

URINARY CALCULI IN SINGAPORE—A STUDY OF 254 PATIENTS

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SYNOPSIS

Two hundred and fifty four patients with urinary calculi in Singapore were investigated. The male:female ratio was 2.2:1 despite the virtual absence of patients with idiopathic hypercalciuria. Bladder stones were radiologically demonstrated in only five patients, three of whom had associated stones in the upper urinary tract. Sterile pyuria was noted in 22 patients (8.7%) in the absence of any evidence for tuberculous infection. Primary hyperparathyroidism was diagnosed in 3 patients (1.2%).

During a three month period, November 1969 to January 1970, 254 patients with urinary calculi were examined in two teaching hospitals in Singapore. The results of our findings are reported in this paper.

PATIENTS AND METHODS

Our criteria for the diagnosis of urinary calculi consisted of either a statement by the patient or his medical practitioner that "a stone" had been passed or removed, or of the urographic demonstration of radio-opaque material or radiotranslucent filling defects in the urinary passages, or of a "classical" history of renal colic as defined by arbitrary criteria (Blackman *et al*, 1967). About 70% of the patients had been previously diagnosed and were recalled by a circular letter requesting them to attend for further investigations. The remainder were new patients who presented during the period of the study.

The methods used in this study were similar to those used by Lavan *et al* (1971) with the following exceptions:

1. Ammonium chloride was given as a liquid rather than in capsule form.

2. The atomic absorption method was employed in the measurement of serum and urine calcium. A series 1 Unicam SP90 atomic absorption spectrophotometer was used and the serum was diluted 1:26 with 0.75% disodium ethylene diamine tetracetic acid while the urine samples were diluted 1:13.5 in 1% strontium chloride.
3. Urine magnesium was not measured.
4. Total urine cystine was measured by the method of Lee and Ow (unpublished).

RESULTS

Table I shows the sex distribution of the 254 patients and the ethnic origins of the patients compared with the ethnic origins of the total population of Singapore. The male:female ratio was 2.2:1 in the stone formers compared to 1.05:1 in the total Singapore population (Census of Population, 1970).

The male:female ratio was significantly ($p < 0.001$) higher amongst Indian patients than amongst other ethnic groups. This was partially accounted for by the different age distribution of the Indian population of Singapore. In 1970, 55% of the male Indian population was aged 20-59 years while only 43% of the male Chinese population was in this age group (Census of Population, 1970).

Urinary calculi were randomly distributed amongst the various Chinese communities (Hokkien, Teochew, Hainanese etc).

Table II shows the age of onset of symptoms in the 254 patients. As in other series (Melick and Henneman, 1958, Lavan *et al*, 1971) almost 70% of patients first developed symptoms in the third to sixth decades of life. This is of greater significance in Singapore than in Australia or the U.S.A. as the age group 20-59 accounts for only 37% of the total population (Census of Population, 1970).

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TABLE III

ABNORMALITIES OF CALCIUM
METABOLISM IN 254 PATIENTS WITH
URINARY CALCULI

	M	F	Total
Hypercalcaemia (two or more occasions)	5*	—	5
Hypercalcaemia (once only)	6	—	6
Hypercalciuria (normal serum calcium)	11	3	14
No abnormality	138	69	207
Inadequate data	14	8	22
TOTAL	174	80	254

* Three of these patients had parathyroid adenomas removed surgically.

TABLE IV

PREVALENCE OF URINARY INFECTION
IN 254 PATIENTS WITH URINARY
CALCULI

	M	F	Total
No cells, no organisms	121	36	157 (62%)
**Cells but no organisms	14	8	22
Organisms but no cells	6	5	11
Organisms and cells	33	30	63* (25%)
Inadequate Data	—	1	1
TOTAL	174	80	254

* 30 of these patients had staghorn calculi.

** "Cells" means 5 or more pus cells per high power field.

TABLE I

ETHNIC ORIGINS OF 254 PATIENTS WITH URINARY CALCULI

	M	F	Total	Percentage of Total	Percentage of Ethnic Group in Singapore
Chinese	108	69	177	69.7	76.2
Malay	19	5	24	9.4	15.0
Indian*	45	4	49	19.3	7.0
Others	2	2	4	1.6	1.8
TOTAL	174	80	254	100.0	100.0

* Indians (including Pakistanis and Ceylonese) comprised 14.3% of all outpatients at Outram Road General Hospital, Singapore, in 1968.

