Original Article

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Prevalence of Prostatic Intraepithelial Neoplasia in Patients Diagnosed as Benign Prostatic Hyperplasia Underwent Transurethral Resection of the Prostate at a Rural Teaching Hospital, India

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Abstract

Introduction: High grade prostatic intraepithelial neoplasia (HGPIN) is the most likely precursor of prostatic adenocarcinoma. In recent years, many studies have been shown that HGPIN is a major precursor of prostate cancer. It is very important to diagnose and correctly use the term HGPIN and to avoid confusion with other atypical entities of the prostate, which may differ with respect to clinical significance.

Purpose: To determine the prevalence of HGPIN in patients who underwent transurethral resection of the prostate (TURP) for benign prostatic hyperplasia (BPH).

Materials and Methods: It is a retrospective study, data collected from the medical records for the duration from January 2009 to September 2014, patients who underwent TURP for BPH at RL Jalappa Hospital, Kolar, India. Histopathology reports of all the patients who underwent TURP were analyzed, and reports with PIN tabulated.

Results: In the above study, 348 patients underwent TURP during the period enclosed. Among the above, a total 66 patients were found with histopathology showing with PIN (n = 66). Of which, HGPIN patients were 16 ($n1$ = 16) and Low grade PIN patients were 50 ($n2$ = 50).

Discussion: Earlier studies have shown that low grade PIN was significantly different from HGPIN in terms of cancer risk and was not associated with an increased risk of cancer any more than is the initial negative biopsy. Despite its histologic similarity to carcinoma *in situ*, a precursor to invasive cancer that arises in other organs (e.g. breast or skin). The finding of HGPIN with adjacent small atypical glands indicates a situation quite different from isolated HGPIN.

Conclusion: The study has conclusively shown there is a high prevalence of HGPIN in prostatic specimens and reported as BPH clinically in our hospital. The identification of increased number of HGPIN has an important implication for the management of the patient.

Key words: Benign prostatic hyperplasia, Neoplasia, Transurethral resection of the prostate

INTRODUCTION

High grade prostatic intraepithelial neoplasia (HGPIN) is a pathologic reading, something that the pathologist might see on a needle biopsy or on a prostate that's been surgically removed. HGPIN is a most likely precursor of prostatic adenocarcinoma.[1,2] The usual cell type comprising HGPIN is a glandular secretory epithelial cell. Squamous differentiation has been described in the benign prostate and prostatic carcinoma, but to our knowledge has not been previously reported in HGPIN. In recent years, many studies have shown that HGPIN is the major precursor of prostate cancer.

Most foci of PIN in young men are low grade, with increasing frequency of HGPIN with advancing age. The

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volume of HGPIN also increases with patient's age.[3] Race and geographic location may also influence the incidence of HGPIN. African and American men have a greater prevalence of HGPIN than whites in the 50-60 years age group. In contrast, Japanese men living in Osaka, japan has a significantly lower incidence of HGPIN than men residing in the United States and Asians have the lowest clinically detected rate of prostate cancer.[4]

In contrast to HGPIN, the presence of low grade PIN is distinctly different ND has no clinical significance. As a result, men with low grade PIN do not require a repeat biopsy unless other clinical indicators are present. In addition, using the term low grade PIN in the pathology report can lead to confusion with HGPIN.

PIN does not significantly elevate serum prostatic specific antigen (PSA) concentration and cannot be detected by ultrasonography.[5] It is very important to diagnose and correctly use the term HGPIN and to avoid confusion with other atypical entities of the prostate, which may differ with respect to clinical significance. This study aims to clarify the diagnostic terms used in pathology reports and implications of the terminology upon clinical management.

Objective

To determine the prevalence of HGPIN in patients who underwent transurethral resection of the prostate (TURP) for benign prostatic hyperplasia (BPH).

MATERIALS AND METHODS

It is a retrospective study; data collected from the medical records for the duration from January 2009 to September 2014, in patients who underwent TURP for the BPH at RL Jalappa Hospital, Kolar, India.

Histopathology reports of all the patients who underwent TURP were analyzed and reports with PIN tabulated. In our study, total number of 348 patients who underwent TURP for BPH was included.

