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Original Research Article

HISTOLOGICAL ANALYSIS OF AGE RELATED VARIATIONS IN HUMAN PROSTATIC GLANDULAR TISSUE

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ABSTRACT

Background: The human prostate is a compound tubulo-alveolar organ. The secretion of prostate forms a considerable part of seminal fluid and provides nourishment to the sperm. Aging and hormonal influences induce morphological and histological alterations in the prostatic glandular tissue exhibiting changes at macroscopic and microscopic levels. The aim of this study is to elucidate the normal age related changes occurring in the glandular tissue of human prostates.

Materials and Methods: The research was conducted in the department of Anatomy, Government T.D. Medical College, Alappuzha. The study employed an observational design examining the changes in the prostatic glandular tissue in different age groups. 100 human prostate specimens, obtained from department of Forensic Medicine and department of Pathology of Government T.D. Medical College, Alappuzha were studied and changes in the glandular tissue were noted.

Results: In the fetal prostate glands, the glandular tissue was rudimentary. In the adult prostate glands, there were numerous follicles with multiple epithelial infoldings. Simple columnar epithelium was predominantly seen in all the age groups except in 61-75 years age group which showed stratified columnar epithelium in 28% of specimens. After 60 years, few specimens showed follicles with regular outline without any infoldings.

Conclusion: In the adult prostate glands, the glandular component was predominant due to the increased secretory activity. The proliferation of glandular elements observed after 60 years may be part of the normal aging process and hyperplasia of the gland. The diminution in the size of acini and the absence of papillary infoldings might be due to decrease in the secretory activity and atrophy of prostate gland. Understanding the age related changes in the glandular tissue of prostate may facilitate a deeper comprehension of prostate gland pathology and more effective management of prostate related disorders.

Keywords: prostate, gland, follicle, epithelium.

INTRODUCTION

The development of prostate begins in the 10th week as a cluster of endodermal invaginations of posterior embryonic urogenital sinus. The ducts originate as mesenchymal epithelial buds that profusely branch and combine to form tubulo-alveolar glands. The function of glandular secretion commences on the 13th week of gestation in the prostate.^[1]

The glandular tissue of prostate gland consists of numerous follicles with papillary infoldings that may allow the expansion of their lumen as secretory reservoirs. Follicles open into canals that join to form 12-20 main ducts. The follicles are separated by loose connective tissue supported by extensions of the fibrous capsule and muscular stroma and enclosed in a delicate capillary plexus. Follicular epithelium is variable but predominantly columnar, and either

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single layered or pseudostratified. Prostatic ducts are lined by pseudostratified epithelium in which the luminal layer is columnar and basal layer is lined by small cuboidal cells. Secretions from the prostate gland and seminal vesicles form the bulk of seminal fluid. Histological sections just above the level of seminal colliculus reveal two concentric zones of glandular tissue, the larger outer peripheral zone and the inner transition zone. The outer zone contains long, branched glands with ducts that open mainly into the prostatic sinuses and the inner zone consists of glands with ducts that open on the floor of the prostatic sinuses and seminal colliculus, and a group of simple mucosal glands that surround the intramural part of the urethra. [2,3]

McNeal established the concept of prostatic zones. Approximately 70% of the prostate is composed of glandular elements, while the remaining 30% is occupied by non-glandular region which is the anterior fibromuscular stroma. The peripheral zone is located at the apex as well as the major part of tissue is located posteriorly near the capsule. The central zone is cone-shaped with the apex of the cone at the confluence of the ejaculatory ducts and the prostatic urethra at the verumontanum. The transition zone is composed of two equal parts of glandular tissue located laterally to the urethra in the mid-gland. [6]

In the past, prostate was considered as a physiologically inert structure. But steadily with time and more studies with renewed interest in prostate the concept of prostate as an inert organ began to decline and it was considered to be a potentially active organ of the male reproductive tract. In men over 30 years, the prostate gland begins to show variety of deviations from normal morphology. [5] The prevalence and extent of these changes progressively increase with age such that most prostates turn quite heterogenous in histologic composition by seventh decade of life. [19-22]

The aim of this study is to determine the normal changes occurring in the glandular tissue of human

prostates. Knowledge of these alterations may help differentiate normal aging from pathological processes facilitating more accurate diagnosis of various clinical conditions of prostate gland.

