Renal Function and Renal Volume of Children Born with Very Low Birth Weight

Sharath Babu M. V.[1], Parvathi R.[2], Mini M. V.[3]

[1]Assistant Professor, Department of Paediatrics, DM Wayanad Institute of Medical Sciences, Wayanad, Kerala, India. [2]Additional Professor, Department of Paediatrics, Government Medical College, Thrissur, Kerala University of Health Sciences, Kerala, India. [3]Assistant Professor, Department of Radiodiagnosis, Government Medical College, Thrissur, Kerala University of Health Sciences, Kerala, India.

ABSTRACT

BACKGROUND

Low birth weight is a risk factor for hypertension and renal disease later in life. Impaired nephrogenesis in low birth weight babies is a postulated cause. Monitoring these babies for kidney size and glomerular function as they grow is important.

METHODS

A cross sectional study was conducted on school aged children born with birth weight below 1500 gms on follow up in the high risk newborn clinic of a government hospital in South India. Medical records were reviewed to assess the perinatal risk factors that could contribute to nephron loss. Anthropometric measurements and blood pressure were recorded. Renal volume was measured by ultra sound examination and renal function by glomerular filtration rate.

RESULTS

The study population consisted of 50 children between 6 to 8 years born with very low birth weight. Seven children had stage 1 hypertension. Glomerular filtration rate (GFR) was abnormal in forty-two (84%) children. Renal volume was found to be reduced in 33 (66%) children (p=0.013). A significant association was found between maternal pregnancy induced hypertension (PIH) (p=0.09), antenatally detected intrauterine growth restriction (IUGR) (p=0.018) and reduced renal volume. Weight of 40 (80%) and height of 45 (90%) of these children were found to be in the normal range as per WHO growth charts.

CONCLUSIONS

Renal volume was found to be reduced in more than two thirds of children born with very low birth weight, especially those born to mothers with PIH and those with IUGR. Continued follow up is necessary to detect deterioration of renal function in these babies.

KEYWORDS

Very Low Birth Weight, IUGR, Renal Volume, Glomerular Filtration Rate

Corresponding Author:
Dr. Parvathi R,
G4, Navani Apartment,
Z anana Mission Road,
Chembukkavu- 680020,
Thrissur, Kerala.
E-mail: drparvathimohan@gmail.com

DOI: 10.18410/jebmh/2020/324

How to Cite This Article:
Sharath Babu MV, Parvathi R, Mini MV. Renal function and renal volume of children born with very low birth weight J Evid Based Med Healthc 2020; 7 (31), 1541-1544. DOI: 10.18410/jebmh/2020/324

Submission 28-05-2020,
Peer Review 10-06-2020,
Acceptance 15-07-2020,
Published 01-08-2020.

BACKGROUND

Low birth weight is defined by the World Health Organization as weight at birth of less than 2,500 grams, and less than 1,500 gms is called Very Low Birth Weight.[1] Low birth weight (LBW) is the result of preterm birth and intrauterine growth restriction (IUGR). In India, nearly 20% of newborns have LBW and 3-14% have weight less than 2 Kg.[2] The specialized care in the Neonatal ICUs complemented by the increase in the number of well-trained staff and better equipment have helped to improve the survival chances of babies born prematurely and with very low birth weight. These survivors have an increased risk of hypertension cardiovascular events & altered renal function in adult life.[3] The renal structure, especially nephron number is a major determinant of blood pressure and renal function.[4] In humans, formation of the nephron is complete at 36-40 weeks and no new nephrons are formed after birth. Nearly 60% of nephrons develop in the third trimester. So, nephron numbers are reduced in preterms. Intrauterine growth restriction especially in the third trimester can also lead to reduction in number of nephrons. These babies born with an incomplete complement of immature nephrons are also exposed to a variety stressors like hypoxia, hypotension, sepsis, nephrotoxic drugs and acute kidney injury that can affect kidney development or cause nephron loss.[5] Oligonephronemia can lead to glomerular hyperfiltration compensatory hypertrophy, increase in glomerular size, hypertension glomerular damage and sclerosis leading on to chronic kidney disease with impaired renal function.[6]

The objectives of this study were to assess the renal function and renal volume and growth of school children born with very low birth weight and to look for any association between the renal volume and maternal and neonatal risk factors.

