PAPERS AND ORIGINALS

Regional variations in the incidence of upper urinary tract stones in England and Wales

D J P BARKER, S P B DONNAN

British Medical Journal, 1978, 1, 67-70

Summary and conclusions

Data from the Hospital In-patient Enquiry were used to define the regional patterns of hospital discharge rates for upper urinary tract stones and renal colic in England and Wales. By combining the rates for stones and colic, and by distinguishing emergency from planned admissions, the biases produced by repeated admissions of the same patient and by regional variations in diagnosis and coding may be reduced.

There are regional variations in incidence of upper urinary tract stones: Wales and the southern regions of England have a generally higher incidence than northern regions. These variations may be related to regional differences in diet or occupation; or they may partly depend on associations between stone incidence and atmospheric temperature, exposure to ultraviolet irradiation, and hardness of drinking water.

Introduction

Since the beginning of the century in Britain and other industrialised countries a progressive and unexplained increase in the incidence of renal and ureteric stones has occurred.¹ Epidemiological studies in Europe, America, Australia, and among the armed services have suggested that the disorder is associated with a number of environmental influences, including occupation, diet, and atmospheric temperature.² These influences vary among the different regions of England and Wales, and this is reflected in the considerable regional differences in overall mortality, and in mortality from particular

diseases—for example, ischaemic heart disease. To find out whether the incidence of upper urinary tract stones varies from one region to another, we studied the regional patterns of hospital discharge rates for renal and ureteric stones and renal and ureteric colic.

Methods

Information on patients discharged from hospital with a diagnosis of renal stones or renal colic was obtained from the Hospital In-patient Enquiry (HIPE), which is based on a one-in-ten sample of all discharges from (or deaths in) hospitals in England and Wales. The source of HIPE data is the HMR1 form completed at the time of discharge. Data for the four years 1968, 1970, 1972, and 1973 were analysed and relate to patients with the diagnostic ICD codings (8th revision, 1967) for calculus of the kidney or ureter (ICD 592) or renal colic (ICD 786.0, which encompasses other forms of pain referable to the urinary system—namely, strangury, vesical pain, and tenesmus). The patients were subdivided according to region of residence. Numbers of discharges were related to the 1971 population, and the resulting rates were adjusted using the HIPE regional correction factors. These factors allow for regional differences in the precise sampling fraction achieved when the notional one-in-ten sample is drawn. Since the correction factors change each year, rates in each region have been multiplied by the mean of the factors for the four years.

Results

Table I shows average annual discharge rates by region for renal stones. The rates relate only to discharges for which calculus of the kidney or ureter was coded as the main diagnosis. The regions are listed in descending order of the overall rates. The highest rate for males and females combined, 26.6 per 100 000, was in Leeds, but the other northerly regions (Newcastle, Manchester, Liverpool, and Sheffield) had average or below-average rates, and the lowest rate of any region, 14.6 per 100 000, was in Sheffield. Wales had an above-average rate, as did three of the four Metropolitan regions. In each region male rates were higher than female rates, so that the overall rates in England and Wales were 27.0 per 100 000 (males) and 14.8 per 100 000 (females). The ranking of regions by rates was generally similar for male and female rates, though the North-west Metropolitan Region had the highest male rate of 37.1, but a below-average female rate of 13.1.

Community Medicine, South Block, General Hospital, Southampton SO9 4XY

D J P BARKER, MRCP, PHD, reader in clinical epidemiology
S P B DONNAN, FRCS, MSC, lecturer in clinical epidemiology

TABLE I—Average annual discharge rates* per 100 000 population for renal and ureteric stones (ICD 592) as main diagnosis 1968, 70, 72, 73. Numbers of cases in Hospital In-patient Enquiry (HIPE) sample given in parentheses

Region of residence	Total	Males	Females
Leeds	26.6 (330)	34.2	19.6
SW Metropolitan	25.3 (303)	33.5	17.8
Wales	25.0 (263)	32.5	18.0
NW Metropolitan	24.8 (383)	37.1	13.1
Wessex	23.8 (172)	33.3	15.0
NE Metropolitan	21.9 (260)	29.8	14.4
Oxford	21.9 (155)	26.8	17.1
East Anglia	21.5 (127)	27.9	15.4
South-western	21.3 (230)	27.4	15.7
Liverpool	20.8 (171)	25.7	16.3
Newcastle	19.1 (220)	24.3	14.1
SE Metropolitan	18.4 (229)	24.7	12.7
Manchester	17.3 (293)	21.7	13.2
Birmingham	17.2 (329)	21.6	13.0
Sheffield	14.6 (266)	16.7	12.6
England and Wales	20.7 (3731)	27.0 (2362)	14.8 (1369)

*Rates given in tables I-V have been adjusted using mean of HIPE regional correction factors.

