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Ovarian Cancer & Aging: Associations, Factors and Prevention

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ABSTRACT

Aging is a natural inevitable process that involves a gradual decline in the physiological functions of an organism over time. Almost all the systems of the body are affected by aging mostly reproductive system. The female reproductive system is key for the health of women's well-being. Ovarian cancer is the seventh most common cancer in women and is the eighth most common cause of death in females due to cancer. Its risk increases with age, peaking in the late 70s. Several factors are responsible for ovarian cancer out of which aging is the most important one. One cannot stop her aging with passing life but the incidence of gynecological problems like ovarian cancer can be successfully reduced and overcome to some extent by following some preventive measures. This review article emphasizes the role of aging in ovarian cancer and how it can be controlled for the better health of the female in old age.

1. INTRODUCTION

Aging is a universal phenomenon observed in all living organisms, including humans. It is natural process but it is triggered by developmental genetic defects, environmental factors, sedentary lifestyles, and some pathological conditions like chronic disease (Harman, 2001). Aging produces many diverse changes in the body (Kohn, 1985; Zurcher and Slagboom, 1992). In the world, the number of people with age more than 60 is gradually increasing. That ratio in 1960 was 8.1 % and in 2000 it became 10% and now it is about 23 % in 2020 (Marengoni *et al.*, 2011). The most important factor of aging is the gradual loss of function and degeneration that occur at the molecular level, organism level, tissue level, and cellular level (Williams, 2001).

The mechanisms of aging are complex and multifaceted, involving a combination of

genetic, cellular, and environmental factors (Fig 1). Genetic factors influence the rate of aging and can contribute to an individual's susceptibility to age-related diseases (Fulop *et al.*, 2010). DNA can be damaged by various factors, such as UV radiation, toxins, and metabolic byproducts. While cells have mechanisms to repair DNA damage, over the time, the accumulation of unrepaired damage can contribute to aging (Gill *et al.*, 2015). Telomeres on the chromosomes are protective structures that naturally shorten with each cell division. When telomeres become critically short, cells may enter a state of senescence, where they cease to divide and function properly (Ottinger, 2010). Along with the genetic factors some cellular changes like Mitochondrial Dysfunction also leads to a decline in energy production, an increase in reactive oxygen species (ROS), and impaired cellular function. In turn the increase in reactive

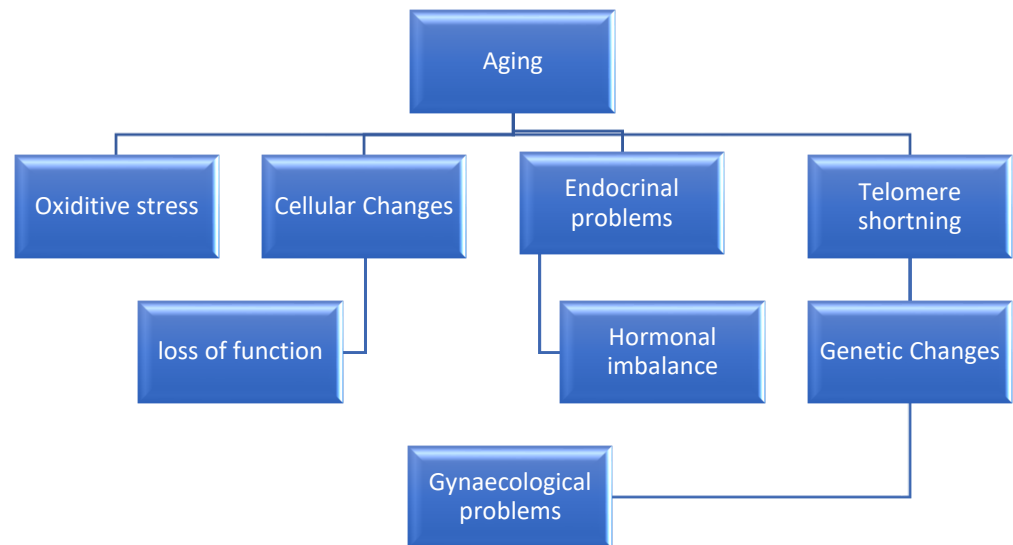


Figure 1. Factors associated with aging leading to female reproductive problems

oxygen species (ROS) leads to oxidative stress, causing damage to proteins, lipids, and DNA (Juan, 2021). Alterations in hormone levels, such as a decline in sex hormones like estrogen and testosterone, are associated with the aging process and can impact various physiological functions. All these mechanisms are interconnected, and the aging process is likely influenced by the interplay of multiple factors.

1.1 Ovarian Changes Associated with Aging

As women age, the female reproductive system undergoes various physiological and pathological changes, many of which are associated with the natural process of aging. These changes can affect different components of the reproductive system, especially the ovaries leading to alterations in hormonal levels, organ structure, and functionality. Here are some common pathological changes in the female reproductive system with advancing age (Wing and Schiffman, 2021). Ovarian aging is a pathological as well as physiological

aging process that is characterized by the low level of quantity and quality of oocytes, ovarian cancer, ovarian tumor, endometriosis, adenomyosis, polyp, and fibroid formation (Park *et al.*, 2021).

