A Pilot Study on Thickened Blood Vessels in Endometrial Curettage in Dysfunctional Uterine Bleeding

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Abstract

Background: Dysfunctional uterine bleeding (DUB) is a common disease. About 10% of patients registered with DUB in Gynecology OPD for treatment in developing countries. There has been a change in the rhythmic cyclic menstruation that causes excessive and irregular bleeding. Lack of ovulation or oligo-ovulation leads to permanent estrogenic effects without opposing the progesterone effects. Other causes of the estrogen domain may have similar effects. The relative estrogen domain causes several changes in the uterine vascular system that causes menstrual bleeding.

Objective: To determine the frequency and significance of thickened blood vessels in curettage of the endometrium in dysfunctional uterine bleeding.

Materials and methods: It was a Retrospective cross-sectional pilot study conducted at Department of Gynecology and Obstetrics, Jinnah Hospital Lahore for one-year duration from January 2017 to December 2017. Hematoxylin and eosin (H&E) stained sections 30 consecutive incident cases of endometrial curettage due to dysfunctional uterine bleeding were examined by an optical microscope, with particular regard to the number of thickened blood vessels. All patients with history of endometrial curettage with dysfunctional uterine bleeding were included while curettage of uterine mucosa in patients with a specific etiology, such as endometritis, atypical hypertrophy, retained products, intrauterine devices (intrauterine device) were excluded.

Results: Over 50% of patients were perimenopausal, i.e. 40-55 years of age. All endometrial procedures included thickened blood vessels. On average, there were about 8 blood vessels thickened by curettage of the endometrium.

Conclusion: Estrogen-induced vascular lesions result in greater permeability, which can lead to the accumulation of various plasma proteins with increased intramural vascular thickening. These thickened veins may not contract properly, causing excessive bleeding and prolongation.

Introduction

Excessive menstruation is common in perimenopausal women. Endometrial curettage produces a "hemorrhagic endometrium" characterized by thin-walled, brittle, fragile uterine stromata dripping red blood cells and fibrin clot, usually indicative of an anovulatory cycle(1,2). However, endometrial curettage can also be endometrial hypertrophy, endometrial polyps and thick walls of blood vessels(3). These thick-walled blood vessels can play an important role in maintaining excessive bleeding. We examined 30 endometrial curettes to detect the presence of thick-walled blood vessels; individually or in groups (4,5,6).

Materials and Methods

It was a Retrospective cross-sectional pilot study conducted at Department of Gynecology and Obstetrics, Jinnah Hospital Lahore for one-year duration from January 2017 to December 2017. Thirty endometrial biopsies with a history of dysfunctional uterine bleeding (DUB) were microscopically examined. All curettage of the endometrium had been specially evaluated for the presence of thickened blood vessels. Slides routinely processed with hematoxylin and eosin was examined and appropriate lesions taken as needed. The presence of large, thick blood vessels was determined and reported in each biopsy individually or in focus groups.

Hematoxylin and eosin (H&E) stained sections 30 consecutive incident cases of endometrial curettage due to dysfunctional uterine bleeding were examined by an optical microscope, with particular regard to the number of thickened blood vessels. All patients with history of endometrial curettage with dysfunctional uterine bleeding were included while curettage of uterine mucosa in patients with a specific etiology, such as endometritis, atypical hypertrophy, retained products, intrauterine devices (intrauterine device) were excluded.

Results

All biopsies contained thick walled blood vessels. Parts of the endometrium reveal variable patterns. In many places, thick
glasses were sent alone or in groups. The walls of the ships were significantly thickened with a relatively narrow light. The walls looked quite fibrotic. (Figure 1). Sometimes these vessels squeeze the endometrial glands, which cause cystic changes in the glands and further aggravate the hemodynamics of the endometrial vessels (Figure 2). On the other hand, the clusters of vessels at places were arranged in rounded clusters clearly leading to the pseudo-polyp formation (Figure 3). These clusters of thickened vessels also appeared in parallel giving rise to pedicle of pseudo polyp formations (Figure 4). Frequently observed a pattern of hemorrhagic endometrium which is characteristic of anovulatory cycle. There was exudation of the plasma and scattered stromal hemorrhages mostly due to fragile more permeable thin walled vessels. These vessels themselves also become cystically dilated due to increased pressure of edematous stroma. The glands themselves in these areas were small and simple perhaps due to ischemia secondary to frequent small hemorrhages (Fig 5).

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<tr>
<th>Serial #</th>
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<td>1</td>
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Table 1: Number of thick blood vessels in individual endometrial biopsies

Figure 1: Clusters of thickened vessels (H&E X 100)

Figure 2: Thickened vessels compressing and distorting the glands (H&E X 100)

Figure 3: The vessels are arranged in nodular configuration leading to pseudo-polyp formation (H&E X 100)
Discussion

Menstrual bleeding usually occurs in the perimenopausal period, with an increased incidence of ovulation and oligo-ovulation. However, this can also happen in relatively young age groups(7,8). The relative increase in estrogen is considered the most important etiological factor. This leads to several morphological symptoms at microscopic level. One of them is similar to an increase in angiogenesis, and the other thickens the blood vessels causing cramps, which contributes to permanent bleeding(10).

