

## Clinicopathological association between BPH and prostatitis

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### ABSTRACT

This was a prospective study done in Nepal Medical College Teaching Hospital, Kathmandu, Nepal to find out the relationship between BPH and BPH associated with prostatitis as regards their symptoms and histopathology. We looked at the symptoms of both disease processes and tried to establish whether we could differentiate between the two entities on a clinical basis. Our study included thirty six patients who were operated for symptoms suggestive of LUTS due to BPH. Prior to the operation they were asked about their symptoms and we correlated these for the two conditions. We analysed the results of the symptoms statistically according to the odd's ratio. We found that the most common symptom associated with BPH with prostatitis was dysuria, however, there was a lot of overlap of the symptoms. So unless there is a high degree of suspicion on the part of the health care worker it is difficult to make a diagnosis of prostatitis based on symptoms alone and it is difficult to distinguish between the two conditions. The histopathological specimens were analysed and it was found that 19 of the 36 patients had prostatitis associated with BPH. This was done by scrutinising the received histopathological specimens. Here it was found that the most common type of prostatitis associated with BPH was the stromal inflammatory pattern.

**Keywords:** BPH, prostatitis, symptoms, histopathology.

### INTRODUCTION

Benign prostatic hyperplasia is one of the most common benign diseases affecting men. There has been evidence to show that this disease progresses with age.<sup>1</sup> However, it has been suggested that prostatitis is also relatively common and affects quite a percentage of men. In fact, data shows that the two diseases seem to co-exist in a high percentage of cases. However, the diagnoses of prostatitis is based on clinical symptoms, some clinical findings, culture results and in some cases demonstration of inflammation in prostate fluid and a vast majority have overlapping symptoms of BPH and prostatitis.<sup>2</sup> Clinical prostatitis can be divided into acute and chronic bacterial prostatitis (National Institute of Health category I and II), rare infectious diseases of the prostate gland, the much more common chronic prostatitis/chronic pelvic pain syndrome (category III chronic prostatitis/chronic pelvic pain syndrome or CP/CPPS) and asymptomatic inflammatory prostatitis (category IV).<sup>3</sup> Histological prostatitis refers to the confirmation of prostate inflammation by microscopic examination. Asymptomatic prostate inflammation would be categorised as Category IV.

Prostatitis has traditionally been considered a condition which inflicts younger men, but it is apparent that it is common in older men.<sup>4</sup> Prostatitis is characterized primarily by pain. Pain and/or discomfort on ejaculation is one of the most common and bothersome symptoms,

but also the most differentiating symptom experienced by men with chronic prostatitis.<sup>5</sup> On the other hand BPH is associated with lower urinary tract symptoms (LUTS) associated with benign prostatic enlargement (BPE) causing bladder outlet obstruction (BOO). Here the symptoms are divided into obstructing or voiding and irritative or filling symptoms.<sup>6</sup> These symptoms include decreased flow in urine, hesitancy, intermittency, post maturation dribbling and feeling of incomplete voiding. They also include urgency, urge incontinence, increased frequency and nocturia. Dysuria is a symptom which may also be present and may include pain/discomfort over the perineal, prostate or suprapubic region. Patients also give a history of burning maturation which is classically dysuria. Having said this however, LUTS is also associated with other disease conditions, such as prostatitis, prostate cancer and obstructed or neurogenic bladder conditions.

In this study we are trying to find out if there is an association between BPH and prostatitis and if the two diseases co-exist in certain cases. We are also trying to determine whether the health care providers have sufficient suspicion of prostatitis to make a diagnosis before hand and whether this will help in subsequent treatment of the patient.

