

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

<u>www.wjpmr.com</u>

<u>Review Article</u> ISSN 2455-3301 WJPMR

A CRITICAL APPRAISAL ON PHYSIOLOGY OF MENOPAUSE WSR TO RAJO NIVRUTTI

C. S. Bhuvana^{1*}, H. M. Spoorthi Prasad² and Kamath Nagaraj³

^{1,2}PG Scholar, ³Associate Professor

Department of Kriya Shareera, Sri Dharmasthala Manjunatheshwara College of Ayurveda & Hospital, Hassan, Karnataka, India.



*Corresponding Author: C. S. Bhuvana

PG Scholar, Department of Kriya Shareera, Sri Dharmasthala Manjunatheshwara College of Ayurveda & Hospital, Hassan, Karnataka, India.

Article Received on 25/04/2025

Article Revised on 15/05/2025

Article Accepted on 03/06/2025

ABSTRACT

Menopause refers to permanent cessation of menstruation due to loss of ovarian follicular activity. The ovaries produce less oestrogen and progesterone, resulting in physiological, psychological, and social changes. *Ayurveda* depicts menopause as '*Jara Pakva Avastha*' with *Rajo Nivrutti* being a coined term. *Rajo Nivrutti* refers to cessation of *Artava Pravrutti* and is associated with *Vata Dosha* dominated stage of life. The phases of menopause can be compared to a female's *Madhyamavastha*. Menopause (*Rajo Nivrutti*) is a physiological process. Menopause is a natural aspect of aging even *Rajo Nivrutti* is mentioned as *Jarajanya Avastha*. It can be categorised as natural cause (*Kaalaja*) and unnatural cause (*Akaalaja*). Both conditions have a common set of clinical signs and symptoms. *Vata Pradhana* and *Pitta Pradhana* clinical signs and symptoms are predominantly observed in this phase. Menopause (*Rajo Nivrutti*) have an impact on both physical and mental health where especially counselling and reassurance similar to *Satvavajaya Chikitsa* aids in its management. The concepts of Menopause and *Rajo Nivrutti* are closely related.

KEYWORDS: Menopause, Oestrogen, Rajo Nivrutti, Raja Nasha, Rajo Kshaya.

INTRODUCTION

Menarche, puberty, pregnancy, parturition, and menopause are important biological stages in female. Menopause is term used in females who undergo hormonal changes. Menopause is the permanent cessation of menstruation at the end of reproductive life due to loss of ovarian follicular function.^[1] It is part of the natural aging process in which the ovaries produce less oestrogen and progesterone. Female spends onethird of her life duration without menstruation. Menopause typically occurs between the ages of 45 and 55. Menopause occurs in four phases, which include Pre menopause, Peri menopause, Menopause and Post menopause.^[2] Pre menopause occurs when a woman reaches her reproductive years. The first cycle is recognized as the start of pre menopause. Perimenopause implies close to or around menopause. Oestrogen levels will fluctuate, resulting in hot flashes, irregular menstruation, dry skin and so forth. Menopause is the last stage of a woman's natural transition into menopause. Woman's ovaries cease to produce ovum as a result, making it impossible for her to conceive naturally. Menstrual periods that entirely stop for at least a year is indicative of it. Post-menopause occurs one year

following the last menstrual cycle where a woman will spend the remainder of her life in this stage.

Endocrine axis in menopause is Hypothalamus-Pituitary-Ovary Axis (HPO Axis).^[3] The hypothalamus releases gonadotropin-releasing hormone (GnRH) in a pulsatile manner, stimulating the anterior pituitary to release FSH and LH. In reproductive years, the HPO axis maintains a delicate hormonal balance. As ovarian function declines, the HPO axis compensates with elevated gonadotropin levels (FSH and LH), but the ovaries fail to respond effectively. Changes are decreased Oestrogen production: Oestradiol is primarily produced by ovarian follicles. As follicles decline, oestradiol production sharply decreases. Post-menopause, estrone (E1), a weaker oestrogen, becomes the predominant oestrogen, produced by peripheral conversion of androstenedione in adipose tissue. Reduced Progesterone Levels: With the cessation of ovulation, the corpus luteum no longer forms, leading to a significant drop in progesterone levels. Increased FSH and LH: Oestrogen usually provides negative feedback to the hypothalamus and pituitary gland, suppressing gonadotropin production. As oestrogen levels fall, FSH and LH levels rise markedly. Decline in Inhibin: Inhibin A and Inhibin B, produced by ovarian

