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Original Research Article

Age Related Changes in the Fibromuscular Stroma of Human Prostate Gland: An Observational Study

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Abstract:

Background: The prostate is the accessory gland of male reproductive system. The primary function of prostate gland is to secrete a clear, slightly alkaline fluid that contributes to the formation of seminal fluid. With advancing age, the gland undergoes significant changes both microscopic and macroscopic. The aim of this study is to demonstrate the normal changes occurring in the fibromuscular stroma of human prostate glands in various age groups.

Method: An observational study on age related changes in fibromuscular stroma of human prostate gland was conducted in the Department of Anatomy, Government T D Medical College, Alappuzha. 100 specimens of human prostate glands were obtained from the Department of Forensic medicine and Department of Pathology, Government T D Medical College, Alappuzha. The pattern of changes in fibromuscular stroma in different age groups was studied using Haematoxylin, Eosin and other special stains.

Results: The fibromuscular stroma was predominant in pre-pubertal prostate specimens. In post pubertal and adult prostate specimens, there was a relative reduction in the amount of stroma. In 61-75 years age group, there was an increase in the proportion of fibromuscular stroma compared to glandular tissue in 60% of specimens.

Conclusions: The present study shows that significant changes occur in the fibromuscular stroma of prostate glands beginning from birth to old age. The results of this study may be helpful in histopathological correlation of various diseases of prostate gland.

Keywords: Prostate; Stroma; Tissue; Fibres.

Introduction

The prostate is a fibro-musculo-glandular organ which surrounds the proximal part of the male urethra. The secretion of prostate forms a considerable part of semen. The gland is situated in the lesser pelvis below the neck of the bladder above the urogenital diaphragm and behind the lower part of symphysis pubis. Anatomically the prostate is divided into three lobes, median and two lateral. Surgically it is divided into five lobes, median, anterior, posterior and two lateral. The median lobe is bounded in front by the urethra, behind and on each side by the ejaculatory duct, behind and in the median plane by the prostatic utricle. The two lateral lobes are separated superficially by a posterior median sulcus. The continuity of lateral lobes is described surgically as the posterior lobe. The lateral lobes, in front of the urethra are connected by the fibromuscular isthmus. In fetal life the isthmus contains glands, hence known as the anterior lobe. The structure of the prostate consists of one fourth fibrous, one fourth muscular and half glandular tissue. The glands of prostate are arranged in three concentric layers around the urethra namely, inner mucous glands, intermediate submucous glands and outer main glands. The outer glands present numerous follicles and longer ducts which open into the prostatic sinuses. The follicles are lined by simple columnar epithelium and are provided with numerous infoldings after puberty [1]. The stroma of the prostate is composed of non-striped muscle and fibrous tissue. The muscular tissue constitutes the proper stroma of the prostate and the connective tissue is very scanty which form thin trabeculae between the muscle fibers. The stroma supports the acinar epithelium through its fibromuscular substance. [4]. The prostate gland begins its growth and development in the fetal life and is completed at the phase of sexual maturity. In post-pubertal males, the growth of the gland is almost entirely

due to follicular development and this is associated with stromal condensation which diminishes relative to the glandular tissue. After the third decade, the size of the prostate remains virtually unaltered until 45-50 years. As age advances, one of the two extremes of changes is observed, the prostate may progressively increase in size or it undergoes atrophy [1,2]. Androgen has a pivotal role in the development of prostate [5]. In the presence of normal circulating and intraprostatic levels of androgens and estrogens, a homeostatic equilibrium exists between proliferative and apoptotic processes in the prostate gland. An imbalance between the two with increasing age, could cause a progressive growth and enlargement of the gland manifesting as benign prostatic hyperplasia (BPH) [6,7].

The normal prostatic tissue undergoes vigorous changes in response to the variation in hormonal levels with age. The frequency of prostate disorders like prostatitis, benign prostatic hyperplasia and prostate cancer has increased. Numerous studies are being conducted on the aetiology and changes in hyperplastic prostates. Recent literature shows very few histological studies on the age changes in microstructure of prostate. The present study is an attempt to demonstrate the normal changes occurring in the fibromuscular stroma of prostate glands in different age groups.

Materials and Methods

An observational study on age related changes in fibromuscular stroma of human prostate gland was conducted in the Department of Anatomy, Government T D Medical College, Alappuzha. 100 specimens of human prostate gland were collected from the Department of Forensic medicine and Department of Pathology of Government T D Medical College, Alappuzha over a period of one and a half years from January 2016 to June 2017. The protocol for this study was approved by Institutional ethics committee, Govt.TD Medical College, Alappuzha.

