Health outcomes of children born to mothers with chronic kidney disease: a pilot study

Indrani Banerjee,[1] Stephen Powis,[2] Mark Shevlin,[3] Jacqueline Barnes,[4] Audrey Soo,[1] Alastair G. Sutcliffe[1]

[1]General and Adolescent Paediatrics Unit, Institute of Child Health, University College London;

[2]Centre for Nephrology, University College London Medical School (Hampstead Campus);

[3]Psychology Research Institute, School of Psychology, University of Ulster;

[4]Institute for the Study of Children, Families and Social Issues, Birkbeck, University of London, UK

Abstract

This study aimed to study the health of children born to mothers with chronic kidney disease. Twenty-four children born to mothers with chronic kidney disease were compared with 39 matched control children born to healthy mothers without kidney disease. The well-being of each child was individually assessed in terms of physical health, neurodevelopment and psychological health. Families participating with renal disease were more likely to be from lower socio-economic backgrounds. Significantly fewer vaginal deliveries were reported for mothers with renal disease and their infants were more likely to experience neonatal morbidity. Study and control children were comparable for growth parameters and neurodevelopment as assessed by the Griffiths scales. There was no evidence of more stress amongst mothers with renal disease or of impaired bonding between mother and child when compared to controls. However, there was evidence of greater externalizing behavioral problems in the group of children born to mothers with renal disease. Engaging families in such studies is challenging. Nonetheless, families who participated appreciated being asked. The children were apparently healthy but there was evidence in this small study of significant antenatal and perinatal morbidity compared to controls. Future larger multi-center studies are required to confirm these early findings.

Introduction

Historically it was said that *children of women with renal disease used to be born dangerously or not at all (not at all if their doctors had their way*[1]), reflecting an early view of the effect of kidney disease on pregnancy. In 1971, Confortini *et al*.[2] reported the first conception and successful delivery in a woman on maintenance hemodialysis. The first successful pregnancy following maternal renal transplantation was reported in 1963.[3] The donor and recipient were identical twin sisters and this child was 48-years old on March 10, 2006.[4] Subsequent progress in management of end-stage renal disease, most notably by means of renal transplantation, has resulted in many more women surviving to child bearing years. Such women were often discouraged from planning a family due to concerns about possible adverse effects on renal grafts and the potential offspring.[5] With advances in modern medical care, some are well enough to contemplate pregnancy without putting their health at significant risk.[6-9] However, no detailed developmental studies of their children has been performed.

It is well recognized that parents' physical illness can be detrimental to the well being of children (e.g. lower self esteem, higher levels of depression and poor academic attainment).[10] Similarly, mothers who are burdened with ill health and treatment face added challenges with parenting. Numerous potential psychological issues arise in families where, for example, the mother has undergone renal transplantation, which may influence the development of a child. These include maternal anxiety regarding her health as well as that of her children.

Mothers may also worry about the possibility of renal disease in their children. Owing to the side effects of the drug treatment, breast-feeding is often precluded in this group of women despite the increasing encouragement in the community for mothers to breast-feed. This situation may adversely affect a woman's perception of her "mothering skills" and increase her anxieties that her infant is not receiving care that is optimal for healthy development.

Partly due to relatively recent advances in care of renal disease, and partly as children born after obstetric disease are often overlooked by those teams (who also do not have the capacity or knowledge to do such studies), there is little structured research beyond the neonatal period in this at risk group of children. There are some single center studies[5] and data from the National Transplantation Pregnancy Registry[11] regarding the well-being of renal transplant recipient mothers' offsprings. Only two controlled studies[5,12] which involved pediatric assessments beyond the neonatal period have been reported. Only one study[12] carried out a neurodevelopmental screening, the Denver Developmental Screening test, i.e. a non-formal assessment using a contemporary neurodevelopmental scoring system. The study,[12] unlike our study, did not carry out hands on assessment of all children seen. Some families were contacted by telephone and follow-up data regarding child development was collected via telephone interview.

Correspondence: Alastair Sutcliffe, General and Adolescent Paediatrics Unit, Institute of Child Health, University College London, WC1N 1EH, UK. E-mail: a.sutcliffe@ich.ucl.ac.uk

Key words: maternal, renal, pregnancy, outcome, children.

Acknowledgments: we would like to thank participating families. We would also like to thank Mr. T. Fesshaie, database manager of the Renal Unit at the Royal Free Hospital and Ms. P. Whitehead, Departmental Administrator of the Renal Unit at the Royal Free Hospital. We also thank Jayne Hui Lim for her contribution in designing and maintaining the study database.