### MATERIALS AND METHODS

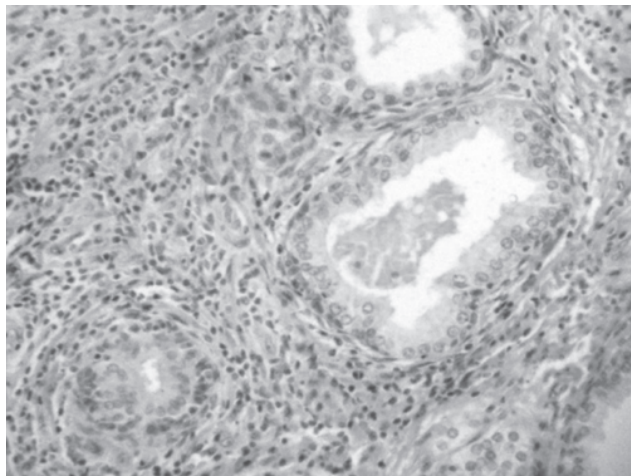
This is a two year prospective study conducted in Nepal

**Table-1:** The grade and inflammatory pattern of prostatic inflammation in cases of bph with prostatitis

Inflammatory pattern	Peri-glandular			Glandular			Stromal			Peri-urethral		
	1	2	3	1	2	3	1	2	3	1	2	3
Inflammatory grade	1	2	3	1	2	3	1	2	3	1	2	3
Frequency	4	7	1	2	3	0	5	7	1	3	1	0
Total	12			5			13			4		

Medical College Teaching Hospital (NMCTH), Kathmandu, Nepal. The study period was from November 2009 to November 2011 where we examined 36 patients who underwent surgery for LUTS. The histopathology slides were studied to confirm their diagnoses of both BPH and prostatitis. The slides were scrutinised to evaluate acute and/or chronic intraprostatic inflammation (ACI) based on the presence of oedema, vascular congestion, lymphoplasmacytic infiltrates and numerous neutrophils within prostatic acini infiltrating the lining epithelium with extension into the surrounding stroma. The sections were stained with haematoxylin and eosin and examined using light microscopy. Based on a study done by Nickel, we categorised prostatitis according to the amount of inflammatory infiltrates present within certain areas of the prostatic tissues.<sup>7</sup> The categories included periglandular, stromal, glandular and periurethral areas. These were further subdivided into grades 1 to 3 depending on the number of inflammatory infiltrates. On identifying slides and confirming the histopathological diagnosis of prostatitis we went through the record files for these patients. Here we looked through the symptoms they had presented with and tried to correlate them with the ultimate histopathology diagnoses. This was with a view to find out if the clinician had previously suspected symptoms which would suggest a diagnosis of prostatitis.

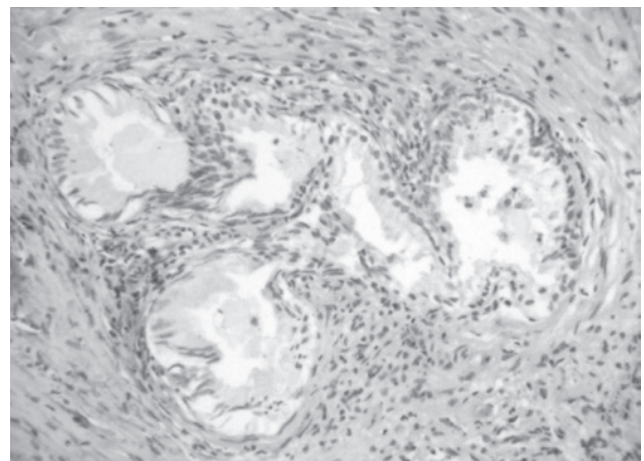
The data were analyzed using SPSS 19 by logistic regression using the odds ratio.



**Fig. 1.** Peri-glandular inflammation: Grade 1: scattering of chronic inflammatory cell infiltrates (typically lymphocytes). (H & E X100).