Inclusion Criteria

1. Fetal specimens obtained from human fetuses subjected to autopsy due to intrauterine death and still birth.
2. Adult prostate specimens taken within eight hours of death.

Exclusion Criteria

1. Fetuses with congenital abnormality.
2. Specimens with gross pathology of prostate gland.

PROCEDURE: During autopsy, after removing the abdominal viscera, the prostate gland was approached through retropubic route and was removed [8]. The specimens were immediately transferred to a labeled bottle containing fixative solution, 10% formalin. Preparation for microscopy: The five lobes of the prostate gland were identified and dissected [1,9]. From each specimen, 2 tissue bits were taken from each of the 5 lobes of the prostate gland and processed by standard methods. Four slides were prepared from each block and stained with routine Haematoxylin and Eosin stain and with special stains namely Van Gieson and Orcein stain to demonstrate collagen and elastic fibres respectively [10]. Mounted sections were observed under low power and high power objectives of a binocular microscope with built in light source. The predominant tissue in each slide was inspected carefully under low power and high power objectives and the following parameters were observed:

A) Fibromuscular stroma / glandular tissue
B) Fibrous tissue / Muscular tissue
C) Collagen / Elastin

Results

100 specimens were obtained and they were categorized into five age groups [Table1].

The microstructure of the prostate gland showed tubulo-alveolar glands embedded in fibromuscular stroma. The stroma consisted of abundant smooth muscle and connective tissue fibres.

Group I included fetal and prepubertal prostates. The stroma of fetal prostate glands chiefly contained connective tissue with relatively smaller proportion of muscle fibres [Figure 1]. The glandular tissue was rudimentary. The amount of muscular tissue was found to be increased in the stroma of pre-pubertal prostates compared to fetal prostate glands [Figure 2]. The fibrous tissue was mainly made up of collagen fibres.

14 year old prostate showed follicles with irregular outline. The stroma was condensed around each alveoli and it was filled with a fairly high proportion of smooth muscle fibres [Figure 3]. These features were similar to the histologic picture of adult prostate.

In group II, III and IV, the amount of fibromuscular stroma was reduced and glandular tissue was found to be predominant. The stroma contained abundant smooth muscle fibres. The fibrous tissue component included collagen fibres mainly and elastic fibres were very less [Figure 4]. Collagen fibres were observed using Van Gieson stain and elastic fibres using Orcein stain [Figure 6].

In Group V, fibromuscular stroma was predominant in 60% specimens compared to glandular tissue. The acini were small and widely separated in these specimens. The stroma contained higher proportion of smooth muscle fibres [Table2, Figure 5]. The connective tissue fibres were mainly

collagen. There were only minimal amount of elastic fibres [Figure 7].

Table 1: The number of specimens collected for study

Age group			No. of specimens (n)
Group I	-	37weeks-15 years	6
Group II	-	16-30 years	10
Group III	-	31-45 years	30
Group IV	-	46-60 years	29
Group V	-	61-75 years	25
TOTAL			**100**

Table 2: The predominant type of tissue in each age group: Glandular / Fibromuscular. N-number of specimens in each age group

Age group	Glandular N (%)	Fibromuscular N (%)	p value
Group 1 (n = 6)	1 (16.7%)	5 (83.3%)	< 0.001
Group 2 (n = 10)	10 (100%)	0 (0%)	
Group 3 (n = 30)	30 (100%)	0 (0%)	
Group 4 (n = 29)	29 (100%)	0 (0%)	
Group 5 (n = 25)	10 (40%)	15 (60%)	

p value < 0.001; the association between age and predominant tissue type is statistically significant

Table 3: The predominant component in the fibromuscular stroma in each age group: Muscular/Fibrous tissue. N-number of specimens in each age group

Age Group	Fibrous	Muscular	P Value
Group 1 (n = 6)	3 (50%)	3(50%)	<0.001
Group 2 (n = 10)	10 (100%)	0 (0%)	
Group 3 (n = 30)	30 (100%)	0 (0%)	
Group 4 (n = 29)	29 (100%)	0 (0%)	
Group 5 (n = 25)	25 (100%)	0 (0%)	

p value < 0.001; the association between age and predominant tissue in the stroma is statistically significant