Contribution: IB and AGS contributed to study conception and design, acquisition of data, analysis and interpretation of data, and wrote the initial draft; MS performed the statistical analyses of the data; AS contributed to the analysis of data. All co-authors contributed to writing the manuscript.

Conflict of interest: the authors report no conflict of interest.

Received for publication: 22 December 2009.
Revision received: 15 February 2010.
Accepted for publication: 15 February 2010.

Pediatric Reports 2010; 2:e7
doi:10.4081/pr.2010.e7

Materials and Methods

We hypothesized that children born to mothers with chronic kidney disease are expected to have the following complications in comparison to age-matched children born to well mothers:

a. reduced longitudinal growth;
b. greater occurrence of difficult temperament and emotional or behavioral problems;
c. possible effects on neurodevelopment;

These effects would be a continuum from healthy children to those with the above morbidity depending on antenatal exposures/disease severity.

We also hypothesized that families where

Table 1. Serum creatinine, blood pressure and urine protein dipstick results 6 months prior to conception, during pregnancy and postpartum.

Time period	Range of serum creatinine (μmol/L)		Mean serum creatinine (μmol/L)	Range of urine protein dipstick results		Mean urine protein dipstick result	Average blood pressure
	Highest	Lowest		Highest	Lowest		
6 months prior to conception	106	88.78	96.14	1.07	0.53	0.72	-
During pregnancy	106.26	90.67	96.50	1	0.61	0.72	127/77
Post partum	134.08	104.33	107.84	-	-	-	123/76

children are born to mothers with chronic kidney disease would experience the following:

a. differences in maternal bonding;
b. more stress in parent child relationship;
c. other difficulties in parenting (related to the pressures of renal disease and treatment).

This was a population-based, case-control study carried out in London. Qualifying families were contacted by post to obtain written informed consent to participate (or not). In order to attain a minimum one to one ratio of study to control children, the local child health database was used to recruit control children. Written consent was obtained from all participating control families and they were assessed in an identical manner to study children. The local research ethics committee approved the study.

Children under the age of eight years whose mothers were known to have chronic kidney disease at the point of positive pregnancy test were eligible. Mothers were identified after searching the database of a large regional renal service, based at the Royal Free Hospital, which serves a population of around 1.3 million residents of North London.

Control children were identified from a Community Child Health System, a community database system with 500,000 children within a group from North London presently involving nine Primary Care Trusts (PCT). The details kept include: demographic, birth, immunizations, examinations, medical details, e.g. ICD 10 codes and health professional involvement.

Families were contacted to participate in the study. These children were matched for age, sex, maturity (gestational age), ethnicity and postcode (as a proxy for socio-economic status).

Children aged over eight years were not recruited as they were not eligible for Griffiths Mental Development Testing. This particular test has an upper age limit of seven years and 11 months.

All case children were singletons and would be born to mothers with chronic renal disease (*see above*).

Outcome measure

The primary outcome measure was neurodevelopmental scoring and the secondary outcome measures were family functioning, and any (initial) evidence of growth problems or other physical abnormalities.

Table 2. Parental social class, educational attainment, birth details and mode of delivery.

	Case frequency (%)	Control frequency (%)	P
Mother			
Age months (SD)	37.04 (4.11)	39.81 (1.77)	0.001
Height cms (SD)	166.13 (8.52)	165.57 (8.11)	0.29
Social class IV or lower	7 (29)	1 (3)	0.00
Smoker	0 (0)	1 (3)	0.42
Alcohol units (SD)	1.27 (2.73)	3.47 (4.61)	0.04
Married/Cohabiting	24 (100)	31 (86)	0.06
Education: school matriculation or less	3 (13)	6 (17)	0.65
Father			
Height cms. (SD)	177.65 (6.40)	178.77 (6.30)	0.50
Social class VI or lower	1 (4)	1 (3)	0.75
Smoker	3 (13)	2 (6)	0.34
Alcohol units (SD)	3.18 (5.04)	6.16 (6.24)	0.06
Education: School matriculation or less	5 (23)	3 (9)	0.14
Birth details			
Support	20 (83)	37 (100)	0.01
Spontaneous birth	12 (60)	26 (79)	0.14
Intend to breast feed	15 (65)	33 (94)	0.00
Illness during pregnancy	11 (45)	10 (27)	0.13
Postpartum complications	11 (48)	8 (21)	0.03
Medication during pregnancy	17 (71)	7 (19)	0.00
Mode of delivery			
Normal vaginal	9 (37.5)	27 (73)	
Planned caesarean	4 (16.7)	4 (10.8)	
Emergency caesarean	6 (25)	4 (10.8)	
Forceps	5 (20.8)	2 (5.4)	