Many patients admitted to hospital with renal stones suffer from renal or ureteric colic. Hence the main diagnosis at discharge may sometimes be coded as renal colic. Whether or not this occurs may depend not only on clinical factors, such as the certainty with which stones are identified radiologically, but also on local coding practices. Table II shows average annual discharge rates by region for renal colic. There were above-average rates in Wales and the Metropolitan regions, which also had above-average rates for renal stones (table I). The highest rate for renal colic (39.9 per 100 000) was in Wales, while Sheffield (20.3 per 100 000) was again ranked lowest. Leeds, which had the highest renal-stone rate had a below-average rate for renal colic, and there was also considerable disparity in the rankings of Wessex and Manchester in the two tables. The northerly regions Sheffield, Liverpool, and Newcastle, however, had below-average rates, as for renal stones.

The combined regional discharge rates for renal stones and renal colic (table III) may more closely reflect the regional variations in

TABLE II—Average annual discharge rates per 100 000 for renal and ureteric colic (ICD 786.0) as main diagnosis 1968, 70, 72, 73. Numbers of cases in HIPE sample given in parentheses

Region of residence	Total	Males	Females
Wales	39.9 (419)	57.2	23.5
NW Metropolitan	35.9 (555)	50.7	21.9
NE Metropolitan	32.7 (388)	48.6	17.5
SW Metropolitan	30.6 (367)	46.0	16.7
Manchester	30.0 (508)	40.9	19.9
SE Metropolitan	29.0 (362)	42.7	16.7
Oxford	28.2 (200)	42.7	14.0
South-western	27.7 (298)	40.7	15.6
Birmingham	27.3 (522)	39.1	15.8
East Anglia	24.6 (145)	38.2	11.4
Leeds	23.9 (296)	34.2	14.2
Newcastle	23.0 (266)	29.4	17.0
Liverpool	21.9 (180)	27.7	16.5
Wessex	20.6 (149)	30.2	11.8
Sheffield	20.3 (370)	28.6	12.3
England and Wales	27.9 (5025)	39.9 (3488)	16.6 (1537)

TABLE III—Combined average annual discharge rates per 100 000 for renal and ureteric stones (ICD 592) and renal and ureteric colic (ICD 786.0) as main diagnosis 1968, 70 72, 73

Region of residence	Total	Males	Females
Wales	64.9	89.7	41.5
NW Metropolitan	60.7	87.9	35.0
SW Metropolitan	55.8	79.5	34.5
NE Metropolitan	54.5	78.4	31.9
Leeds	50.5	68.4	33.8
Oxford	50.1	69.4	31.1
South-western	49.0	68.1	31.3
SE Metropolitan	47.4	67.4	29.3
Manchester	47.3	62.5	33.1
East Anglia	46.1	66.1	26.8
Birmingham	44.5	60.7	28.7
Wessex	44.5	63.5	26.7
Liverpool	42.7	53.4	32.3
Newcastle	42.1	53.7	31.0
Sheffield	35.0	45.4	24.9
England and Wales	48.7	66.9	31.4

incidence of stones than the discharge rates for stones alone. The rates for Wales (64.9) and Sheffield (35.0) were the highest and lowest respectively. Southerly regions had generally higher rates than northerly, though the rate for Leeds (50.5) was above average, while East Anglia (46.1) and Wessex (44.5) were below average.

In HIPE data no distinction is made between first admissions and readmissions for the same disease. Patients with renal stones are liable to repeated admissions. For example, a ureteric stone that fails to pass spontaneously may cause repeated attacks of colic necessitating eventual surgical removal of the stone. Many factors influence the likelihood of a patient being admitted more than once. Surgeons' views of the ideal timing for surgical intervention may vary. In some centres patients needing surgery may be transferred directly from medical to surgical wards, whereas in others they may be discharged home from the medical wards for a brief period and then readmitted to the surgical wards. Regional variations in surgical policies or in the organisation of medical and surgical services, or in the readiness of general practitioners to refer patients with renal colic or other symptoms to hospital may produce regional inequalities in the frequency of repeated admission. This in itself may produce an apparent regional variation in disease incidence.