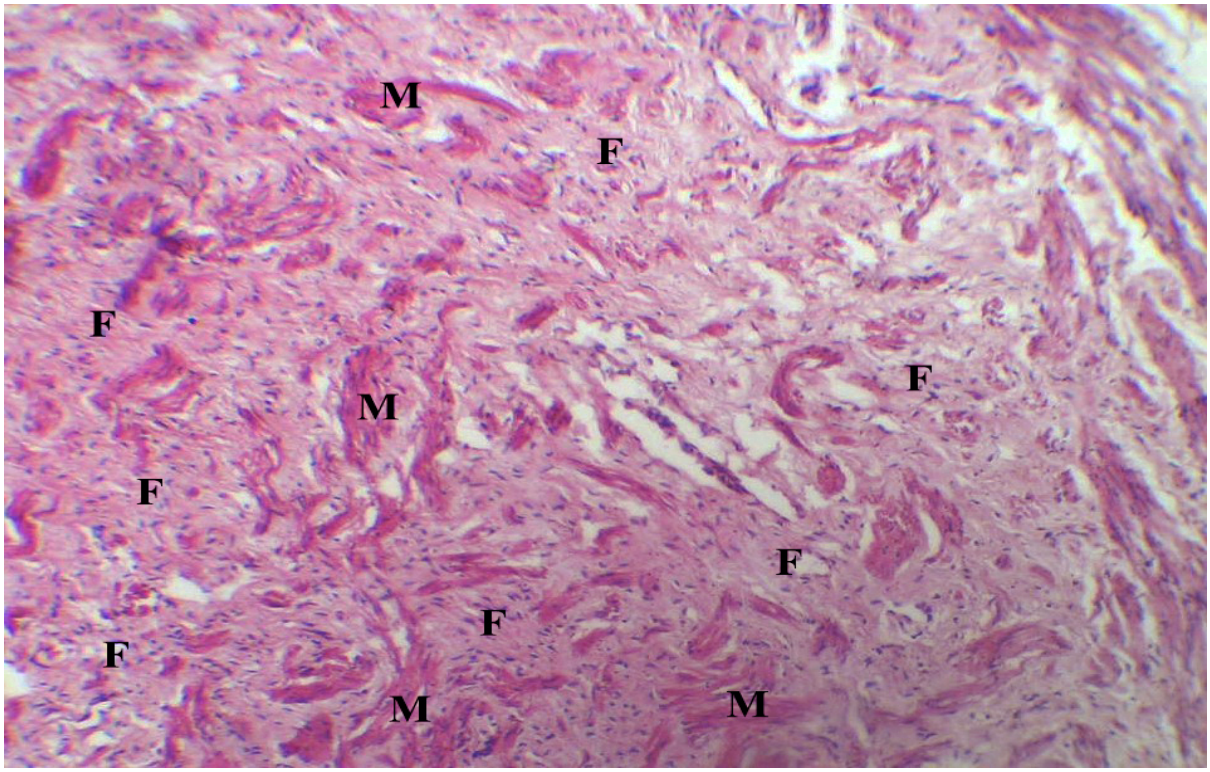

Figure 1: Section of 37 weeks old prostate showing predominant fibromuscular stroma. Stroma contain mainly fibrous tissue. M: Muscular Tissue, F: Fibrous Tissue 100X, H&E

