A histological study of uterus in reproductive and postmenopausal women

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Abstract

Background and aims: The “Uterus” or “Womb” is a part of the female reproductive tract that receives the fertilized ovum from the oviduct, provides the bed for implantation and establishes the vascular connections necessary for sustenance of the embryo throughout its development. Due to increasing rate of infertility, the reproductive organs are gaining importance. The aim of the study is to ascertain that the research work could be utilized for investigation and guidance for management of infertility cases. The knowledge of normal histological architecture of the uterus will be of help to isolate any pathological changes. Materials and methods: Ten samples each from reproductive and postmenopausal women were collected from fresh unembalmed human cadavers. The slides were prepared using the standard laboratory procedure. Stress was given on the structure of endometrium, cervical mucosa and squamocolumnar junction. Endometrial and cervical mucosal thickness were measured in both groups. Results: Significant differences of histological architecture were noted between the two groups. The average endometrial thickness as measured by micrometer scale was 4.29 mm and 1.64 mm in reproductive and post-menopausal women respectively. The average cervical mucosal thickness was 2.76 mm and 1.55 mm in reproductive and postmenopausal women respectively. Conclusion: Knowledge of the normal histological structure of the uterus is of prime importance to have the basic knowledge of various pathological entities.

Key words: endometrium, cervical mucosa, squamocolumnar junction, glandular epithelium, myometrium
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product of conceptus, abnormal uterine anatomy, pathology of the pelvis were excluded from the study.

From the different dissected parts of the body and cervix, approximately 3-5 mm size pieces were taken and fixed in 10% formalin and labelled separately. Tissues were kept in 10% formalin for 24-48 hours. The fixed tissues were processed for embedding in paraffin and sectioned at 5 µm thickness in a 'Rotary microtome'. Sections of tissues were stained by routine Haematoxylin and Eosin according to standard method of Carleton.

Different layers of uterus, epithelial lining and glandular structures were observed under both low and high power objective. Endometrial thickness of uterine body and mucosal thickness of cervix were measured with the help of a 'Spencer ocular' lens and objective micrometer scale. One division of the ocular micrometer scale was equivalent to 5µm at 400 magnification.

Calculation of the micrometer scale

2 divisions of ocular micrometer coincide with 1 division of objective micrometer. Therefore, 1 division of ocular scale=1/2 division of objective micrometer scale.

As one division of objective micrometer scale measures 0.01mm, hence 1/2 division = 1/2 x 0.01 = 0.005 mm = 5µm (since 10^{-3} mm = 1µm)

Therefore, 1 division of ocular micrometer scale = 0.005mm

Statistical Analysis

The data on endometrial thickness (mm) and cervical mucosal thickness (mm) were analyzed by standard statistical methods. The data were analyzed to calculate the mean and t test was applied to find out the significant difference between mean values.

Results

In the present study uteri were grouped into two as follows:

Group A: Reproductive (14 years to 49 years)
Group B: Postmenopausal (50 years and above)

Micro anatomical features of human uterus were observed as follows:

Endometrium

In reproductive age group the endometrium or mucosal lining of the uterus was found to be composed of simple columnar epithelium and a layer of connective tissue i.e. the endometrial stroma or lamina propria. The epithelium consisted of non-ciliated, secretory columnar cells. The glands were tubular running perpendicular to the luminal surface and penetrated up to the myometrial layer.

In postmenopausal age group the endometrium was found to be consisting of only the stratum basalis. The glandular epithelial cells were cuboidal or low columnar with no mitotic figures. The secretory activity was absent in glandular epithelial cells.

During reproductive age the endometrium was variable in thickness measuring between 1.5 mm to 6.2 mm at different stages of menstrual cycle. In post-menopausal age the endometrium was thin and atrophic. The average endometrial thickness as measured by micrometer scale was 4.29 mm and 1.64 mm in reproductive and post-menopausal age group respectively (Table 1). The inter-group variation of endometrial thickness has been shown with the help of bar diagram (Fig 1).

Since calculated value of ‘t’ is greater than 1% table value of ‘t’ for 18 d.f., it is highly significant. Therefore endometrial thickness in reproductive and postmenopausal women differs significantly.

