

Role of Infection in Bladder Stone Disease in Children

Pages with reference to book, From 132 To 137

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Abstract

The urine from 180 children with bladder stone disease (BSD) was cultured for evidence of urinary tract infection. Fifty eight (22.2%) BSD children had positive urine culture. E. Coli was the commonest organism (52%) followed by B. Proteus (31%). There was a significant relationship ($P < 0.001$) between high urinary pH and growth of B. Proteus whereas E. Coli was positively correlated with lower urinary pH. On correlating urinary tract infection with surface constituents of analysed stones, uric acid was more commonly seen in sterile urine ($P < 0.05$). On infrared spectroscopic analysis of calculi calcium phosphate occurred significantly more frequently ($P < 0.01$) in the group with infected urine (JPMA34: 132, 1984).

Introduction

The association between infection and stone formation was scientifically studied in the early part of the present century. Rosenow and Meisser (1922) implanted organism from stone formers in dogs to provide a focus of subsequent urinary tract infection. Hagar and Magath (1928) demonstrated the formation of vesical calculi in urinary bladder of rabbits after instilling bacterial colonies into their bladders.

Some authors have reported urinary tract infection to be an important cause of stone formation (Yendt, 1970; Westbury, 1974; Rose and Harrison, 1974). Others (Malek, 1976; Resnick and Boyce, 1979) failed to find a cause effect relationship between infection and calculus formation. The relationship of poorly mineralized 'matrix' calculi seen commonly with urinary tract infection was thought to be immunologically distinct (Boyce and Garvey, 1956; Boyce, 1969) while others disproved its specificity in stone disease and considered it an adventitious adsorbate on crystals (Vermeulen and Lyon, 1968). Although the relationship between infection and calculogenesis needs further investigation, nucleation of bacteria together with desquamating cells may have some role just as precipitation of phosphate in high urinary pH has a role in the formation of phosphate stones especially with B. Proteus urinary tract infection.

Material and Methods

One hundred eighty children with bladder stone disease and 50 normal children were included in the study done at urology ward, Civil hospital Karachi between July 1979 and June 1982. Detailed history of BSD children was recorded. Both stone formers and controls were examined. Early morning urine specimen from stone formers and normal children was subjected to analysis (Varley, 1969). More than 10 WBC per high power field was classified as pyuria and more than 3 RBC per high power field as haematuria. Crystals were examined by the method described by Hailson and Rose (1976). Urine was cultured by standard laboratory method (Cruickshank et al., 1973). A bacterial count of more 105 per millilitre of urine was considered positive.

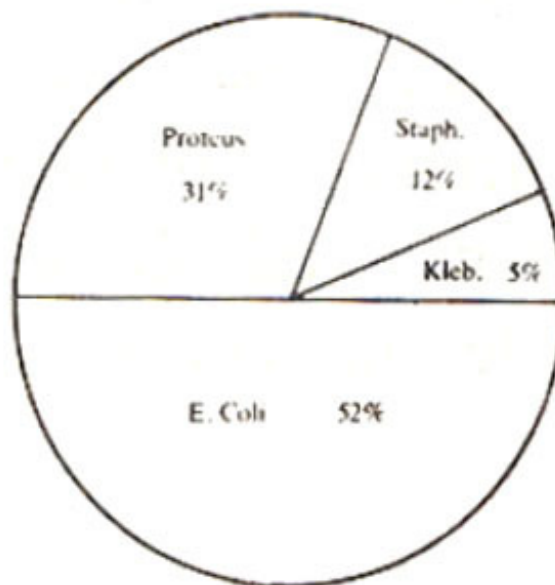
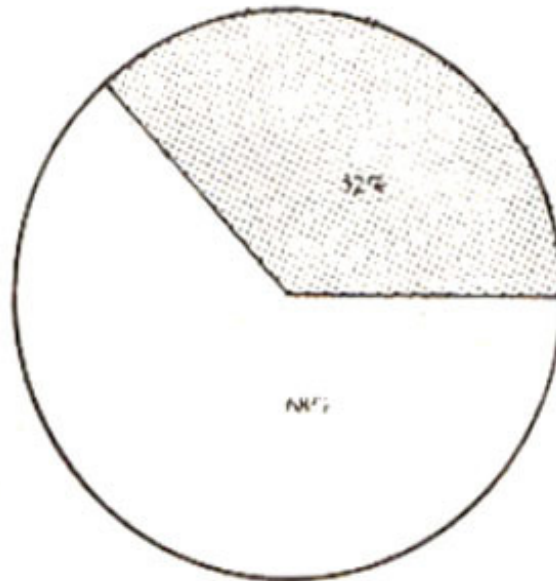
Urinary calculi were analyzed by chemical method (Winer and Mattice, 1942) and by infrared spectroscopy (Tsai, 1961).