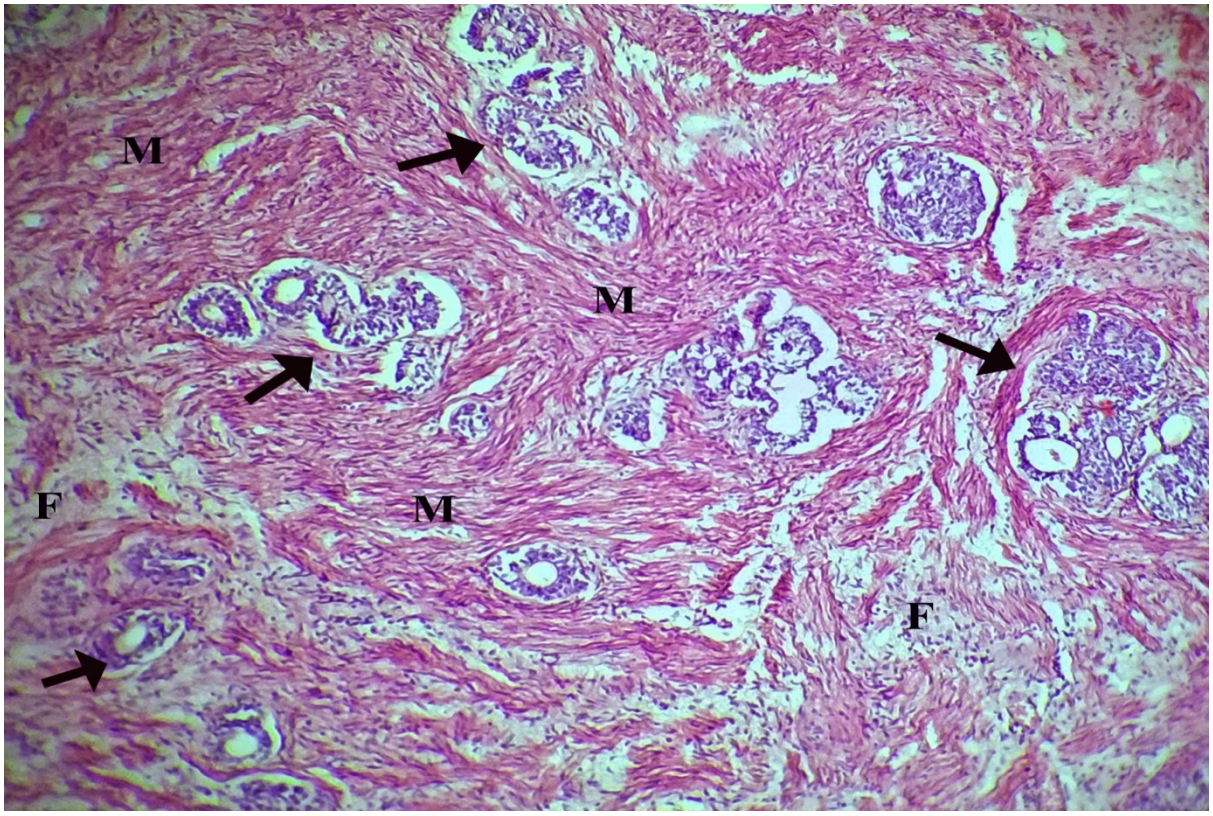

Figure 2: Section of 11year old prostate. Stroma showing predominantly muscular tissue. Glandular tissue (arrow) is rudimentary. M: Muscular Tissue, F: Fibrous Tissue 100X, H&E

