TJVS Turkish Journal of Vascular Surgery

Turk J Vasc Surg 2023;32(Supplement 1):31-3
DOI: 10.9739/tjvs.1970.01.220

Available online at www.turkishjournalofvascularsurgery.org

Invited Review

Possible link between pelvic venous disorders and fertility

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Received: 01 November, 2023 Accepted: 22 November, 2023 Published online: 30 November 2023

Abstract

Pelvic venous disorders (PeVD) is characterized by chronic pelvic pain for at least 6 months as a result of varices or the insufficiency of pelvic veins. It usually manifests as chronic pelvic pain, dyspareunia, dysmenorrhea and varicosities of atypical localizations. One of the most important issue in this field pertains to the impact of PeVD on female reproductive function, particularly its influence on pregnancy and the significance of timely treatment in this regard. The analysis of the studies presented in current review, despite rather scarce data, indicates that the presence of pelvic venous disorders affects the reproductive activity of women. However, due to the weak evidence, future investigations are extremely needed.

Keywords: Pelvic venous disorders, pelvic vein embolization, fertility, pregnancy

INTRODUCTION

Chronic Pelvic Pain (CPP) is a condition characterized by persistent pain symptoms originating from the pelvic organs, typically lasting for a duration exceeding six months, as defined by the American College of Obstetricians and Gynecologists. This condition is frequently associated with adverse cognitive, behavioral, sexual, and emotional consequences, along with symptoms suggestive of dysfunction in various systems, including the lower urinary tract, sexual function, bowel, pelvic floor, myofascial structures, and gynecological aspects [1]. A systematic review conducted by the World Health Organization (WHO) has revealed that approximately one in seven women in the United States is affected by chronic pelvic pain. The prevalence is similar to conditions such as migraine headaches, asthma, and chronic back pain [2]. Among the different factors contributing to chronic pelvic pain, pelvic congestion syndrome accounts for 16% to 31% of cases, ranking second in prevalence only to endometriosis [3]. The management of pelvic venous congestion syndrome (PVCS), encompassing its diagnosis, investigation, and treatment, necessitates a collaborative, multidisciplinary approach involving gynecologists, vascular surgeons, diagnostic and interventional radiologists, urologists, neurologists, psychologists, and psychiatrists, [4,5] which is particularly challenging due to the significant disparities in strategies adopted by different specialists. One most important issue in this field pertains to the impact of pelvic venous disorder (PeVD) on female reproductive function, particularly its influence on pregnancy and the significance of timely treatment in this regard.

Borghi et al. noted that the etiology of PeVD remains poorly understood and likely results from a combination of factors, including genetic predisposition, anatomical abnormalities, hormonal influences, venous wall damage, dysfunctional valves, reverse blood flow, hypertension, and venous dilation [6]. Mechanical compression of ovarian tissue by varicose ovarian veins can induce local hypoxia and subsequent ischemia in the ovarian cortex, contributing to a decline in ovarian reserve, particularly in reproductive-age patients, except other causes leading to this condition. Hormonal factors play a pivotal role in PeVD development, with the influence of female sex hormones being of paramount significance. Estrogen, for instance, prompts increased nitric oxide secretion, leading to vein dilation and

CITATION
Lazarashvili Z. Possible link between pelvic venous disorders and fertility. Turk J Vasc Surg. 2023;32(Supplement 1):31-3.

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valve stress. Progesterone also weakens venous valves within the pelvic veins [7]. During pregnancy, there is a substantial increase in the circulatory volume flowing through ovarian and pelvic veins, with a potential up to 60-fold rise in ovarian vein flow. This heightened venous demand, driven by pregnancy-induced physiological changes and hormonal shifts, results in chronic venous insufficiency [8]. It is worth noting that postmenopausal women typically experience the resolution of PeVD symptoms, emphasizing the role of hormonal imbalances and hemodynamic changes in the morphological alterations of female reproductive structures. In particular, women with pelvic congestion syndrome (PCS) tend to exhibit larger uterus and cystic changes in their ovaries compared to healthy counterparts, attributed to venous congestion and estrogen overstimulation. These cystic changes can manifest as classic polycystic appearances or clusters of small four to six cysts of 5-15mm in diameter in bilaterally enlarged ovaries [9,10].

Theoretically, it is evident that hemodynamic, hormonal, and morphological changes of this nature should exert a significant influence on female reproductive function. However, the paucity of clinical research in this domain diminishes the strength of the evidence.

