Examination of renal function in infants with a history of intrauterine growth restriction up to 36 weeks gestation compared to infants with normal growth

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Sri Lanka Journal of Child Health, 2017; **46**(2): 152-154

Abstract

Background: Intrauterine growth restriction (IUGR) will increase the risk of impairment of renal function in the future.

Objective: To assess renal function in infants with a history of IUGR up to 36 weeks gestation compared to infants with normal growth.

Method: Laboratory examination of urine microalbumin, urine creatinine and a cystatin C blood test were done on day 7 after birth in infants with a history of IUGR and in infants with normal growth up to 36 weeks gestation and compared.

Results: On day 7 after birth, mean urine microalbumin levels of IUGR and normal weight infants were 15.83 ± 31.32 mg/ml and 1.9 ± 0.97 mg/ml respectively ($p<0.01$). Mean urine creatinine levels of IUGR and normal weight infants were 17.19 ± 9.84mg/L and 8.22 ± 2.85 mg/L respectively ($p<0.01$). Mean albumin/creatinine ratios of IUGR and normal weight infants were 198 ± 627.63 µg/mg and 24.75 ± 14.07 µg /ml ($p<0.01$). Mean cystatin C levels of IUGR and normal weight infants were 1.47 ± 0.28mg/ml and 1.45 ± 0.19mg/ml respectively ($p>0.05$).

Conclusions: Mean urine albumin level, mean urine creatinine level and mean urine albumin/creatinine ratio of IUGR infants were significantly higher than those of normal weight infants. There was no significant difference between the mean cystatin C levels of IUGR infants and normal weight infants.

DOI: http://dx.doi.org/10.4038/sljch.v46i2.8272

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(Received on 31 July 2016: Accepted after revision on 23 September 2016)

The authors declare that there are no conflicts of interest

Personal funding was used for the project.

(Keywords: Renal function of infants with IUGR, microalbumin, creatinine, cystatin C)

Introduction

Barker Hypothesis 1995 emphasizes the close relationship of intrauterine growth restriction (IUGR) to hypertension, coronary heart disease, diabetes mellitus and peripheral vascular disease in adulthood[1]. The World Health Organization (WHO) defines small for gestational age (SGA) as a neonatal weight of less than 2500g at term[2]. The terms IUGR and SGA are commonly used interchangeably. A more widely used definition of IUGR in the developed countries is an estimated weight less than the 10th percentile for gestational age or a weight that is less than two standard deviations below the anticipated value for the gestational age[3]. IUGR is reported to affect 10-15% of pregnant women[4].

Objectives

To assess renal function in infants with a history of IUGR up to 36 weeks gestation compared to infants with normal growth.

Method

The study was conducted at the H. Adam Malik Hospital Medan, Dr. Pirngadi Hospital Medan and practices of obstetricians and gynecologists. Ethical clearance was obtained from the Health Research Ethical Committee, Medical Faculty of Universitas Sumatera Utara/ H. Adam Malik General Hospital. Informed consent for the study was obtained from the pregnant mothers. The cases were pregnant mothers whose fetuses had IUGR at 28-36 weeks gestation, while controls were pregnant mothers whose fetuses had normal weights and who were matched for gestational ages as the cases. The cases were followed up and ultrasound examination was conducted every 2 weeks until 36 weeks gestation or until there was an improvement in the weight to normal values, in which instance these cases were excluded. Weighing infants was done after birth along with measurement of body length and recording Apgar scores. On day 7, examination of urine albumin, creatinine and cystatin C blood test were done.

In this study, the number of cases and controls were 20 each. The sample size was chosen for

convenience. The first 20 eligible consenting mothers who attended the antenatal clinic from the time the study was commenced were chosen as the cases. The data obtained was analysed descriptively (number, size and description) along with use of student t test analysis and if it did not have normal distribution Mann-Whitney test was then conducted with SPSS version 19 with the significance level at 5%.

Results

Table 1 shows the characteristics of the research subjects.