Myometrium

In both the age groups the main bulk of uterus was found to be consisting of smooth muscle i.e. myometrium, which was composed of interlacing bundles of long and slender fibers arranged in ill-defined layers. All the muscle layers were seen intermingled with each other in both the age groups. The thickness of the myometrium was more in reproductive age than that of postmenopausal age. The myometrium in postmenopausal age was thin and atrophic.
### Table 1: Comparison of endometrial thickness (mm) of uterus in reproductive and postmenopausal age group

<table>
<thead>
<tr>
<th>No of Specimen</th>
<th>Reproductive Age (Group A)</th>
<th>Post Menopausal Age (Group B)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age in Years</td>
<td>Endometrial Thickness</td>
</tr>
<tr>
<td>1</td>
<td>15(NP)</td>
<td>3.1</td>
</tr>
<tr>
<td>2</td>
<td>17(NP)</td>
<td>1.5</td>
</tr>
<tr>
<td>3</td>
<td>22(NP)</td>
<td>3.4</td>
</tr>
<tr>
<td>4</td>
<td>25(NP)</td>
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<td>8</td>
<td>38</td>
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<td>9</td>
<td>40</td>
<td>4.5</td>
</tr>
<tr>
<td>10</td>
<td>42</td>
<td>4.8</td>
</tr>
</tbody>
</table>

Mean: $\bar{x} = 4.29$, $\bar{y} = 1.64$

NP = Nulliparous

Calculated value of $t = 5.95327$; d.f. = 18; Table value of $t$ at 1% level of significance = 2.88; $p$-value = 1.240365E-05

### Table 2: Comparison of cervical mucosal thickness (mm) in reproductive and postmenopausal age group

<table>
<thead>
<tr>
<th>No of Specimen</th>
<th>Reproductive Age (Group A)</th>
<th>Post Menopausal Age (Group B)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age in Years</td>
<td>Mucosal Thickness</td>
</tr>
<tr>
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<td>17(NP)</td>
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<td>2.7</td>
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<tr>
<td>10</td>
<td>42</td>
<td>2.6</td>
</tr>
</tbody>
</table>

Mean: $\bar{x} = 2.76$, $\bar{y} = 1.55$

NP = Nulliparous

Calculated value of $t = 10.09698$; d.f. = 18; Table value of $t$ at 1% level of significance = 2.88; $p$-value = 7.69668
Cervical mucosa

The epithelial lining of the cervix in the upper part of the cervical canal was seen to be simple columnar epithelium. The cells were tall in the reproductive group with light stained cytoplasm and basally placed nuclei. In the lower part of the canal the epithelium was stratified squamous epithelium of non-keratinized variety.

The squamocolumnar junction was abrupt in most of the tissues. In the upper part of the canal there were patchy areas of cilia which were maximum in the reproductive age group.

The stroma was found to contain the cervical glands which opened into the luminal surface of the epithelium. The proportion of the glands was more in the reproductive group than that of post menopausal group. The glands were lined by non-ciliated simple columnar epithelium.

The mucosal thickness as measured by micrometer scale was found to be thicker in reproductive age group. The average thickness of the cervical mucosa was 2.76 mm and 1.55 mm in reproductive and postmenopausal age group respectively (Table 2). Inter-group variation of cervical mucosal thickness has been shown with the help of bar diagram (Fig 2).

Since calculated value of 't' is greater than 1% table value of 't' for 18 d.f., it is highly significant. Therefore cervical mucosal thickness in reproductive and postmenopausal group differs significantly.

Cervical musculature

The muscular layer was found to consist of smooth muscle along with dense connective tissue containing both collagen and elastic fibers. It was noticed that proportion of muscle was more in reproductive age group than that of postmenopausal group. In postmenopausal group the elastic and collagen fibres were replaced by fibrous tissue.

Discussion

This study has revealed several points of interest having marked importance in practical life with the hope that it will help in the investigation and management of various pathological conditions related to the uterus.

