

## **Cancer and Pregnancy: becoming parents after an oncological diagnosis in women**

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## **Abstract**

The issue of cancer and pregnancy will be increasingly topical giving the rising trend of women diagnosed with cancer during childbearing period. Although oncological progress has allowed women who receive cancer diagnosis before or during pregnancy to satisfy their desire for maternity and to carry on gestation, there is still few awareness.

In this chapter we present our research project and results carry out to date. The aim is to better understand challenges of women who experience pregnancy after or during cancer compared with non-oncological sample.

We focus on the impact of cancer in the construction of prenatal attachment and related psychological aspects. We study resilience considered as a protective factor in the construction of mother-fetus relationship. Then, we present the results of a qualitative study conducted in order to have a deeper understanding of the psychological dynamics that help women with cancer diagnosis to develop their maternal identity. We explore the topic of breastfeeding in women with cancer history, investigating how the feeding method is related to mother's mood states. Finally, we present the results about the cortisol concentration measurement during pregnancy.

Our results show how is very important to give women with oncological diagnosis the adequate support during puerperium.

## **Keywords**

Cancer; Pregnancy; Prenatal attachment; Resilience; Maternal Representations; Cortisol

There is no clinical context that is not influenced by the results of the research which, in addition to providing new intervention tools and allowing to assess their effectiveness, improves the quality of care.

This is particularly true in psycho-oncology, a professional discipline that focuses on the psychosocial and behavioural dimensions of neoplastic diseases, as part of a comprehensive and global approach to the patient and his family.

In the last 20 years, the research activity in psycho-oncology has grown considerably, offering important contributions on the most significant aspects of the disease experience and providing timely and personalized responses to the needs not only of patients, but also of the family members and of the nursing staff. Psychological research on the complex issue of women diagnosed with cancer at childbearing age is still in its infancy.

In Italy, about half of women with an oncological diagnosis express the motherhood desire, but due to the age, the diagnosis and the type of treatment, only few of them succeed in this project. An adequate counselling about onco-fertility could sustain the motherhood desire in women with cancer history. Since this topic will become more and more frequent, emerges the need and the importance to create multidisciplinary support interventions, in order to allow the young women to face not only the hard path related to cancer, but also the challenge related to motherhood.

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### *Introduction*

Pregnancy complicated by a medical diagnosis makes woman face a *double risk*: motherhood's desire is counterbalanced by the difficult and painful experience of illness that deeply undermine her safety and future planning.

In particular, when oncological and onco-hematological diagnosis are made during the childbearing period, they profoundly affect the woman's wellbeing and her future motherhood's project. A cancer diagnosis alters psychological protective factors that are fundamental to effectively cope with both pregnancy and post-partum period; specifically, an oncological diagnosis represents a challenge for the construction of prenatal and postnatal attachment.

With *cancer and pregnancy* we refer both to a cancer diagnosed during pregnancy or within 12 months from childbirth (gestational cancer), but also to a pregnancy occurring after diagnosis and treatment (pregnancy after cancer).

During perinatal period it's not rare that cancer diagnosis is delayed due to the misinterpretation (of pregnant women, but also of the medical staff) of physical symptoms. For example, hormonal changes caused by gestation, *puerperium* and breastfeeding may alter the normal appearance of breasts, thus retarding diagnosis [1,2]. Moreover, many of the first symptoms of malignancies may be confused by common pregnancy signs, such as tiredness, nausea, abdominal pain, vaginal discharge and pigmented lesions of the skin [2].

When an oncological diagnosis occurs during pregnancy, chemotherapy can be safely administered after the first trimester, without harming the fetus [3, 4, 2]. Moreover, antitumoral treatments giving during gestation do not impact negatively on the future child's health, including cognitive and cardiac development [3]. Nonetheless, there is an increased risk of a preterm birth, intrauterine growth restriction, hematopoietic suppression and stillbirth [2].

Women diagnosed with cancer in childbearing age have noteworthy doubts about fertility and recurrence, especially those who may wish to have a child [5]. On one side, although it is true that tumor and its treatments can reduce fertility, onco-fertility innovations allow to delay pregnancy at the end of the oncological *iter*. Therefore, health care provider (oncologist, gynecologist and psychologist) should be ready to discuss with patients in childbearing age all the relevant information about future fertility, pregnancy and breastfeeding, in other words to offer an oncofertility counseling. It is important to note that pregnancy after most cancers is not linked to an increased risk of recurrence. Actually, at least for breast cancer, there are data that pregnancy is a protective factor for recurrence and mortality [6] even if the *healthy mother effect* (i.e. self-selection of patients at better prognosis who get pregnant) should not be underestimated [5].

Given the rising trend of women delaying first gestation in their thirties and early forties, when cancer diagnoses are increasing [2], the issue of oncological pregnancy will be increasingly topical. In 2019, about 21.000 Italian women have been diagnosed with malignancies during the childbearing period [7] and 500-600 women have been diagnosed during pregnancy.

