



A Review of the Gastrointestinal Causes of Infertility from the Perspective of Persian Medicine

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Abstract

Infertility affects about 10-15% of couples in reproductive age, and puts a lot of economic burden on communities. Persian Medicine (PM) introduces perspectives on causes of infertility that can be useful in prevention and treatment of this common healthcare problem. Gastrointestinal problems are one of the causes of infertility based on PM literature. The purpose of this study was to collect evidence of gastrointestinal problems associated with infertility in conventional medicine, and ultimately compare the results with the viewpoints of PM. By reviewing literature on PM, we classified the digestive causes of infertility and then, by searching the keywords "infertility" and "gastrointestinal disorders" and symptoms such as, "duodenal ulcer", "peptic ulcer", "dyspepsia", "fatty liver", "maldigestion", "H. Pylori infection", "celiac", "inflammatory bowel disease", and "obesity" in databases of SCOPUS, PubMed, Web of Science. Based on the review of the literature on PM, gastrointestinal causes of infertility include digestive failure, liver weakness, and inappropriate eating habits. There is also a growing scientific evidence of this connection in modern medicine. Attention to the treatment of gastrointestinal disorders in patients with infertility can help to treat unknown causes of infertility.

Keywords: Persian medicine; Avicenna; Digestion; Gastrointestinal; Infertility

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Introduction

The Practice Committee of the American Society for Reproductive considers infertility as a disease, defined by an unprotected intercourse between couples which does not result in pregnancy after a period of more than 12 months or more than 6 months in women over 35 [1]. In a study by WHO on 8500 infertile couples, infertility was observed in 37% women, and 8% men and 35% couples, in other cases, the cause of infertility was not found or couples were pregnant during the study [2]. Therefore, it seems that a high percentage of the etiology of infertility is still unknown [3]. On the other hand, the treatment of this disease requires a lot of medical costs; In a study conducted in California in 2011, 198 infertile women for 18 months had followed, which the average cost of treatment was estimated to be \$ 61,000 [4]. So, people's general interest in using complementary medicine is increasing worldwide as an effective and low-cost way of preventing and curing diseases [5,6]. In a study conducted in the United States in 2002, about 62 percent of adolescents used complementary therapy in treating their illness [7]. Persian Medicine (PM) with many recommendations, especially in the field of lifestyle, can play an important role in prevention and treatment of diseases [8]. From the perspective of PM, digestive problems are a bunch of causes of infertility. In recent studies, some digestive problems have been associated with infertility. So far, no review has been done on the scattered studies carried out, and a coherent result

has not been achieved. This study aims to collect and review the digestive causes of infertility based on conventional medical studies, and ultimately compare the results with viewpoints of PM.

Method

In this review, sources of Persian medicine and current medicine on fertility were assessed. First, the authoritative sources of Persian medicine were studied using infertility keywords including, pregnancy, infertility, digestion weakness, dyspepsia, liver weakness and dietary habits. The sources of Persian medicine are included, "the Canon of Medicine" (Avicenna, 11th century AD), "Kamel al-Sanaah al-Tibbiyah" (Ali ibn al-'Abbas al-Majusi, 10th century), "Kholasa't ol Hikma" (Aghili, 18th century), "al-Mansouri fi Al-Tibb" (Razi, 10th century AD), "Exir-e-Azam" (Nazem Jahan, 19th century), "Bahr al-jawahir" (Heravi, 16th century) "Zakhireh kharazmshahi"(Jurjani, 12th century). Also, the sources of current medicine are investigated and list of disorders and digestive symptoms was prepared by the writers' team and then using the keyword infertility and gastrointestinal disorders and symptoms such as duodenal ulcer, peptic ulcer, dyspepsia, fatty liver, mal-digestion, H. Pylori infection, celiac, inflammatory bowel disease, and obesity required searches were done in databases of SCOPUS, PubMed, and Web of Science.

