HISTOPATHOLOGIC PATTERN OF PROSTATIC LESIONS OBSERVED IN AUTOPSY SERIES

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Abstract

Incidental autopsy findings may be important to study about the prevalence of prostatic lesions among the male population which remains undiagnosed. Histology is the unique method for diagnosis of silent prostatic disease. The present cross sectional study was carried out with an aim to evaluate the histopathological pattern of prostatic lesions such as nodular hyperplasia of prostate (NHP), the precancerous lesions and the latent cancer in autopsy series over the age of 40 years of male. A total number of 120 specimens of prostates were collected from the dead bodies on whom postmortem examination was done by the Department of Forensic Medicine, Dhaka Medical College and Hospital, Dhaka. All these autopsies were done for medicolegal purposes. This study confirms previous observations and concluded that nodular hyperplasia of prostate was the commonest lesion. Of the total 54 cases of NH, 27 were accompanied with transitional cell metaplasia (TCM), Squamous metaplasia, basal cell hyperplasia (BCH), low grade prostatic intraepithelial neoplasia (LGPIN), inflammation, atypical adenomatous hyperplasia (AAH), high grade prostatic intraepithelial neoplasia (HGPIN) and prostatic carcinoma (PCa). Only 27 cases were NH. Most common pattern of inflammation associated with NHP was chronic inflammation. LGPIN was present in 8 (6.6%) cases and majority were with NH. But none of the LGPIN and metaplasias were associated with carcinoma or HGPIN. The commonest age group of presentation for NH was in fifth decade and increased with advancing age. It can be concluded that many prostatic lesions can remain silent and are diagnosed only at autopsy. Considering the HGPIN and prostate cancer to be silent, the development of screening programs to detect the latent cases of the disease is recommended.

Key words: *prostatic lesion, autopsy, histopathology.*

Introduction

A wide range of neoplastic and nonneoplastic diseases are associated with the prostate gland, which are responsible for significant morbidity and mortality among adult men. Some of them are prostatitis, nodular hyperplasia and prostate cancer. Nodular prostatic hyperplasia is universal and develops spontaneously in aging men. Prostate cancer is a common cancer in males, and is a large public health problem. It is currently the most common neoplasm and the second leading cause of cancer death in males in westerns countries[1]. Among the male cancer patients attending the National Institute of Cancer Research Hospital (NICRH), Bangladesh, prostate cancer is not even in the top 10 malignancies. According to WHO data 2011 death rate from prostate cancer is 0.7 in our country. In world health ranking of prostate cancer Bangladesh is in 187 position[2].

Nodular prostatic hyperplasia represents benign growth of the prostate that

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spontaneously develop in the aging population[3]. Histological evidence of NH is rarely observed in males prior to the fifth decade of life. The development of NH is an unavoidable phenomenon for the majority of aging males. Several studies show that after certain age almost 100% male develop NH, though this age varies from country to country[4].

Autopsy studies that have defined the incidence and morphological evolution of prostatic lesions have been confined largely to hospital autopsy of men with more than 40 years of age. Several studies show that after 45-50 years the prostate undergoes benign hyperplasia[5].

Prostatic intraepithelial neoplasia (PIN), which is dysplasia of the lining epithelium of prostate glands, is a probable precursor of prostatic carcinoma. It can be divided into low grade and high grade PIN. Low grade PIN may be found even in men of middle age. In recent years, many studies have shown that high grade porstatic intraepithelial neoplasia (HGPIN) is the major precursor of prostate cancer[6].

In 1954 one autopsy study demonstrated that approximately 30% of all men in the sixth decade of life and 67% at those between 80 and 90 years had carcinoma of the prostate, although the tumor was not always the cause of death[7]. Accurate prediction of prostate cancer prevalence and mortality, however, are hindered in some populations by the absence of relevant epidemiological data, including the frequency of clinically not diagnosed or incidental tumors[8]. Prostatic carcinoma starts silently and may not be noticed until the postmortem examination. The term "latent PCa" is used to define PCa that is clinically silent and determined during postmortem examination. Latent PCa cases are found in autopsies[9].

In a series of prostate obtained at autopsy, PIN was more likely to be found in men with prostate cancer than in those without cancer[10].

In Bangladesh no study has been done to observe the frequency of prostatic lesions. As biopsy of prostate without symptoms is not indicated, so the autopsy specimen can be an alternative to asses the volume of prostatic lesion in a population.

The present study was designed to determine the frequency of salient prostatic diseases such as NH, the precancerous lesions and the latent cancer in autopsy series.

Materials and methods:
This is a descriptive cross sectional study which was carried out at the Department of Pathology, Dhaka Medical College, during the period of July, 2011 to June, 2013. The study was done on autopsy specimens of prostate that were received from unclaimed dead bodies that went under postmortem examination in the Morgue of Department of Forensic Medicine, Dhaka Medical College. Out of the total 125 cases selected, 5 were excluded from the study having gross extensive deterioration due to autolytic change.