To lessen possible biases resulting from repeated admissions table IV shows only emergency admissions for renal stones. In England and Wales as a whole 47% of admissions in which renal stones was the principal diagnosis were emergencies. The emergency admission rate was 9.8 per 100 000 compared with the total admission rate of 20.7 (table I). Overall the rankings of regions in table I and table IV are similar. Table IV also shows the percentage of admissions for renal stones in each region which were emergencies. Regions with high emergency admission rates tended to have a high proportion of admissions as emergencies. The percentage of emergency admissions was higher among men (52%) than among women (39%).

TABLE IV—Average annual emergency admission rates per 100 000 for renal and ureteric stones as main diagnosis (No of cases = 1756)

Region of residence	Rate	Emergency admissions (% of all admissions)
Leeds	14.8	56
SW Metropolitan	13.1	52
NW Metropolitan	12.6	51
Wales	12.4	50
Liverpool	11.6	56
Wessex	10.7	45
South-western	10.7	50
East Anglia	9.8	46
NE Metropolitan	9.6	44
Newcastle	9.4	49
Oxford	9.3	42
SE Metropolitan	8.4	46
Sheffield	6.5	45
Birmingham	6.5	38
Manchester	6.4	37
England and Wales	9.8	47

Not unexpectedly, most patients with renal colic were admitted as emergencies, so that the emergency admission rate for renal colic in England and Wales is 80% of the total admission rate. If there are regional variations in diagnostic and coding practices that influence whether patients are classified as having renal stones or renal colic this would be most evident among emergency admissions. One possible explanation for the findings shown in tables I and IV is that the above-average discharge rates for renal stones in some regions (notably Leeds) were partly determined by an increased incidence of patients with renal colic being coded as having renal stones. This difference in coding would be reflected in the greater proportion of emergency admissions for renal stones in these regions, and in the ratio of discharge rates for renal stones to rates for renal colic. In Leeds, for example, the ratio is 1.1:1, whereas in Wales it is 0.6:1.

Combined average annual emergency admission rates for renal stones and renal colic (table V) are a measure of the incidence of renal stones which is to some extent free of biases produced by repeated admissions of the same patient and regional variations in diagnosis and coding. The ranking of regions is similar to that of the total combined rates (table III), but the trend of higher rates in the southern regions of England compared with the north is accentuated. Only Leeds and Wessex are at variance with this trend. Standardisation of the rates to allow for regional differences in population age-sex structure does not change the regional rankings. HIPE data include up to three diagnoses for each patient. The emergency admission rate

TABLE V—Combined average annual emergency admission rates per 100 000 for renal and ureteric stones and renal and ureteric colic (No of cases = 5782)

Region of residence	Total
Wales	45.2
NW Metropolitan	40.6
SW Metropolitan	38.2
NE Metropolitan	36.7
South-western	34.4
Leeds	34.4
Oxford	31.2
SE Metropolitan	31.2
East Anglia	30.0
Liverpool	29.0
Manchester	28.9
Birmingham	28.5
Newcastle	28.4
Wessex	26.8
Sheffield	22.5
England and Wales	32.2

for renal stones in England and Wales rises from 9.8 per 100 000 (table IV) to 11.2 if cases in which renal stones was the second or third diagnosis are included. The inclusion of these cases has little influence on the relative rates of the regions.

Table VI shows the rates for admissions during which surgery was performed, either for removal of a renal calculus (OPCS operation code 563) or removal or a ureteric stone (codes 580 and 587.2). Surgery is performed in only 18% of admissions for renal stones and the numbers of cases in each region are therefore small. But the ranking of regions according to operation rates (table VI) differs from that for all admissions for renal stones. Wales in particular has comparatively low operation rates, and the pattern of generally higher rates for regions in southern England is no longer apparent.

There is considerable seasonal variation in the number of emergency admissions for renal colic, with more admissions in the summer than in the winter (figure). Emergency admissions for renal stones show a similar but less pronounced seasonal variation.