All the patient's reports are tabulated as different groups as reports patients with normal prostatic cells, reports with low grade PIN and HGPIN.

RESULTS

In the above study, out of 348 patients who underwent TURP during study period of four years 9 months, we found the following biopsy reports. Biopsy reports of TURP specimen: (1) BPH, (2) PIN, (3) adenocarcinoma, (4) squamous metaplasia, (5) basal cell hyperplasia, and (6) chronic prostatitis.

Among the above, a total 66 patients were found with histopathology showing with PIN (n = 66). Of which, HGPIN patients were 16 ($n1$ = 16), and low grade PIN patients were 50 ($n2$ = 50) (Figures 1 and 2) (Table 1).

DISCUSSION

HGPIN has a high predictive value as a marker for adenocarcinoma. A repeat biopsy is generally indicated in men with HGPIN. Earlier studies showed that low grade PIN was significantly different from HGPIN in terms of cancer risk $P < 0.05$, $P < 0.001$, and $P < 0.01$ and was not associated with an increased risk of cancer any more than is the initially negative biopsy.[6-8]

HGPIN is considered as a precancerous lesion. HGPIN is often diagnosed in a prostatic specimen obtained for a

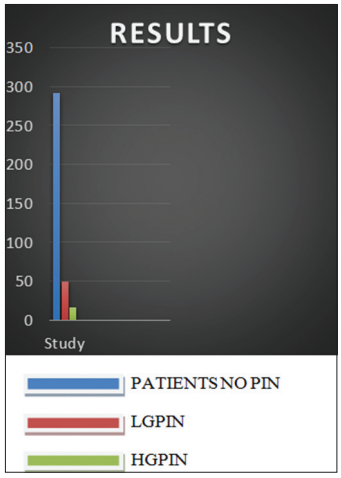

Figure 1: Number of patients with PIN

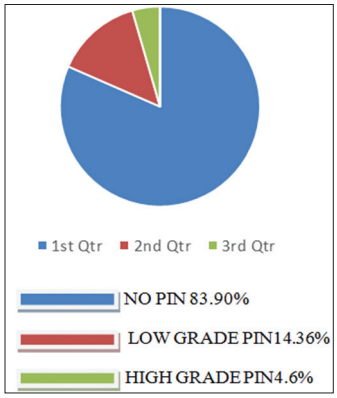

Figure 2: Percentage of patients with PIN

Table 1: Age distribution of patients studied

Years	N
61-70	124
71-80	157
81-90	52

diagnostic test (needle core biopsy) or for the treatment of non-neoplastic prostate pathology (such as TURP specimens for BPH). HGPIN is a non-invasive neoplastic process, which does not form a tumor mass or cause clinical symptoms.

Despite its histologic similarity to carcinoma - *in situ*, a precursor to invasive cancer that arises in other organs (e.g. breast or skin).[9] PIN is a condition in which some prostate cells have begun to look and behaved abnormally. Abnormal cells located in two areas such as acini and ducts when PIN develops. The epithelial cells lining acini and ducts become abnormal, but lining itself remains intact. In contrast, when cancer develops, the epithelial lining is ruptured, and the malignant cells penetrate into the tissues of the prostate gland itself (Figures 3 and 4).

Originally, PIN was classified as Grades I, II, or III, according to increasing degree of abnormality. But 1989, a consensus conference recommended classification to low grade PIN (Grade I) and HGPIN (Grades II and III).[10]

This classification is important because low grade PIN does not increase developing cancer while HGPIN might. HGPIN is often multifocal and coexists with carcinoma in high frequency in radical prostatectomy specimens.[11-13]

The reported incidence varies widely from 2.1% to 16.5%. Studies of men who have undergone prostate biopsies have found that anywhere from <1% to more than 20% had HGPIN.