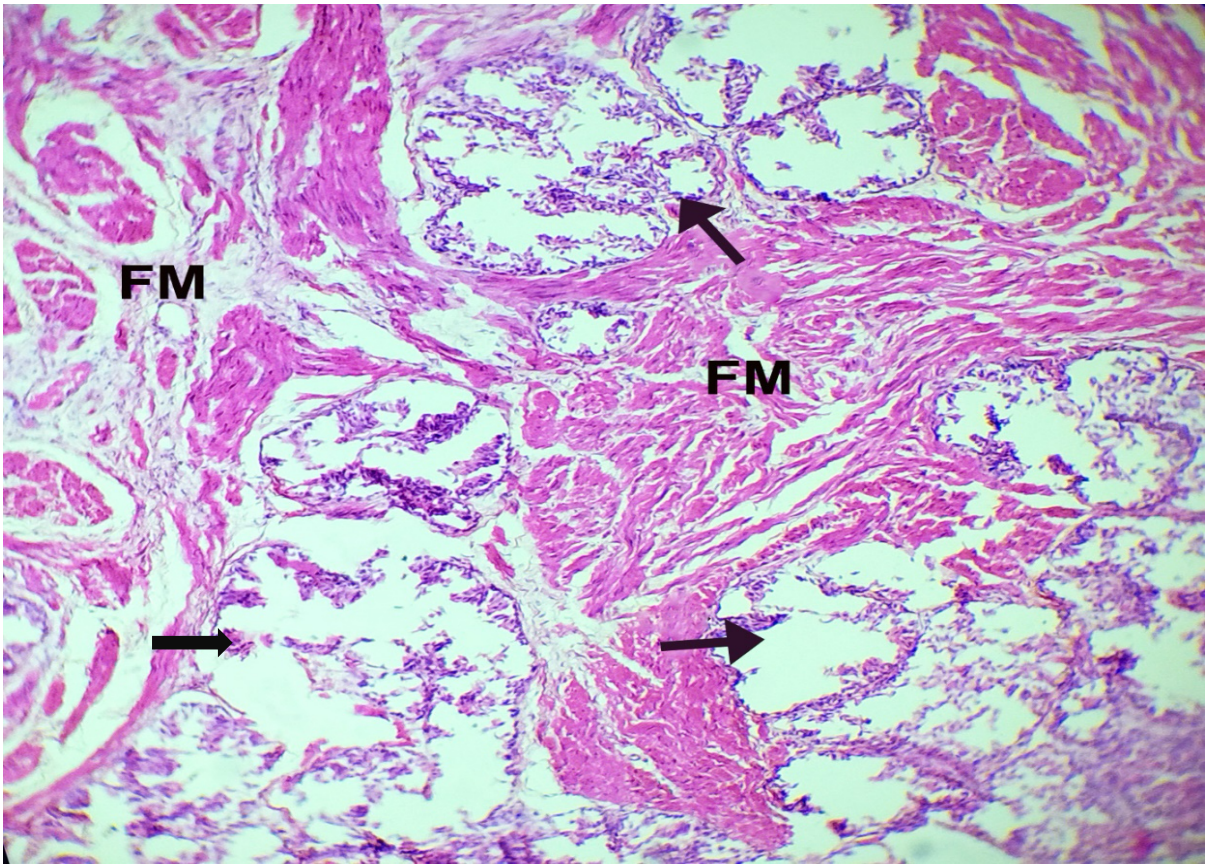

Figure 3: Section of 14 year old prostate with predominantly glandular tissue (G). 100X, H&E. FM: Fibromuscular stroma; Arrow-Glandular tissue

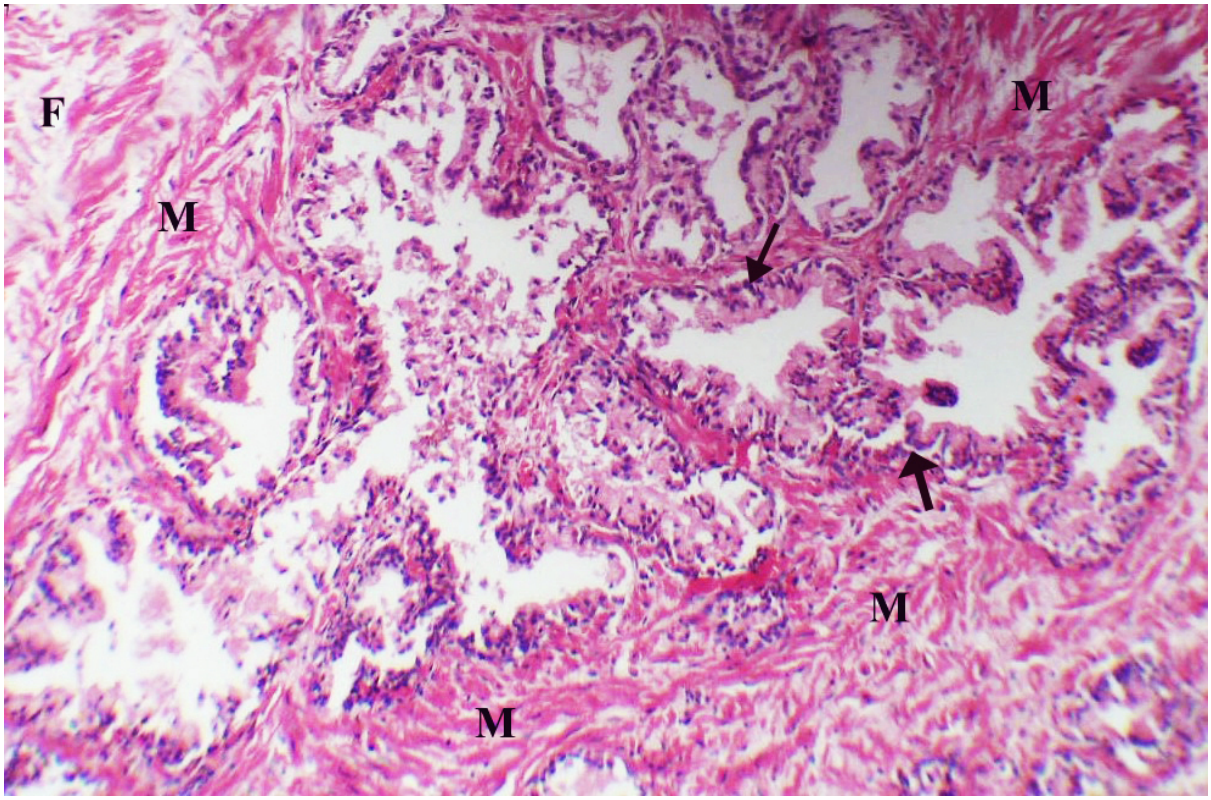

Figure 4: Section of 40 year old prostate with stroma showing predominantly muscular tissue. 100X, H&E. M: Muscular tissue, F: Fibrous tissue ;Arrow-Glandular tissue