In 1991, Galkin et al. postulated that persistent ovarian varicoceles might induce ovarian hypo-function and, similar to testicular varicoceles, could potentially lead to infertility. In support of this theory, they presented data from 49 patients who underwent successful intervention on the gonadal veins. Within 4-18 months after intervention, improved clinical outcomes and functional diagnostic test results were observed in 46 patients. Among them, 19 patients exhibited patent uterine tubes, with 14 of them subsequently achieving pregnancy [11]. Tarazov et al. reported two cases of pregnancy in infertile women following successful trans-catheter embolization of ovarian varices. According to their report, "Both patients achieved pregnancy after successful ovarian vein embolization. In the first case, the pregnancy resulted in a normal delivery. Extra-uterine pregnancy in the second case can be attributed to multiple contributing factors, including prior recanalization of the fallopian tubes" [12]. Kim et al. conducted a study examining hormonal level changes before and after embolization therapy and concluded that there were no statistically significant differences in hormone levels. The mean basal follicle-stimulating hormone levels were 15±24 mIU/mL before the procedure and 18±29 mIU/mL at follow-up (P=.3). Mean estradiol levels were 61±53 pg/mL before the procedure and 62±53 pg/mL at follow-up (P=.5). Mean luteinizing hormone levels were 8.1±13.1 mIU/mL before the procedure and 9.4±12.9 mIU/mL at follow-up (P=.3) [3]. In the same study, they reported that four patients attempted conception after embolotherapy, with two achieving successful pregnancies. The two who did not conceive had pre-existing fertility difficulties before the procedure.

Goncalves et al. described two cases of embolization of ovarian varicose veins in patients with a confirmed diagnosis of premature ovarian failure who resumed menstruation after treatment. 13 Interesting data from 24 women is provided by Venbrux et al. regarding the impact of embolization on menstruation: The range of follow-up was approximately 6–24 months. No significant changes in menstrual cycle interval or cycle length were noted. Before the embolizations, the mean menstrual cycle interval was 27.4 days and the mean cycle length was 4.9 days. After embolization, the mean menstrual cycle interval was 27.6 days and the mean cycle length was 4.6 days (P=NS) [14]. Senechal et al., analyzed the results of embolization therapy of 312 patients with pelvic congestion syndrome, While ovarian function was not specifically investigated in their study, they noted that "17 women (6%) became pregnant during the follow-up and delivered full-term babies. Furthermore, the absence of significant menstrual cycle-related alterations suggests that pelvic vein embolization did not have a detrimental impact on ovarian function" [15].

A very interesting case was reported by Ghosh A et al. including a 21-years old, multiparous woman with an 8-month history of right iliac fossa pain. Diagnostic laparoscopy revealed grade 1 endometriosis, along with tortuous vessels around both uterosacral ligaments. Despite laparoscopic ablation/cauterization of endometriotic lesions and conservative treatment with progesterone, her symptoms worsened, leading to marked dyspareunia and a significant impact on her quality of life. Subsequent laparoscopy four months later showed no abnormalities in pelvic organs, and the aberrant blood vessels around the uterosacral ligaments remained unchanged. A sclerosing agent, ethanolamine maleate, was bilaterally injected into the perivascular area, resulting in her becoming pain-free within a month, and she remained so even a year later. She subsequently became pregnant, experiencing an uneventful antenatal period and delivering vaginally without complications. Six months post-delivery, she remained pain-free [16].

Dos Santos et al. published data on eight patients who had previously undergone pelvic vein embolization for pelvic venous reflux before and after pregnancy. Parity before embolization ranged from 1 to 5 (mean 2.8). The authors detected differences in outcomes between 6 weeks post-embolization and post-pregnancy based on ultrasound findings. While pelvic venous reflux was completely eliminated in five patients, two achieved complete elimination of truncal reflux with very minor vulval reflux, and one patient had persistent mild reflux in the right internal iliac vein after embolization. After pregnancy and delivery, pelvic venous reflux was completely eliminated in three patients, while five patients displayed pelvic venous reflux in at least one truncal vein, with or without concurrent vulval reflux. Notably, no patient experienced coil displacement or embolization due to pregnancy. The authors concluded that pregnancy is associated with recurrent reflux in pelvic veins in women previously treated

with coil embolization. Following post-pregnancy recovery, repeat embolization can effectively eliminate recurrent reflux, and pregnancy appears to be safe following coil embolization of pelvic veins [17]. Liu et al. presented cases of pregnancy after pelvic vein embolization, where pelvic congestion syndrome was the sole cause of infertility [18]. Data from 12 women were collected, with 66.7% (8/12) experiencing subsequent pregnancies and complete relief from pelvic pain, and 33.3% (4/12) achieving partial pain relief. Among these cases, six resulted in intrauterine pregnancies leading to live births. However, one patient experienced an ectopic pregnancy in the right fallopian tube, leading to laparoscopic salpingectomy, and another patient had embryo cessation during the early stage of pregnancy, necessitating abortion. There were no significant differences in hormonal levels before and after the procedure, both in terms of mean values of follicle-stimulating hormone and luteinizing hormone.

Lastly, it is worth noting the significant role of dyspareunia and prolonged post-coital pain in women's reproductive activity. Dyspareunia, which occurs in 40-85% of cases of pelvic venous disorders, is a major factor affecting sexual relationships between partners and, consequently, reducing women's chances of becoming pregnant.

CONCLUSION

In conclusion, the analysis of the studies presented, despite rather scarce data, indicates that the presence of pelvic venous disorders affects the reproductive activity of women. Pelvic vein embolization, considered a "gold standard" of treatment of PeVD, can play a crucial role in certain cases of female infertility without adversely affecting reproductive function. However, due to the weak evidence, future investigations are extremely needed.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: All authors contributed equally to the article.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

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