Results

The frequency of microscopic pyuria in stone formers was 41% and that of microscopic haematuria was 37.7%. None of the normal children had microscopic pyuria or haematuria within the limits of our protocol. This difference between the normal children and stone formers was highly significant ($P < 0.001$).

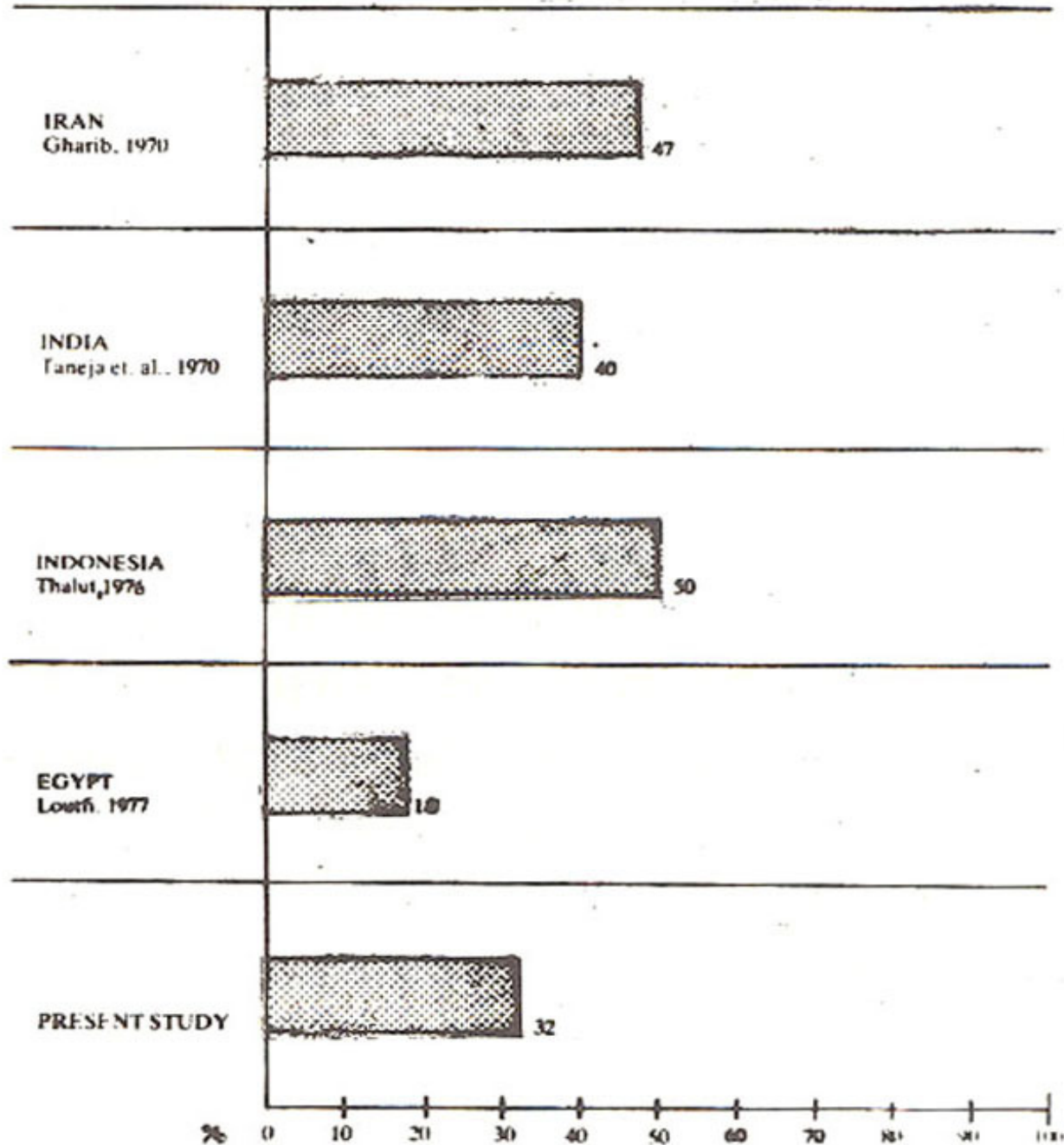
Of 180 stone formers 58 (32%) had positive urine cultures. *E. Coli* was the commonest organism (52%) of all positive cultures followed by *B. Proteus* (31%) (Fig. 1).