MATERIALS AND METHODS

The study was conducted in the department of Anatomy, Government T.D. Medical College, Alappuzha over one and a half years from January 2016 to June 2017. An observational study was done on the glandular tissue of 100 human prostate specimens which were collected from department of Forensic Medicine and department of Pathology of Government T.D. Medical College, Alappuzha. The permission for this study was approved by the Institutional Ethics Committee, Government T.D. Medical College, Alappuzha. Prostate specimens collected within eight hours of death from autopsy cases died in road traffic accidents were included. Prostate specimens with gross deformity were excluded from the study.

Procedure: The abdominal cavity was opened and after removing the viscera, the prostate gland was identified and removed by the retropubic approach. The specimens were immersed in labelled bottle containing 10% formalin for tissue fixation. The lobes of prostate gland were identified and two tissue bits were taken from each lobe. From each block, four slides were prepared. Staining was done using Eosin and Hematoxylin stains. Mounted sections were inspected under low and high power objectives of light microscope.

RESULTS

The glandular tissue of 100 human prostate specimens was studied. They were divided into 5 age groups and the following findings were observed [Table 1].

Table 1: The predominant type of epithelium of the glandular acini in each age group: Simple columnar/ Stratified columnar

	Simple Columnar	Pseudostratified Columnar	Total
Age group	n (%)	n (%)	n (%)
Group I 37weeks-15years	6 (100%)	0	6 (100%)
Group II 16-30years	10 (100%)	0	10 (100%)
Group III 31-45years	30 (100%)	0	30 (100%)
Group IV 46-60years	29 (100%)	0	29 (100%)
Group V 61-75years	18 (72%)	7 (28%)	25 (100%)

In group I, the fetal prostates consisted of very few nascent glands and the ducts were present within a wide fibromuscular stroma [Figure1]. In the prepubertal prostates, proliferating series of ducts were found. Alveoli were not fully developed [Figure2]. Pubertal prostate specimens revealed follicles with irregular outline and the epithelium of their alveoli showed extensions into the lumen. The follicles were lined by columnar cells with basally disposed nuclei. In group II, III and IV the glandular tissue was found to be hypertrophied with an increase in the number of

acini exhibiting numerous papillary projections into the lumen. Simple columnar epithelium was predominant in the specimens of these age groups [Figure 3,4].

In group V, proliferation of glandular tissue was observed in some specimens. In these specimens there were numerous follicles with irregular outline. The follicles had papillary projections [Figure 5]. In few specimens, some of the fields showed follicles with regular outline without any infoldings. The height of the epithelium was found to be reduced in

such cases [Figure 6]. The glandular tissue showed atrophy in some specimens [Figure 7]. In 72% cases, the most common type of follicular epithelium observed was simple columnar. Pseudostratified epithelium was predominant in 28% specimens of this age group [Table 1]. Pseudoacinar formation was observed, that is, an acinus formed within the epithelial wall of a larger acinus [Figure 8].

[Table 1] shows simple columnar epithelium as the predominant type of epithelium lining the glandular acini in all the age groups. Pseudostratified epithelium is found to be predominant in 28% specimens of group V.

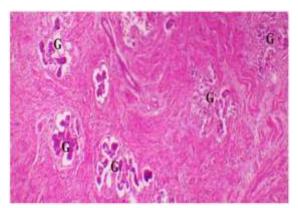


Figure 1: 38 weeks old prostate showing rudimentary glandular tissue(G) embedded in fibromuscular stroma. 100X, H&E

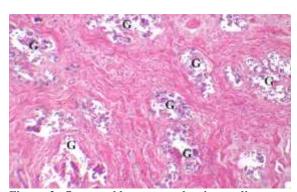


Figure 2: 7 year old prostate showing rudimentary glandular tissue (G) embedded in fibromuscular stroma. 100X, H&E

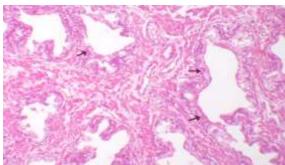


Figure 3: Section of 18 year old prostate. Arrow showing follicles lined by simple columnar epithelium. 100X, H&E

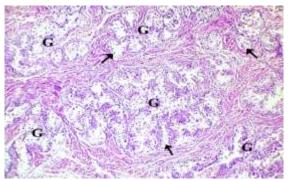


Figure 4: Section of 42 year old prostate. Stroma showing predominantly glandular tissue (G)-arrow shows follicles with numerous papillary infoldings. 100X, H&E

