

Original research article

Morphogenetic evaluation of the prostate gland in human foetuses: an observational studyDr. Suman Kumari¹, Dr. Rajendra Prasad²¹Assistant Professor, Department of Anatomy, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India.²Professor and HOD, Department of Anatomy, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India.

Corresponding Author: Dr. Suman Kumari

write2mesuman17@gmail.com

Abstract**Aim:** evaluate the morphogenesis of the prostate gland in human foetuses.**Materials and methods:** The present study was conducted in Department of Anatomy. Total 100 discarded placentae were collected at random from deliveries (both vaginal and caesarian) conducted Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India, for 1 year. Total 100 foetuses of different gestational ages ranging from 14 weeks (80 mm) to 40 weeks (450 mm), products of terminated pregnancies under MTP Act of India, 1971 and stillbirths were collected from the Department of anatomy. Only those foetuses which were free from any gross anatomical abnormality were selected for the present study. The age of the foetuses were assessed from the obstetrical history, crown rump length (CRL) and gross features before fixation. The foetuses were preserved in 10% formalin for 12 to 15 days. The specimen were categorised into different age groups for study.**Results:** The first time of appearance of the prostate gland to the naked eye till its definitive adult shape (at term) is studied in detail. GROUP I: 14 Weeks: In the earliest specimen of this series (14weeks; CRL-7.7 cm), the developing prostate is seen as jelly like, slight fusiform bulge along the upper half of the developing urethra i.e. in the lower part of the urogenital sinus. GROUP II: 14 -18 Weeks: Prostate is more prominent and better defined than the previous age group and has gained in size, but still its length is more than its transverse measurement. GROUP III: 18 -22 Weeks: At subsequent age groups i.e. at 20 weeks it increases in size. Posterolaterally, the prostate is more prominent and the posterior surface looks flat. GROUP IV: 22-26 Weeks: At this stage, there is overall increase in size in all dimensions, thus gain in anteroposterior and transverse measurements resulting as lateral convexities. the transverse dimension is more than the vertical and anteroposterior dimensions. GROUP V: 26-30 Weeks: The prostate shows more increase in its transverse dimension. The posterior aspect seems to support the lower part of the urinary bladder in a funnel shaped way. Thus at around 30 weeks, it has a stunted pear shape appearance whose anterior portion has developed into a firm mass. GROUP VI: 30-34 weeks: With further increase in size in all dimensions, the shape of the prostate assumes as that of an adult. GROUP VII: 34-40 weeks: With further growth in this age group, there is overall increase in all dimensions. The posterior surface is flattened and the upper and lateral surface is occupied by the two lateral lobes.**Conclusion:** Increase in vertical and transverse dimensions, assumption of adult shape were noted as the age changes and at term, it has all the three components of the adult tissues although it is not as mature as in adult. This signifies that the growth of the prostate continues postnatally.**Key words:** Prostate gland, human foetuses, morphology and development.

Introduction

The human prostate is a walnut sized organ at the base of the urinary bladder. It is the seat of three major causes of morbidity; benign prostatic hyperplasia (BPH), prostate cancer and prostatitis. As such it commands more attention than might be expected from an organ of this size. Anatomical illustrations of the prostate have been published dating at least as far back as the mid-16th century when Andreas Vesalius, in 1543, published his observations of the male accessory glands.¹ The links between testicular and prostatic function have also been known for hundreds of years. John Hunter, writing in 1786 in "Observations on the glands situated between the rectum and the bladder, called vesiculae seminales" said "the prostate and Cowper's glands and those of the urethra which in the perfect male are soft and bulky with a secretion salty to the taste, in the castrated animal are small, flabby, tough and ligermentous and have little secretion".² The adult prostate is a compound tubular-alveolar gland found in most mammals.³ The gross structure differs considerably between species. Much of the descriptive work on the development of the prostate from its origins in the hindgut to descriptions of the adult organ was performed by anatomists and pathologists working in the early to mid-20th century. Subsequent work has outlined the molecular basis for these descriptions. Interest in prostate biology is centered around the human organ and that of the species, notably rats and mice used to model human diseases. A clear understanding of the differences in the structure of human and rodent prostates is important in assessing the results of animal studies. Prostatic development is dependent on both epithelial-mesenchymal interactions and androgens, whose effects are mediated via androgen receptors (ARs). The prostate develops from the embryonic urogenital sinus, which is composed of urogenital sinus epithelium (UGE) and urogenital sinus mesenchyme (UGM). Interactions between UGM and UGE are obligatory for prostatic development, and thus prostatic development only occurs when UGM and UGE are associated and are grown in the presence of androgens. During androgen-dependent prostatic development, UGM specifies prostatic epithelial identity, induces epithelial bud formation, elicits bud growth and ductal branching, promotes epithelial differentiation into secretory epithelial cells and determines the types of secretory proteins expressed.⁴⁻⁸