URINARY PATHOGEN



None of the 50 normal children had a colony count of more than 105 per ml. of urine.

COMPARISON OF FREQUENCY OF INFECTION IN CHILDHOOD BSD IN SELECTED REPORTED SERIES AND PRESENT STUDY



No significant relationship between the type of organism and the age of stone formers could be seen (Table 1).

Table-1**Relationship of Type of Urinary Organisms With Age Group.**

Age in years	No.	E. Coli	Proteus	Staph	Klebsiella
0 – 6	41	21	14	4	2
6 – 12	17	9	4	4	1
Total	58	30	18	7	3

No pattern could be seen between the frequency of different symptoms in the infected and non infected groups of stone formers . Haematuria was more frequently seen in the infected group (34%) compared to the uninfected (20%). The type organisms showed no relationship with either the symptomatology or the duration of symptoms.

All the 18 children with B. Proteus infection had urinary pH greater than 6.5 (Table II).

Table – II**Relationship of Type of Organisms With Urinary pH**

Group	No.	E. Coli	Proteus	Staph	Klebsiella
PH > 6.5	30	8	18**	3	3
PH < 6.5	28	22*	0	4	0

*P < 0.02

**P < 0.001

E. Coli was seen in significantly higher number of cases (P < 0.02) with lower urinary pH.

A positive correlation was found between the occurrence of phosphate crystals and B. Proteus urinary infection (P < 0.01) (Table III).

Table – III**Relationship of Organisms With Crystalluria.**

Type of organisms	No.	Type of Crystals		
		Oxalate	Urate	Phosphate
E. Coli	30	14	13	1
Proteus	18	1	2	17*
Klebsiella	3	—	1	2
Staphylococcus	7	3	3	2

* P < 0.01

A significantly higher ($P < 0.001$) occurrence of post operative complications occurred in patients with urinary tract infection (67.3%) compared to the group with no complications in whom the occurrence of infection was 17.9% (Table IV)

Table– IV**Relationship of Urinary Tract Infection With Post–Operative Complications.**

Group	Urinary tract infection present	
Complications absent (106)	19	(17.9%)
Complications present (52)	35*	(67.3%)

*P < 0.001

A relationship between the urinary infection and surface constituents of calculi was sought. Uric acid occurred on the surface of calculi in significantly higher number ($P < 0.05$) in patients who had sterile urine (table V).

Table –V
Relationship of Urinary Infection of Surface Constituents of Calculi.

Group	Calcium oxalate	Ammonium urate	Calcium Phosphate	Uric acid	Magnesium ammonium phosphate
Urine infection present (26)	25 (96.1%)	10 (38.5%)	14 (53.8%)	2 (7.7%)	3 (11.5%)
Urine infection absent (53)	53 (100%)	16 (30.2%)	12 (22.6%)	18* (40%)	3 (5.7%)

* P < 0.05 Note Surface layer analysis was alone in 79 samples .

On infrared spectroscopic analysis of calculi calcium phosphate occurred significantly more frequently (P < C.05) in the group with infected urine (Table VI).

Table – VI
Relationship of Urinary Infection to Occurrence of Common Constituents of Calculi by Infrared Spectroscopy.