granulosa cells, suppress FSH production. With reduced ovarian activity, inhibin levels drop, further increasing FSH secretion Androgen Changes: Ovaries continue producing androgens (testosterone and androstenedione) even after menopause, but levels gradually decline with age. Peripheral tissues convert these androgens to oestrogens, contributing to minimal oestrogen activity post-menopause.

The cause for menopause can be divided into two categories: natural and induced.^[4] A) Natural causes include depletion of ovarian follicle and gonadotropininduced follicular insensitivity. Depletion of Ovarian Follicles: At birth, the ovaries contain about 1–2 million primordial follicles. By puberty, this number decreases to around 3,00,000, and only around 400 follicles ovulate over a woman's reproductive life. By the time of menopause, very few follicles remain, and their functional capacity is greatly diminished. Oocytes diminish due to lower mitochondrial efficiency and increased oxidative stress, resulting in atresia. Mitochondrial effectiveness is necessary for proper maturation. Follicular Insensitivity oocvte to Gonadotropins: Aging follicles become less responsive to follicle-stimulating hormone (FSH) and luteinizing hormone (LH), leading to impaired ovulation and reduced oestrogen and progesterone production. B) Induced causes include primary ovarian insufficiency oophorectomy. and bilateral Primary ovarian insufficiency- A condition that develops when a woman's ovaries cease to function normally before the age of forty. It is caused by chromosomal abnormalities (fragile x syndrome), auto immune disease, radiation and chemotherapy (treatment induced) and an idiopathic cause. Bilateral oophorectomy- The ovaries are the primary producers of oestrogen and progesterone. In oophorectomy hormone bilateral levels decline dramatically, causing menopausal symptoms.

Menopausal changes can be divided into three categories: Physiological, psychological and social.^[5] A) Physiological changes -Lack of oestrogen and progesterone alters the physiology of women. Hyperlipidaemia- Oestrogen regulates the metabolism of lipids in the liver.^[6] As a result, a decrease in oestrogen levels leads to an increase in LDL cholesterol and triglycerides. Osteoporosis- Oestrogen plays a key role in regulating the balance between bone-forming osteoblasts and bone-resorbing osteoclasts.^[7] A decrease in oestrogen levels affects the osteoblasts, causing an imbalance in the bone remodelling process. A decrease in oestrogen levels affects osteoclasts, causing calcium to flow out of the bone, leaving it fragile and prone to fracture, resulting in a fall in bone density. Changes in the digestive system- Oestrogen helps to control the cortisol levels.^[8] When oestrogen levels fall, cortisol levels rise, which can disrupt the GIT and cause sluggish motility. Changes in the urinary system- Oestrogen catalyses the formation of antimicrobial compounds in the urinary bladder and strengthens the urinary tract