TABLE II

AGE OF ONSET OF SYMPTOMS IN 254 PATIENTS WITH
URINARY CALCULI

Age of onset (years)	M	F	Total	Percentage of Total	Age group as percentage of total Singapore population
0 - 9	1	—	1	0.4	24.9
10 - 19	3	2	5	2.0	25.8
20 - 29	35	16	51	20.1	16.2
30 - 39	42	20	62	24.4	12.0
40 - 49	47	13	60	23.6	8.8
50 - 59	13	12	25	9.8	6.6
60 - 69	13	5	18	7.1	4.0
70 and above	3	1	4	1.6	1.7
Incomplete data	17	11	28	11.0	
TOTAL	174	80	254	100.0	100.0

Hypercalcaemia was noted on two or more occasions in 5 patients (Table III). Three of these had parathyroid adenomas removed surgically. The fourth patient was a boy of six in whom venepuncture was difficult and sufficient serum for specific gravity was not obtained. The fifth patient had concurrent thyrotoxicosis. He has since become euthyroid on carbimazole therapy but nevertheless remains hypercalcaemic. The urine calcium exceeded 301 mg. per 24 hours in only 14 patients and in 9 of these the urine creatinine, measured in the same specimens, was 2 gm. per day or more.

Table IV summarises our bacteriological findings. There were 157 patients (62%) in whom the urine was normal on microscopy and culture. Twenty two patients (8.7%) had sterile pyuria while 11 patients (4.3%) had positive cultures but no pus cells. In 63 patients (25%) the centrifuged deposit of urine contained 5 or more leukocytes per high power field and cultures were positive. Only this last group of patients was classified as infected. Fig. 1 shows that urinary infection was more prevalent amongst patients with branched calculi than amongst patients with stones that were not branched. *Proteus* species or staphylococci were cultured from 20/53 patients with branched stones and from 5/201 patients with simple calculi.

Table V shows the urinary pH after oral ammonium chloride in 254 stone formers. It is seen that 198 patients (84% of patients with adequate data) acidified normally. In another 10 patients there were obvious causes for non-acidification such as proteus or staphylococcal infection of the urine. There were 27 patients who failed to acidify in the absence of obvious causes and in 8

of these, this defect was confirmed on a second occasion.

Four patients (three males and one female) had uric acid calculi according to the stringent criteria stated by Lavan *et al* (1971). Two of these patients, one male and one female, had chronic myeloid leukaemia.

Six patients had a positive cyanide nitroprusside reaction for cystine. Only one patient, a male Chinese, excreted abnormal amounts of cystine (280 mg. per day and 548 mg. per day in two separate 24 hour specimens).

There were 5 male patients in the series who had radiologically visible bladder stones at the time of the survey. Three of these had associated stones in the upper urinary passages.

TABLE V

URINARY ACIDIFICATION IN 254 STONE FORMERS

	M	F	Total
Normal pH (5.5 or below)	136	62	198
Abnormal pH (5.6 or above)			
Proteus or Staph. infection	4	4	8
Ileal Bladder	1	—	1
Nephrotic Syndrome	—	1	1
Failure to acidify	20	7	27
Inadequate Data	13	6	19
TOTAL	174	80	254

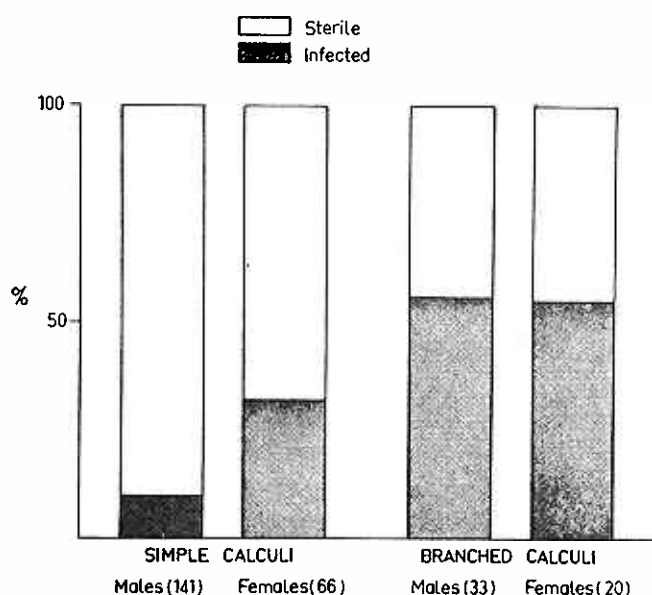


Fig. 1. The prevalence of urinary infection amongst various groups of stone formers. Amongst patients with branched calculi more than 50 per cent have infected urine.