In reproductive age group the endometrium was seen to be lined by a simple columnar epithelium (Fig.3). This finding is analogous with that of Dawn, Cunningham et al. Just after menstruation the epithelium was found to be cuboidal and later became columnar. Similar observation was made by Wilson et al., Jones, Novak and Woodruff, Clayton et al., Tindall and Healy et al. In the early part of menstrual cycle the endometrial glands were simple straight tubes lined by columnar epithelium with large oval nuclei (Fig.3). But later on the glands became curved or tortuous (Fig.5,6). Similar observations were noted by Clayton et al., Fox and Buckley, and Healy et al. Subnucleolar vacuolation was also noticed in the endometrial glands (Fig.6). This was also noted by authors like Passmore and Robson, Rao and Roy Choudhury, Padubidri and Daftary. This vacuolation is considered as the presumptive evidence of ovulation.

In contrast to reproductive endometrium the postmenopausal endometrium was found to be thin and atrophic and was composed of stratum basalis only (Fig.4). This finding corroborates with that of Massani, Rao and Roy Choudhury and Young et al. The endometrial glands were sparse and inactive, which was also reported by Tindall and Young et al. The glandular epithelium in the postmenopausal age group consisted of low columnar or cuboidal epithelium with no mitotic figure (Fig.7). This finding was similar to findings of Massani, Fox and Buckley, Young et al.

In the present study endometrial thickness was found to be variable in reproductive age group depending on different phases of the menstrual cycle (Table 1). Similar observation was made by other authors (Table 3).

The average thickness of the postmenopausal endometrium was found to be 1.64 mm (Table 1). This corroborates with the findings of Padubidri and Daftary, who mentioned that at menopause the endometrium is only 1-3 mm in thickness.
The difference in endometrial thickness might be due to the fact that the endometrium is very refractory to the hormones i.e. oestrogen and progesterone secreted by ovary. Hence the endometrial thickness in reproductive age group suggests high level of oestrogen in the plasma whereas atrophic endometrium in post-menopausal group indicates low oestrogen level in plasma. This observation was also made by several authors - Fox and Buckley\textsuperscript{19}, Cunningham et al\textsuperscript{11} and Padubidri and Daftary\textsuperscript{22}.

In both the age groups the myometrium was found to be composed of interlacing bundles of long and slender fibres arranged in ill defined layers (Fig.8,9). The outermost and innermost layers were thin and consisted of chiefly longitudinal and obliquely dispersed fibres. This finding was also supported by Bloom and Fawcett\textsuperscript{4}, Gartner and Hiatt\textsuperscript{12} and Healy et al\textsuperscript{18}.

The thickness of myometrium was more in reproductive age. In postmenopausal age the myometrium was thin, fibrous and atrophic (Fig.9). This observation was supported by Rao and Roy Choudhury\textsuperscript{21}, Young et al\textsuperscript{24}. These atrophic changes could possibly be due to atrophy of the muscle fibres and increase in fibrous connective tissue due to absence of oestrogen in the postmenopausal age.

It was observed in the present study that the mucosal thickness in the upper part of cervical canal was 2.76 mm and 1.55 mm in reproductive and postmenopausal age respectively. It could be due to increase in number of glands present in reproductive age. The mucosal thickness matches with the findings of Bloom and Fawcett\textsuperscript{4} and Bannister and Dyson\textsuperscript{26}.

The epithelial lining of the cervix in the upper part of the canal i.e. endocervix was found to be simple columnar type. Similar observation was made by Anderson and Genadry\textsuperscript{27}, Dawn\textsuperscript{10}, Impey\textsuperscript{28}, Young et al\textsuperscript{24} and Gartner and Hiatt\textsuperscript{12}. In the upper part of the canal there were patchy areas of cilia which were maximum in the reproductive group. This was also observed by Fluhmann and Dickmann\textsuperscript{29}, Ham and Cormack\textsuperscript{30} and Moghissi\textsuperscript{31}. These ciliae probably help in the transport of sperm towards the body the uterus.