tissue, making it more difficult for bacteria to thrive in the bladder's deeper layers. When oestrogen levels fall, the tissue lining the urethra and bladder becomes dryer, thinner, and less elastic, which can contribute to increased micturition frequency and an increased risk of developing urinary tract infections.^[9] Changes in the genital tract- Uterus- Oestrogen strengthens and protects the mucous membrane that lines the uterus.^[10] Additionally, it controls the thickness and flow of mucus secretions from the uterus. Oestrogen deprivation causes the uterus to shrink and become fibrotic as a result of muscular atrophy.^[11] Ovaries- Oestrogen promotes follicular growth. Oestrogen insufficiency causes reduction in the size of ovaries with impaired endocrine activity.^[12] Vagina- Oestrogen maintains the thickness of vaginal wall and promotes lubrication. The vaginal mucosal membrane thins and loses its rugosity when there is insufficient oestrogen.^[13] Vaginal production reduces, making the vagina dry and resulting in dyspareunia. Eventually, vaginal secretions disappear completely. Vulva- Oestrogen helps keep the vulvar skin and mucosa soft, elastic, and well-lubricated, maintaining subcutaneous fat in the area.^[14] It stimulates collagen production, which maintains tissue strength and elasticity. Reduced oestrogen causes vulvar atrophy, loss of elasticity and suppleness, dryness, and discomfort, which can result in itching, irritation, or burning sensation. Breast- Oestrogen promotes the development of milk ducts and fat accumulation.^[15] Reduced oestrogen levels cause a decrease in breast size and suppleness, which contributes to sagging. Changes in general appearance- Skin- Oestrogen is essential for preserving skin's structural and functional integrity.^[16] It promotes skin hydration, sebum production, enhanced stratum corneum barrier function and enhances collagen and elastin content.^[17] Reduced oestrogen causes elasticity loss and thin skin as elastin and collagen are lost from the skin. Weight- Oestrogen regulates the body weight by reducing the appetite and enhancing the feeling of satiety.^[18] Reduced oestrogen leads to weight gain from irregular eating habits caused by mood swings, as well as increased fat deposition around the hips, buttocks, and waist. Hair- Oestrogen binds to receptors in the hair follicles, stimulating growth and regulating sebum production in the scalp.^[19] Voice- Oestrogen and progesterone regulate vocal harmonies.^[20] Reduced oestrogen induces thickening of vocal cords, resulting in deepening of voice. Changes in the vasomotor system-Changes in hormone levels influence the body's temperature regulation. The changes seen are- Hot flash-It is a quick sensation of heat that travels mostly through the face, neck, and chest. It can cause tachycardia which causes sudden perspiration as body tries to reduce the temperature. Night sweat- It happens when hot flashes occur at night. It has the ability to awaken a woman from her sleep. Abrupt awakening might induce palpitations and even panic attacks. Tachycardia creates quick perspiration as the body seeks to lower the temperature. B) Psychological changes- Inadequate levels of oestrogen cause psychological disturbances.^[21] Oestrogen helps to maintain serotonin levels. Decrease in the oestrogen level results in the low density of $5HT_2A$ receptors and low activity of serotonin.^[22] Drop in serotonin levels lead to irritability, anxiety, fatigue, depression, emotional disturbance, etc. C) Social changes-The psychological effects caused by drop in oestrogen levels can result in social humiliation, discomfort, and so on.

Counselling and prevention are part of management. Prevention of hot flash and night sweat by dressing in layers which allows to remove clothing when hot flash and night sweat starts. Opting for cotton clothing is recommended for optimal skin ventilation. Counselling includes providing emotional support and reassurance to the woman experiencing anxiety and depression. Treatment comprises of both non-hormonal treatment and hormone replacement therapy (HRT). Non-hormonal include lifestyle modifications, treatments the consumption of phytoestrogen-rich foods, calcium and vitamin D supplements, fluoride, which protects osteoporosis and improves bone matrix, calcitonin, which slows bone resorption, the avoidance of smoking and alcohol, etc. Hormone replacement treatment is advised in women to address the short- and long-term implications of oestrogen insufficiency. It includes oral, vaginal and transdermal routes. Oral HRT treatments include Oestrogen-Conjugated oestrogen (0.625-1.25 Progestin-Medroxyprogesterone mg/day), (100-300)mg/day), and so on. The vaginal route comprises vaginal pessaries, creams, and rings. The transdermal approach includes subdermal implants, percutaneous oestrogen gel, and subdermal patches.

