INTRODUCTION

Endometriosis is a common gynecological disease, occurring in about 10% of all women and up to 60–80% of women with infertility problems or pelvic pain. Despite a number of theories concerning the origin of endometriosis the precise pathogenetic mechanisms remain enigmatic ***(Vinatier et al., 2001).***

Proposed mechanisms include genetic predisposition, involvement of the immune system, changes in the peritoneal fluid, peritoneum and endometrium, and retrograde menstruation ***(Valle, 2002).***

The ability of endometrial fragments to implant is of particular interest in the pathogenesis of peritoneal endometriosis. A number of studies, both in vivo and in vitro, indicate that endometrial fragments in the menstrual fluid might survive and adhere to an intact peritoneal surface ***(Witz et al., 2001).***

Little is known about the regulation of growth of the ectopic endometrium and the recruitment of blood vessels to the endometriotic lesions. It is known, however, that down regulation of ovarian activity by use of contraceptive pills, gestagens or GnRH analogues usually reduces the activity of endometriotic lesions and relieves the pain. The effects of these

treatments are thought to be due to a reduction in the levels of oestradiol in the pelvic region ***(DeMayo et al., 2002).***

Vascular endothelial growth factor (VEGF) is a sub-family of growth factors, more specifically of platelet-derived growth factor family of cystine-knot growth factors. They are important signaling proteins involved in both vasculogenesis [the *de novo* formation of the embryonic circulatory system] and angiogenesis [the growth of blood vessels from pre-existing vasculature],***(Liu et al., 2007).***

The most important member is VEGF-A. Other members are Placenta growth factor [PlGF], VEGF-B, VEGF-C and VEGF-D (Table 1). The latter ones were discovered later than VEGF-A, and before their discovery, VEGF-A was called just VEGF. A number of VEGF-related proteins have also been discovered encoded by viruses [VEGF-E] and in the venom of some snakes [VEGF-F], ***(Bergers & Hanahan, 2008).***

Recent studies have demonstrated an association between endometriosis and immunologic events such as apoptosis, extracellular matrix remodeling, and angiogenesis ***(Gazvani & Templeton, 2002).***

Type	Function

VEGF-A	• Angiogenesis
	  ○ ↑ Migration of endothelial cells
	  ○ ↑ mitosis of endothelial cells
	  ○ ↑ Methane monooxygenase activity
	  ○ ↑ αvβ3 activity
	  ○ creation of blood vessel lumen
	  ○ creates lumen
	  ○ creates fenestrations
	• Chemotactic for macrophages and granulocytes
	• Vasodilatation (indirectly by NO release)

VEGF-B	Embryonic angiogenesis
VEGF-C	Lymph angiogenesis
VEGF-D	Needed for the development of lymphatic vasculature surrounding lung bronchioles
PlGF	Important for Vasculogenesis, Also needed for angiogenesis during ischemia, inflammation, wound healing, and cancer.

Table (1): Comparison between types of V.E.G.F.

One of the substances involved in angiogenesis is the vascular endothelial growth factor [VEGF] , whose functions include induction of endothelial cell proliferation , prevention of cell senescence, promotion of cell resistance to apoptotic stimulus, induction of matrix metalloproteinase production , promotion of macrophage chemotaxis, and increments in vascular permeability ***(Tan et al., 2002).***

The presence of neovascularization has been well established in endometriotic implants, and larger and more active implants have been observed in well-vascularized areas than in poorly vascularized ones. Moreover, red peritoneal lesions and ovarian endometriosis show higher concentrations of VEGF. There is evidence suggesting a strong correlation between VEGF levels and menstrual cycle phases, with possible implications for the development of endometriosis. Variations in VEGF mRNA throughout the menstrual cycle have been observed in endometrial tissue, with increased expression during the secretory and menstrual phases. In addition, analysis of endometrial tissue and peritoneal fluid samples showed higher mean VEGF levels during the late secretory phase in women with endometriosis than in those without the disease ***(Brenner et al., 2002).***