METHODS

This cross-sectional study was conducted in the High-Risk Clinic of the Department of Paediatrics, Govt. Medical College, Thrissur during a period of 18 months from January 2015 to June 2016. All consecutive children coming for follow up and born with birth weight less than 1500 gms, aged between 6-8 years during the study period were enrolled Ethical clearance from the Institutional ethical review board and informed consent from the parents of the children were obtained. Children with renal anomalies and those with acquired renal diseases like pyelonephritis, nephrotic syndrome, acute glomerulonephritis, Henoch Shonlein purpura and septicaemia beyond the neonatal period were excluded. Maternal and neonatal data were obtained from records maintained in the High Risk Clinic. Birth weight was measured at the time of delivery by an electronic weighing machine. The babies were classified as small for gestational age (SGA) and appropriate for gestational age (AGA) by using Fenton's chart.[7]

Gestational age was assessed from first trimester ultrasound and by the New Ballard scoring system.[8] The children were subject to a detailed physical examination and blood pressure was recorded. Blood pressure (BP) was measured with a standard sphygmomanometer. Subjects were seated and after 5 minutes of rest, the BP was measured with a cuff two thirds the size of the upper arm length. Average of three readings was taken. Assessment of growth was done using precise measuring equipment's (seca weighing scale and stadiometer). Weight was measured by a seca electronic scale with an accuracy of ±10 gms. Standing height was measured to the nearest 0.5 cm by a wall mounted seca stadiometer using standard technique. Head circumference was measured using a non-stretchable tape. Percentile scores of anthropometric measurements were calculated using gender specific WHO growth charts.[9] Investigations done included urine routine examination, urine protein creatinine ratio, blood urea and serum creatinine. Blood urea was estimated by urease GLDH method, reagent provided by Erba Mannheim and serum creatinine by Jaffe's method.[10] Glomerular filtration rate (GFR) was calculated by Schwartz formula.[11] Laboratory investigations were done in the Department of Biochemistry except for urine sodium estimation which was done by ion selective electrode method in private laborotary. GFR less than 90 mL/min per 1.73 m^2 was considered as abnormal.[12] The number of glomeruli indicates the renal mass but both theses parameters are difficult to measure. Hence the renal volume which is proportionate to renal mass is used as a surrogate marker of low nephron number. Renal volume was measured by ultrasonography using a Philips real-time mechanical sector scanner of 3.5-5 MHZ frequency with electronic callipers length, width and thickness of each kidney with the child placed in a supine oblique position was measured. The maximal renal length was recorded after re-positioning the probe in several angulations. Renal width was measured at the renal hilum and thickness was recorded from transverse scans showing the maximum dimension. All the measurements were made by a qualified radiologist. Renal volume was calculated using an equation of an ellipsoid: Length x transverse diameter x anterior-posterior diameter x 0.523 (cm^3). The combined renal volume was obtained by adding the left and right renal volumes. The relative kidney volume was calculated as combined renal volume corrected to BS. Renal size in terms of renal volume was compared with reference values mentioned in the study by Otiv A, Mehta K, Ali U and Nadkarni M conducted in 2011 in Mumbai on 1000 Indian children in the age groups 1 month to 12 years.[13]

Statistical Analysis

Data was analysed using SPSS version 18. The linear association between the normally distributed variables was assessed by Pearson's correlation coefficients and independent T test.

RESULTS

Fifty one children on regular follow up in the high risk clinic and who fulfilled the criteria for enrolment were included in the study. One child had to be excluded as he was found to have horse shoe kidney on ultrasound examination. More than half 29 (58%) of the children were in the 7-year age group, 5 (6%) were in the 6 year and 16 (32%) in the 8-year group There were almost equal number of girls 26 (52%) and 24 (48%) boys. Out of the 50 children 40 (80%) had very low birth weight, between 1500 gm and 1000 gms and 10 (20%) were extremely low birth weight, with weight at birth below 1000 gms. The majority of babies were preterm 41 (82%) and 9 (18%) were term SGA babies. Among the preterms 9 (18%) were appropriate for gestational age and 41 (82%) were small for gestational age. None were large for gestational age. The majority of preterm babies were between 33-36 weeks. Stage 1 hypertension was detected in 9 (18%) of the children. Urine routine examination urine protein creatinine ratio, urine sodium analysis and serum electrolytes were also estimated and found to be normal. Serum creatinine was also in the normal range for age. However, the estimated glomerular filtration rate (GFR) based on Creatinine value which reflects renal function was found to be abnormal in 42 (84%) children. The children were categorized based on the age, into three groups for comparison of the renal volume with the reference value for Indian children of Otiv A et al. Renal volume measured by ultrasound examination was found to be reduced in 34 (68%) children when compared with the reference values. Among 6-year olds, the mean kidney volume of cases compared with the reference value was 24.8±6.9 and 34.2±9.4 respectively but this difference was not statistically significant (p value was 0.588). Among 7 year olds the mean kidney volume of cases was 28.92±8.7 and the reference value was 44.6±12, this difference was statistically significant (p value 0.0350).Among children aged 8 years, the mean kidney volume of cases was 33.4±6.6 and the reference value was 49.8±14.8 respectively, this difference was also statistically significant (p value - 0.001.).