Ayurveda depicts menopause as 'Jara Pakva Avastha'.^[23] Rajo Nivrutti is a coined term. The word Rajah is used synonymously with Artava. Hence Rajah indicates menstrual blood and Nivrutti means cessation. So, the term Rajo Nivrutti refers to cessation of Artava Pravrutti. Although *Rajo Nivrutti* is not a distinct term in classical Ayurvedic scriptures, it is referred as Rajo Kshaya and Rajo Nasha.^[24,25] Twelve years of age is the Kaala of Artava Pravrutti, and fiftieth year is the Kaala of Artava Nivrutti.^[26] Furthermore, the fiftieth year is indicated as the most likely age rather than the precise one. In the context of "Rajah Utpatti Hetus," Acharyas mentions Paripurnata of Sharirika Dhatus, Vaya Parimana and Swabhavash Dhatu Paripurnata, Kala, Swabhava, Yoni Abhivriddhi, and Vaya, Upchaya Roopa Vriddhi, Sodhana Prakriya, Apana Vayu Kriya and the influence of *Chandra* and *Mangal Grahas*.^[27] These factors can be alternatively regarded as Rajah Nivrutti Hetus too. In addition, a few particular factors Kaala, Swabhava, Vayu, Karma, Dhatu Kshaya, Dosha-Dhatu-Mala, Abhighata, Ahara, Vihara, Manasika hetus etc can be considered as the causative factors for Rajonivrutti. Since there is no explicit mention of Rajonivritti Lakshanas in the Ayurvedic classics, Rajonivrutti Lakshana can be regarded as a set of symptoms caused by the degenerative process of the body. Ayurveda defines

degenerative changes as Dhatu Kshaya Lakshana. Hence the clinical symptoms manifested by the patients of Rajonivritti are the manifestations of Dhatu Kshaya Lakshanas along with vitiated Doshas. Vataja Lakshana's are Shirahshoola, Hrid Spandana, Hasta Pada Suti, Shabda Asahishnuta, Bala-Kshaya, Adhmana, Vibandha, Anidra/Alpanidra, Bhrama, Anavasthita Chitatvam, Vaichitya, Vishaada, Chinta, Smritimandhya, Krichchhra Vyavayata, Maithuna asahishnuta, Vak Sang, Katishool, Vali, Asthivedana, Sandhi Vedana. Vamanatvam, Angamarda, Yoni Vedana, Yoni Shushakta, Prabhutamutrata, Mutrakrichhrata. Pittaja Lakshana Osha. Atisveda. Amarsha, Yoni Daha. Yoni Daurgandhya, Mutradaha. Kaphaja Lakshana Atisthaulava, Yoni Kandu, Yoni Srava.^[28] It is essential to understand physiology of menopause from both modern and Ayurvedic perspective. Therefore, an attempt is being made here to critically link the two concepts.

AIMS AND OBJECTIVES

To critically analyse menopause from modern and Ayurvedic perspective.

MATERIALS AND METHODS

The concepts of Menopause were studied from modern physiology and gynaecology textbooks, the knowledge concerned with *Ayurveda* was taken from classical *Ayurveda* texts. Scientific research articles were analysed from reputable websites and journals. Hypothesis was made to establish a relation between menopause and *Rajo Nivrutti*.

DISCUSSION

Relation between the classification of age- The human age can be broadly categorised as young age, middle age and old age which is similar to *Balya*, *Madhyama* and *Vruddha Vaya* as per *Ayurveda*.^[29,30] Concerning to reproductive period in a female, middle age in modern and *Madhya Vaya* in *Ayurveda* can be classified as Pre menopause (10-16 years) which is similar to *Vruddhi* (15-20 years), Peri menopause (35-45 years) similar to *Yavvana* (20-30 years) and *Dhatu Sampurna* (30-40 years), Menopause (45-50 years) and post menopause (above 50 years) similar to *Parihani* (40-70 years). Menopause marks the shift from middle to elderly age whereas *Rajo Nivrutti* is a transition from *Madhyamavastha* to *Vruddavastha*.