Results

Four digestions play a role in the production

and performance of the sperm and ovum. Any disturbance in digestion can lead to fertility disorder. The four digestions include gastric digestion, hepatic digestion, blood-vessel digestion and tissue digestion [9]. The concept of digestion, as described in PM literature, is an extensive process that encompasses all acts of the body on food from the time it is consumed until it enters the interstitial fluid and takes part in cell growth and proliferation cycles [10]. Gastric digestion means digestive changes on the food from the mouth to the intestines. This stage of digestion in Persian medicine is the same process that is called digestion today [11]. The second digestion is hepatic digestion, in which the liver induces changes on the absorbed material from the digestive system. This results in the production of quaternary humors (blood-phlegm - yellow bile - black bile). Quaternary humors are the same material that forms blood and the content within it. Today we know that there is a large vascular connection between the intestines, the liver and the content of mesenteric vessels that covers the entire intestine. Finally, it enters the liver through the vein. The third phase is vascular digestion during which other changes occur on the products of hepatic digestion, so that the cells can better use the digestive product and finally, in tissue digestion, the body cells prepare the food received from the vessels for their use any disorder in these stages can affect the production of sperm and ovum [9,12]. Persian scientists strongly emphasize that the processes involved in the production and fertilization of the sperm and ovum are

a result of healthy function of all these four stages and in assessing and treating infertility, none of these steps should be neglected. In PM, digestive disorders referred to underlying causes of infertility include digestive weakness, indigestion, liver weakness and inappropriate food habits, which we will continue to explain each one.

Weakness of digestion and indigestion (Digestive Failure)

Digestion in PM involves four stages and includes a long way from entering the food to use of it, though the intent of digestive weakness is in particular a weakness in first digestion. The same thing is called gastric digestion in Persian medicine [13]. It should be noted that what is called the PM of gastric digestion today is equivalent to digestion and absorption, and the term gastric digestion in PM also encompasses absorption. According to PM experts, digestion requires moderate heat and moisture in the stomach. Based on the principles of Persian medicine, there are four qualities of hotness, coldness, wetness and dryness in all cells of the body. Each of these qualities provides specific properties to body tissues and organs. Moisture, for example, facilitates the acceptance of new shapes and changes, while on the contrary, dryness preserves the existing structure and does not accept changes and new structures [14]. Today, gastric motility and gastric secretions for ideal digestion are examples of the concept of moderate heat and moisture in the stomach [11]. Therefore, if indigestion occurs in the stomach, gastric digestive failure will occur

[12]. In PM, the term “dystemperament” refers to the body or an organ diverted from its natural temperament. The temperament of each organ is a quality that results from the interactions between the four humors of blood, phlegm, yellow bile and black bile in the body. In normal temperament, the organ is completely healthy and performs its own actions correctly, while the dystemperament means a disorder in the organs performance. According to this definition, dystemperament in the stomach means a disorder in the stomach’s performance, i.e. digestion. In this case, symptoms of poor digestion, such as indigestion, having pain in the stomach, which are known as dyspepsia symptoms today [15], will show up with bloat and also belching [16,17]. In digestion failure, foods cannot be completely transformed to body tissues and cannot be used properly [18]. If this disorder intensifies, until the digestion performance is completely overturned, indigestion or digestion failures will occur. In such cases, no digestive performance in the stomach is performed, so indigestion is the exacerbated condition of weakness of digestion [19]. Persian scholars believed that digestion failure or inadequate digestion of food in the gastrointestinal system is one of the causes of infertility. Therefore, patients should be examined and treated accordingly.

Liver weakness

Liver weakness is one of the causes of infertility in PM. Humor is a liver product that plays a role in feeding the organs, so a patient

with liver weakness will have weakness in the body tissues. Incidence of weight loss in the body, loss of appetite, facial swelling, and loss of facial brightness, white urine, and small and dark stool are other signs of weak liver digestion [23]. Of course, not all of these symptoms are necessarily observed in all patients. Swelling of the face can be very mild and just some puffiness which can sometimes be considered natural. It should be noted that one of the causes of liver weakness is the progression of digestive disorders in the stomach due to inappropriate product. This can be due to an impairment of the second or liver digestion, which ultimately causes problems in the four stages of digestion.