The perinatal risk factors for nephron loss considered were maternal pregnancy induced hypertension (PIH),intrauterine growth restriction (IUGR),placental abruption, birth asphyxia, sepsis and acute kidney injury. We did not have data regarding the use of nephrotoxic drugs in all patients, so this factor was not considered for analysis. Among the risk factors, significant association could be found only between maternal PIH and IUGR. Among the children whose mothers had pregnancy induced hypertension. 80.2% had reduced renal volume (p value 0.04) and 84.6% of children with antenatally detected intrauterine growth restriction also had reduced renal volume (p value 0.018) Renal volume was also found to be lower in small for gestational age babies but this was not statistically significant (p value 0.09). Among the 50 children enrolled in the study, 7 had neurodevelopmental disabilities and renal volume was found to be reduced (p value 0.05) in all of them. On analysing the anthropometric data only 10 (20%) children enrolled in the study were under weight and 5 (10%) had stunting as per the WHO reference charts. Head circumference was found to be below the 3rd percentile in 12 (24%) children.

Age	Renal Volume of Cases Mean (SD)	Renal Volume as Per Reference Value Mean (SD)	P Value
6 yrs.	24.8 (6.9)	34.2 (9.4)	0.588
7 yrs.	28.92 (8.7)	44.6 (12.7)	0.035
8 yrs.	33.4 (6.6)	49.8 (14.8)	0.001

Table 1. Comparison of Renal Volume of Children in Different Age Groups with Reference Values

	Abnormal (n = 33)	Normal (n = 17)	P Value
Age	7.29 ± 0.58	7.06 ± 0.68	0.218
Birth weight	1.13 ± 0.21	1.21 ± 0.15	0.175
Hb	12.62 ± 0.96	12.55 ± 1.01	0.8126
Blood Urea	19.68 ± 4.82	18.38 ± 4.75	0.375
Creatinine	0.703 ± 0.15	0.819 ± 0.20	0.0275
GFR	86.49 ± 20.6	73.96 ± 12.7	0.0299

Table 2. Comparison of Investigation Results of Children with Reduced and Normal Renal Volume

Maternal Risk Factors	Reduced Volume (n = 33)	Normal Volume (n = 17)	P Value
*PROM	11 (33.3)	7 (41.1)	0.613
Oligohydramnios	13 (39.3)	4 (23.5)	0.849
#PIH	21 (63.6)	5 (29.4)	0.04
&IUGR	23 (69.6)	4 (23.5)	0.018
$APH	2 (6)	1 (5)	0.002

Table 3. Association of Maternal Risk Factors with Renal Volume

*PROM: premature rupture of membrane, #PIH: pregnancy induced hypertension, & IUGR: intrauterine growth restriction, $APH: antepartum haemorrhage

DISCUSSION

In this study on the 'Renal function and Renal size of children born with very low birth weight, we were able to recall 50 survivors between 6-8 years of age for a cross sectional study. Of them, the majority were born preterm between 33-36 (84%) weeks as survival in our centre during the study period was higher in this gestational age group. There were 10 (20%) extremely low birth weight babies. We were able to pick up stage 1 hypertension in 9 (18%) children. Barker et al. have described the tendency of low birth weight children especially those with intrauterine growth restriction to develop metabolic syndrome in adulthood.[14] Other studies have also reported early onset of hypertension in VLBW infants.[15] Reduced nephron number is one of the links between LBW and hypertension in addition to developmental programming of blood pressure.[4] Renal size in terms of renal volume when compared with reference values mentioned in the study by Otiv A et in Indian children in the age groups 1 month to 12 years, we found that 33 (66%) of the children in our study had reduced renal volume when evaluated between 6-8 years of age. Renal volume was found to be reduced in 33 out of 50 children in our study. These children have to be followed up for early predictors of metabolic syndrome and chronic kidney disease. Renal function when assessed in terms of estimated glomerular filtration rate (GFR) calculated by Schwartz formula, forty-two (84%) children enrolled in the study had abnormal GFR. Zaffanello M et al from the university of Verona Italy in a cross-

sectional study on the renal function and volume of 69 infants born with a very low birth-weight have not reported any abnormality in renal function in preschool age.[16] The weight and height of the children in this study group was not much affected. The majority of children had weight and height in the normal range between the 3rd and 50th percentile as per the WHO charts. Only 10 children (20%) were underweight and 5 (10%) had stunting. Similar findings have been reported by Hack, et al. in a study on babies born with very low birth weight at 20 years of age.[15] None of the children were obese.