To do this study ethical clearance was taken from institutional ethical committee of Dhaka Medical College. Prostate glands were received from the dead body of men aged above 40 years for pathological examination. Moderate to marked autolytic changes were seen in the specimens as they were brought by the police and reached the pathology department quite late, Most of the deceased had died from traffic accidents and other unnatural death and no clinical histories were available since these men had not been hospitalized.

The age and heights of the deceased were recorded from the documents that accompanied the prostate specimen. The specimens were weighed and measured in three dimensions (width x height x length). Any abnormalities like increase in weight/ size and gross features like nodular and cystic changes were noted.

Macroscopic examination and sectioning were done through following steps. In the first place, through a transverse section the prostate was split into anterior and posterior halves. Then various consecutive coronal sections were cut through the prostate, from the apex to the base at a distance of 3-5 mm from the anterior and posterior halves. At least 6 sections were obtained from each prostate. Two samples were

taken from peripheral part of each halves and one from inner side.

The inner block was embedded as A and block from peripheral portion as B. Further sections were taken if any suspicious area was observed in terms of color or consistency. All of the blocks obtained were fixed in 10% formalin and processed routinely. The paraffin blocks were sectioned at 4-5 micrometer thickness and stained with haematoxylin and eosin (H & E).

Results:

The present study was carried out to evaluate the histopathological pattern of prostatic lesions in autopsy specimens. Prostate of 120 deceased male were observed, of which 112 (93.3%) were well preserved and 8(6.7%) were partially autolysed. Total cases were grouped according to their age falling in decades. Highest number of cases were in fifth decade and their mean age was found to be 47.2±7.57 years with range from 40 to 70 years.

In the histopathology findings the highest number of cases were nodular hyperplasia. Of the total 54 cases of nodular hyperplasia, 27 were accompanied by different other findings such as squamous metaplasia, transitional metaplasia, basal cell hyperplasia, atypical adenomatous hyperplasia, inflammation, low grade prostatic intraepithelial neoplasia, high grade prostatic intraepithelial neoplasia and carcinoma. Only nodular hyperplasia was observed in 27(22.5%) cases.

There were 8 cases low grade prostatic intraepithelial neoplasia of which 4 were associated with nodular hyperplasia, 2 with basal cell hyperplasia and 2 with inflammation. In the total 120 cases, 2 cases high grade prostatic intraepithelial neoplasia were observed and they were associated with nodular hyperplasia and adenocarcinoma. According to zonal distribution Majority of the nodular hyperplasia were observed in transitional zone. Most of the LGPIN and 2 case of HGPIN with adenocarcinoma were found in peripheral zone. The mean weight of the gland was calculated in different age group and gradual increase of weight was observed after 41 years. The scatter diagram shows significant positive correlation

between age a weight of prostate. The highest weight of prostate was observed in NHP with inflammation. Lesions without NH had lower weight than lesions with NH. On analysis there were 23 cases of 40 years of age of which 7 (30.4%) had
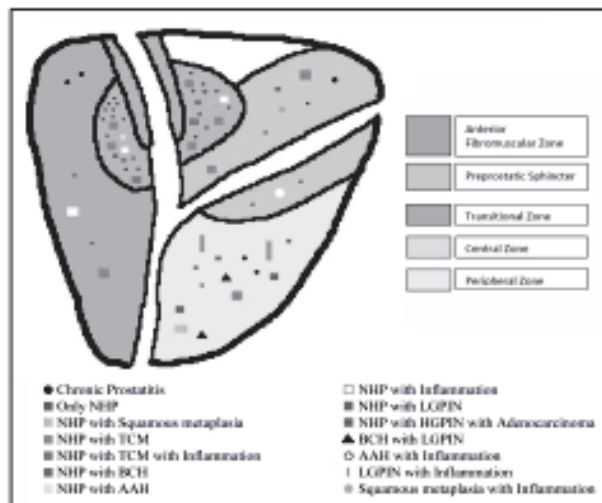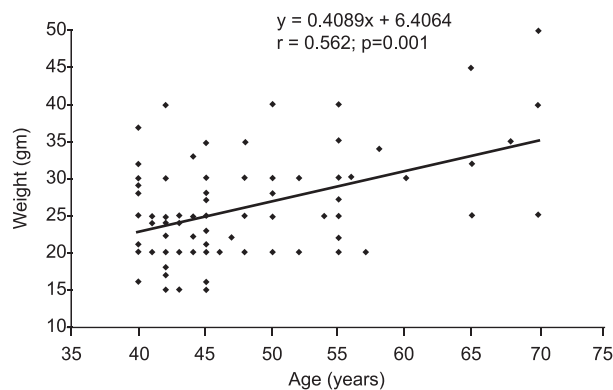