Raviv *et al.* claimed that abnormal digital rectal examination (DRE) ($P = 0.008$), abnormal TRUS ($P < 0.001$) and

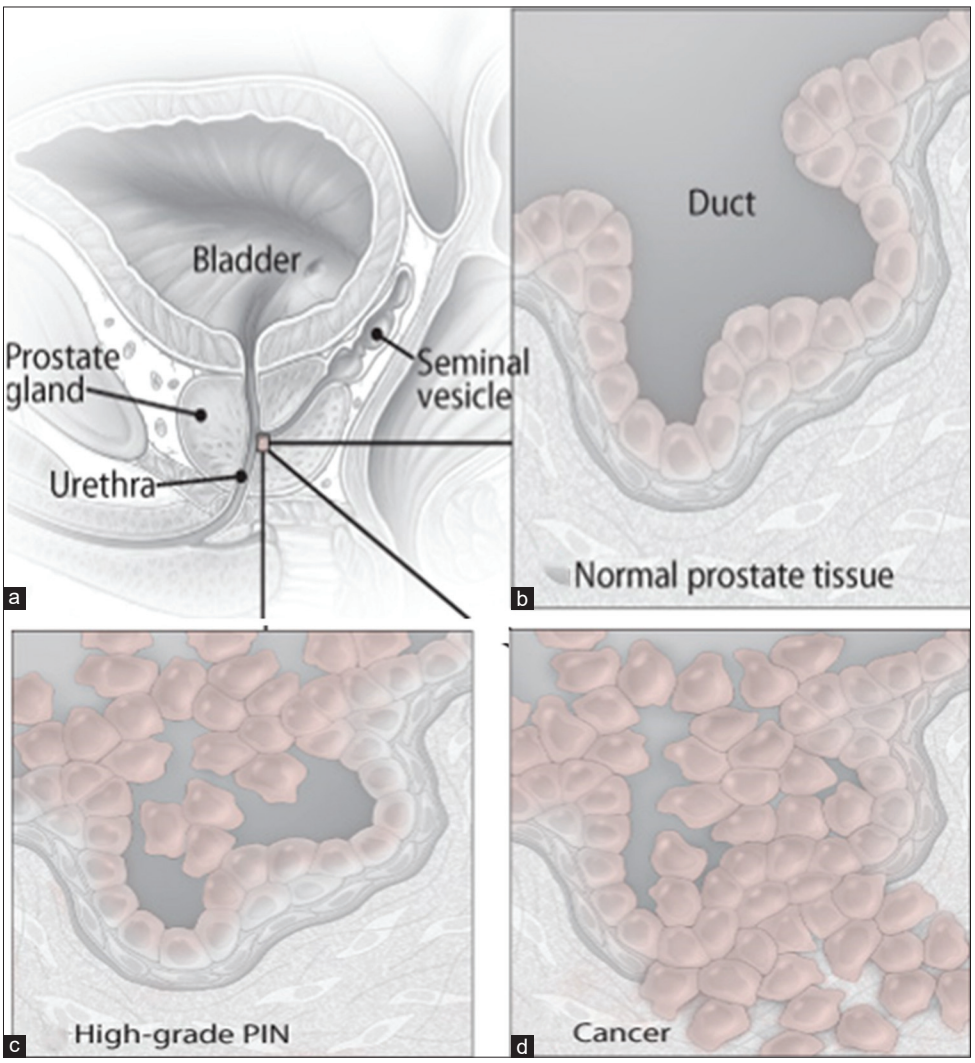

Figure 3: Normal epithelial cells line the ducts (a) that carry fluid from prostate gland to the main ejaculatory duct. In the case of high grade prostatic intraepithelial neoplasia (b), the cells become abnormally shaped. Their nuclei enlarge. Over time, these cells may become malignant and proliferate wildly, filling the duct and rupturing the epithelial lining (c). They can then penetrate into prostate gland tissue. (Source: 2014 Annual Report on Prostate Diseases by Harvard Medical School + Harvard Health Publications. Originally published Oct. 1, 2007)

Table 2: Incidence of isolated HGPIN in prostatic transurethral resections

References	Patient population	Men, *n*	Incidence of PIN (%)
Gaudin *et al.*,1997[14]	Consecutive TURPs without cancer at Johns Hopkins Hospital	158	3.2
Pacelli and Bostwick, 1997[15]	Consecutive TURPs without cancer at Mayo Clinic	570	2.8
Skjorten *et al.*, 1997[16]	Consecutive TURPs from 1974-1975 at Ullevaal and Lovinsenberg Hospitals, Oslo, Norway	731	33

HGPIN: High grade prostatic intraepithelial neoplasia, TURP: Transurethral resection of the prostate