We evaluated the association between antenatal risk factors and renal volume. 80.2% of children with maternal PIH had reduced renal volume (p=0.04) and 84.6% children with antenatally detected IUGR also had decreased renal volume (p=0.018). Both these results were found to be statistically significant. Studies conducted in Aboriginal children also show comparable findings.[17] A number of autopsy studies have also reported a significant reduction in nephron number as a result of IUGR.[10,18] We could not find any association between GFR and renal size. Renal volume was lower in small for gestational age babies (p=0.09) Renal function was also abnormal in small for gestational age (p=0.89).But both these observations were not statistically significant. Among the 50 children in our study, 7 had neurodevelopmental disabilities including cerebral palsy, mental retardation, learning disability, blindness and hearing impairment. All these 7 children had reduced renal volume (p=0.05). This implies that hypoxic ischemia and prematurity can have long term effects on vital organs especially kidney and brain. The strength of our study is the survival and follow up of 50 VLBW babies up to the age of 6-8 years of age with the limited facilities we have in a government hospital. The drawbacks include the lack of a normal control group and the inability to do more investigations to detect renal impairment.

CONCLUSIONS

Renal size of VLBW babies was found to be smaller when compared to normal Indian children at school age. Reduced renal size had significant association with IUGR and pregnancy, induced hypertension.

Financial or Other Competing Interests: None.

REFERENCES

[1] Stoll BJ, Chapman IA. The high-risk infant. In: Kliegman R, Behrman R, Jenson H, et al. eds. Nelson Text book of Pediatrics. 18th edn. Philadelphia, USA: Saunders Elsevier 2007.
[2] Palve S, Shenoy A. Study to assess sociodemographic factors affecting low birth weight baby in urban slum of Mumbai, Maharashtra, India. International J Sci Res 2016;5 (2):234-235.
[3] Ingelfinger JR. Pathogenesis of perinatal programming. Curr Opin Nephrol Hypertens 2004; 13 (4):459-464.
[4] Guyton AC, Coleman TG, Cowley AV Jr, et al. Arterial pressure regulation. Overriding dominance of the kidneys in long-term regulation and in hypertension. Am J Med 1972; 52 (5):584-594.
[5] Carmody JB, Charlton JR. Short-term gestation, long-term risk: prematurity and chronic kidney disease. Pediatrics 2013; 131 (6):1168-1179.
[6] Stritzke A, Thomas S, Amin H, et al. Renal consequences of preterm birth. Molecular and Cellular Pediatrics 2017; 4 (1):2.
[7] Fenton TR. A new growth chart for preterm babies: Babson and Benda's chart updated with recent data and a new format. BMC Pediatr 2003;3:13.
[8] Ballard JL, Khoury JC, Wedig K, et al. New Ballard Score, expanded to include extremely premature infants. J Pediatr 1991; 119 (3):417-423.
[9] WHO Multicentre Growth Reference Study Group. Enrolment and baseline characteristics in the WHO Multicentre Growth Reference Study. Acta Paediatrica 2006; (Suppl 450):7-15.
[10] Fuchs TC, Hewitt P. Biomarkers for drug-induced renal damage and nephrotoxicity—an overview for applied toxicology. The AAPS Journal 2011; 13 (4):615-631.
[11] Pottel H, Hoste L, Dubourg L, et al. An estimated glomerular filtration rate equation for the full age spectrum. Nephrology Dialysis Transplantation 2016; 31 (5):798-806.
[12] Hunley TE, Kon V, Ichikawa I. Glomerular circulation and function. In: Avner ED, Harmon WE, Niaudet P, et al, eds. Pediatric Nephrology. 6th edn. Heidelberg, Germany: Springer-Verlag 2009: p. 31-64.
[13] Otiv AS, Mehta K, Ali U, et al. Sonographic measurement of renal size in normal Indian children. Indian Pediatrics 2012; 49 (7):533-536.
[14] Barker DJP. The developmental origins of adult disease. Journal of The American College of Nutrition 2004; 23 (Suppl 6):588S-595S.
[15] Hack M, Schluchter M, Cartar L, et al. Growth of very low birth weight infants to age 20 years. Pediatrics 2003; 112 (1 Pt 1):e30-e38.
[16] Zaffanello M, Brugnara M, Bruno C, et al. Renal function and volume of infants born with a very low birth weight: a preliminary cross-sectional study. Acta Paediatrica 2010; 99 (8):1192-1198.
[17] Spencer J, Wang Z, Hoy W. Low birth weight and reduced renal volume in Aboriginal children. American Journal of Kidney Diseases 2001; 37 (5):915-920.
[18] Hinchliffe SA, Lynch MRJ, Sargent PH, et al. The effect of intrauterine growth retardation on the development of renal nephrons. British Journal of Obstetrics and Gynaecology 1992; 99 (4):296-301.