## RESULTS

We looked into thirty-six patients who had surgery for LUTS suggested to be due to BPH. The histopathology slides were examined and the diagnosis of BPH was confirmed. Those patients who were suggested to have prostatitis were categorised as glandular, periglandular, stromal or peri-urethral and the inflammatory cell density graded from 1 to 3.<sup>7</sup> Out of a total number of 36 patients who underwent surgery for LUTS we found out that 19 of them had associated prostatitis with BPH. The rest of them had only BPH. This meant that out of the total number of patients who underwent a procedure for LUTS due to BPH 52.7% of them had BPH associated with prostatitis. Out of 19 cases of prostatitis we found stromal infiltration of inflammatory cells to be predominant, followed by periglandular infiltrates. However, there was also an overlap in most of the specimens between periglandular, glandular, stromal and periurethral inflammatory infiltrates (Figs. 1-4). Hence, the total numbers of stromal infiltrates were 13, followed by periglandular which were 12 and glandular and periurethral being 5 and 4 respectively (Table-1). These infiltrates were further divided into grades ranging from 1 to 3 based on the number of inflammatory cell infiltrates which is shown in the chart. As can be seen grade 2 infiltrates were found to be the most in the stromal and periglandular inflammatory pattern. The average age of people who had BPH alone was 70.71 and that with BPH with associated prostatitis was 69.37 years. We did not find a significant difference between the ages at the time of operation.



**Fig. 2.** Glandular inflammation: Grade 2: heavier intraepithelial and luminal inflammatory infiltrates with areas of epithelial destruction. (H & E X 100).

**Table-2:** Odds ratio of the different variables analyzed while comparing cases of bph and bph with prostatitis

Variables	Odds Ratio
Dysuria	3.3
Frequency	0.935
Urgency	1.28
Hesitancy	2.722
Intermittency	0.889
Incontinence	0.889
Hematuria	0.882

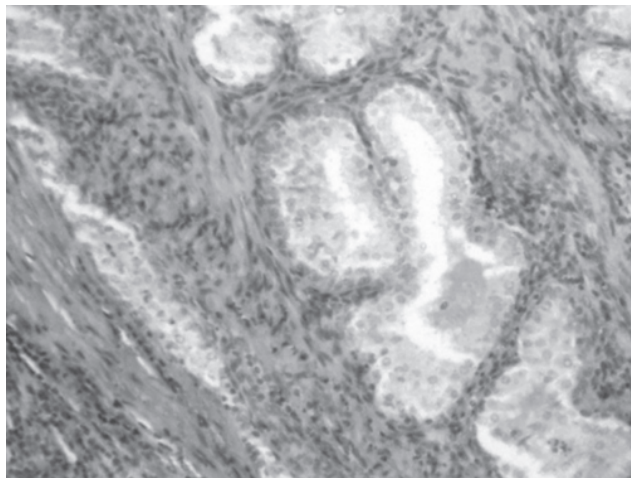
We also looked at the symptoms that were related to BPH alone and with BPH associated with prostatitis. We found that the predominant LUTS presentation for patients with BPH alone and with BPH associated with prostatitis were very similar. However, it was noted that certain symptoms were more prominent in patients with associated prostatitis (Fig. 5). Our findings suggested dysuria as one of the predominant symptoms of patients with prostatitis. This was followed by frequency and urgency. We proceeded to take out the odds ratio using SPSS version 19 to see if there was any statistical significance as regards the symptoms at presentation. Our results are displayed in the table. As can be seen the chances of someone having associated prostatitis along with BPH is 3.33 times more if that person presents with symptoms suggestive of dysuria. This is only 0.935 with frequency, 1.2 times with urgency, 2.72 with hesitancy, 0.889 with intermittency, 0.889 with incontinence, and 0.882 with haematuria (Table-2).