All children were assessed in accordance with an identical protocol which included medical history, physical examination and psychometric scoring using the Griffiths Scales of Mental Development.[13] Family functioning/child socio-emotional development was assessed using the maternal General Health Questionnaire[14] for maternal mental health status, the Toddler Temperament Scales[15] for child behavior, Parental Acceptance Rejection Questionnaire[16] and Parenting Stress Index (short version)[17] for parental attitudes to the child. Parental information included age, social class, and educational attainment. Social class was determined based on occupation and grouped as being Class IV or below, or III M or above. Social class was ascertained according to the Office of National Statistics classification. This is a scale for classifying people into five groups (represented by roman numerals), one subdivided, based on occupation (formerly the Registrar General's Social Class). Educational attainment was based on highest educational qualification achieved and grouped as school matriculation or less, and degree level or higher.

Differences on quantitative variables were analyzed using t-tests and qualitative variables were analyzed using χ^2 tests.

Results

Twenty-four case and 39 control children were assessed. The case children were born to mothers, 8 of whom had renal transplant, 3 with chronic renal failure and the remainder (11) were mothers attending the general nephrology clinic and had renal disease of a milder nature. The general nephrology conditions included various diagnoses: focal segmental glomerular sclerosis, congenital absent kidney, single hypertrophied kidney, autoimmune renal disorder, proteinuria, hematuria, raised blood pressure, nephritis, pyeloplasty, reflux nephropathy with nephrectomy and reimplantation of ureters, IgA nephropathy

and renal stones (secondary to increased oxalate level). None of the mothers' were pregnant while on dialysis but one mother required dialysis post pregnancy.

These mothers' renal function six months prior to pregnancy, during pregnancy and postpartum (including serum creatinine, urine protein dipstick and average blood pressure) are described in Table 1. These participants were from the original group of 80 families approached.

Eighty families were approached of which 35 (43.75%) were willing to participate and finally 24 (30%) children born between August 1997 and October 2005 came for assessment. Participants in the renal disease group were more likely to be from socio-economically poorer backgrounds than the control families (Table 2). During pregnancy there were significant differences in the antenatal and perinatal factors considered in this study (Table 2). Mothers with renal disease had a higher proportion of instrumental and operative deliveries and significantly fewer vaginal deliveries were reported (Table 2).

Babies born to mothers with renal disease were more likely to experience neonatal morbidity (Table 3).

Case and control children were comparable for growth parameters (Table 4). They showed no evidence of neurodevelopmental differences as assessed by the Griffiths scales of mental development (Table 5). There was no evidence, as judged by the Parenting Stress Index, of more stress (Table 5) amongst mothers with renal disease nor was there any evidence of impaired bonding between mother and child in comparison with controls (Table 5). The Child Behaviour Check List (CBCL) for 1½ - 5 years and 6-18 years, which provides a standardized rating and descriptive details of children's functioning as seen by parents, showed significant differences between the case group and the control group (Table 5). The mothers in the case group reported a significantly higher perception of externalizing problems like rule breaking and aggressive behavior in their children. The case mothers also reported a significantly higher perception of other problems when compared with the control group. The total scores of the CBCL were also higher in the case group reflecting that these mothers perceived difficulties in their children's functioning more commonly.

Discussion

Of the initial 80 children found to be eligible, only 35 (44%) responded to the invitation and finally 24 (30%) of the eligible children were assessed. We identified this weakness as the study progressed. Eleven families (14%),

Table 3. Neonatal information on cases and controls.

	Case frequency (%)	Control frequency (%)	P
Sex (male)	13 (50)	16 (43)	0.404
1st Child	12 (44)	15 (40)	0.467
Resuscitation	6 (25)	3 (8)	0.070
NICU	8 (33)	3 (8)	0.012
Ventilator	4 (17)	1 (3)	0.052
Babies not exclusively breast fed	9 (39)	4 (11)	0.011
	Case mean (SD)	**Control mean (SD)**	**P**
Weight (in grams)	2842.57 (886)	3414.07 (488)	0.002

Table 4. Physical development of children at time of evaluation.