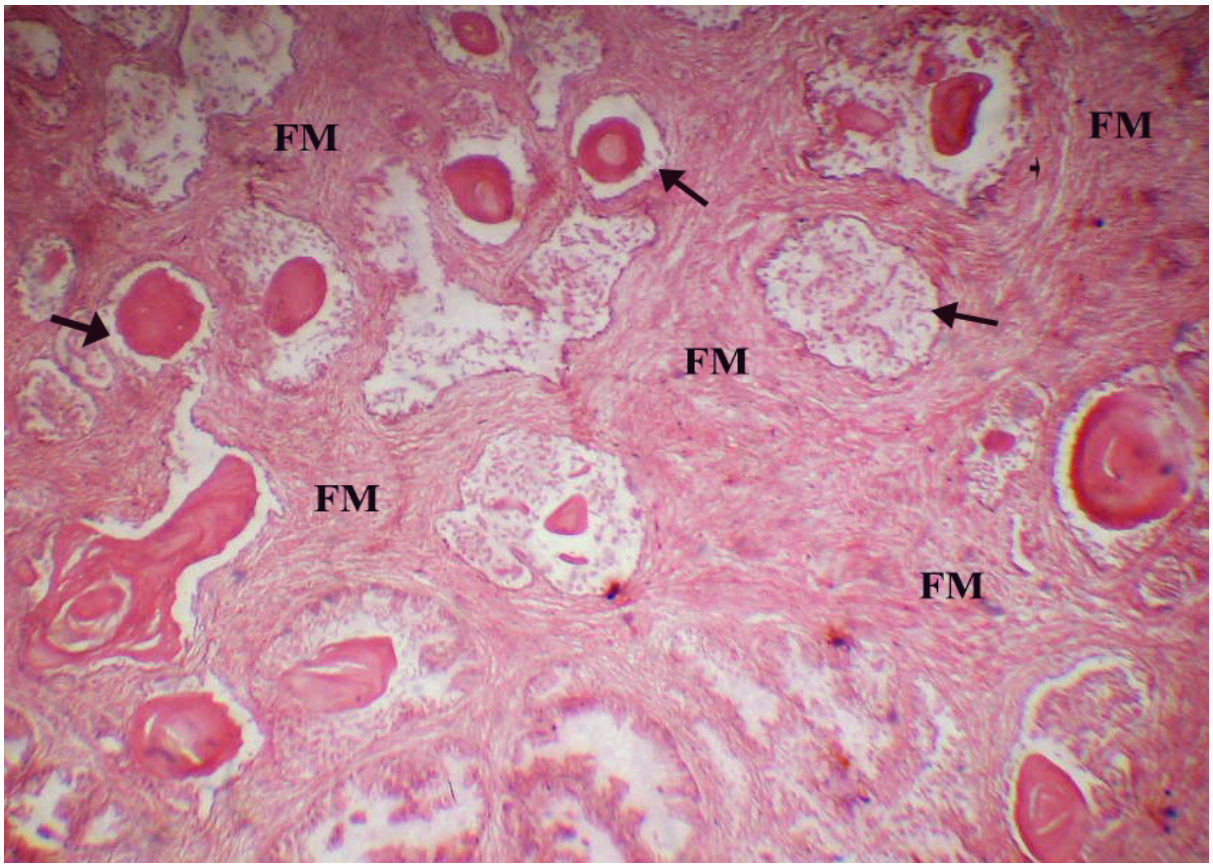

Figure 5: Section of 70 year old prostate. Fibromuscular stroma is predominant compared to glandular tissue (arrow). 100X, H&E. FM: Fibromuscular stroma