Materials and methods

The present study was the conducted in Department of Anatomy. Total 100 discarded placentae were collected at random from deliveries (both vaginal and caesarian) conducted Anugrah Narayan Magadh Medical College and Hospital, gaya, Bihar, India, for one year. after taking the approval of the protocol review committee and institutional ethics committee. Total 100 foetuses of different gestational ages ranging from 14 weeks (80 mm) to 40 weeks (450 mm), products of terminated pregnancies under MTP Act of India, 1971 and stillbirths were collected from the Department of anatomy . Only those foetuses which were free from any gross anatomical abnormality were selected for the present study. The age of the foetuses were assessed from the obstetrical history, crown rump length (CRL) and gross features before fixation. The foetuses were preserved in 10% formalin for 12 to 15 days. The specimen were categorised into different age groups as follows for easier study and observation.

Group 1- Up to 14 weeks

Group 2- 14-18 weeks

Group 3 -18-22 weeks

Group 4 -22-26 weeks

Group 5- 26-30 weeks

Group 6 -30-34 weeks

Group 7- 34-40 weeks

After proper fixation (for about 2 weeks) the foetuses were dissected. The abdomen was opened by a left paramedian incision. The incision was extended inferiorly to cut through the cartilage of the hip joint thus exposing urinary bladder and the prostate from the left. The specific age at which the gland first appeared in situ and was visible to the naked eye just below the urinary bladder was noted. The prostate gland was finally removed along with the urinary bladder and was studied for the growth and development and its changing size, shape and volume.

Results

The first time of appearance of the prostate gland to the naked eye till its definitive adult shape (at term) is studied in detail. Growth and development at specific age period at different age groups are described as below.

Group I: 14 Weeks: In the earliest specimen of this series (14weeks; CRL-7.7 cm), the developing prostate is seen as jelly like, slight fusiform bulge along the upper half of the developing urethra i.e. in the lower part of the urogenital sinus . A mild angulation also exists in between the proximal swollen part and the caudal part of the developing urethra. Posteriorly, the anlage of the developing prostate is seen enveloping the cephalic end of the developing urethra.

Group II: 14 -18 Weeks: Prostate is more prominent and better defined than the previous age group and has gained in size, but still its length is more than its transverse measurement and thus it has an elongated look and is tapered distally . The developing prostate is discernable both on anterolateral as well as on posterior aspects as a swollen fold of tissue enveloping the upper third of the developing urethra. It can be demarcated from the urinary bladder by a shallow groove and prostate is seen more prominent on the posterior aspect . Viewed from the side, the developing prostate looks like a tongue shaped structure merging with each other on the anterior aspect of the urethra.

Group III: 18 -22 Weeks: At subsequent age groups i.e. at 20 weeks it increases in size. It is seen developing transversely across the cephalic end of the urethra and at this stage, it assumes a more rounded appearance with increase in both transverse and anteroposterior measurements. There is increase in prostatic volume throughout from all its aspects. The prostatic swelling appears harder and more fibrous at this stage than the earlier stages. It is seen as a greyish white structure which could be the beginning of the formation of the capsule. Posterolaterally, the prostate is more prominent and the posterior surface looks flat.

Group IV: 22-26 Weeks: At this stage, there is overall increase in size in all dimensions, thus gain in anteroposterior and transverse measurements resulting as lateral convexities. The convexity on lateral aspect is more prominent as two protruding bodies whilst the dorsal surface is nearly flat with a median longitudinal groove. The prostate at 22 weeks is seen to have a greyish white covering which is glistening and is probably the beginning of the capsule formation. It is firmer in consistency as compared to the previous age group. The development of the prostate is more enhanced posteriorly and is seen as two lateral protruding masses from the cephalic end of the developing prostate. There is a pyramidal shaped elevation on the anterior aspect tapering toward the apex which is recognized as the anterior lobe. From the anterior view, the two lateral lobe rudiments are seen as ovoid swelling jutting out from the main tissue. On lateral view, a small ovoid swelling with rough surface is recognizable as the representative of the lateral lobes. From the posterior aspect, the two lateral swellings got merged with each other behind to form a flattened posterior lobe. The posterior surface is bigger than the lateral and anterior lobes. Thus the growth of the developing prostate is responsible to give a conical appearance with the broader cephalic end and a narrow tapered end caudally. In this age group, there is overall growth in all dimensions however, the transverse dimension is more than the vertical and anteroposterior dimensions.