	Case mean (SD)	Control mean (SD)	P
Height (cm)	99.55 (21.34)	97.72 (13.79)	0.69
Weight (kg)	16.98 (7.67)	15.34 (4.23)	0.29
Head (cm)	50.30 (3.77)	50.14 (2.60)	0.85

Table 5. Group differences on the overall and subscale score on neurodevelopmental and psychometric scales.

	Case Mean (SD)	Control Mean (SD)	p
Griffiths Scales			
Locomotor subscale	108.84 (14.77)	108.91 (17.23)	0.98
Personal social subscale	105.04 (19.16)	106.77 (13.79)	0.69
Hearing speech subscale	107.66 (26.55)	109.60 (16.15)	0.73
Eye hand subscale	101.02 (18.37)	98.57 (15.58)	0.59
Performance subscale	107.60 (25.90)	106.06 (14.50)	0.74
Practical reasoning subscale	103.01 (43.33)	112.12 (13.31)	0.37
Griffiths General Quotient	106.29 (18.48)	105.65 (11.60)	0.87
Parental Stress Index Scales			
Parental distress	26.48 (9.52)	26.65 (8.59)	0.94
Parent child dysfunctional interaction	18.76 (9.09)	17.22 (5.35)	0.41
Difficult child	28.45 (7.60)	25.16 (7.37)	0.11
Total clinical score	73.80 (20.70)	69.03 (17.32)	0.36
Parental Acceptance Rejection Questionnaire			
PARQ warmth- affection	23.16 (3.64)	24.22 (4.65)	0.39
PARQ aggression-hostility	25.11 (7.03)	27.35 (7.75)	0.29
PARQ neglect-indifference	21.00 (5.07)	20.43 (4.20)	0.65
PARQ rejection	15.53 (5.50)	14.73 (4.56)	0.56
PARQ total	84.79 (18.22)	86.73 (17.50)	0.70
Toddler Temperament Scales			
Activity	4.43 (0.13)	4.08 (0.54)	0.18
Rhythmicity	2.49 (1.05)	2.79 (0.89)	0.52
Approach	3.62 (0.98)	3.04 (0.60)	0.12
Adaptability	3.40 (0.79)	2.92 (0.40)	0.07
Intensity	4.06 (0.91)	3.80 (0.81)	0.56
Mood	3.31 (1.03)	2.82 (0.55)	0.18
Persistence	3.30 (1.26)	3.19 (0.82)	0.82
Distractibility	3.56 (1.09)	3.80 (0.90)	0.63
Threshold	4.49 (0.50)	4.34 (0.85)	0.72
General Health Questionnaire			
GHQ_A	1.09 (4.78)	1.59 (2.39)	0.59
GHQ_B	1.80 (2.24)	1.64 (2.40)	0.82
GHQ_C	0.47 (0.81)	1.18 (1.89)	0.10
GHQ_D	0.28 (0.71)	0.35 (0.94)	0.78
GHQ Total	4.57 (4.95)	4.75 (6.49)	0.91
Child Behavior Check List			
Internal 1	7.81 (5.45)	5.15 (3.57)	0.087
Internal 2	50.93 (8.56)	45.25 (8.24)	0.051
External 1	13.31 (7.96)	7.35 (6.28)	0.017
External 2	53.06 (8.91)	43.60 (10.73)	0.008
Other Problems	11.72 (4.26)	5.05 (3.36)	0
CBCL Total 1	33.81 (18.60)	19.90 (11.80)	0.010
CBCL Total 2	52.12 (9.46)	43.80 (9.07)	0.011

even though they responded initially, later did not participate. Restrictions on the ethical approval meant we were not allowed to investigate reasons of non-participation but some mothers wrote that even though they saw the need for the research and morally agreed they personally found it not suitable to participate. There is a possibility that these mothers had a worry about the consequences of their illness on the child and did not want to know about it any further. It is also possible that they perceived their children as well and did not want to delve any deeper into the issues in case a problem did emerge. We also found that participation of mothers with renal transplant was much better; this possibly reflecting that having a well child after transplant provided a stronger motivation when compared with mothers who had mild renal impairment.

