

CLINICAL SCIENCE

SONOGRAPHIC ASSESSMENT OF RENAL GROWTH IN PATIENTS WITH BECKWITH-WIEDEMANN SYNDROME: THE BECKWITH-WIEDEMANN SYNDROME RENAL NOMOGRAM

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BACKGROUND: Beckwith-Wiedemann syndrome is a disorder of somatic overgrowth. Evidence of kidney overgrowth is a diagnostic criterion that may be used to help identify those patients who are at the greatest risk of developing Wilms tumors. In such subjects, kidney size is typically larger than that of age-matched normal controls.

OBJECTIVE: The purpose of our study was to generate a nomogram that could be used to measure renal dimensions in children with Beckwith-Wiedemann syndrome in a clinical setting.

MATERIALS & METHODS: All of the Beckwith-Wiedemann syndrome patients followed at our institution from 1996 to 2004 were eligible for inclusion in our study. Renal length was measured with a curvilinear transducer and with the patient supine. Renal lengths were measured for both kidneys using real-time ultrasound for all patients. Their data were compared with those of age-matched controls reported in the 1984 study by Rosenbaum et al.

RESULTS: Ninety-six children with Beckwith-Wiedemann syndrome were followed from 1996 to 2004. Forty-three of these patients met our criteria for inclusion in the study: 28 girls (65%) and 15 boys (35%). We identified a linear relationship between kidney length and patient age. No statistically significant differences in renal length were found between boys and girls ($p=0.2153$) or between the kidneys on either side of the body ($p=0.9613$).

CONCLUSION: Our study provides a practical, simple renal growth chart that offers a reasonable, sensitive method for evaluating kidney size in children with Beckwith-Wiedemann syndrome.

KEYWORDS: Beckwith-Wiedemann syndrome; Renal length; Wilms Tumor; Renal nomogram; Practical chart.

INTRODUCTION

Beckwith-Wiedemann syndrome (BWS), a disorder of somatic overgrowth first described by Beckwith in 1963¹ and subsequently by Wiedemann in 1964,² is a congenital disorder associated with the disruption of the genomic imprinting of one or more genes in the 11p 15.5 region.³ Many of these genes are involved in the promotion

or suppression of growth.⁴ The cardinal features of the syndrome include macroglossia, abdominal wall defects, and macrosomia.¹ A number of other features have been documented, including neonatal hypoglycemia and hemihyperplasia.^{1,2} Patients with BWS also have an increased risk of developing embryonal tumors, the most common of which is the Wilms tumor.⁵ Other lesions reported include hepatoblastoma, neuroblastoma, adrenocortical carcinoma, and rhabdomyosarcoma.¹

Given the increased risk of embryonal tumors, screening protocols have been implemented to detect tumors in children at a younger age and earlier stage of disease. Evidence of kidney overgrowth is a diagnostic criterion that may be used to help identify those patients who are

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at greatest risk of developing Wilms tumors.⁵ A number of entities, both acute and chronic, can cause deviations in renal size. For BWS, the size of the kidney is typically larger than that of age-matched normal controls.⁵ There exist numerous sonographic reports^{1,3,5-6} of morphological changes, tumors, and other associated processes for patients with BWS, although no renal chart depicting the expected growth of kidneys for these patients has ever been published.

When children with BWS are examined using ultrasound, the renal length is measured and compared with published nomograms to determine whether kidney size is normal for the patient's age or is outside the usual ranges. Since no nomograms have ever been established for children with BWS, we use either nomograms for unaffected children or no nomograms at all.

The aim of this study was to create a nomogram that could be used to assess renal growth in children with BWS because this is an integral part of their clinical care. Such a chart should serve as a predictive tool to evaluate expected renal growth in this patient population.

MATERIALS AND METHODS

All BWS patients followed at our institution from 1996 to 2004 were eligible to participate in this study. Patients were

excluded from the study if they had a urinary tract infection at the time of their examination, hydronephrosis, a previous or partial nephrectomy, a tumor, or a solitary kidney. In our study group, nine patients had Wilms tumors at the time of their diagnosis; consequently, we had no information about the baseline size of these patients' kidneys. If the images for a patient were of poor quality or if serial studies were unavailable, that patient was also excluded from the study.