TABLE VI—Average annual discharge rates per 100 000 for renal stones as main diagnosis and operative removal of renal stone (OPCS 563) or ureteric stone (OPCS 580 and 587.2) (No of cases = 673)

Region of residence	Rate
Newcastle	5.5
Birmingham	5.0
NW Metropolitan	4.5
Manchester	4.3
SW Metropolitan	4.0
NE Metropolitan	3.7
SE Metropolitan	3.5
Leeds	3.4
Oxford	3.4
Wales	3.2
Liverpool	3.0
South-western	3.0
East Anglia	2.9
Wessex	2.8
Sheffield	2.3
England and Wales	3.7

Discussion

This study shows considerable regional variations in hospital discharge rates for renal stones and renal colic in England and Wales. When interpreting these variations the limitations of hospital discharge records as an indicator of the incidence of renal stones must be considered. Possible biases produced by local differences in coding practices and in hospital admission practices can be reduced by using combined rates for renal stones and renal colic and by restricting attention to emergency admissions (tables III and V). Nevertheless, these biases cannot be eliminated, and in Leeds, for example, which is a centre for the study of renal stones, the high discharge rates compared with other northern regions may reflect different hospital admission practices.

Another possible source of bias is the criteria used to establish the diagnosis of renal stones. Unless the stone is removed at operation or passed spontaneously the diagnosis will usually depend on radiological findings, whose interpretation may

vary from one observer to another. Nevertheless, the similarity in the regional patterns of renal stones (table I) and renal colic (table II) suggests that regional variation in diagnostic criteria is not a dominant influence on the variations in discharge rates for renal stones.

We conclude that the pattern of hospital discharge rates reflects regional variations in the incidence of upper urinary tract stones, such that Wales and the southern regions of England have a generally higher incidence than the northern regions. Among the regional variations in mortality and morbidity that have been documented, higher incidence of a disease in the south of England is an unusual finding. There is an increased incidence of renal and ureteric colic, and to a lesser extent stones, during the summer. The disparity between regional discharge rates and operation rates for removal of renal or ureteric stones (table VI) presumably reflects regional variations in surgical policies.

Our findings conflict with those of Rose and Westbury,³ which showed a higher incidence of renal calculi in northern England. Their study, however, was based on only 24 hospital groups in Britain, and their data were limited to the number of admissions for renal stones and the total numbers of all admissions during the same period. The incidence of renal stones was then expressed as the ratio of these two numbers. Proportional morbidity rates of this kind are a crude index of disease incidence and, as the authors themselves comment, are subject to errors. The incidence of a disease, expressed in this way, may vary solely because of variations in the numbers of admissions for other diseases. Thus true rates, relating numbers of cases to the total population, are usually used.

In Czechoslovakia regional variations in renal calculi have also been recorded⁴: the incidence of stones was negatively correlated with the total hardness of drinking water. In England, however, the distribution of upper urinary tract stones shows a positive correlation since the areas of hard water are mainly in the south and east of the country. The drinking water in Wales generally has a low calcium content. In Czechoslovakia⁴ the incidence of renal stones was higher in regions with a higher standard of living. This accords with the world distribution of urolithiasis. Upper urinary tract stones are found in the affluent industrialised countries, in contrast to vesical calculi, which are found predominantly in non-industrialised countries.² In so far as general

Numbers of emergency admissions for renal stones and colic by month of admission.

socioeconomic indices show the south and east of England to be more affluent than the north and west, the findings in the present survey support an association between upper urinary tract stones and a high standard of living. But the finding of a higher incidence of stones in Wales than in England cannot be explained in this way. An association between living standards and stone incidence in England and Wales might partly depend on occupation, for several surveys have shown that the condition is more common among those in sedentary occupations.² Further occupational data on patients with upper urinary tract stones in Britain are required.

The composition of urine is greatly influenced by diet, and it has been suggested that the increase in incidence of upper urinary tract stones in Europe during this century results from changes in diet. This hypothesis is strengthened by the temporary decline in incidence observed in Norway during the war years.¹ The National Food Survey has shown appreciable regional differences in diet in England and Wales. There is no obvious association between any single dietary constituent recorded in this survey and the incidence of upper urinary tract stones; but the data are relatively crude, and a more detailed study of this association is indicated. Interestingly, the regional patterns in upper urinary tract stones and ischaemic heart disease⁵ are almost the reverse of each other, yet they are both disorders whose steep rise in incidence in industrialised countries has been attributed to diet.

