German study where it was found that high-grade ventricular arrhythmias seemed to be related to more depressed ventricular function.3 (Table 1).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Death</th>
<th>No Death</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syncope</td>
<td>Yes</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>High grade ventricular arrhythmias</td>
<td>Yes</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Intraventricular conductive defect</td>
<td>Yes</td>
<td>6</td>
<td>8</td>
</tr>
</tbody>
</table>

Mean LVEDD among males and females were 56.1mm and 55.56 mm respectively. 44(64.7%) patients had EF <35%. RVD was noted in 24 cases (35.29%). EF<35% and RVD had good relation with severity of symptoms. Contrary to certain reports, the severity of symptoms did not correlate with LVEDD in our patients.2 (Table 2).

<table>
<thead>
<tr>
<th>Echo parameters</th>
<th>Moderate to severe symptoms</th>
<th>Mild Symptoms</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ejection Fraction &lt;35%</td>
<td>26</td>
<td>4</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>&gt;35%</td>
<td>14</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Left ventricular end diastolic dilatation Yes</td>
<td>26</td>
<td>8</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>No</td>
<td>14</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Right ventricular dilatation Yes</td>
<td>22</td>
<td>4</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>No</td>
<td>12</td>
<td>12</td>
<td></td>
</tr>
</tbody>
</table>

In conclusion, the present study shows that younger patients and females with IDCM have a favorable outcome. Syncope is a strong predictor of mortality in these patients irrespective of the NYHA class. Electrocardiographic evidence of IVCDs and high-grade VAs is associated with poor prognosis. Reduced ejection fraction and right ventricular dilatation is associated with severe symptoms; whereas left ventricular end diastolic dimension do not have any prognostic value.


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Mycobacteriuria – Whether a Forerunner of Manifest Tuberculosis?

Sir,

Diagnosis of tuberculosis continues to be a challenge. Difficulty in localization of the active lesion and its inaccessibility for appropriate sampling – account for the diagnostic uncertainty. At present, diagnosis of Tuberculosis relies upon tissue diagnosis, mycobacterial culture, polymerase chain reaction (PCR—tuberculosis) and detection of acid fast bacilli (AFB) in appropriate diagnostic material.

Sputum smear for AFB has been a standard diagnostic method for pulmonary tuberculosis, while detection of AFB in urine has been equated to urinary tract tuberculosis in the text books. In our experience, a case has been encountered with AFB in urine without evidence of urinary tract tuberculosis. Conversely, detection of AFB in urine without any evidence of tuberculosis at that time has been harbinger of extrapulmonary tuberculosis eventually. A purposive follow-up of two proven cases of tuberculosis showed urine positive for AFB. With this background, 607 cases suspected/proven to be tuberculosis, were followed up with various investigations including 24 Hour urine analysis for AFB. The results indicate that the latter has high predictive value for tuberculosis at varied sites in body. There appears to be a justification to consider this investigation as confirmatory or predictive of tuberculosis.

Case – I : An eleven years male, case of end-stage renal disease (ESRD) due to bilateral extensive nephrolithiasis was scheduled for renal transplant. His 24-hour urine was tested for AFB as routine transplant work-up. It showed presence of AFB in urine consistently. After six weeks of anti-tubercular therapy (ATT), renal transplant was done along with bilateral nephroureterectomy under the presumption of removing tuberculous focus. Diligent gross and microscopic examination of both kidneys and ureters did not reveal any tubercular focus.

Case – II : A 35 years male with complaints of post dinner chills lasting 5-10 minutes. Twenty-four hour urine tested positive for AFB and PCR-tuberculosis. No clinical and imaging evidence of tuberculosis was found. Treatment was not instituted. He later developed backache and was detected to have Pott’s spine 4 months after urine tested positive for AFB.

Case – III and IV : Twenty-four hours urine was tested for AFB in one case each of (a) Biopsy confirmed Tuberculous lymphadenitis and (b) sputum AFB positive pulmonary tuberculosis. Both cases predictably revealed AFB in urine deposit.

Based on these observations a pathogenic mechanism
intermittent bacillemia and bacilluria in tubercular pathology was thought of. Observations in a larger series buttress this hypothesis.

Twenty-four hour urine deposits of 607 patients suspected of or known cases of tuberculosis were tested for presence of AFB. Ten apparently healthy volunteers were tested for AFB in urine on 3 consecutive days as controls. Urine samples were collected in clean plastic bottles rinsed with formalin and dried by spirit. A 50 ml aliquot of gravity sediment of the sample was divided in 4 tubes and centrifuged at 2000 rpm for 30 minutes. One smear was made from each tube deposit and stained by Ziehl-Neelsen (ZN) method, the decolouriser being 20% acid and alcohol. At least 300 oil immersion fields were screened in each smear before reporting as negative. Negative cases were retested on two more occasions preferably on consecutive days. Three negative tests were deemed as “Negative for AFB”. Fifty AFB positive samples were submitted for PCR-tuberculosis at another laboratory. Ten AFB positive samples were tested for AFB culture in our laboratory.