At our institution, a renal ultrasound is performed every six months for this population. The renal ultrasound examination consists of imaging the kidneys with the patient supine in the longitudinal and transverse planes. The kidneys are also assessed, if possible, with the patient in the prone position. We collected kidney measurements for each patient enrolled in the study from 1996 to 2004. All ultrasound studies were performed using ATL (Advanced Technological Laboratories, Bothel, WA) 3,000 or 5,000, Acuson Sequoia, and General Electric Ultrasound Systems (Brookfield, WI). The curvilinear and linear transducers ranged from 3 to 12 MHz. The length of the kidney was measured with a curvilinear transducer and with the patient supine. The lengths of both kidneys were measured with real-time ultrasound for all BWS patients.

We compared the data for the patients in our study with those of age-matched controls reported by Rosenbaum et

Table 1 - Mean renal lengths for patients with Beckwith-Wiedemann syndrome and age-matched controls

Age interval	Length of Kidneys (cm)				p-Value
	Children with BWS		Normal Children*		
	No. (n=43)	Mean (SD)	No. (n=43)	Mean (SD)	
8 days to 4 mo	11	5.73 (0.56)	54	5.28 (0.66)	0.48806
4 to 8 mo	16	6.35 (0.66)	20	6.15 (0.67)	0.76564
8 mo 1 day to 1 y	16	6.69 (0.61)	8	6.23 (0.63)	0.46343
1 y 1 day to 2 y	42	7.06 (0.60)	28	6.65 (0.54)	0.47972
2 y 1 day to 3 y	44	7.57 (0.53)	12	7.36 (0.54)	0.69462
3 y 1 day to 4 y	50	7.87 (0.58)	30	7.36 (0.64)	0.40027
4 y 1 day to 5 y	58	8.15 (0.48)	26	7.87 (0.50)	0.56625
5 y 1 day to 6 y	56	8.52 (0.51)	30	8.09 (0.54)	0.41112
6 y 1 day to 7 y	39	8.66 (0.56)	14	7.83 (0.72)	0.17597
7 y 1 day to 8 y	20	8.79 (0.65)	18	8.33 (0.51)	0.43919
8 y 1 day to 9 y	10	9.00 (0.66)	18	8.90 (0.88)	0.90277
9 y 1 day to 10 y	5	9.10 (1.03)	14	9.20 (0.90)	0.91583
10 y 1 day to 11 y	8	10.12 (0.53)	28	9.17 (0.82)	0.22533
11 y 1 day to 12 y	7	10.11 (0.64)	22	9.60 (0.64)	0.43248
12 y 1 day to 13 y	3	10.05 (0.83)	18	10.42 (0.87)	0.67396
13 y 1 day to 14 y	3	10.50 (1.26)	14	9.79 (0.75)	0.40917

Note. — No.= Number of measurements, since some patients were assessed more than once. SD=Standard Deviation. *Normal kidney length from Rosenbaum et al ⁶

al.⁶ We correlated morphometric kidney data, such as kidney length, with the patient's age in months during the first year and then with years of age, using linear regression.

We superimposed growth charts for kidney lengths and 95% confidence limits for patients in our study population onto measurements of kidney lengths in normal children from the 1984 study of Rosenbaum et al.⁶ We used linear regression models to establish the linear relationship between age and the average length of the kidneys for children with BWS and for the age-matched controls (Table 1). We used two-sample t-tests to compare average kidney sizes in our study with normal kidney sizes as reported by Rosenbaum et al.⁶ for different age groups.

We used SAS version 8.2 (SAS Institute, Cary, NC) for data manipulation and analysis. We considered a p-value ≤ 0.05 statistically significant.

RESULTS

Ninety-six children with BWS were followed from 1996 to 2004. Forty-three of these patients met our criteria for inclusion in the study: 28 girls (65%) and 15 boys (35%).

A linear relationship between length of kidney and patient age was found for both patients with BWS and for

normal controls as reported by Rosenbaum et al.⁶ (Figure 1). No statistically significant difference in the length of kidneys was found between boys and girls ($p=0.2153$). There were no differences between the left and right kidneys ($p=0.9613$).

Nonparametric smooth curves fitted to both right (Figure 2) and left (Figure 3) kidney lengths clearly show the linear relationship between kidney length and age in months for children less than 1 year, and age in years for children older than 1 year. The slope of the regression lines changes at 12 months. Since the nonparametric smooth curves fitted to the data for the left and right kidney lengths were almost identical (Fig. 4), we used the average of the lengths of the left and right kidneys in our linear regression models to estimate the relationship between kidney size and age among children with BWS.

Eight of our 43 patients with BWS were less than 3 months of age. Of these eight patients, the length of the kidneys in five children (63%) was normal. In the 35 patients older than 3 months of age, kidney size was enlarged.