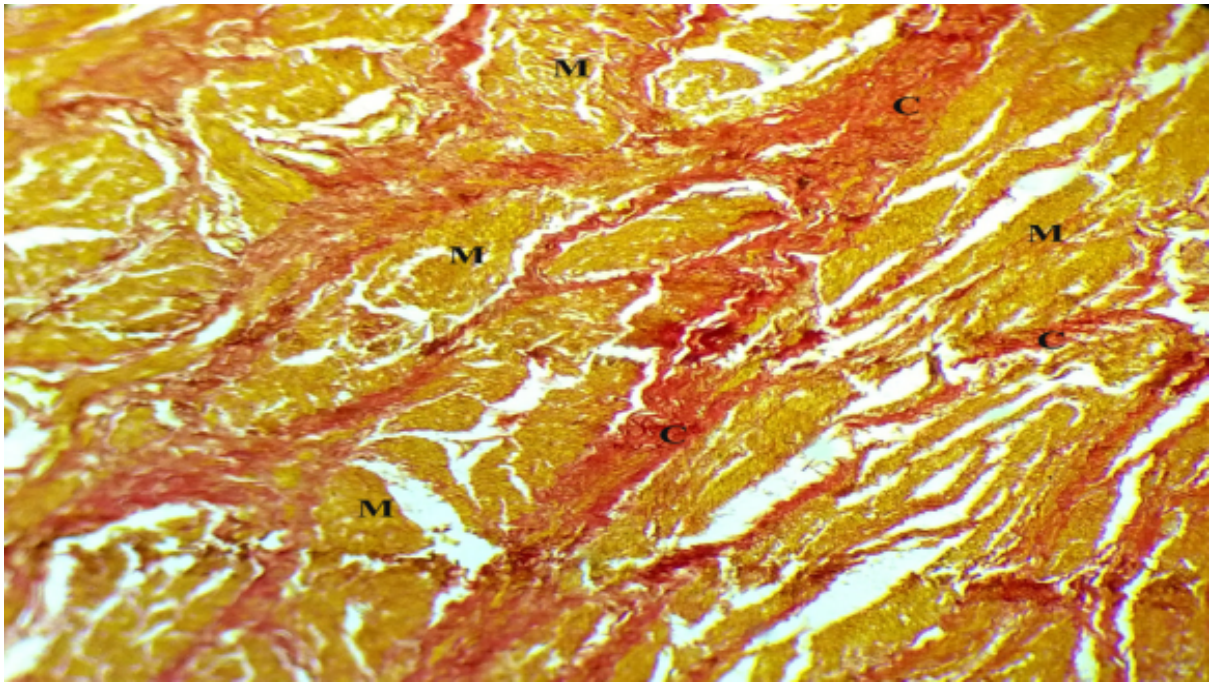

Figure 6: Section of 55 year old prostate. Stroma showing predominance of muscular tissue compared to fibrous tissue. Van Gieson staining 100X. C: Collagen fibres, M: Muscular tissue

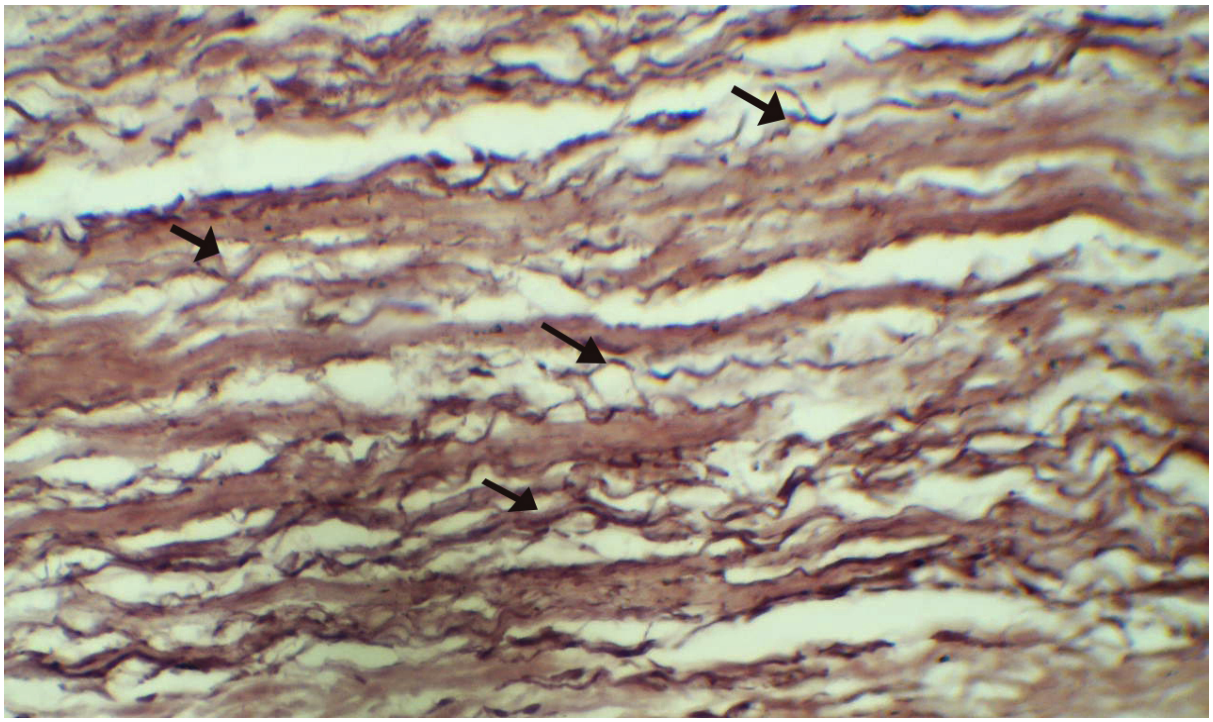

Figure 7: Stroma of 70 year old prostate showing the presence of elastic fibres (arrow mark). Orcein staining 400X

Discussion

Prostate is an androgen dependent fibromuscular and glandular organ. The glandular part of the prostate is developed in the third fetal month as solid endodermal outgrowths from the pelvic part of urogenital sinus and the fibromuscular part is developed in the fourth fetal month from the splanchnic mesoderm [1,3]. Lowsley described the origin of the prostate gland from five independent groups of tubules which begin to develop at about twelfth week of gestation [9].