Inappropriate nutritional habits

One of the most important features of PM with numerous references in PM texts is the emphasis on the regulation of nutritional habits. One of the main aspects of life style in PM is eating and drinking [20]. The frequent recommendations in this area include issues such as no overeating, no eating all kinds of different foods at a meal, no water and drinking between meals and up to an hour after meals, respect for food diversification in various meals. Among all these recommendations, it is very important to avoid drinking cold water and drinking plenty of water in PM. PM experts consider one of the causes of infertility in women to be high water consumption or cold water consumption. Cold water consumption causes liver weakness and thus, infertility [12].

Gastrointestinal disorders affecting infertility from the perspective of current medicine

Infertility in men is a disturbance in the process of spermatogenesis and mitosis and meiosis divisions, it is also evolution of epithelium of the seminiferous of testicles, which is affected by the testosterone hormones, LH and FSH [21]. However, infertility in women results in impaired ovarian activity and steroid hormonal secretion, as well as disruption of the secretion of LH and FSH hormones, ultimately leading to fertility disorders [22]. In order to investigate the association between the gastrointestinal system and infertility, we will investigate the both, individually.

H-pylori infection

H-pylori is a gram-negative bacterium that is colonized in the stomach and plays a role in the development of gastritis and peptic ulcer [24], dyspepsia without ulcer [25]. In the studies, there is a correlation between H-pylori infection and infertility in men and women [26,27].

Celiac

Celiac is an autoimmune gastrointestinal chronic disease along with indigestion and malabsorption, which is caused by ingestion of gluten-containing foods. The main symptoms of this disorder are belching, bloating, diarrhea, weight loss and anemia. Liver involvement is observed in some patients. Celiac disease in men and women can also be accompanied by infertility.

In women with celiac disease, delayed menarche, amenorrhea, early menopause and reduced pregnancy rates are commonly observed. Celiac in men may be associated with hypogonadism and reduced semen quality [29,30].

Inflammatory bowel disease (IBD)

Gastrointestinal inflammatory diseases are divided into two major causes of ulcerative colitis and Crohn's disease. Gastrointestinal symptoms in inflammatory bowel disease include abdominal pain, diarrhea and bleeding [31,32]. The lesion in the crohn is transmural, and in the ulcerous colitis occurs in the mucous layer [32]. Fertility rate is low in women with Crohn's disease, but not with ulcerative colitis [33-35].

Chronic liver diseases

Fatty liver is one of the most common chronic liver diseases ,which reduces the quality of sperm and gonadal hormones [36]. The liver plays a significant role in the metabolism of steroid hormones [37]. Also studies have been demonstrated that the prevalence of fatty liver disease in women with polycystic ovarian syndrome is one of the most common causes of infertility in this group[38,39].

Obesity

Obesity is a metabolic disorder, resulting in poor eating habits and one of the causes of infertility in men and women [40,41].