DISCUSSION

This study does not constitute a true epidemiological survey as it was carried out over a short period of three months and the majority of patients seen were those who responded to a written request to report for further investigations. Nevertheless certain findings appear of interest.

The preponderance of males which has been observed in other series (Melick and Henneman, 1958, Clark and Nordin 1969, Lavan *et al*, 1971) was again noted in Singapore in spite of the virtual absence of patients with idiopathic hypercalcaemia (Melick and Henneman, 1958). This suggests that the predominance of males amongst stone formers may be due to factors other than the calcium content of the urine.

The age of onset of symptoms and the site of stone formation were those seen in "developed" countries (Anderson, 1969). Whatever factors

cause bladder stone formation in children in certain geographic areas such as rural Thailand (Lonsdale, 1968, Anderson, 1969) these were absent in Singapore.

Indian males accounted for 17.7% of all patients in this survey compared to 4.2% in the Singapore population. This finding is partly explained by the greater proportion of Indians in the outpatient population of the relevant hospitals (Table I) and partly by disproportionately large number of Indians among the age group at risk. The prevalence of hyperparathyroidism in this series was 1.2% which was similar to that found by Milne (1954) and by Gordan (1962).

We were impressed by the large number of patients with sterile pyuria (Table IV) in the absence of any clinical, radiological or bacteriological evidence of tuberculous infection. It is possible that a number of our patients were taking analgesic preparations or had partially treated urinary infections in spite of their statements to the contrary. We consider it more likely that sterile pyuria in stone-forming patients is due to inflammatory changes induced in the urinary epithelium by a foreign body (Huth, 1967). In our series this observation was made in 22 patients (8.7% of the entire series.)

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REFERENCES

1. Anderson, D.A.: "Historical and Geographical Differences in the Pattern of Incidence of Urinary Stones Considered in Relation to Possible Aetiological Factors", in 'Proceedings of the Renal Stone Research Symposium.' Edited by Hodgkinson, A. and Nordin, B.E.C., Churchill, London, 1969.
2. Blackman, J.E., Gibson, G.R., Lavan, J.N., Learoyd, H.M. and Posen, S.: "Urinary Calculi and the Consumption of Analgesics." *Brit. Med. J.*, 2, 800, 1967.
3. Census of Population, Singapore, 1970.
4. Clark, P.B. and Nordin, B.E.C.: "The Problem of the Calcium Stone", in 'Proceedings of the Renal Stone Research Symposium.' Edited by Hodgkinson, A. and Nordin, B.E.C., Churchill, London, 1969.
5. Gordan, G.S., Eisenberg, E., Loken, H.F., Gardner, B and Hayashida, T.: "Clinical Endocrinology of Parathyroid Hormone Excess." *Recent Progr. Hormone Res.*, 18, 297, 1962.
6. Huth, E.J.: "Nephrolithiasis and Nephrocalcinosis", in 'Renal Disease.' Edited by Black, D.A.K., Blackwell Scientific Publications, Oxford, 431, 1967.
7. Lavan, J.N., Neale, F.C. and Posen, S.: "Urinary Calculi: Clinical, Biochemical and Radiological Studies in 619 Patients." *Med. J. Aust.*, 2, 1049, 1971.
8. Lonsdale, K.: "Human Stones." *Science*, 159, 1199, 1968.
9. Melick, R.A. and Henneman, P.H.: "Clinical and Laboratory Studies of 207 Consecutive Patients in a Kidney Stone Clinic." *New Engl. J. Med.*, 259, 307, 1958.
10. Milne, J.: "Primary Hyperparathyroidism." *New Engl. J. Med.*, 251, 307, 1954.
11. Ooi, G.B.: "The Demographic Structure of Modern Singapore", in 'Modern Singapore.' Edited by Ooi, G.B., University of Singapore, 1969.