**DISCUSSION**

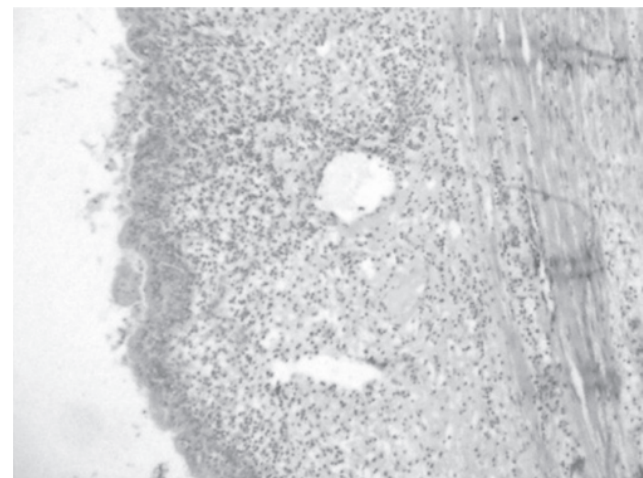
BPH is a common clinical syndrome among aging men that is typically diagnosed with the onset of lower urinary tract symptoms (LUTS), increased prostate size, and

decreased urinary flow rates in the absence of other causes.<sup>8,9</sup> Similarly prostatitis is the most common presenting diagnosis for men less than 50 years of age in outpatient urology clinics with an estimated prevalence ranging from approximately 2% to 16%, depending on the population studied, and the definition used.<sup>10-12</sup> This data is predominantly what is seen in the Western countries. However studies in our part of the world have shown the incidence of prostatitis to be as high as 51% and 46.4% as mentioned in the study conducted by Mishra et al and Asgari and Mohammadi.<sup>13,14</sup> In our study of all the people who underwent surgery for LUTS 52.7% of them had prostatitis on histopathological examination which is similar to the previous mentioned two studies. It is important to mention that our results were based on people who underwent surgery which is considered the end point for people who suffer from LUTS. This high prevalence of prostatitis is something that needs to be studied further. This is in regard to most studies which have questioned whether prostatitis plays a role in ultimately developing BPH.<sup>15,16</sup> The interesting thing to note however is that in our study we did not find a significant age difference between patients who had BPH and BPH associated with prostatitis. This may be due to the fact that people in our country do not seek immediate medical attention for symptoms unless they become severe enough to warrant surgical intervention.

One of the reasons for conducting this study was also to find out if prostatitis could be identified in patients with overlapping BPH prior to surgery and histopathological diagnosis. The thinking was that if this could be done then maybe treating prostatitis may prevent people from developing BPH, as some studies suggest that there may be a relation between prostatitis and ultimate development of BPH.<sup>17, 18-20</sup> As suggested all our patients



**Fig. 3.** Stromal inflammation: Grade 3: sheets of confluent stromal inflammatory cells. (H & E X 100).



**Fig. 4.** Peri-urethral inflammation: Grade 2. Heavy inflammatory infiltrate with confluent areas and edema in submucosa and adjacent stroma. (H & E X 100).