The results of this study were generally reassuring for the families where the mother has chronic renal disease and has had children. Study and control children were comparable for growth parameters and neurodevelopmental scores as assessed by the Griffiths scales of mental development. The data, albeit small in terms of numbers, does provide reassurance to a group of mothers with a variety of renal diseases that there was no effect related to maternal disease or medications used on growth and development of the children.

The study highlights significant differences in externalizing behavior (e.g. rule breaking and aggressive behavior) between the study and the control groups. The numbers involved were small and further studies would be needed to establish this. The result might relate to the comparative social disadvantage (as assessed by the social class classification) seen in a higher proportion of case mothers than control mothers.

There was no difference in the temperamental characteristics perceived by mothers in study and control groups. There was no evidence of more stress amongst mothers with renal disease or evidence of impaired bonding between mother and child in comparison with controls. There have been concerns about psychological health of women with chronic renal disease and also how it might affect parenting. The current data are reassuring but numbers were small and thus further studies are needed.

Two groups were chosen: the children born after maternal chronic renal disease and a control group of children born to mothers who did not have any reported renal impairment. All the children were assessed by the same pediatrician (IB), providing consistency in assessments and negating interobserver bias. The control group provided a standard of 'normal' by which to compare the case children. These children were from the same geographical area and in this way attention can also be given to the family structure and educational status of the parents.

This preliminary study is the first detailed control matched study published on children born to mothers with chronic renal disease. Although the number of cases is small, the study does provide provisional reassurance that these children do not have any overt problems over and above those known to be at risk from being born early and with a low birth weight. This preliminary study showed that the methodology is viable to assess a larger group of children.

Conclusions

This modest but unique study shows early evidence of well-being in mature children born to mothers with renal disease in pregnancy. However, it also shows evidence of increased perinatal risks. A larger registry based study would seem one of two ways to confirm the key findings. Alternatively, this could be investigated via a prospective cohort study where further evidence of health status can be obtained.

References

1. Pregnancy and renal disease. Lancet 1975;2:801-2
2. Confortini P, Galanti G, Ancona G, et al. Full term pregnancy and successful delivery in a patient on chronic hemodialysis. Proc Eur Dialysis Transplant Assoc 1971; 8:74-80
3. Murray JE, Reid DE, Harrison JH, Merrill JP. Successful pregnancies after human renal transplantation. N Engl J Med 1963; 269:341-3
4. McKay DB, Josephson MA. Pregnancy in recipients of solid organs-effects on mother and child. N Engl J Med 2006;354:1281-93
5. Willis FR, Findlay CA, Gorrie MJ, et al. Children of renal transplant recipient mothers. J Paediatr Child Health 2000; 36:230-5
6. Davison JM. Renal disorders in pregnancy. Curr Opin Obstet Gynecol 2001;13:109-14
7 Hou S. Pregnancy in chronic renal insufficiency and end-stage renal disease. Am J Kidney Dis 1999;33:235-2
8. Jones DC, Hayslett JP. Outcome of pregnancy in women with moderate or severe renal insufficiency. N Engl J Med 1996;335: 226-32
9. Toma H, Tanabe K, Tokumoto T, et al. Pregnancy in women receiving renal dialysis or transplantation in Japan: a nationwide survey. Nephrol Dial Transplant 1999;14:1511-6
10. Barnes J, Stein A. Effects of parental physical and psychiatric illness on child development. In M.G.Gelder, Lopez-Ibor II Ir and Andreasen NC eds. New Oxford Textbook of Psychiatry. Oxford University Press, Oxford: 2000; 1848-55
11. Stanley CW, Gottlieb R, Zager R, et al. Developmental well-being in offspring of women receiving cyclosporine post-renal transplant. Transplant Proc 1999;31:241-2
12. Sgro MD, Barozzino T, Mirghani HM, et al. Pregnancy outcome post renal transplantation. Teratology 2002;65:5-9
13. Griffiths R. The Griffiths Mental Development Scales 1996 revision. Association for Research in Infant and Child Development (Printed by Test Agency), Henley: 1996.
14. Goldberg DP, Hillier VF. A scaled version of the General Health Questionnaire. Psychol Med 1979;9:139-45
15. Carey WB. The Carey Temperament Scales, Test Manual. Behavioral-Developmental Initiatives, Scottsdale, AZ: 2005.
16. Handbook for the Study of Parental Acceptance and Rejection. Ronald Research Publications, Storrs, CT: 2005.
17. Abidin R. Parenting Stress Index Test Manual. Pediatric Psychology Press, Charlottesville, VA: 1990.