simptoma infekcije mokraćnog sustava, su u riziku od nastajanja bubrežnog oštećenja i može ih se prepoznati temeljem rizičnih činilaca.