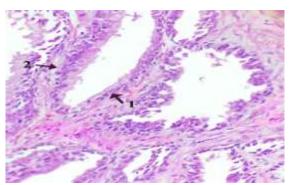


Figure 5: Section of 68 year old prostate showing follicles with papillary projections. Follicles are lined by simple columnar (1) and pseudostratified epithelium (2). 400X, H&E

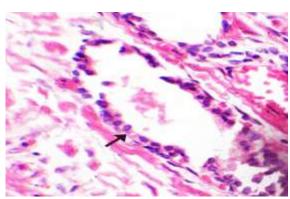


Figure 6: Section of 74 year old prostate. Follicle showing decrease in height of the epithelium (arrow mark).400X, H&E

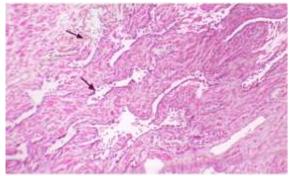


Figure 7: Section of median lobe of 74 year old prostate. Arrow showing atrophy of glandular tissue. 100X, H&E

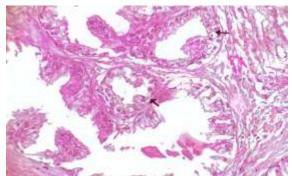


Figure 8: Section of 70 year old prostate showing pseudoacinar formation (arrow mark). 400X, H&E

DISCUSSION

In fetal prostates, the glandular tissue was rudimentary. Only partially developed follicles and ducts were observed. This was in agreement with the findings of Swyer. He documented that the fetal prostate glands showed duct system embedded within the stroma and the ducts radiated outwards from its origin in the urethra. Follicles were represented by small end buds on the ducts.^[7]

In this study, in pre-pubertal prostates, the glandular part was not fully developed and there were proliferating series of ducts. The sections obtained from pubertal prostates showed follicles with numerous papillary projections extending from the follicular epithelium into the lumen of the acini. In adult prostate glands, the glandular component was predominant. The glandular tissue was composed of tubulo-alveolar glands. An increase in the number of acini was identified. The follicular epithelium also increased which was reflected by the numerous epithelial infoldings which projected into the lumen of the follicles. This was in accordance with the observations of Moore, Higgins and Gosling, Aumuller.

Moore reported that at 10 years of age, the growth of prostatic epithelium begins and between 12th and 14th years, highly branching alveoli with numerous papillae become evident.[8] According to Swyer, at puberty when the secretion of the male sex hormone commences, there occur rapid growth of the prostate gland and within 6 months to one year, the prostate is transformed into an adult type of gland. In the third decade, however, the glands have reached a high degree of complexity and closely resemble true prostatic glands with an epithelium having numerous peninsular extensions. Such a condition is usual up to the age of about 45 years.^[7] Higgins and Gosling studied the structure of adult prostate gland and reported that the central portions of the gland contained larger acini with numerous prominent epithelial folds within the lumen.^[9] Aumuller described post-natal development of the human prostate proceeds in three phases: a regression period after birth, a quiescent period up to 12-14 years, and a maturation period between 14 and 18 years.^[10] According to Gray, during the third decade, the

glandular epithelium grows by irregular multiplication of the epithelial infoldings into the lumen of the follicles.^[3] This was in accordance with the findings of the present study.

In this study, after 60 years, some of the specimens showed proliferation of glandular tissue. There were numerous follicles with papillary projections. Zirkin and Strandberg studied quantitative changes in the morphology of the aging canine prostate. They concluded that proliferation of glandular and stromal components, increase in epithelial cell numbers and increase in epithelial cell size resulted in prostatic enlargement during aging.^[11] The proliferation of glandular components in this study might be part of the aging process of the prostate gland.