In the present study, the fetal prostates chiefly consisted of fibromuscular stroma and glandular elements were poorly developed. The stroma showed more of fibrous connective tissue than smooth muscle. This was in agreement with findings of Amma et al. Amma et al reported that the fetal prostate glands showed rudimentary duct system

embedded in fibromuscular stroma and the stroma formed the bulk of the gland during the fetal period [11]. Cunha et al studied the development of fetal prostate glands and observed the distribution of smooth muscle. They concluded that human prostatic stroma is only partially differentiated at 19 weeks of gestation [12]. Swyer commented that the prostate gland at birth is chiefly composed of connective tissue with a relatively small proportion of smooth muscle[13].

In pre-pubertal prostates too, the fibromuscular stroma was predominant compared to glandular tissue, however, there was a gradual decrease in connective tissue fibres and the amount of smooth muscle fibres was seen to be increased. According to Andrews, from the fourth month until the age of 13 years the only change observed was a slight increase in the size of the prostate due to an increase in stroma and in the prostates of this age group, the tubules were widely separated by stroma [14].

The sections obtained from 14 year old prostate were similar to that of adult prostate and the amount of stroma was reduced. In the adult prostate glands, the number of acini increased and there was a reduction in the amount of stroma relative to the glandular tissue. D J Horsfall et al demonstrated that the stromal volume proportion of the prostate in both guinea pigs and men decreases at puberty due to the expansion of the epithelial cell compartment [15]. Lowsely reported the comparison between glandular tissue and stroma in youth before puberty is about one to five. After puberty in the adult, the ratio is one to three and in normal old age the ratio is one to four [16].

The muscular tissue formed the main portion of stroma in all the age groups other than group 1. Hutch et al suggested that the muscular tissue in the stroma is mainly non-striated [17]. This was in agreement with the present study. Sensibar et al identified that the percent of smooth muscle cells increases and the cellular shape changes with increasing age [18]. According to Moullin, the stroma of the prostate consisted of muscular and fibrous tissue and the muscular fibres are arranged concentrically around the alveoli [19].

The fibrous tissue in the stroma of prostate glands in all the age groups was constituted by collagen fibres mainly and elastic fibres were minimal. Moore reported that the stroma of prostate gland contained bundles of smooth muscles and a moderate amount of collagenous connective tissue and elastic fibres in between the muscle fibres [20]. In this study, although a moderate amount of collagen fibres was observed; the amount of elastic fibres was very less. In 61-75 years age group, there was a notable increase in the amount of fibromuscular stroma in 60% specimens. In these specimens, the follicles of the glands were smaller. Horsfall et al found that during aging, increased stromal mass was seen as the prominent histologic feature [15]. Arenas et al commented that in histologically normal prostates, with aging, an increase in the total volume of prostate was observed; this increase was caused by an increase in the stromal volume [21]. An expansion of stroma noted in the present study might be a part of aging process due to shrinkage of the follicles.

Deering et al demonstrated that the largest component of BPH was stroma, and it comprised approximately 50%-75% of the total hyperplastic tissue [22]. Chagas et al found an increase in the stromal component in prostate with BPH; both smooth muscle fibres and connective tissue markedly increased [23]. The increase in the amount of stroma observed in the present study could also be a hyperplasia of stromal elements due to benign hyperplasia of prostate.

Conclusions

In the present study, in fetal as well as pre-pubertal prostates, the fibromuscular stroma was present in higher proportion compared to glandular tissue until puberty. In post pubertal and adult prostate specimens, the glandular tissue was predominant and there was a reduction in the amount of fibromuscular stroma. This might be due to the hormonal influence at puberty and adulthood when the testosterone levels are high. In group V, increase in the amount of fibromuscular stroma observed in 60% of specimens could be considered as a part of normal aging process and can be attributed to reduced secretory activity of the glands of this age group due to fall in testosterone levels.

The increased stromal mass may also indicate a proliferation of stromal elements and could possibly be due to benign hyperplasia of prostate gland. These observations underscore the dynamic nature of prostatic tissue with advancing age, emphasizing the importance of further research to elucidate the underlying mechanisms and potential implications for prostatic health.

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