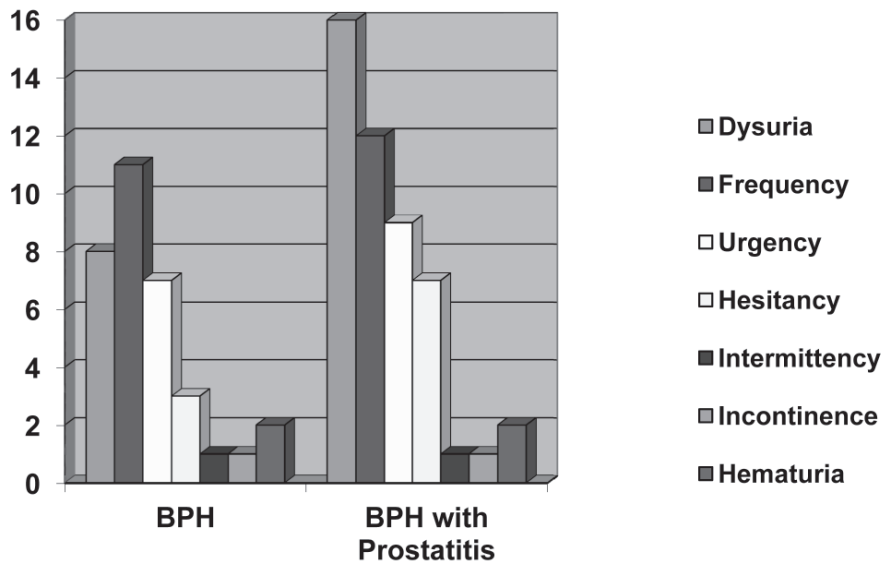


Fig. 5. Frequency of various symptoms in bph and bph with prostatitis

had reached the end point of their disease process which in cases is taken as the need for surgery. However, it remains to be seen if these patients were given proper medication for prostatitis would it have prevented them from having to undergo surgery. The other question is whether it would have postponed surgery further by a few more years. These questions although being hypothetical may have been answered if the clinicians had a higher degree of suspicion for cases having prostatitis along with BPH. This could probably have been done by identifying symptoms for prostatitis. This is obviously very difficult as there is an overlap of symptoms as previously mentioned. However, in all studies it has been suggested that pain or dysuria may favour a diagnosis of prostatitis.<sup>6,21,22</sup> In our study also people have given a history of dysuria but they have unfortunately not commented exactly on the type of pain experienced. In spite of this it has been shown statistically that dysuria was 3 times more common as a symptom in patients who had BPH associated with prostatitis. The other factor which is more in favour of prostatitis was suggested to be painful ejaculation.<sup>23-25</sup> However, this finding was difficult to elicit among our patient group in spite of repeated leading questions. This may be due to the fact that these kinds of questions are still taboo in our society.

In our study as suggested earlier we studied the specimens and categorized them into various patterns of inflammatory infiltrates. This was the basis of diagnosing prostatitis. The stromal pattern of infiltrates predominated followed by periglandular infiltrates. This was found to be different compared to the study done by Nickel, Downey, Young and Boag who found that periglandular inflammation was the most common single pattern of prostatic inflammation.<sup>7</sup> In fact they described

grade 1 periglandular infiltrates to be present in all their specimens, whereas we only had 21% of patients having this pattern. Our most common pattern as mentioned earlier was grade 2 stromal infiltrations which accounted for 36.8% of the cases. This was in contrast to the above mentioned study which showed their predominant pattern to be grade 1 inflammation in all the categories. No substantial conclusion could be drawn on the basis of these finds in our study regarding the significance of these infiltrative patterns. Nickel, Downey, Young and Boag in their

study have also come up with the conclusion that there was no correlation between the degree and pattern of inflammation, catheterization, presence of bacteria, serum PSA or PSA density in cases of asymptomatic category IV chronic prostatitis associated with BPH.<sup>7</sup> Prostatic inflammation is an extremely common histological finding in patients with symptoms of BPH who have no symptoms of prostatitis. We do acknowledge the presence of dysuria in cases of prostatitis associated with BPH. But only 62.5% of dysuria cases had histopathologically confirmed diagnosis of BPH with prostatitis. 21% cases of BPH with prostatitis had no clinical symptoms. Hence the clinical significance of asymptomatic Category IV chronic prostatitis associated with BPH and the various patterns of inflammation have yet to be determined.

In our study, we looked at the association between patients with BPH alone and BPH with prostatitis as regards to their lower urinary tract symptoms. As shown in previous studies it is difficult to come to a definite conclusion due to an overlap of symptoms in both patient groups. However, patients with BPH associated prostatitis do definitely give a history of dysuria/ pain more frequently than the other group. Having said this, the health care worker does need a high degree of suspicion to diagnose prostatitis. Again as demonstrated in previous studies, there seems to be a relation between prostatitis and the development of BPH, which has also been seen with the histopathological slides. In our study the most common histopathological type of prostatitis associated with BPH was the stromal inflammatory pattern. However, we cannot draw a definite conclusion from this study alone. Our study was hampered due to the small sample size, hence, we recommend studies with more number of patients to verify our findings.

ACKNOWLEDGEMENTS

We would like to thank the staff of the Department of Pathology at NMCTH along with Mr. Prem Pant from the Department of Community Medicine for their help.

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