

## Research Article

# Consequences of Reproductive Age Events, Disorders, Therapies and Elderly Women's Health

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## Abstract

**Introduction:** Events, disorders, therapies during reproductive age of women have sequelae in later life. It may not be possible to prevent events, disorders therapies, it is essential to know possible consequences, so that prevention is attempted by controlling other risk factors to prevent disorders in later age.

**Objective:** Aim of this simple review was to get information about consequences of reproductive life events, disorders and therapies in later stages of a woman's life.

**Materials and Methods:** Literature was searched with various search engines like Google, Google Scholar, Bing, PubMed, UpToDate, BMJ etc. Information from discussions and personal experiences was added.

**Evidence:** About some disorders in elderly women, there is clear evidence that they have direct linkages to events, disorders and/or therapies during reproductive life, others require more research. Early menarche and late menopause have been linked to endometrial carcinoma. Polycystic ovarian syndrome, in young women has been linked to occurrence of diabetes, hypertension and Coronary Artery Disease (CAD) in later life.

Infertility is known to be associated with endometrial cancer, ovarian cancer later.

Hypertension during pregnancy has been associated with CAD in future life. Ovarian dysfunction and ovulation therapies during reproductive life have direct linkage to CAD. Oral contraceptives have some linkages to CAD, cervical cancer in later life. Birth trauma is responsible for genital prolapse, bowel, bladder, sexual dysfunction later, in many.

**Conclusion:** Events, disorders, therapies during reproductive age affect life of elderly women. So attention needs to be given to other risk factors to attempt healthy life for elderly women.

**Keywords:** Disorders; Elderly women; Reproductive health events; Consequences

## Introduction

Many events, disorders and therapies during reproductive life of women have sequelae in later life. It may not be possible to prevent events, even disorders or therapies, it is essential for women to know the future possibilities, so that prevention is attempted by controlling other risk factors for protecting the health of elderly women. It is especially important because older women are more likely than men to be living in poverty, which affects their health seeking, non-affordability of visiting specialist doctors, medications for disorders and other essential health care needs [1].

## Objective

The aim of the review was to get information about consequences of events, disorders and therapies during reproductive stages of women which affect their life in later years.

## Materials and Methods

Literature was searched with various search engines like Google,

Google Scholar, Bing, and sites like PubMed, Up To Date, BMJ etc. Information from discussions and personal experiences was added.

## Evidence

About some disorders in elderly, there is clear evidence that they have direct linkages to events and therapies during reproductive life, others need more research.

## Menarche and menopause

There is evidence that women who have early menarche and/or late menopause are more likely to have endometrial carcinoma. This seems to be due to longer duration of oestrogen. Breast cancer may also be commoner in such women [2]. And also late menarche or early menopause has association with osteoporosis in later life [3-8]. Again this could be due to less of oestrogenic life.

## Polycystic ovarian syndrome

The Polycystic Ovarian Syndrome (PCOS) affects 5 to 10 percent women. Evidence and knowledge about PCOS is rapidly evolving,

as commonest endocrinopathy among women of reproductive age, a common cause of infertility, an important harbinger of future metabolic disorders such as diabetes and heart disease with an increased risk of obesity too [9-12]. Around, 8% of affected women are likely to develop type 2 diabetes annually [13]. Women with PCOS have been found to have more extensive coronary artery disease, detected during angiography [14]. Hypertension is also observed more frequently in these women [12]. Although, to date, most attention has been paid to the management of symptoms, signs and infertility, it is becoming more and more obvious that, due to the complexity of the PCOS a number of metabolic and other implications of woman's health may have to be confronted in the future.

There is considerable evidence that reproductive factors play a definite role in the aetiology of endometrial cancer [15-21]. Prolonged anovulation which characterizes PCOS, considered to be the main mechanism responsible for continued unopposed oestrogen and as a consequence, increased risk of endometrial carcinoma. Irregular menstrual cycles are common in perimenopausal age, so women with PCOS need to be specially monitored. Researchers have reported that the true risk of endometrial carcinoma in women diagnosed with PCOS has not been clearly defined. La Vecchia [22] reported that recent appraisal of the evidence for association between PCOS and endometrial cancer was inconclusive. However the risk of developing endometrial cancer is known to be increasing with obesity, long-term use of unopposed oestrogens, nulliparity, infertility, hypertension and diabetes. All these pathophysiological conditions are known to be associated with PCOS, so such patients need to take necessary measures for quality life [14,23-25]. Other reproductive factors may also influence the risk of endometrial cancer by affecting relative estrogen/progesterone exposures. There is emerging evidence of strong connections between PCOS and ovarian and breast cancer too [26,27]. However, there are only a few studies addressing the possibility of association of PCOS and ovarian cancer with conflicting evidence. Globally ovarian and breast cancers kill many women and PCOS also occurs in many adolescent and young women around the world, so research needs to continue.

### Infertility

Infertility especially when it is because of progesterone deficiency or anovulation has been linked to increased risk of endometrial cancer in several studies [20,28-32]. A woman who has a pregnancy anytime has less than half the risk of endometrial cancer, compared with a woman who was never pregnant. There has been much debate and concern about the risk of ovarian cancer in women with anovulation, particularly because of the extended use of ovulation inducing drugs [27]. However analysis of a possible causal relationship between fertility medications and the risk of ovarian cancer often is confounded by the established effects of low parity and infertility on this risk. However researchers reported infertility and 'incessant ovulation' as risk factors for the development of ovarian cancer [33-37]. The hyperstimulatory effects of fertility medications on the ovary are etiologically important in the genesis of some cases of ovarian cancer. Clinical evidence of a possible link, though not necessarily causal, between gonadotropins and ovarian cancer was described in a case reported by Bandera et al. [38]. Also the apparent link between fertility drugs and ovarian cancer may not be a causal one, but rather one of hastening or stimulating tumor growth. Bristow [39] reported

that it may be that the select population of infertile women that carry a significant risk for the development of ovarian cancer, regardless of fertility drug use. Rossing et al [33] reported the risk of ovarian tumors associated with long-term use of clomifene increased among both the women with ovulatory abnormalities and those with no known ovulatory abnormalities.