Table .1 Effects of digestive problems on infertility

Disease/disorder		Female factor	Male factor
H- pylori Infection		Reduced capacity of fertilization due to production of free radicals [26]	Reduced Sperm quality[27]
IBD		1-Nutritional deficiency 2-Active inflammation 3-Occlusion of ovarian tube [34, 35] 4-Increased Leaky gut and resulting in passage of bacterial endotoxin from the gut lumen in to circulation and then triggered inflammation that impairing ovarian steroid production [43]	1- Nutritional deficiency 2- Active inflammation 3- Medications [42]
Celiac		1- Deficiency of folic acid, zinc, and selenium, resulting in impaired synthesis and secretion of LH and FSH and impaired proliferation of tissues such as embryo [29,30] 2- Increased Leaky gut resulting in passage of bacterial endotoxins from the gut lumen into circulation, and then triggered inflammation that impairs ovarian steroid production [43]	1-Deficiency of folic acid, vitamin A, E, resulting in impaired spermatogenesis (proliferation and maturation); and secretion of semene proteins [30,44] 2- Androgen resistance [30,45]
Liver disease		Altered metabolism of sex hormones resulting in amenorrhea [37,46,48]	-Altered metabolism of sex hormones resulting in [39,48] decreased testosterone and hypogonadism [36,46-47]
obesity		1- Increased Leaky gut and passage of bacterial endotoxins from the gut lumen into circulation triggering inflammation and oxidative stress that decreases ovarian steroid production and LH [41,43,50-52] 2-reduced implantation of the embryo [53]	-Altered metabolism of sex hormones resulting in [40,49] decreased testosterone and hypogonadism increased scrotal adiposity resulting in increased heat of scotoma and impaired spermatogenesis [40]
Poor eating habit	Cold water		Chronic stress induced of cold water resulting in Decrease Motility, morphology, and sperm count [54,55] High fat diet causing reduction in sperm quality [56]
	High fat diet		

Discussion

According to the PM literature, for the creation of an ovum and a suitable sperm for fertilization, gastrointestinal digestion and hepatic digestion and metabolism are two basic pillars. Weak-digestion, mal-digestion and weakness of liver are common causes

of infertility as well as inappropriate dietary habit such as cold water drinking. As a result of impaired digestion of the gut and liver, the fourth digestion in the ovaries and testicles is disrupted, ultimately sperm and ovum are not suitable for fertilization. On the other hand,

with inappropriate digestion of the tissue during digestive and hepatic digestion, the uterine tissue won't be suitable for implantation. Healthy lifestyle in Persian medicine is regulated through the regulation of six axes in the lives of patients and healthy people. These six axes are the air and climate, eating and drinking, sleeping and wakefulness, motion and rest, the process and dynamics of retention or disposing of the material from the body, and ultimately emotional states. Eating and drinking are the most prominent of these axes in the development of diseases. Persian medical scholars have provided a wide range of suggestions on this issue, which can help eliminate or improve digestive disorders without prescribing drugs and their effectiveness can also be studied in patients with infertility. In conventional medicine for digestive diseases such as celiac, inflammatory bowel disease with indigestive and malabsorption symptoms, chronic liver disease such as fatty liver and cirrhosis, and obesity as a metabolic disorder, as well as bad dietary habits such as drinking cold water are accompanied by infertility due to abnormal spermatogenesis and non-ovulation [9,57,12].

Inflammatory bowel disease and celiac, cause infertility by reducing the absorption of effective nutrition in the production of sexual hormones, sperm and ovum, followed by the leaky gut mechanism (increased gastrointestinal permeability) and stimulation of inflammatory pathways, thereby reducing gonadal hormones. From the perspective of

Persian medicine, digestion weakness and indigestion, are causes of infertility. Celiac and inflammatory bowel diseases can be regarded as instances of indigestion [41,43,51-52]. H-pylori infection associated with non-ulcer dyspepsia causes infertility due to reduced sperm quality and oocyte fertilization capacity. Regarding the signs of H-pylori infection, we find that H-pylori infection causes weakness gastric digestion which causes infertility based on Persian medicine literature [26,27]. Hepatic and liver failure disease due to metabolic diseases and obesity leads to a defect in the metabolism of sexual hormones, followed by defects in natural spermatogenesis and normal ovulation. As mentioned, liver weakness plays an important role in infertility according to PM [36,46-48].

Drinking cold water decreases the quality of sperm and its mobility, thereby leading to infertility [54,55]. According to PM, cold water causes weakness of the liver and thus leads to infertility.

Conclusion

As PM scholars believed in the association of digestion and infertility, today, there is a growing scientific evidence of this association. It is suggested that more clinical studies be conducted on the angles of this etiology and accompaniment. Attention to the treatment of gastrointestinal disorders in patients with infertility can open up a new perspective to treatment of this disorder and may also help to treat couples with unknown causes of infertility.

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