Fig.-1: *Zonal distribution of different prostatic lesions.*

Figure 1 shows various prostatic lesions in different zone. Majority of the nodular hyperplasia were observed in transitional zone. Most of the LGPIN and 2 case of HGPIN with adenocarcinoma were found in peripheral zone.

y= weight (gm)
r=Pearson's correlation coefficient
x= Age (years)
p= P value

Fig.-2: *Scatter diagram of positive significant correlation (r=0.462; p=0.001) between age and weight of prostate.*

Table-I

Frequency of different prostatic lesions observed by histologic evaluation in autopsy series with 95% CI (n=120)

Diagnosis	Frequency
Normal	55
Chronic prostatis	05
NHP (Nodular hyperplasia of Prostate	27
NHP with squamous metaplasia	02
NHP with TCM (Transitional cell metaplasia)	09
NHP with TCM with inflammation	02
NHP with BCH (Basal cell hyperplasia)	04
NHP with AAH (Atypical adenomatous hyperplasia)	01
NDHP with inflammation	03
NHP with LGPIN (Low grade prostatic intraepithelial neoplasia)	04
NHP with adenocarcinoma with HGPIN (High grade prostatic intraepithelial neoplasia)	02
BCH with LGPIN	02
AAH with inflammation	01
LGPIN with inflammation	02
Squamous metaplasia with inflamation	01
Total	120

Table-II

Distribution of different histopathological pattern of prostatic lesions according to age group (Number with percentage)

| Age years | Nor mal | Chr. Pros | Only NHP | NHP with | | | BCH | AAH | Inflam mation | LG-PIN | Ca with HG-PIN | BCH with LG-PIN | AAH with Inflam mation | LG-PIN with Inflam mation | Squa mous Metap lasia Inflam mation | Total |
				Squam ous metapl asia	TCM	TCM with Inflam mation										
>40	14 68.9%	02 8.7%	04 17.4%	0	01 4.3%	01 4.3%	01 4.3%	0	0	0	0	0	0	0	0	23
41-50	37 51.4%	03 4.2%	15 20.8%	01 1.4%	04 5.6%	01 1.4%	02 2.8%	0	0	03 4.2%	0	02 2.8%	01 1.4%	02 2.8%	01 1.40%	72
51-60	04 23.5%	0	05 29.5%	0	04 23.5%	0	01 5.9%	01 5.9%	01 5.9%	01 5.9%	0	0	0	0	0	17
>60	0	0	03 37.5%	01 12.5%	0	0	0	0	02 25.0%	0	02 25.0%	0	0	0	0	08
Total	55	05	27	02	09	02	04	01	03	04	02	02	01	02	01	120

$y = 0.4089x + 6.4064$
$r = 0.562; p=0.001$
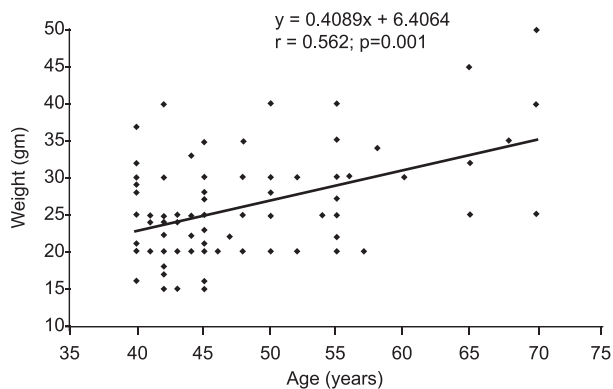
Fig-3: *Percentage of NHP in different age group (n=120)*

Discussion

In this present study it was observed that highest number of cases were in fifth decade with their mean age, 47.2±7.57 years, ranging from 40 to 70 years. A similar study was done by Ghartimagar[11] on medicolegal autopsy cases and his mean age was 39.44± 16.04 years. His finding is lower than the present study. The cause may be majority of his cases being below 40 years of age. In present series the mean weight of the prostate gland was 25.7±6.7g. This is similar as observed by Okani which was 30.9±17.0g. In our series there was increase in weight of the gland with age, though before 50 years it was minimum. Marked increase of mean weight was observed after 50 years of age. In the current study different histopathological lesions were observed in prostate. The most frequent finding in this current study was nodular hyperplasia. Of the total 54 (45%) cases of NH, 27 were accompanied by different other findings such as TCM, BCH, Sq. metaplasia, inflammation, LGPIN, HGPIN and carcinoma. Nodular hyperplasia only, was observed in 27(22.5%) cases. Okani[4] also reported that the most common lesion identified in his series was nodular hyperplasia, accounting for 64 (81%) of the cases, which is higher than present study and that by Ghartimagar[11]. It can be stated that the frequency of NH is lower in our population and Indians, than the Africans and Caucasians. Nodular hyperplasia is a progressive condition which increases with age. In present series and all others studies a

sharp rise in the frequency of NH was observed, after 60 years of age. However it can be concluded that at extreme later age, all prostates develop nodular hyperplasia.