However, the Danish studies have suggested that infertility on its own increased the risk of borderline and invasive ovarian tumors [40,41].

### Ovarian dysfunction and therapy

Normal ovarian function is believed to be cardioprotective. The role of estrogen in heart disease is not well understood. The relationship between heart disease and the female reproductive system often is usually overlooked. It has been reported that fewer cardiac events occur before menopause, an effect most likely related to relatively higher estrogen levels during reproductive age. Low estrogen levels, oral contraceptive use, affect oestrogen. Stress is also known to affect menstruation and stress has been linked with Cardiovascular Disease (CVD) also. So linkage is possible. Some studies showed a link between irregular menstruation and later development of CVD which again is linked to circulating hormones. Autopsies of women as young as 34 years revealed that even mild changes in ovarian function increased CVD risk [42]. Pathologic changes, such as atherosclerosis have been reported in women with ovarian dysfunction. In a large study that followed 28,000 women in Denmark for a decade, revealed that women with irregular menstrual cycles (28%) were more likely to develop CVD than those with regular menstrual cycles [43]. In a study Bertuccio *et al.* [44], demonstrated that menstrual and reproductive factors along with smoking increased a woman's risk of nonfatal myocardial infarction. So additional risk factors need to be always remembered. Although women may not be able to change their menstrual cycles, they can work to lower CVD risks by looking at other risks factors, such as smoking, obesity, and hypertension [42]. Until about 10 years ago, Hormone Replacement Therapy (HRT) was commonly prescribed for menopausal women to relieve menopausal symptoms and protected against cardiovascular problems and osteoporosis. After the Women's Health Initiative (WHI) data [45], great controversy arose. Maclaran *et al* [46] have reviewed many studies and found HRT having no benefits in preventing CVD and actually increased associated risks. Later reevaluation of their study, as well as other studies, suggested that starting HRT during the perimenopausal and early postmenopausal periods does have cardioprotective effects, whereas for women in late postmenopause, HRT could be detrimental at worst or ineffectual at best. Globally women were given and are still being given HRT. This needs more research, awareness and advocacy.

### Disorders during pregnancy

Pregnancy is a physiological event but turns into pathology many times. Some studies suggested a link between complications during pregnancy and later CVD development. A 2012 study revealed that women with preeclampsia which is not uncommon globally were at increased risk for ischemic heart disease, hypertension, and other CVD later in life [42]. Since hypertensive disorders are common it is essential that women are aware. Gestational diabetes affected 3-10% of pregnancies, depending on the population studied [47,48]. Donovan

[49] reported that women with unmanaged gestational diabetes were at increased risk of developing type 2 diabetes mellitus (or, very rarely, latent autoimmune diabetes or Type 1) after pregnancy. Research on various other disorders associated with reproductive age of women needs to continue to enhance better understanding of their consequences, prevention and treatment, specially which occur during pregnancy with not much known about their etiology.

### Births

Trauma during birth could cause genital prolapse and all associated problems like urinary, bowel dysfunction etc. Genital prolapse is known to occur after birth trauma or in women who have many births women have to suffer because of prolapsed and their surgical morbidity. Inadequate treatment of birth related Postpartum Depression (PPD) puts women at risk for the sequelae of untreated affective illness, and the depression may become chronic, recurrent, and/or refractory [50,51]. It is estimated that one in six women over the age of 50 have osteoporosis [52], a major cause of morbidity and mortality in postmenopausal women globally [53]. Women around the globe suffer with backache, fractures and so on.

### Contraception

Oral Contraceptive Pills (OCPs) are used globally, young girls to women of reproductive age and CVD have been associated with deep vein thrombosis, stroke, and *myocardial infarction*. However when OCPs were introduced in the 1960s, they contained large estrogen doses. These doses were associated with blood clots, nausea, and weight gain. Over the years, studies found that much lower estrogen doses were just as effective. Modern OCPs have lower estrogen doses. But all OCPs do pose some risk for thrombosis, MI and stroke. In a recent review by the Food and Drug Administration, it was revealed that, contraceptives containing drospirenone (a synthetic progesterone form) had higher risk of blood clots than other progestin-containing contraceptives [54]. Oral contraceptive risks in women may be mediated by factors such as age, overall health, and smoking history, genetic and hereditary conditions. One study showed a higher incidence of ischemic stroke in women with inherited prothrombotic conditions (including factor V Leiden, prothrombin G20210A, and methylenetetrahydrofolate reductase C677T genotype). This study is important because women do not get routinely tested for inherited prothrombotic conditions before using OCPs and thus do not realize that they may be at greater risk for stroke [55]. The risk of adverse effects of OCPs increases with age and certain other related factors. Therefore, the decision to use OCPs should be considered carefully [42]. OCP are used globally for control of fertility and for many disorders too. Risks need to be remembered and women made aware.

### Conclusion

Many events during reproductive age, disorders and their therapies affect life of women in later years. It is essential that women know and take precautions, because it may not be possible to prevent events, disorders and avoid therapies. Action to look into other risk factors to prevent disorders during later life of women and timely management is always possible. A few things are beyond control, but timely management helps in survival with quality.

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