Menopause and *Rajo Nivrutti* as physiological processes- Menopause is characterized by gradual physiological changes in the digestive, urinary, and genital systems as a result of age-related decreases in oestrogen and progesterone levels. A woman's reproductive potential is bound to cease in the normal course of life. Similarly, *Rajo Nivrutti* is caused due to advancing age. With advancing age, progressive vitiation of *Vata Dosha* due to its *Ruksha, Laghu, Sheeta* and *Sookshma Gunas's* further precipitate the *Soshana* and *Kshaya* of different *Dhatus*. The progression of ageing with *Dhatu Kshaya* again adds to the increase in the *Vata*

dosha. Dhatu Kshaya leads to Vata Prakopa.^[31] The dominant Vata Dosha specially with Laghu and Ruksha Guna results in reduction in Dravata of Rasa Dhatu. Raja is a Upadhatu of Rasa Dhatu and the function of all Dhatus is better in Madhyama Avastha, which reduces during the Vruddha Avastha. This further leads to Dhatu Kshaya starting from Rasa Dhau, further respective Upadhatu Kshaya takes place both quantitatively and qualitatively. Thus, leading to Raja Nasha and Rajo Nivrutti. Hence, physiologically this stage of life is dominated by Vata dosha. Menopause is a natural aspect of aging even Rajo Nivrutti is a Jarajanya Avastha.

The etiology of menopause and Rajo Nivrutti- It can be categorised as natural cause (Kaalaia) and unnatural cause (Akaalaja). Natural decline of reproductive hormones can be regarded as the natural cause (Kaalaja). Whereas primary ovarian insufficiency, hysterectomy, bilateral oophorectomy, radiation and chemotherapy can be considered as the unnatural cause (Akaalaja). Old age is the inevitable outcome of time. Menopause is therefore a time-related process that occurs naturally between the ages of 45-50 years of age. Rajonivritti, like Jaravastha, is a condition that occurs spontaneously in all women and is referred as Kaalaja Hetu. Hence the natural decline of reproductive hormones can be considered as the Kaalaja Hetu. Akaalaja Rajo Nivrutti refers to the occurrence of the menopause before or after 45-50 years of age. Karma can be categorised into two i.e. Poorva Janmakruta Karma and Ajanmakruta Karma.^[32] Chromosomal abnormality can be the resultant of the Poorva Janmakruta Karma. Ajanmakruta Karma can be understood with the Prajyaparadha that women engage in, such as alcohol intake or smoking cigarettes. Primary ovarian insufficiency is caused by chromosomal abnormalities, alcohol intake, smoking and so on. Therefore, primary ovarian insufficiency which is a result of Karma can be regarded as one of the causes of Akaalaja Rajo Nivrutti. Viddhata of the Artavavaha Srotas Moola can be regarded as Abhighataja Nidana i.e., Vidhhata to the Garbhashaya and Artavavahi Dhamanis will lead to Artavanasha. This can be considered as one of the reasons to Akaalaja Rajo Nivrutti. Hysterectomy, bilateral oophorectomy, radiation and chemotherapy where the injury occurs to the uterus and the blood vessels supplying it, can be regarded as Akaala Rajo Nivrutti due to Abhighata.

Similarities between menopausal and *Rajo Nivrutti* symptoms

Rajo Nivrutti alludes to *Jara Pakwa Avastha*, indicating the dominance of *Vata Dosha* in this stage. Hence the *Vata Pradhana* clinical signs and symptoms are predominantly observed during this period.^[33] *Pitta Pradhana* clinical signs and symptoms are also more prevalent since it is a shift from the *Pitta* dominant stage to the *Vata* dominant stage.^[34] The following *Lakshanas* can be considered in terms of *Dosha* dominancy.

<u>Vata Pradhana</u>
<u>Aniyamita Masika</u> Chakra
<u>Gaada Varcha</u>
Nidra Nasha
<u>Asthi Shoola</u>
Alpa Bala
Yoni Shushkata
Sandhi Vedana
Maithuna Krichrata