Female gametes are produced during embryonic life that is gradually decreased during women's life span. during early life 2000 germ cells migrate to gonadal ridges and within 20 weeks that number is increased 5 times (Schmidt *et al.*, 2012; Pelosi *et al.*, 2015; Consortium *et al.*, 2016; Adebayo *et al.*, 2023). Women are born with a finite follicle pool that constantly decline without renewing (Pelosi *et al.*, 2015). Furthermore, with advancing age oocyte quality also decreases (Block, 1952; Consortium *et al.*, 2016). Less than 0.1% of oocytes present at birth will be ovulated during gestational life. The remaining oocyte will be destroyed by atresia. These vast number of events occurring in the female ovary may get affected in any stage of life but with advancing age the chances of pathology and loss of function increases which make a female

vulnerable to ovarian cancer and other related pathologies (De Pol *et al.*, 1997).

1.2 Risk of Ovarian Cancer

The risk of certain gynecological cancers, such as ovarian, uterine, and cervical cancers, increases with age. Ovarian Cancer is age-related degenerative disease. It starts from the beginning and reaches at its peak at the midpoint of life span therefore cancer is not different from other diseases of aging (Res, 2009; Jemal *et al.*, 2010). Epithelial ovarian cancer is a gynecological cancer half of the cases occur above the age of 65 year of age (Siegel *et al.*, 2018). With this cancer, the women's survival rate gradually decreased with five-year survival rates below 45%. The reason for the aggressiveness of this cancer is poorly understood. Without this cancer, a woman of 75 years can survive for 12 years, and of 85 years women can further survive for 7 years (Muñoz *et al.*, 1997; Hilpert *et al.*, 2007). Epithelial ovarian cancer can interact

with the host immune system. This cancer first involves the shedding of tumor cells from primary ovarian mass to peritoneal fluid (Shield *et al.*, 2009).

1.3 Prevalence of Ovarian Cancer

Ovarian cancer is not diagnosed at early stage but often at an advanced stage making it more challenging to treat. According to global cancer statistics, ovarian cancer is the eighth most common cancer in women worldwide. However, the incidence rates can vary significantly by region and are generally higher in developed countries (Reid *et al.*, 2017). It has been studied in several researches that the percentage of ovarian cancer in females above 50 years is much greater than the number of ovarian cancers in females below 30 years of age. In China the percentage of ovarian cancer in females above 50 years is 18 while in females below 30 years of age is just 3. (Table 1).

Table 1. Percentage of ovarian cancer in females during various reproductive years of life

Age (year)	25-29	30-34	35-39	40-44	45-49	>50	reference
United States	4.83	6.44	8.89	13.26		13.16	(Quirk <i>et al.</i> , 2005)
China	3.16	2.84	4.77	8.49	14.60	18.07	(Wang <i>et al.</i> , 2014)
India	-	14.11		26.38		23.93	(Puri <i>et al.</i> , 2018)
Pakistan	-	14		22		24	(Nasreen, 2002)
Egypt	-	5		12.4		35.5	(Alshahrani <i>et al.</i> , 2018)

1.4 Factors Causing Ovarian Cancer

Several factors can influence female reproductive health and the functioning of the ovaries (Hassan *et al.*, 2024). These factors encompass a combination of genetic, environmental, lifestyle, and healthcare-related elements (Richie, 2024). (Fig 2)

Conditions affecting the endocrine system, such as polycystic ovary syndrome (PCOS) or

thyroid disorders, can impact hormonal balance and menstrual cycles (Bungau *et al.*, 2024). Adequate nutrition is crucial for reproductive health. Poor nutrition, obesity, or extreme weight loss can affect hormonal balance and fertility. Intense or excessive exercise can lead to irregular menstrual cycles and, in some cases, amenorrhea (absence of menstruation). Tobacco and excessive alcohol consumption have been linked to fertility issues and can increase the risk of miscarriage.



The type and use of contraception can influence reproductive health. Some methods, such as hormonal contraceptives, can have temporary effects on fertility (Ames *et al.*, 2024). Infections such as chlamydia and gonorrhea can cause pelvic inflammatory disease (PID), which may lead to fertility problems if left untreated (Naghdi-Dorabati *et al.*, 2024). Exposure to certain chemicals, pollutants, and toxins in the environment may impact fertility. Occupational exposures to certain substances may also play a role (Margiana *et al.*, 2023). Chronic stress can

affect the menstrual cycle and may contribute to fertility issues. Mental health conditions, such as anxiety and depression, can also impact reproductive health (Vladimirovna *et al.*, 2023)]. Conditions like diabetes, autoimmune disorders, and other chronic illnesses can influence reproductive health. Many treatments of cancers, especially radiation and chemotherapy, affects the fertility negatively (Andreoli *et al.*, 2023). Hereditary abnormalities of the reproductive system can also have negative effects on reproductive health and fertility (Van Lunsen, 2023).