Group V: 26-30 Weeks: It acquires a greyish white appearance losing its glistening jelly like appearance of previous age group at 26 weeks and the posterior surface shows reddish brown spots which are just visible to the naked eye and these spots may probably be the developing blood vessels (venous plexus). The prostate shows more increase in its transverse dimension. The posterior aspect seems to support the lower part of the urinary bladder in a funnel shaped way. The two lateral lobes are bulkier than the earlier age group and they fuse and get merged with each other in the same plane and form the posterior lobe. From the lateral view, the two lateral lobes are slightly higher than the anterior lobe and extend upwards and laterally. The capsule formation goes on and is well enhanced by 27 weeks as evidenced by a clear cut lower margin of the developing prostate and well separated out by a groove which demarcates it from the developing urethra. The upper margin is also separated out from the developing urinary bladder. The prostate thus acquires a firm looking appearance and is more fibrous and looks pinkish grey (because of the blood supply). The anterior lobe is represented by a band of fibromuscular tissue connecting the two lateral lobes in front of the urethra adjoining the neck of the bladder and is continuous posterolaterally to become the well formed lateral lobes. Thus at around 30 weeks, it has a stunted pear shape appearance whose anterior portion has developed into a firm mass.

Group VI: 30-34 weeks: With further increase in size in all dimensions, the shape of the prostate assumes as that of an adult. The prostate is well formed and has a firm nodular look and is reddish brown in color. As viewed from the front, the gland is firm due to more condensation of the fibres and muscles. The anterior lobe can be visualized which has a fibromuscular texture and is rougher than the other lobes. The two lateral lobes, as two eminences show more growth posterolaterally and are extended on the posterior lobe and are seen merging with each other on the posterior aspect. The inferior margin of the prostate is well developed and surrounds the urethra all around it delineating it thus showing the well developed capsule. On the posterior surface is seen a network of blood vessels by 30 weeks visible to the naked eye.

Group VII: 34-40 weeks: With further growth in this age group, there is overall increase in all dimensions. The prostate is firmer in consistency, harder than before and by 36 weeks, the two lateral protrusions are well developed and have a nodular rounded look presenting as two lobes with the central area flattened. Firm anterior lobe of the prostate is seen as a pyramidal shaped strip of prostatic tissue in front of the upper part of the urethra and neck of the bladder. The two lateral lobes seem to extend anterolaterally more or less assuming the adult shape. The false capsule is more distinct on the lateral lobes and is better defined as compared to the earlier age group. The vertical dimension decreases as seen from the anterior view and is about half of the horizontal dimension. The anterior lobe has a ratio of about one third of the lateral lobes. The posterior surface is flattened and the upper and lateral surface is occupied by the two lateral lobes.

Discussion

Development of the prostate begins with the growth of prostatic buds from the urogenital sinus at about 10th week of fetal development in Majority of the workers have laid more emphasis on histogenesis. The prostate gland begins to develop in the 10th week as a cluster of endodermal evaginations that bud from the pelvic urethra and grow into the surrounding mesenchyme.⁹ The prostate gland develops during the third month from interactions between the urogenital sinus mesenchyme and the endoderm of the proximal part of the urethra.^{10,11} The multiple endodermal outgrowths arise from the prostatic part of the urethra and grow into the surrounding mesenchyme. The glandular epithelium of the prostate differentiates from these endodermal cells.¹² In males the inferior portion of the primitive urogenital sinus gives rise to the pelvic urethra and to penile urethra. By 6th week, the germs cells migrating from the yolk

sac begin to arrive in the mesenchyme of the posterior body wall. The arrival of germ cells in the area just medial to the mesonephroi at the 10th thoracic segment induces cells of the mesonephroi and adjacent coelomic epithelium to aggregate into somatic sex cords that invest the germ cells. The sexual differentiation of genetic males begins at the end of the 6th week when a specific gene on the Y chromosome (SRY) is expressed in the sex cords cells. The product of this gene called the SRY protein initiates a development cascade that leads to the formation of the testes, the male external genitalia and the entire constellation of male secondary sex characteristics. The paramesonephric ducts degenerate. During the 3rd month the prostate and bulb urethral glands grow from the adjacent pelvic urethra.¹³ The present workers while studying on developmental gross anatomy notice a gradual change in the size of the prostate as age advances. In the present study, the youngest prostate studied is of a 14-week old foetus and the prostate is visible as a longitudinal strip of mesenchymal induration which is pearly white and jelly like surrounding the upper half of the developing urethra. The prostate is described to have four surfaces anterior, posterior and two inferolateral surfaces.¹⁰ The posterior surface is flat transversely and convex vertically. It is characterised by a midline groove that is wider toward the base of the gland and serves to partially separate the gland posterior into right and left lateral lobes.¹⁴ The posterior surface superiorly presents an annular groove through which the two ejaculatory ducts enter into the prostate. This annular groove subdivides this surface into upper smaller and lower larger parts. The latter is again subdivided by a median vertical groove into two lateral right and left lobes. The upper or superior part belongs to the median lobe and intervenes between the two ejaculatory ducts posteriorly and the prostatic urethra anteriorly. The lateral lobes are connected together anteriorly in front of the urethra by a fibromuscular band known as the isthmus which has no glandular tissue.¹⁰ The posterior surface is described as nearly flat.¹⁵ According to our present study, the posterior surface is seen as a merging surface from the two bulge of lateral lobes in a funnel shape with a V shaped trough toward upper end in which seminal vesicles are also converged towards the midline. The numbers 4,3,2 indicate the transverse, vertical and anteroposterior dimensions of the gland in cms.¹⁰ In our present study, the anteroposterior, transverse and vertical dimensions are measured. The mean transverse dimension of 38-42 week old foetus is 14.92mm, that of vertical is 10.25 mm, and the anteroposterior dimension is 7.21mm.