Group	No.	Calcium oxalate	Calcium phosphate	Uric acid	Magnesium ammonium phosphate
Urine infection present	27	22 (81.5%)	19* (70.4%)	6 (22.2%)	6 (22.2%)
Urine infection absent	53	48 (90.6%)	12 (22.6%)	27 (50.9%)	3 (5.7%)

*P < 0.01

Occurrence of phosphate in surface and the central portions of calculi was seen in less than one third samples on chemical analysis (Table VII).

Table – VII

Occurrence of Common Constituents in Surface And Central Layers of Calculi.

Stone layer	Calcium oxalate	Ammonium urate	Calcium phosphate	Uric acid	Magnesium ammonium phosphate
Surface (80)	78	26	26	20	6
Centre (73)	59	46	20	12	4

Discusswn

Most authors have considered haematuria and pyuria in childhood BSD, but in the connotations of clinical presentation. However Aurora et al. (1970) analysed 38 urines and found more than 5 WBC per HPF in 36.8% cases, which is in agreement with the present study, but they found no relationship of RBC and WBC to each other or the presence or absence of infection. The absence of microscopic haematuria and pyuria in about 60% of our BSD patients shows that majority of children presented as uncomplicated cases. Haematuria and pyuria appears more an indicator of obstruction, trauma and infection which is more often seen in renal lithiasis (Ghazali, 1975; Scholten et al., 1976. Malek and Kelalis, 1975).

Many workers have reported the incidence of urinary tract infection in childhood BSD ranging from 18 to 50% (Fig.2). There is a broad agreement that *E. Coli* is the commonest organism followed by *B. Proteus* (Eckstein, 1961; Taneja et al., 1970; Gbarib, 1970; Rizvi, 1975; Thalut et al., 1976; Loutfi and Abdel-Hamid, 1977). In the West where childhood urolithiasis, is predominantly of upper tract type, the incidence of infection has varied from 29 to 75% and *B. Proteus* as the commonest isolate (Ghazali et al., 1973; Gaches et al., 1975; Noronha et al., 1974; Brueziere et al., 1977). The difference not only in the type of organism but in the frequency of infection between upper and lower tract stone disease needs further investigation.

No significant relationship could be seen between the type of organism and the age groups, nor were the symptoms or their duration related to the different isolates. There are no studies that have focussed attention on this aspect.

All 18 children who had *B. Proteus* infection had a urinary pH higher than 6.5 (range 6.5-8) and phosphate crystalluria was positively correlated with *B. Proteus* infection (Table III). *B. Proteus* is a urea splitting organism due to the action of nickel metalloenzyme urease on urinary urea (Fishbein, 1981). The urea is hydrolysed to NH_3 and HCO_3 which causes a sharp rise in the urinary pH so that the formation product of apatite and struvite is exceeded, forming insoluble precipitate (Fishbein, 1981) which is excreted as phosphate crystals and their aggregates.

In the present study *E. Coli* was associated with lower urinary pH ($P < 0.02$) and oxalate (as well as urate) crystalluria. Loutfi et al. (1974) have reported a similar finding. Aurora et al. (1970) showed no correlation between crystalluria and urinary tract infection. Our findings can be explained on the propensity of proteus infection to cause alkalinity of urine resulting in precipitation of phosphate. *E.*

Coli is known to grow in acid urine where the formation product of urate (and oxalate) is more likely to be exceeded.

It is not surprising that the frequency of post-operative complications (wound infection being the commonest) were higher in the infected group. A mandatory urine culture and measures like appropriate antibiotics, high fluid intake (and change of urinary pH in suitable cases) preoperatively is strongly advocated.

The significance of uric acid on the surface of stone in sterile urine is explicable on the low urinary pH in uninfected children where the formation product of urate is more likely to be exceeded, resulting in urate crystalluria, which is likely to form the surface layer on the existing calculus.

The analysis of central portions (containing the nucleus) showed that less than one third calculi had phosphate in the form calcium phosphate (CaP) or magnesium ammonium phosphate (MAP). Some workers have classified stones containing predominance of CaP & MAP as infection stones (Griffith et al., 1976; Robertson and Peacock, 1982). Thus the role of infection in childhood BSD does not appear to be primary but rather incidental facilitated by the presence of stone acting as a foreign body in the bladder. However, proteus infection known to cause high urinary alkalinity may cause crystallization of phosphate leading to formation of phosphate stone.

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