In this study, in few specimens, some of the fields showed follicles with regular outline without any infoldings. There was decrease in the size of acini and they were widely separated. The height of the epithelium was found to be decreased in such cases. These features indicate atrophy of glandular tissue. This result agreed with the findings of Moore and Franks. Moore documented that atrophy is a conspicuous feature of presenile period, that is, before 60 years and this may involve only the epithelial cells or the acinus or both may be combined. Atrophy of the epithelium results in a decrease in the height of the epithelium. In simple acinar atrophy, acini are small and closely packed together.[8] These features suggesting atrophy were observed in the present study but they appeared only after 60 years. According to Franks, simple atrophy involves both epithelium and stroma. The epithelial cells lost their activity and become smaller and more cuboidal. The lumen becomes narrow and slit-like.^[12] This is in agreement with the present study. McNeal observed changes of prostate with age. He found both focal and diffuse atrophy with age. He reported that, diffuse atrophy occurred as part of aging and begins as early as the fifth decade.[19] In this study, the features of atrophy were noted after 60 years. According to Liavag, benign prostatic hyperplasia forms in the central portion of the prostate during the age of 40 years and the peripheral portion shows progressive atrophy with increasing age. The atrophy involves both epithelium and stroma and leads to reduced secretion. The epithelium becomes cuboidal and even flat and may be shed into the lumen of the acini and the ducts.[13] Gardner et al studied atrophy and proliferation in the young adult prostate and considered atrophic and proliferative changes in the prostate gland as initial stages of middle age and characterized the prostates of older men.^[14] Amma et al studied the age related changes in glandular and stromal elements of prostate gland using light microscopy and stated that in fetal stage, prostate gland contained underdeveloped ducts and in the later phase, glandular hyperplasia occurred and the occurrence of atrophic changes was observed after age of 60.^[15] These findings are in concordance with the present study.

Epithelium of glandular acini: In the present study, in fetal prostate, the duct system and the partially developed alveoli were lined by low columnar cells. This was in accordance with findings of Swyer. According to him, the ducts of fetal prostate gland are lined by cubical or low columnar cells with centrally placed nucleus. In general, the epithelium of the end buds resembles that of the ducts. They are lined by columnar cells with basal nuclei similar to that of the active adult prostatic alveoli.^[7]

In all other age groups, the epithelium was formed of tall columnar cells. Pseudostratified epithelium was prevalent after the age of 60 years. Pseudoacinar formation, that is, acinus formed within the epithelium of the wall of a larger acinus was observed. Mostofi suggested that the hyperplasia occurring after the age of 40 years reaches its maximum intensity at about 60 years and continues to be present in sufficient amount to cause changes in the rest of life. [16]

In group V, 28% of the prostates showed pseudostratified epithelium as the predominant type, which was suggestive of hyperplasia. According to Swyer, the epithelium of acini of prostate gland in older age is generally composed of small cuboidal cells and some degree of hyperplasia was found more commonly.^[7] This result is in accordance with the present study. According to Moore, hyperplastic cells, pseudoacinar formation and atrophy are features of presenile period, which occurs before 60 years.^[8] This was contradictory to the findings of the present study. In this study, the predominance of pseudostratified columnar epithelium which is a feature of hyperplasia and pseudoacinar formation were observed only after 60 years. Berry et al studied the development of benign prostatic hyperplasia with age. He observed sequence of events like epithelial proliferation, prolonged survival of epithelial population, hypertrophy of acini marked by increase in volume fraction and thickness of acinar epithelium are relevant for the growth and expansion of the hyperplastic glandular tree.[17] Chapman highlighted in his research that prostatic enlargement should be regarded as an anatomical feature of old age and this becomes a disease only when obstruction to the urine flow occurs.^[18] The increase in epithelial cells noted in the present study could be attributed to hyperplastic change of the prostate with age.

CONCLUSION

In fetal prostate, the glandular tissue was rudimentary and they were lined by low columnar epithelium. In the pre-pubertal prostates, the glandular part was not fully developed and there were proliferating series of ducts. In the sections of pubertal prostates, several follicles with papillary projections extending from the follicular epithelium into the lumen of the acini were seen. This clearly indicated that hormonal influence at puberty has led to proliferation of glandular elements and transformation into adult type

of gland. In the adult prostate glands, the glandular component was predominant. The follicular epithelium increased which was evident from the numerous epithelial infoldings which projected into the lumen of the follicles. This suggests the increased secretory activity of adult prostate gland. After 60 years, the glandular component was predominant in few specimens and numerous follicles with papillary infoldings were present. This suggested the proliferation of glandular elements perhaps, as part of normal aging process and hyperplasia resulting in enlargement of the prostate gland. In few specimens, some of the fields showed follicles with regular outline without any infoldings. The height of the epithelium was found to be decreased which suggest the decreased activity of epithelium. The acini were found to be small and widely separated. This indicated atrophy of the glandular tissue. In the present study, the alveoli were lined by simple columnar epithelium. Pseudostratification of lining epithelium seen after the age of 60 years, indicating hyperplasia of cells and pseudoacinar formation could be considered as features of old age. Insight into the changes in histological characteristics of glandular tissue of prostate gland may provide valuable information that could aid clinicians in the diagnosis and management of various prostatic disorders.

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