Pitta <mark>Pradhana</mark>	
Daha	
<u>Santapa</u>	
Krodha	

Aniyamita Masika Chakra- One of the Karmas of Apana Vata is Artava Nishkramana.^[35] In the years near to Rajo Nivrutti, Apana Vata Karma i.e. Artava Nishkramana is hampered. So initially Aniyamita Masika Chakra is observed which later results in Rajo Nivrutti. Gaada Varcha- One of the Vata Pradhana Lakshanas is gaada Varcha^[36] which is the result of Rooksha Guna of Vata. Nidra Nasha^[37]- The Rooksha Guna of Vata is the cause of this Vata Pradhana Lakshana. Asthi Shoola^[38]-The Rooksha Guna of Vata is the cause of this Vata Pradhana Lakshana. Alpa Bala^[39]- Vata Vriddi leads to Uttarottara Dhatu Kshaya. Rasadhatu will be reduced both qualitatively and quantitatively, resulting in Alpa Bala. Yoni Rookshata caused by Rooksha guna of Vata. Yoni Shushkata- Sphik Shushkata is a Lakshana of Mamsa Kshaya.^[41] Sphik can be regarded as pelvic region, hence it can be corelated with vaginal atrophy. It is caused by Rooksha and Khara Guna of Vata. Sandhi Vedana- It is a Lakshana of Mamsa Kshaya.^[42] Maithuna Krichrata- It is one of the Lakshanas of Shukra Kshaya^[43] caused by Rooksha Guna of Vata. Daha, Santapa and Krodha^[44,45,46]- Are Pitta Pradhana clinical signs and symptoms caused by Ushna Guna of Pitta.

Involvement of mental health- Along with the physiological symptoms, a menopause woman also presents with the psychological symptoms like irritability, anxiety, fatigue, depression, emotional disturbance, etc due to inadequate levels of oestrogen.^[47] Similarly in *Rajo Nivrutti, Manasika lakshanas* such as *Smriti Hrasa, Utsaha Hani, Anidra, Chinta* are seen due to the prevailing *Vata Dosha*.^[48] *Vata Dosha*, which is prominent in *Raja Guna*, governs the *Manas*.^[49] When *Vata Dosha* reaches *Vriddhi* due to the progression of age *Raja Guna* is also elevated, resulting in disruption in the *Manas* and the manifestation of symptoms. *Krodha*, one of *Pitta's lakshanas*, is also present since *Rajo Nivrutti* marks the transition from *Pitta* to *Vata* dominance stage.

Similarity in the treatment- Menopause signifies a shift in both physical and mental health. So, the management aspect in menopause also deals with counselling and reassurance. This is homologous to the *Aswasana* and *Santwana* which are the forms of *Satvavajaya Chikitsa* described in *Ayurveda*.^[50]

CONCLUSION

Menopause occurs due to the natural depletion of ovarian follicles, which reduces oestrogen, progesterone, and inhibin levels, leading to an endocrine imbalance. The hypothalamic-pituitary-ovarian axis adjusts to the declining ovarian function, marked by elevated gonadotropins (FSH and LH) and diminished sex steroid hormones. These hormonal shifts define the transition into menopause. The notions of menopause and Rajo Nivrutti can be critically related. The phases of menopause can be compared with the Madhyamavastha of a female. Menopause (Rajo Nivrutti) is physiological process. Both conditions share a common cause and set of signs and symptoms. Menopause (Rajo Nivrutti) have an impact on both physical and mental health where especially counselling and reassurance similar to Satvavajaya Chikitsa aids in its management.

REFERENCES

- 1. Dutta DC. Textbook of Gynecology. 7th edition. Kolkata: New Central Book Agency, 2016; 55-57.
- Padubidri VG, Daftary SN. Shaw's Textbook of Gynaecology. 17th edition. New Delhi: Elsevier, 2018; 56–58.
- 3. Dutta DC. Textbook of Gynecology. 6th edition. Kolkata: New Central Book Agency, 2013; 55–59.
- 4. Dutta DC. Textbook of Gynecology. 6th edition. Kolkata: New Central Book Agency, 2013; 57–59.
- 5. Rani HS, Pai MR. Clinical Obstetrics and Gynaecology. 2nd edition. New Delhi: Jaypee Brothers Medical Publishers, 2017; 150–155.
- Palmisano BT, Zhu L, Stafford JM. Role of estrogens in the regulation of liver lipid metabolism. Adv Exp Med Biol., 2017; 1043: 227–256.
- Khosla S, Oursler MJ, Monroe DG. Estrogen and the skeleton. Trends Endocrinol Metab., 2012; 23(11): 576–581.
- Young EA, Altemus M, Parkison V. Effects of estrogen versus estrogen and progesterone on cortisol and interleukin-6. Menopause., 2008; 15(6): 1170–1175.
- Robinson D, Cardozo L. The role of estrogens in female lower urinary tract dysfunction. Urology, 2003; 62: 45–51.
- Gargett CE, Schwab KE, Zillwood RM, Nguyen HP, Wu D. Isolation and culture of epithelial progenitors and mesenchymal stem cells from human endometrium. Biol Reprod., 2009; 80(6): 1136–1145.
- 11. Zhang Y, Wang Y, Wang X, et al. Menopauseinduced uterine epithelium atrophy results from autophagy activation. Sci Rep., 2016; 6: 31408.
- 12. Zhang Y, Wang Y, Wang X, et al. Menopauseinduced uterine epithelium atrophy results from autophagy activation. Sci Rep., 2016; 6: 31408.
- 13. Bleibel B. Vaginal Atrophy. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2024. Available from:

https://www.ncbi.nlm.nih.gov/books/NBK559297/

- Gambacciani M, Levancini M. Non-oestrogenic modalities to reverse urogenital aging. Climacteric., 2015; 18(1): 12–17.
- Daniel CW. The mammary gland: a model for development. J Mammary Gland Biol Neoplasia., 1999; 4(1): 5–10.
- Stevenson S, Thornton MJ. Effect of estrogens on skin aging and the potential role of SERMs. Clin Interv Aging., 2007; 2(3): 283–289.
- Shah MG, Maibach HI. Estrogen and skin. An overview. Am J Clin Dermatol., 2001; 2(3): 143–150.
- Clegg DJ. Sex differences in obesity and the regulation of energy homeostasis. Physiol Behav., 2012; 106(2): 169-73.
- 19. Hu H, Zhang S. Estrogen leads to reversible hair cycle retardation through inducing premature catagen and maintaining telogen. PLoS One., 2012; 7(7): e40124.
- 20. Abitbol J, Abitbol P, Abitbol B. Sex hormones and the female voice. J Voice., 1999; 13(3): 424-46.
- 21. Soares CN. Mood disorders in midlife women: understanding the critical window and its clinical implications. Menopause., 2014; 21(6): 635-637.
- 22. Bethea CL, Lu NZ, Gundlah C, Streicher JM. Diverse actions of ovarian steroids in the serotonin neural system. Front Neuroendocrinol., 2002; 23(1): 41-100.
- 23. Singh RH. Menopause: An Ayurvedic perspective. Journal of Ayurveda and Integrated Medicine., 2012; 3(3): 136-142.
- 24. Vaidya Keval Krishna Takral, Sushruta Samhita of Sushrutha with Dalhana's Nibandhasangraha and Shree Gayadas's Nyaya Chandrika commentary, Sharira sthana 3/11. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 42.
- 25. Bhavaprakasha, Bhavamishra, Madhyama Khanda, 15.
- 26. Vaidya Keval Krishna Takral, Sushruta Samhita of Sushrutha with Dalhana's Nibandhasangraha and Shree Gayadas's Nyaya Chandrika commentary, Sharira sthana 3/11. Reprint edition. Varanasi: Chaukhambha Orientalia., 2022; 42.
- 27. Bhardwaj Anita, Kumar Sharma Deepak. Rajonivritti: A Physiological Study. J Ayurveda Integrated Medical Sciences, 2022; 11: 59-66.
- 28. Bhardwaj Anita, Kumar Sharma Deepak. Rajonivritti: A Physiological Study. J Ayurveda Integrated Medical Sciences, 2022; 11: 59-66.
- 29. Kim JH, Park JH, Lee JH. Differences in youngestold, middle-old, and oldest-old patients who visited the emergency department. Clin Exp Emerg Med., 2018; 5(4): 249–255.
- 30. Vaidya Keval Krishna Takral, Sushruta Samhita of Sushrutha with Dalhana's Nibandhasangraha and Shree Gayadas's Nyaya Chandrika commentary, Sutra sthana 35/29. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 389.
- 31. Vaidya Harishchandra Simha Kushavaha, Charaka Samhita of Charaka with Chakrapani Dutta's

Ayurveda Deepika commentary, Sutrasthana 17/76. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 271.