Conclusion

Increase in vertical and transverse dimensions, assumption of adult shape were noted as the age changes and at term, it has all the three components of the adult tissues although it is not as mature as in adult. This signifies that the growth of the prostate continues postnatally.

Reference

1. Vesalius, A.; O'Malley, CD.; Calcar, JSv; Saunders, JBdCM. The illustrations from the works of Andreas Vesalius of Brussels : with annotations and translations, a discussion of the plates and their background, authorship and influence, and a biographical sketch of Vesalius. World Publishing Company; 1950.
2. Geller J. Pathogenesis and medical treatment of benign prostatic hyperplasia. Prostate Supplement. 1989; 2:95-104.
3. Price, D.; Williams-Ashman, H. The accessory reproductive glands of mammals. In: Young, W., editor. Sex and internal secretions. 3. Vol. 1. Williams and Wilkins; Baltimore: 1961. p. 366-448.
4. Cunha GR, Donjacour AA, Cooke PS, Mee S, Bigsby RM, Higgins SJ, et al. The endocrinology and developmental biology of the prostate. Endocrine Rev 1987;8:338 - 62.

5. Cunha GR, Fujii H, Neubauer BL, Shannon JM, Sawyer LM, Reese BA. Epithelial-mesenchymal interactions in prostatic development: I, morphological observations of prostatic induction by urogenital sinus mesenchyme in epithelium of the adult rodent urinary bladder. *J Cell Biol* 1983;96:1662–70.
6. Cunha GR, Sekkingstad M, Meloy BA. Heterospecific induction of prostatic development in tissue recombinants prepared with mouse, rat, rabbit, and human tissues. *Differentiation* 1983;24:174 – 80.
7. Cunha GR, Reese BA, Sekkingstad M. Induction of nuclear androgenbinding sites in epithelium of the embryonic urinary bladder by mesenchyme of the urogenital sinus of embryonic mice. *Endocrinology* 1980;107:1767–70.
8. Cunha GR. Androgenic effects upon prostatic epithelium are mediated via trophic influences from stroma. In: Kimball FA, Buhl AE, Carter DB, eds. *New approaches to the study of benign prostatic hyperplasia*. New York: Liss, 1984. 81–102.
9. Wein AJ. Normal development of the urogenital system. Kavoussi LR, Novide AC, Partin AW, Peters CA. editors. In *pediatric urology*. Vol 4. 9th ed. Philadelphia: Saunders Elsevier; 2007. p. 3137-9.
10. Sahana SN. *Genital System In: Human Anatomy*. 3rd edition. India: Books and Allied Private Limited; 1980. p. 402-5.
11. Hammerich KH, Ayala GE, Wheeler TM. Anatomy of the prostate gland and surgical pathology of prostate cancer. In: Hedvig Hricak, Scardino PT, editors. *Prostate Cancer*. New York: Cambridge University Press; 2009.
12. Moore KL, Persaud TVN. The urogenital system. In: *The developing human, clinically oriented embryology*. 8th ed. Philadelphia: Elsevier; 2008. p. 263- 70.
13. Larsen WJ. Development of the urogenital system. In: *Human embryology*. 3rd ed. Philadelphia: Churchill Livingstone; 2001. p. 282-3.
14. Skandalakis JE, Colborn GL, Badalament RA, Scaljon W, Parrott TS, Galloway NTM et al. Male genital system. Skandalakis JE, Weidman TA, Colborn GL. editors. In: *Skandalakis Surgical Anatomy*. 1st ed. Greece: Paschalidis Medical Publications Ltd; 2004. p. 1415-38
15. Franks LM. Benign nodular hyperplasia of the prostate: a review. *Ann Roy Coll Surg Engl*. 1953; 14(2): 92-106.

Received: 03-09-2020 || Revised: 06-09-2020 || Accepted: 20-09-2020