All of our DUB biopsy cases had several thickened blood vessels. The minimum number of vessels was 4 and the maximum number was 19, with an average of 7.87 (Table 1). Over 50% of 16/40 patients were older than 40 years. Only 5 patients were under 30 years old. None of the patients were younger than 20 years.

Endometrial vessels are very sensitive to estrogen. Increased receptor levels and a change in endometrial morphology have been found to indicate the role of estrogen instead of DUB. Hickey said that prolonged estrogen stimulation can cause irregular withdrawal in bleeding, which is why cyclic progesterone is regularly used to cause withdrawal in bleeding in the second half of the cycle(11).

Due to various mechanisms, such as hormone receptors and angiogenic chemicals, millions of small vessels multiply in stromal edema and counteract without estrogen because of bleeding. However, over time, the walls of the vessels begin to thicken, perhaps due to deposits in the walls of the vessels and components of the red blood cells, followed by intramural fibrosis(12). These thickened container groups may not be effective in shrinking and closing. The persistence of these difficult vessels can cause permanent bleeding. Ischemia can cause atrophy of the glands in focal areas due to microhemorrhage. On the other hand, the estrogen domain can cause glandular growth in areas where ischemia is not effective(13).

Vascular pathology seems to play an important role in causing various divergent conditions, such as smooth fibroids, amytrophic lichen sclerosis, and simple cystic hyperplasia. The complex interaction of vascular pathology, i.e., increased proliferation, increased permeability, stromal edema, can stimulate uterine musculoskeletal smooth muscle, which can reach a peak in the formation of leiomyosarcoma. These vascular changes are not uncommon in leiomyosarcomas. Ischemia and swelling of the skin around the perineum can cause atrophic sclerosis of lichen. The resulting reduced oxygen supply and increased edema permeability may explain various areas and features of lichen sclerosis.

Our work sheds light on some aspects of this puzzle that may be useful to solve. Chang et al., explained Angiogenic growth factors. For example, vascular endothelial growth factor (VEGF) and smooth myoma. VEGF is one of the most important angiogenic growth factors(14). VEGF regulates angiogenesis and mediates cell growth and differentiation caused by sex steroids. VEGF-mediated activities appear to contribute to the pathogenesis of leiomyosarcoma. Genetic differences in VEGF, including polymorphisms, may also be associated with the complex pathogenesis of leiomyomas. Livingstone found that dysfunctional ovarian bleeding (DUB) is associated with a reduction in vasoconstriction and the formation of hemostatic plugs, and the lack of DUB ovulation and advanced bleeding are associated with altered endometrial angiogenesis and vascular fragility.

The role of hormones, especially estrogen, as the etiology of various vascular lesions cannot be denied. This applies to genital and non-genital lesions. Hepatic hemangiomas, amytrophic lichen sclerosis, smooth fibroids, endometrial hyperplasia, etc.(15). To some extent, this is due to deviations of hormones, especially estrogens. Paradoxically, it appears that
hormones are also used to treat certain vascular cancers such as skin hemangiomas. Jaffe said that disease states such as dysfunctional uterine bleeding, endometriosis and endometrial hyperplasia or cancer may be associated with abnormal uterine angiogenesis. The blood vessels are dominant, so there is a tendency to lobules. As expected, these groups of thickened blood vessels are more common in endometrial and cervical polyps that also reflect excessive estrogen (Figure 6).

Ultrastructural studies on vascular abnormalities are very accurate and support primary pathology at the vascular level. It confirmed that obstruction and dilatation of endometrial blood vessels increased in DUB and that there was a positive correlation between the change in angiogenesis and menstrual disorders. It is noted that abnormal angiogenesis and increased vessel fragility support DUB. Ferenczy described the primary vascular lesion in both hypoestrogenic and pre-parenchymal endometrium.

![Image](image-url)

**Figure 6:** Similar changes in Endocervix. Arrow points to the Endocervical glands. Large thickened vessels are marked by red arrow. This may be a precursor to Endocervical polyp formation (H&E x 100).

**Conclusion**

We found thickened blood vessels; individually or collectively in all methods of treating endometrial dysfunctional uterine bleeding. It seems that these thickened blood vessels may contribute to maintaining menstrual bleeding in dysfunctional uterine bleeding (DUB). Because the vessels are very sensitive to various hormonal activities and laser therapy, new methods can be developed to control a wide range of female genital pathologies, including DUB, endometrial hyperplasia, polyps, fibroids and atrophic lichen sclerosis. We plan to carry out more research in these areas in the future.

**Conflict of Interest:** This study has no conflict of interest to declare by any author.

**Disclosure:** None

**Human and Animal Rights:** No rights violated.

**References**