Table 1: ***Characteristics of research subjects***

Characteristic	IUGR *(n=20)*		Normal *(n=20)*		p value
	mean	SD	mean	SD	
Birth weight (g)	2,952.5	330.79	3,306.75	194.18	0.001 (p<0.01)
Body length (cm)	49	0.81	50	0.88	0.012 (p<0.05)
	Number	%	Number	%	
Apgar at 1 minute					
5 or less	03	15	01	05	0.605 (p>0.05)
More than 5	17	85	19	95	
Apgar at 5 minute					
5 or less	0	0	0	0%	
More than 5	20	100	20	100%	
Gender					
Male	10	50	10	50	1.00 (p>0.05)
female	10	50	10	50	

Though there were 3 cases who had an Apgar score at one minute of 5 or less among the 20 infants with IUGR compared with 1 among the 20 normal weight infants, this was not statistically significant. There were no cases where the Apgar score at 5 minutes was 5 or less in either the IUGR or normal weight infants. In both IUGR and normal weight infants, the male: female distribution was 1:1. On day 7 after birth, levels of urine microalbumin of both infant groups were measured. Table 2 shows the different mean albumin levels between normal and IUGR infants. The differences were statistically significant. Table 3 shows the different mean creatinine levels between normal and IUGR infants. The differences were statistically significant. On examination of the albumin/creatinine ratio, by using instantaneous urine sample, it was found that the mean albumin/creatinine ratio for IUGR infants differed significantly from that of normal infants. This is shown in Table 4. Table 5 shows the mean levels of Cystatin C between IUGR and normal weight infants. This was not statistically significant.

Table 2: ***Different mean urine microalbumin levels between normal weight and IUGR Infants***

	Group	Number	Mean	Standard deviation	* p value
Microalbumin (mg/ml)	IUGR	20	15.83	31.32	0.001 (p <0.01)
	Normal	20	1.9	0.97	

*Mann-Whitney

Table 3: ***Different mean urine creatinine levels between normal weight and IUGR Infants***

	Group	Number	Mean	Standard deviation)	* p value
Creatinine (mg/L)	IUGR	20	17.1	9.8	0.001 (p <0.01)
	Normal	20	8.2	2.9	

*Mann-Whitney

Table 4: ***Different mean urine albumin/creatinine ratio between normal weight and IUGR Infants***

	Group	Number	Mean	Standard deviation	* p value
Albumin/ creatinine ratio (µg/mg)	IUGR	20	198	627.63	0.001 (p <0.01)
	Normal	20	24.75	14.07	

*Mann-Whitney

Table 5: ***Mean level of Cystatin C between IUGR and normal weight infants***

	Group	Number	Mean	Standard deviation	* p value
Cystatin C (mg/ml)	IUGR	20	1.47	0.27	0.800
	Normal	20	1.45	0.20	(p>0.05)

* t-test

Discussion

In a study in Sudan in the third trimester of normal pregnancy, the fetal kidney volumes of premature, mature and full-term infants were 5.6 cu mm, 9.8 cu mm and 10.5 cu mm respectively[5]. The occurrence of proteinuria in IUGR infants is caused by reduced number of nephrons, and will increase the risk of hypertension and kidney disease. With the reduction in the number of nephrons, to maintain satisfactory function, rest of the nephrons undergo hyperfiltration and hypertrophy. Hyperfiltration in the nephrons leads to an increase in intra glomerular capillary hydrostatic pressure, which in turn causes damage to the capillary walls. The damage causes a decrease in proteinuria and glomerular filtration[6].

Glomerular filtration rate (GFR) is an important parameter in assessing kidney function. There are several tests for measuring GFR but the substance frequently used to assess renal impairment is creatinine. The increase in creatinine level will occur when there is a decline of GFR more than 50%. Cystatin C measurement is more promising, especially in mild impairment of renal function compared to the use of creatinine[7]. Cystatin C does not pass the placental barrier and there is no correlation between maternal and neonatal levels, unlike creatinine, so levels of cystatin C in the neonate only depicts GFR of neonates, themselves[7].

Since our study is a comparison of renal function of IUGR infants and normal weight infants it is to be expected that the mean weights and body lengths of the IUGR infants will be significantly less when compared to the normal weight group. There were no significant differences in the Apgar scores at 1 and 5 minutes and no significant gender differences between the IUGR group and the normal weight group. Mean urine microalbumin levels in the 20 IUGR infants were significantly higher than the levels in the 20 normal weight infants ($p<0.01$). Mean urine creatinine levels in the IUGR infants were significantly higher than the levels in the normal weight infants ($p<0.01$). Mean urine albumin/creatinine ratios in the IUGR infants were similarly higher than the levels in the normal weight infants ($p<0.01$). However the mean blood Cystatin C levels were not significantly different in the IUGR group and the normal weight group.

Conclusions

Mean urine albumin level, mean urine creatinine level and mean albumin/creatinine ratio of IUGR infants were significantly higher than those of normal weight infants. There was no significant difference between the mean cystatin C levels of IUGR infants and normal weight infants.

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