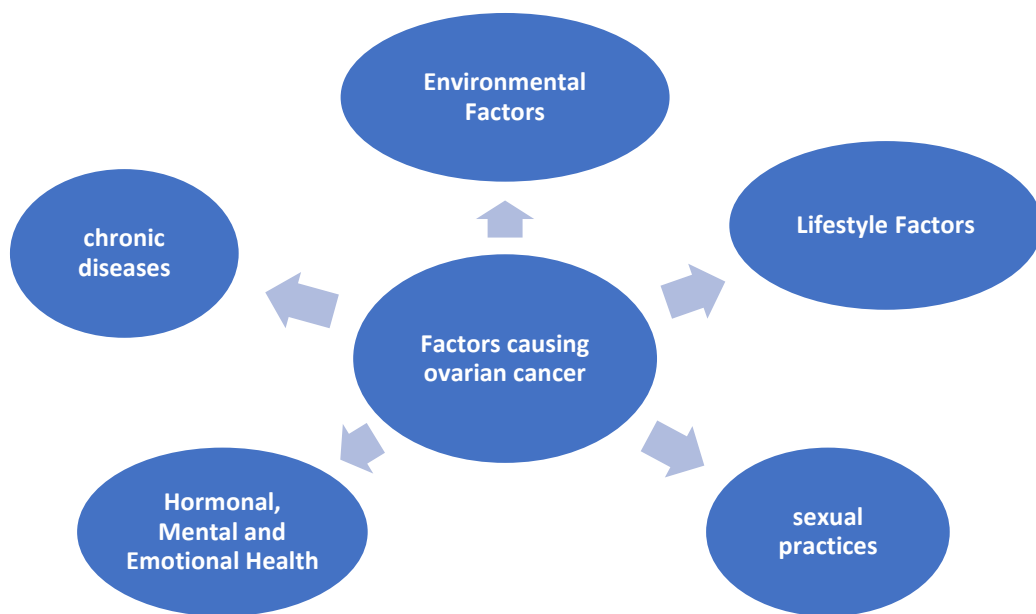


Figure 2. Factors causing ovarian cancer

1.5 Prevention of Ovarian Cancer

Though the phenomenon of aging is natural, certain measures can be taken to keep a healthy reproductive system and to reduce the risk of age-associated problems related to reproductive health associated (Miao and Goltzman, 2023).

- Regular Health Check-ups:** Individuals should be aware of symptoms of any such medical conditions and should seek immediate medical assistance when needed. There should be regular medical check-ups for early detection of any such problems. Moreover, individuals having family history of any such ailments should seek genetic counseling and should go for genetic testing



if needed in order to detect of presence of any relevant genetic mutations that may lead to higher risk of developing such problems (Telman *et al.*, 2023).

- **Healthy Lifestyle:** A healthy lifestyle and a balanced diet is key to maintaining proper health and well-being (Sarwar *et al.*, 2015). Exercise and physical activity also helps to maintain weight, control cholesterol, and other medical problems that arise with the aging (Hill and Wyatt, 2005). Moreover, unhealthy habits such as alcohol consumption and smoking may also contribute to fertility issues (Basic *et al.*, 2023). Weight should be controlled as obesity can cause hormonal imbalances while being underweight can disrupt menstrual cycles, both can contribute to fertility related issues (Stefanaki *et al.*, 2023). Stress can also impact reproductive health. Stress-reducing exercises such as yoga can help overcome it (Janssen *et al.*, 2023).
- **Protection against Sexually Transmitted Infections (STIs):** Practice safe sex to reduce the risk of STIs, which can lead to pelvic inflammatory disease (PID) and affect fertility (Stefanaki *et al.*, 2023).
- **Hormone Replacement Therapy (HRT):** For women experiencing severe menopausal symptoms, hormone replacement therapy under the guidance of a healthcare professional may help manage symptoms and support overall well-being. Long-term use of oral contraceptives has been associated with a decreased risk of ovarian cancer. Discussing the potential benefits and risks of birth control pills with a healthcare provider is important (Holloway, 2023)
- **Cancer Screenings:** Participate in regular screenings for gynecological cancers, such as cervical and ovarian cancers (Radu *et al.*, 2023).

- **Pregnancy and Breastfeeding:** Pregnancy and breastfeeding have been linked to a lower risk of ovarian cancer. Women who have had one or more full-term pregnancies and breastfed may have a reduced risk (Puri *et al.*, 2018).

Conclusion

Ovarian cancer is likely associated with the aging process. One cannot stop aging but can intervene with the pathological changes associated with aging. Healthy lifestyle, regular checkups, exercise and proper diet helps in preventing ovarian cancer.

Conflict of Interest

The authors declare no conflict of interest.

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