Six hundred and seven cases of clinically suspected or biopsy confirmed tuberculosis were screened for AFB in 24-hour urine deposits, during July 2000 to December 2001. Of these, 311 tested positive for AFB by smear microscopy (Fig. 1, 2-A, B). Of these 311 urine AFB positive cases, 72 had a confirmed tissue diagnosis of tuberculosis that consisted of lymph node biopsy (53), Pott’s spine (12), pleural biopsy (2), ileocaecal junction (2), tuberculoma (1), ureteral nodule (1) and kidney biopsy(1).

The 311 urine AFB positive cases had protean clinical presentations, like pyrexia of unknown origin (PUO) (184), lymphadenopathy (73), backache (16), urinary symptoms (12), respiratory symptom (10), abdominal pain (8), CNS symptoms (6) and fatigability (2).

PCR-tuberculosis test was carried out on smear positive urine sample in affording patients only. Of the 50 samples tested, 48 were positive for PCR-tuberculosis with IS 6110 primer at 68°C annealing temperature. Culture for AFB on Lowenstein-Jensen medium was done in 10 cases with a positive result in 8 cases.

Out of apparently healthy volunteers, one tested positive for AFB and PCR-tuberculosis. This person eventually developed cough and fever with AFB in sputum 2 months after urine tested positive. Clearance of urine AFB was noted after 3 months of ATT in 8 cases available for follow-up.

Urine AFB has conventionally been equated with urinary tract tuberculosis in text books. It was fortuitous for us to be able to examine both kidneys and both ureters with no tuberculosis in a urine AFB and PCR positive case (Case - I) suggesting non-renal tuberculosis showing AFB in urine. This was further substantiated by Case - II that was urine AFB positive for 4 months prior to being symptomatic for Pott’s spine as also by one apparently healthy volunteer developing pulmonary tuberculosis 2 months after urine testing positive for AFB.

With evidence based clinical practice, a definitive diagnosis of tuberculosis has become imperative for starting anti- tubercular chemotherapy. Besides biopsy and AFB culture, the other diagnostic methods accepted widely are PCR and serological methods (anti-Tuberculosis IgG, IgM and IgA). However, the costs of PCR and serological tests are prohibitive for patients of tuberculosis in developing countries. Accessibility is a limitation for biopsy of imaging detected lesion. Time required for culture report makes it impracticable investigation for starting therapy. On this background, a simple test as urine deposit smear may be a boon to the poor patients in developing countries.
Recovery of etiological organism from urine in systemic infection is a well established phenomenon, exemplified by salmonella and leptospira. However the detection of AFB in urine attains far more importance especially for extrapulmonary tuberculosis because the yield of AFB from CSF, effusions, aspirates or joint fluids is very low and lesion accessibility for biopsy may be a severe limitation for tissue diagnosis.

As to the identity of AFB in urine, a 96% concordance of PCR-tuberculosis with smear asserts the observed AFB as *Mycobacterium tuberculosis* and rules out *Mycobacterium smegmatis*. Contrary to the groundless yet widely held belief, *M. smegmatis* is a rare contaminant in urine. Webster had observed AFB in urine from cases of skeletal tuberculosis while Munro cultured *M. tuberculosis* from urine of cases without evidence of renal disease. However, in subsequent years these findings were probably lost in cloud of doubt about contamination by *M. smegmatis*.

The observations of – (a) absence of tubercular lesions in Case – I, (b) presence of AFB in urine months ahead of Pott’s spine in Case – II as well as in apparently healthy volunteer, (c) biopsy confirmed cases of non-renal tuberculosis showing AFB in urine and (d) PCR proven identity of *M. tuberculosis* in their urine being positive for AFB – taken collectively indicate that acid-fast bacilluria may (i) confirm tuberculosis in localized indicative lesions; (ii) may corroborate with the clinical diagnosis of Tuberculosis with classical symptoms (iii) may be used as a second line investigation in cases of PUO or backache with equivocal results of first line investigations of routine blood, urine, stools & sputum examination (iv) may herald manifest tuberculosis – particularly in case of contacts of diagnosed cases of tuberculosis. Urine deposits tested positive for AFB in a symptomatic case later on turning negative may have a prognostic value superior at least to ESR that is relied upon today.

Tubercular bacillemia with acid-fast bacilluria appears to be the mechanism that can be hypothesized to explain these findings. Thus, there appears to be a strong case for multi-centric trials for cohort studies for 24 hour urine deposit for AFB as a predictor of tuberculosis. Also, sensitivity, specificity and predictive value for a positive test needs to be worked out with appropriate case-control studies.

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