Surveys in several countries have shown an association between the incidence of upper urinary tract stones and atmospheric temperature. The higher incidence of stones in the south

of England conforms with this association, which may be due to decreased urinary output in warm climates, or the effect of increased atmospheric temperature on urinary composition. There is evidence that urinary calcium excretion is increased among men during the summer in Britain,⁶ and in summer urinary oxalate and urinary crystals may be increased.⁷ Emergency admissions for upper urinary tract colic and stones also increase during the summer months, though admissions diagnosed as stones fluctuate less than those diagnosed only as colic (figure).

We thank Mrs Barbara Gale, who helped with the analysis of the data, and Surgeon Captain N J Blacklock, who gave us helpful advice and criticism. The data were obtained through the courtesy of the Office of Population Censuses and Surveys, and the work was supported by a grant from the Department of Health and Social Security.

References

- Andersen, D A, in *Proceedings of the Renal Stone Research Symposium*, p 7. London, Churchill, 1969.
- Blacklock, N J, in *Scientific Foundations of Urology*, p 235. Edinburgh, Churchill Livingstone, 1976.
- Rose, G A, and Westbury, E J, *Urological Research*, 1975, **3**, 61.
- Mates, J, in *Proceedings of the Renal Stone Research Symposium*, p 59. London, Churchill, 1969.
- Morris, J N, Crawford, M D, and Heady, J A, *Lancet*, 1961, **1**, 860.
- Robertson, W G, *et al*, *British Medical Journal*, 1974, **4**, 436.
- Hallson, P C, and Rose, G A, *British Journal of Urology*, 1977, **49**, 277.

(Accepted 21 October 1977)

Factor VIII—related protein on vascular intima of patients with chronic renal failure and prolonged bleeding times

G REMUZZI, T BERTANI, G MECCA, M B DONATI, G DE GAETANO

British Medical Journal, 1978, **1**, 70-72

Summary and conclusions

To determine whether the prolonged bleeding time so common in chronic renal failure (CRF) was due to defective factor VIII-related activities, as in von Willebrand's disease, vascular-factor VIII-related protein was measured in patients with CRF. Factor VIII-related protein was detected by immunofluorescence on the vascular intima of all 13 patients with CRF and greatly prolonged bleeding times. This protein was also present on the vascular intima of a patient with CRF and moderate von Willebrand's disease.

These findings support a previous suggestion that the disturbed haemostasis in patients with CRF is not linked to defective factor VIII-related activities.

Introduction

Patients with chronic renal failure (CRF) often have prolonged bleeding times.¹ This abnormality has been ascribed to defective platelet function²⁻⁵ or to reduced plasma concentrations of von Willebrand factor (VIII:VWF).⁶ But several workers⁷⁻⁸ have challenged the hypothesis that reduced VIII:VWF concentrations cause prolonged bleeding times because they have found either normal or increased VIII:VWF concentrations in patients with CRF.

Normal endothelium synthesises and releases both factor VIII-related antigen⁹⁻¹⁰ and VIII:VWF,¹¹ and both contain the same single-polypeptide subunit.¹² These activities are possibly functions of the same molecule and may be referred to as factor VIII-related protein.

The relation between plasma and vascular VIII:VWF in determining the haemostatic effectiveness of platelets remains obscure.¹³⁻¹⁴ To complete our previous study on factor VIII concentrations in patients with uraemia,¹ we therefore investigated whether the factor VIII-related protein was immunologically detectable on the vessel walls of patients with CRF and greatly disturbed primary haemostasis. The absence of such a component in the vessel wall of some patients with von Willebrand's disease has been proposed as an explanation for the prolonged bleeding time in von Willebrand's disease.¹⁵

Patients and methods

Fourteen patients (nine men and five women, aged 22-65 years) with CRF were studied just before they started undergoing haemo-

Division of Nephrology and Dialysis, Ospedali Riuniti, Bergamo, Italy

GIUSEPPE REMUZZI, MD, assistant in nephrology
TULLIO BERTANI, MD, assistant in nephrology
GIULIANO MECCA, MD, head of division

Istituto di Ricerche Farmacologiche "Mario Negri,"
Via Eritrea 62—20157 Milano, Italy

MARIA BENEDETTA DONATI, MD, PHD, laboratory chief
GIOVANNI DE GAETANO, MD, PHD, laboratory chief