

IMPACT OF CANCER THERAPY ON FEMALE FERTILITY: A SYSTEMATIC REVIEW

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ABSTRACT

- **Background:** Cancers have become highly prevalent in developing countries and Africa is not far from it. The treatment to these cancers increases the risk of infertility in women. This review aims at understanding the effects of different types of cancer treatments on fertility of women.
- **Method:** A systematic review of published literature was performed on the topic of effects of cancer treatment on fertility of women in South Africa initially, and later expanded to include other countries. Nineteen articles were finally included in the study following PRISMA guidelines.
- **Results:** Overall fertility deficits were observed in female survivors of cancers. Fertility post cancer therapy is influenced by sex, age at diagnosis, prediagnosis parenthood, and diagnostic period. Treatment with alkylating agents, second line therapy and age> 35 years also influence chances of pregnancy. Pre-term delivery was also found to be linked to cancer related therapy. Probability of having first live birth among cancer survivors was low. Site of cancer and age at the onset of cancer were independent predictors of a reduced probability of giving birth after diagnosis. Pelvic radiation was found to be more damaging than abdominal or supradiaphragmatic radiation.
- **Conclusion:** The present study indicates that future measures should be taken to include assessment of women’s desire for future fertility and also provide fertility preservation options. Fertility preservation strategies for women in their reproductive years who have been diagnosed with cancer. Long-term fertility data is required on cancer survivors of South African women. Counseling tools and guidelines for referral to oncofertility specialists should be developed for newly diagnosed young patients.
- **Key words:** Cancer, Survivor, Fertility, Chemotherapy, Radiotherapy, Radiation, Treatment

INTRODUCTION

- Recently, cancers have become highly prevalent in developing countries and Africa is not far from it (Farmer et al., 2010).
- More than 1 million people suffer from cancer in the world every year and these are mostly in their reproductive age (Hawkey et al., 2021).
- Cancer contributed to 650 000 new cases in Africa in 2002 among which sub-Saharan Africa comprised 530 000 people (311 000 males and 338 000 females) (Ferley JF, 2001).
- Cancer treatments and its effects on fertility has been investigated in various studies, mainly focusing on pregnancy and childbirth (Stensheim et al., 2011; Baxter et al., 2013; Brämswig et al., 2015; Armuand et al., 2017; Thouvenin-Doulet et al. 2018).
- The mechanism of cancer therapy related injury, in terms of ovarian reserve has not been understood comprehensively.
- Some of the effects include faster primordial follicle recruitment ('burn-out' effect), ovarian vascularization impairment (Meirow et al., 2007).
- ❖ **Aim:** This particular systemic review aims at understanding the effects of different types of cancer treatments on fertility of women and also assesses their chances to fulfil their desire of parenthood.
- ❖ **Importance:** This study might be helpful in future counselling of such patients and their families, on impact of oncologic treatment on fertility, and might also seek their decisions on fertility preservation, if possible, in future.

METHODOLOGY

- This systematic review was carried out in accordance with the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Liberati et al., 2009).
- Literature searches was carried out on the following databases, such as Cochrane, Google Scholar, PubMed (Medline), Scopus and databases with the appropriate key terms (MeSH) and phrases
- The search was limited to studies in humans. Only articles published in English language were included in this study.

RESULTS

- This review included 19 studies that matched the criteria for inclusion
- Out of the 19 studies included here, 14 studies were retrospective.
- The most common type of cancer that was reported in most of the articles was breast cancer and cervical cancer.
- Most of the studies considered that age group 18-44 (Syse et al., 2007; Cvancarova et al., 2009; Hartman et al., 2013; Stensheim et al., 2011), while some others also considered children <15 years (Pivetta et al., 2011; Madanat et al., 2008; Chow et al., 2016; Hodgson et al., 2007; Byrne et al., 2004; Thouvenin-Doulet et al., 2018; Armuand et al., 2017).
- Chemotherapy and Radiotherapy was the mode of treatment of cancers in almost all the articles.
- The present literature review it can be inferred that the overall fertility deficits were observed in female survivors of cancers.
- This was directly reported by few of the articles such as (van der Kaaij et al., 2012; Byrne et al., 2004; Cvancarova et al., 2009).
- Byrne et al., (Byrne et al., 2004) reported this in female survivors treated with cranial radiotherapy.
- It has also be observed to be influenced by sex, age at diagnosis, prediagnosis parenthood, and diagnostic period with more favorable rates in males than in females (Cvancarova et al., 2009).
- Moreover, treatment with alkylating agents, second line therapy and age> 35 years seem to influence chances of pregnancy (van der Kaaij et al., 2012).
- Age related difficulty in pregnancy was also reported by Hodgson et al., (Hodgson et al., 2007).
- On the contrary, Hodgson et al., (Hodgson et al., 2007) observed that there was no association between age at the time of treatment and number of cycles of chemotherapy and pregnancy among HodgekinsLeukemia (HL).
- Patients with abdominal and brain radiotherapy also reported reduced probability of producing offspring (Reulen et al., 2009).

CONCLUSION

- Female cancer survivors of reproductive age have fertility risks owing to their diagnosis, disease, and treatment. Future studies are required especially in the region of South Africa, where not much work has been done on this.
- The present study indicates that future measures should be taken to include assessment of women’s desire for future fertility and also provide fertility preservation options.
- A very strong survey or RCT is very much required in South Africa. Apart from focusing on only survival, the oncologists should also start considering the fertility preservation strategies for female candidates of reproductive age and also their decision to consider child birth in future.
- Emphasis must be laid on generating long term fertility data for such patients. The development and implementation of counselling tools and standards for referral to oncofertility specialists may also aid newly diagnosed young cancer patients and survivors.

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