Beyond 12 months of age, kidney growth accelerated (Figure 4); renal growth of patients older than 12 months of age was statistically significant ($p=0.03$). In patients younger than 12 months of age, kidney growth was not significantly different ($p=0.05$) for patients with BWS versus control patients.

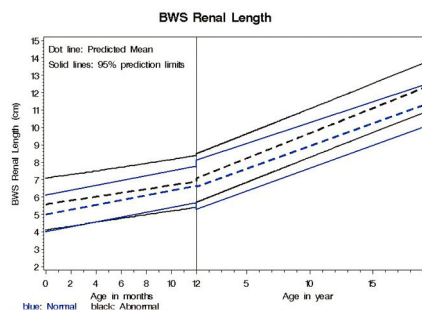


Figure 1 - Renal growth curves for normal control (blue line) age-matched population, as published by Rosenbaum et al.⁶, and patients with Beckwith-Wiedemann syndrome (BWS; black line). Renal growth is parallel and renal length increases continuously at an approximately constant rate above normal that is never above two standard deviations

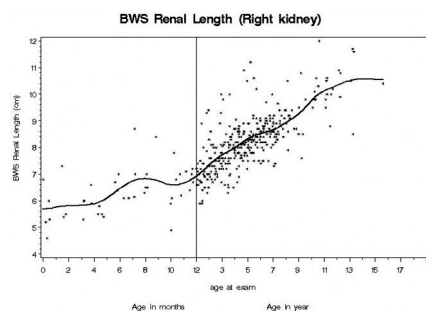


Figure 2 - Renal length and growth of the right kidney of patients with Beckwith-Wiedemann syndrome (BWS)

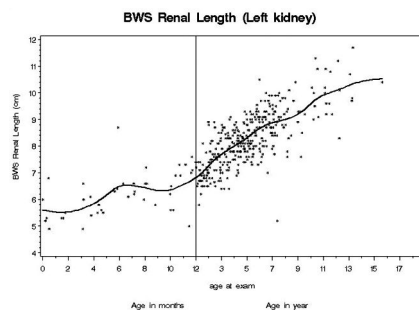


Figure 3 - Renal length and growth of the left kidney in patients with Beckwith-Wiedemann syndrome (BWS)

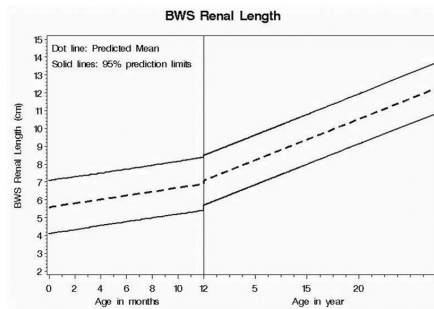


Figure 4 - Growth pattern of kidneys (right and left) for patients with Beckwith-Wiedemann syndrome (BWS). There was no significant difference in the patterns of growth for the right and left kidneys

When the estimated growth charts for kidney length were superimposed on the kidney lengths of normal age-matched controls drawn from Rosenbaum et al,⁶ the differences in the length of the kidneys between controls and patients with BWS were borderline significant ($p=0.05$) for patients younger than 1 year of age and highly statistically significant ($p=0.003$) for patients older than 1 year of age (Table 1).

However, the kidney sizes for patients with BWS across most other age categories were less than one standard deviation larger than those of the age-matched control children (Table 1).

In our study, nine patients presented Wilms tumors at the time of their diagnosis. Although we had no information about the baseline size of these patients' kidneys, at the time of the study, their kidneys were more than two standard deviations larger than expected for their ages. A comparison of the findings of the 1998 study of DeBaun et al⁵ with our results confirmed that, if the lengths of the kidneys of patients with BWS were more than two standard deviations greater than those of their age-matched controls, these patients would be at greater risk of developing Wilms tumors in the future.

DISCUSSION

Our study offers a practical and standardized renal growth chart for the evaluation of kidney size in children with BWS. Based on extensive experience from previous reports,⁷⁻⁹ kidney length is considered the best assessment tool of the size and growth of the kidneys. Our results for 43 children with BWS revealed a linear relationship between the length of the kidney and patient age. Furthermore, the lengths of both kidneys were above the mean control values beginning at 12 months of age and increased linearly over time thereafter. This finding is consistent with that of another study¹⁰ that used sonography to determine the size of normal children's kidneys.

CONCLUSION

Our study offers a practical, simple renal growth chart that is a reasonable, sensitive method for evaluation of kidney size in children with BWS. Our renal growth chart can be used to determine objectively the expected size of the kidneys of patients with BWS. In future, this chart could be used to help develop risk estimates for Wilms tumors and to support better health outcomes in these children.

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