Table 3: Incidence of isolated HGPIN in prostatic needle biopsies

Reference	Patient population	Men, *n*	Incidence of PIN (%)
Screening programs			
Mettlin *et al.*, 1991[17]	American cancer society National Prostate cancer Detection project	330	5.2
Feneley *et al.*, 1997[18]	Screening population in Gwent, England, 1991-1993	212	20
Hoedemaeker *et al.*, 1999[19]	PSA screening study in Rotterdam, The Netherlands	1824	0.7
Urology practice			
Lee *et al.*, 1989[20]	Consecutive biopsies of hypoechoic lesions at St, Joseph mercy Hospital	256	11
Bostwick *et al.*, 1995[21]	Consecutive biopsies at Mayo clinic	200	16.5
Bostwick *et al.*, 1995[21]	Consecutive biopsies at Glendale Hospital, calif	200	10.5
Langer *et al.*, 1996[22]	Consecutive biopsies at University of Pennsylvania medical Centre	1275	4.4
Wills *et al.*, 1997[23]	Consecutive biopsies at Johns Hopkins Hospital	439	5.5
Feneley *et al.*, 1997[18]	Consecutive biopsies at University College London Hospitals, 1988-1994	1205	11
O'Dowd *et al.*, 2000[24]	Consecutive biopsies at UroCor Labs, Okla, 1994-1998	132, 426	2.3
Fowler *et al.*, 2001[25]	Consecutive biopsies of men with suspected carcinoma at Veterans Affairs Medical Center, Miss, 1992-1998	1050	8.9

PSA: Prostate specific antigen, HGPIN: High grade prostatic intraepithelial neoplasia

Table 4: Incidence of prostate cancer on repeat biopsy[26]

Initial biopsy finding	Percentage of men diagnosed with prostate cancer (%)	
	Repeat biopsy before 1995	Repeat biopsy between 1996 and 2000
Normal (benign) tissue	19	26.2
HGPIN	51	30.5

HGPIN: High grade prostatic intraepithelial neoplasia

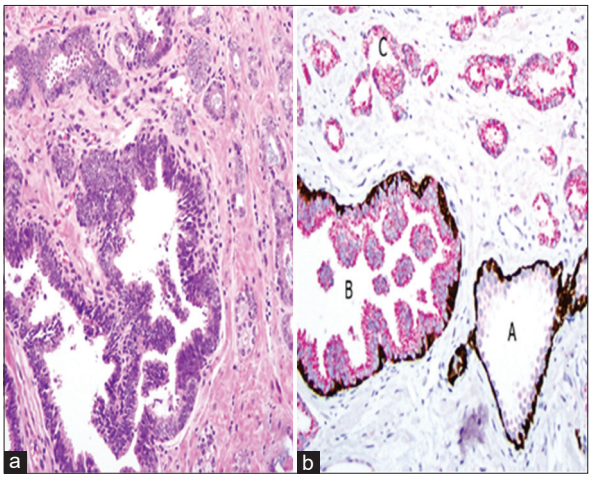

Figure 4: Triple antibody staining (AMACR, p63, and HMWCK). (a) Benign gland with basal cell staining (brown) minimal AMACR staining (red). (b) HGPIN gland with basal cell staining (brown) strong AMACR staining (red) in neoplastic acinar cells. (c) Adenocarcinoma with no basal cell staining but strong AMACR staining in acinar cells (red only) (Source: Int J Clin Exp Pathol 2009;2:327-338)

high PSA and predictive for carcinoma in the subsequent biopsy.[5] The finding of HGPIN with adjacent small atypical glands indicates a situation quite different from isolated HGPIN. In rate of finding, cancer on biopsy is 50%. Hence, close follow-up with biopsy is recommended in men with HGPIN with small atypical glands (Tables 2-4).

CONCLUSION

The study has conclusively shown that there is a high prevalence of HGPIN in prostatic specimens and reported as BPH clinically in our hospital.

The identification of increased number of HGPIN has an important implication for the management of the patient.

Bearing in mind that HGPIN is strongly predictive as a precursor of prostatic carcinoma, patients with the finding of HGPIN report should be closely followed up with serum PSA, DRE and ultrasound, preferably transrectal ultrasound or repeated needle biopsy for a defined period of time.

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