In this series lowest weight was observed in the normal prostates and highest weight was observed in prostate with NH alone or accompanied with other findings. Increased mean weight was also observed in chronic prostatitis and also in LGPIN alone or LGPIN with metaplasia or with inflammation, in comparison to normal prostate. A total of 14 (11%) cases showed prominent inflammation alone or accompanied by other lesions. Only 5 (4.1%) cases had isolated chronic prostatitis. Basal cell hyperplasia is the most common observed epithelial hyperplasia. In present study focal basal cell hyperplasia was noted in 6 (5%) cases, and majority of them were observed above 40 years of age group. Four cases of BCH were associated with NH and two with LGPIN. Study done by Mittal found 5.4 % of BCH which is similar to our findings.

Different metaplastic changes in the glandular lining of prostate were a common findings. Most of these cases were associated with NH. In the present study 14 (11.6%) cases showed metaplastic change, transitional metaplasia being the commonest which was seen in 9% cases, followed by squamous metaplasia in 2.5% cases. A similar study done by Mittal[12]. observed the percentage of transitional metaplasia to be 7.02% which is slightly lower than our series. It may be due to inclusion of periurethral glands which can normally have a transitional lining. Most common observed intraepithelial proliferative disorders are AAH and PIN, which have been recognized as putative premalignant lesions of prostate.

In this present series total LGPIN were seen in 8 (6.6%) cases. Among them 4 (3.3%) cases were associated with NH and 4 (3.3%) other cases were seen with BCH and inflammation. The association of LGPIN with NH was not statistically significant. Rekhi[13] also observed LGPIN as the most common grade of PIN and found it to be significantly associated with NH. However sectioning and larger study may be conclusive. A study done by Mirzaie[14] in a

series of 149 autopsy cases reported 26 (17.4%) of LGPIN. Higher number of LGPIN in his series can be explained by inclusion of more elderly cases as his mean age was 64.5 (SD=3.8) in contrast to our mean age, which is 47.2±7.57. In the present study 7 out of 8 cases of LGPIN were in 41-50 years of age. Only one was in 51-60 years and none over 60 years. So in our study no influence of age can be observed on LGPIN. However a large study can establish or rule out the correlation of age with LGPIN. In the present study none of the 8 cases of LGPIN was associated or accompanied with HGPIN or cancer. Similar findings were reported by Silvestri[15] who did not find any association of LGPIN with prostatic carcinoma or HGPIN. In our study HGPIN was present in only 2 (1.6%) cases. Both were above 60 years of age and associated with the presence of cancer. The obtained Gleason scores in these 2 cases of adenocarcinoma were (2+2)=4. Therefore, in terms of histological classification, they were well differentiated. Both the HGPIN and adenocarcinaoma were seen in peripheral zone of the prostate gland. Ghartimagar[11] In his study had noted 1(1%) case of HGPIN which is similar to the current study.

In two autopsy series of prostate one done in Denmark by Holund[16] and the other in Hungary done by Soos G[8] found 22% and 38.8% of incidental carcinoma respectively. In both of these series, the mean age of the deceased were much higher than the present study, which may be one of the causes. The other reason may be higher life expectancy, improved diagnostic facilities or their genetic constitution. Frequency of HGPIN and prostatic carcinoma may increase with increasing age. Screening program for prostatic carcinoma and mortality rate are other confounding factors that may apparently lower the prevalence of HGPIN & prostatic carcinoma in extreme higher age.

In present series both the two cases of HGPIN had NH. The coexistence of NH with PIN has many controversies. Rekhi[13] in a series of 200 cases did not find any association of HGPIN with NH, though he observed significant correlation of LGPIN with NH. Another study by Nusret[9] observed a strong negative correlation between HGPIN & NH.

It can be stated that among the prostate related lesions, NH is the most frequent presentation in our population, like others. However the frequency is lower than many other countries. But the scenario might change with increase in the life expectancy.

Conclusion

In conclusion the commonest pathology encountered in this study was NH. Incidence of HGPIN and prostatic carcinoma were low and none of the HGPIN or Ca was associated with other lesions such as TCM, BCH, sq. metaplasia, LGPIN, AAH, inflammation. It was observed that incidence of many prostate related diseases such as NH, PIN and carcinoma increase with age. So for developing countries like Bangladesh there is a strong probability of simultaneous increase in the incidence of prostate cancer with increase in life expectancy and diagnostic facilities.

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