In the lower part of the canal i.e. the ectocervix, the epithelium was found to be nonkeratinized stratified squamous type (Fig.10). This is akin to the findings of Anderson and Genadry\textsuperscript{27}, Young et al\textsuperscript{24}, Gartner and Hiatt\textsuperscript{12} and Healy et al\textsuperscript{18}. In the present study, it was observed that after menopause, the stratified squamous epithelium was atrophic and thin (Fig.11). Fox and Buckley\textsuperscript{19} have stated that after menopause the depth

\begin{table}
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\begin{tabular}{|l|l|}
\hline
\textbf{Authors} & \textbf{Endometrial Thickness (mm)} \\
\hline
Novak and Woodruff (1979)\textsuperscript{15} & 1-2mm to 3-8mm \\
Rao and Roy Choudhury (1984)\textsuperscript{21} & 2mm to 5-6mm \\
Tindall (1994)\textsuperscript{17} & 1-5mm \\
Dawn (2004)\textsuperscript{10} & 1-10mm \\
Cunningham et al (2005)\textsuperscript{21} & 0.5-5mm \\
Young et al (2006)\textsuperscript{24} & 1-5mm \\
Healy et al (2008)\textsuperscript{18} & 1-2mm to 6mm \\
Ross and Pawlina (2011)\textsuperscript{25} & 1-6mm \\
Present study & 1.5-6.2mm (mean = 4.29mm) \\
\hline
\end{tabular}
\end{table}
Fig 1: Bar Diagram showing inter-group variation of endometrial thickness of Uterus

Fig 2: Bar diagram showing inter-group variation of mucosal thickness of cervix

Fig. 3: Photomicrograph showing endometrium of reproductive uterus under low power magnification (100X)

Fig. 4: Photomicrograph showing endometrium and a part of myometrium of postmenopausal uterus under low power magnification (100X)

Fig. 5: Photomicrograph showing tubular and tortuous glands in uterus of reproductive age (100X magnification)

Fig. 6: Photomicrograph showing subnuclear Vacuolation (arrow) in the endometrial glands of reproductive uterus (400X magnification)

Fig. 7: Photomicrograph showing endometrial glands lined by low columnar or cuboidal epithelium in postmenopausal uterus (400X magnification)

Fig. 8: Photomicrograph showing myometrium and a part of the endometrium (stratum basalis) in reproductive uterus (100X magnification)
and maturity of cervical squamous epithelium becomes shallow and maturation is arrested. The atrophic mucosa is particularly susceptible to infection.

The squamocolumnar junction—which is an abrupt change of epithelium from columnar to squamous type was found to be situated at or near the external os (Fig. 13). This is supported by similar findings of Tindall[33] and Young et al[24]. This abrupt change is due to the effect of oestrogen which has been experimentally proved on mouse by Graham[32]. The site of squamocolumnar junction was found to be variable. After menopause it was found at a higher level i.e. within the endocervical canal. Similar observation was also made by Ostergard[33] and Anderson et al[27].
The stroma was found to contain the tubular branched cervical glands (Fig.12) which were lined by nonciliated secretory columnar epithelium. Similar findings were noted by Bannister et al.26, Dawn10, Gartner and Hiatt12 and Healy et al.18. The proportion of the glands was more in reproductive group than in the postmenopausal group which was supported by Tindall17.

In the present study the muscle layer of the cervix was found to be composed of smooth muscle along with dense connective tissue- both collagen and elastic fibres. This finding was similar to that of Bannister and Dyson26 and Healy et al.18. The muscle fibres were found to be more abundant in reproductive group than that of postmenopausal group. In the postmenopausal age the elastic and collagen tissues were replaced by fibrous tissue (Fig.11). This observation was akin to that of Blaikely34.

Conclusion

The present study has highlighted the major histological changes of uterus in reproductive and postmenopausal women. Endometrium is the ‘mirror’ of the ovarian cycle because it responds in a consistent manner to the fluctuating concentration of gonadotrophin and ovarian hormones. Hence there is a wide scope for uterus to be studied with advanced techniques for investigation and management of infertility cases. Uterine neoplasia (both benign and malignant) and cervical pathology especially carcinoma are common clinical entities in present era. The knowledge of normal histological structure as well as changes in different age groups may aid in the early diagnosis and treatment of any disease of this part of female reproductive tract.

References


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