- 32. Vaidya Harishchandra Simha Kushavaha, Charaka Samhita of Charaka with Chakrapani Dutta's Ayurveda Deepika commentary, Vimana sthana 3/36. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 616.
- Bhardwaj Anita, Kumar Sharma Deepak. Rajonivritti: A Physiological Study. Journal of Ayurveda Integrated Medical Sciences, 2022; 11: 59-66.
- Bhardwaj Anita, Kumar Sharma Deepak. Rajonivritti: A Physiological Study. Journal of Ayurveda Integrated Medical Sciences, 2022; 11: 59-66.
- 35. Vaidya Keval Krishna Takral, Sushruta Samhita of Sushrutha with Dalhana's Nibandhasangraha and Shree Gayadas's Nyaya Chandrika commentary, Nidana sthana 1/19. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 683.
- 36. Vaidya Keval Krishna Takral, Sushruta Samhita of Sushrutha with Dalhana's Nibandhasangraha and Shree Gayadas's Nyaya Chandrika commentary, Sutra sthana 15/13. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 165.
- 37. Vaidya Keval Krishna Takral, Sushruta Samhita of Sushrutha with Dalhana's Nibandhasangraha and Shree Gayadas's Nyaya Chandrika commentary, Sutra sthana 15/13. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 165.
- Vaidya Ravidutta Tripathi, Ashtanga Sangraha, Sutra sthana 19/5. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 340.
- Vaidya Keval Krishna Takral, Sushruta Samhita of Sushrutha with Dalhana's Nibandhasangraha and Shree Gayadas's Nyaya Chandrika commentary, Sutra sthana 15/13. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 165.
- Paradakara H S Sastri. Ashtanga Hrdaya of Vagbhata, Sutra Sthana 11/17 Reprint edition. Varanasi: Chowkamba Surbharati Prakashan, 2005; 290.
- 41. Vaidya Harishchandra Simha Kushavaha, Charaka Samhita of Charaka with Chakrapani Dutta's Ayurveda Deepika commentary, Sutrasthana 17/65. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 268.
- 42. Vaidya Keval Krishna Takral, Sushruta Samhita of Sushrutha with Dalhana's Nibandhasangraha and Shree Gayadas's Nyaya Chandrika commentary, Sutra sthana 15/9. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 162.
- 43. Vaidya Keval Krishna Takral, Sushruta Samhita of Sushrutha with Dalhana's Nibandhasangraha and Shree Gayadas's Nyaya Chandrika commentary, Sutra sthana 15/9. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 162.
- 44. Paradakara H S Sastri. Ashtanga Hrdaya of Vagbhata, Sutra Sthana 11/7 Reprint edition.

Varanasi: Chowkamba Surbharati Prakashan, 2005; 288.

- 45. Vaidya Keval Krishna Takral, Sushruta Samhita of Sushrutha with Dalhana's Nibandhasangraha and Shree Gayadas's Nyaya Chandrika commentary, Sutra sthana 15/13. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 165.
- 46. Vaidya Ravidutta Tripathi, Ashtanga Sangraha, Sutra sthana 19/5. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 340.
- 47. Santoro N, Epperson CN, Mathews SB. Menopausal Symptoms and Their Management. The Journal of the American Medical Association, 2015; 314(4): 399–400.
- 48. Yadav R, Dei L. Review of clinical studies on Rajonivrutti avastha with special reference to menopausal syndrome. International Journal of Advanced Medicine, 2021; 8: 137-43.
- 49. Vaidya Harishchandra Simha Kushavaha, Charaka Samhita of Charaka with Chakrapani Dutta's Ayurveda Deepika commentary, Sutrasthana 12/8. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 189.
- 50. Vaidya Harishchandra Simha Kushavaha, Charaka Samhita of Charaka with Chakrapani Dutta's Ayurveda Deepika commentary, Sutrasthana 11/54. Reprint edition. Varanasi: Chaukhambha Orientalia, 2022; 183.