Oncological and onco-fertility progresses have allowed women who are diagnosed during pregnancy to carry on gestation [8, 9, 10] and women with a past oncological history to satisfy their desire for maternity [3, 11, 12]

Despite these advances, there is still little information about the adjustments of women who face an oncological diagnosis during pregnancy and the transition to motherhood and about how the cancer event affects the mother-child relationship.

To expand the literature about this issue and to make population aware with target programs, in 2016 a research has been started with the aim of verifying how the cancer event affects the mother-child relationship.

*Research project*

In 2016, we started a project called “*Becoming parents after an oncological diagnosis in women: evaluation of an Italian sample of oncological patients*” (Ethics Committee 196/2016). The project, conducted in collaboration with many different clinical and research centers in Italy, aimed to answer some questions about cancer and pregnancy, to better understand peculiarities and challenges of women who experience pregnancy after or during cancer. In order to reach our goal, we designed a short-longitudinal research in pregnant women with cancer, structured in two phases, the first one in the last trimester of pregnancy and the second one to three months after delivery. We compared a clinical group of pregnant women with cancer experience before or during gestation (and their partners) with a control sample consisting of non-oncological pregnant women and their partners. Subjects with a medical or psychiatric diagnosis of cognitive or psychiatric disorders, which could interfere with the assessment, were excluded from the study.

The research project consisted in the administration of questionnaires (Table 1) which, in addition to detecting important variables about the history of pregnancy, assessed the psychological status of the future mother and father. We evaluated prenatal attachment, negative experiences, the meaning that pregnancy assumes in their life, quality of life and resilience.

| Stages   | Tools   |
|--|---|
| <p style="text-align: center;"><b>Pregnancy</b></p> <p style="text-align: center;">The last trimester of pregnancy</p> | <ul style="list-style-type: none"> <li>• Detection of cortisol levels using blood and urine (24-hours) samples</li> <li>• Demography and clinical history</li> <li>• Prenatal Attachment Inventory (PAI) (Only for mothers) [13, 14]</li> <li>• Maternal Antenatal Attachment Scale (MAAS) (Only for mothers) [15,16]</li> <li>• Multidimensional Scale of Perceived Social Support (MSPSS) [17, 18]</li> <li>• Profile of Mood States (POMS) [19, 20]</li> <li>• Impact of Event Scale-Revised (IES-R) [21,</li> </ul> |

|   |   |
|---|---|
|   | <p>22]</p> <ul style="list-style-type: none"> <li>• Centrality of events scale (CES) [23, 24]</li> <li>• The Interview of Maternal Representations during Pregnancy (IRMAG) [25]</li> <li>• Baby Care Questionnaire (BCQ) [26]</li> <li>• World Health Organization Quality of Life-26 items (WHOQOL-BREF) [27, 28]</li> <li>• Resilience Scale for adults (RSA) [29, 30]</li> <li>• Edinburgh Postnatal Depression Scale (EPDS) [31, 32]</li> </ul>                      |
| <p><b>Postpartum</b></p> <p>Three months after childbirth</p> | <ul style="list-style-type: none"> <li>• Clinical history</li> <li>• Parenting Stress Index - Short Form (PSI-SF) [33, 34]</li> <li>• Multidimensional Scale of Perceived Social Support (MSPSS) [17, 18]</li> <li>• Profile of Mood States (POMS) [19, 20]</li> <li>• Baby Care Questionnaire (BCQ) [26]</li> <li>• World Health Organization Quality of Life-26 items (WHOQOL-BREF) [27, 28]</li> <li>• Edinburgh Postnatal Depression Scale (EPDS) [31, 32]</li> </ul> |

Table 1 – Questionnaires and stage of administration

### *Results*

The research team focused on the following thematic areas.

#### *Impact of cancer in the construction of prenatal attachment*

Women with cancer history have a higher risk of developing psychological difficulties, they frequently report emotional difficulties following diagnosis and treatment [35] and higher levels of anxiety compared with healthy controls [36]. Moreover, younger cancer survivors experience higher levels of depression, more psychological distress, and more difficulties related to their psychosocial roles than older women during the illness trajectory [37, 38]. The higher number of psychosocial needs reported by young cancer survivors may influence negatively prenatal attachment and, subsequently, the building process of a close and positive mother–infant relationship.

A total of 123 pregnant women, of which 36 were cancer survivors and 87 women without a history of cancer, were recruited during their last trimester at different hospitals in Northern Italy [39]. Firstly, we explored mother's mood states and post-traumatic symptomatology comparing the two samples. Secondly, we detected if cancer survivors perceived their pregnancy more as a central event for their life history and for their identity than women without a cancer diagnosis. Additionally, we investigated perceived quality of life and prenatal attachment in both samples, to understand if there were differences. Finally, we explored whether the centrality of the cancer diagnosis, investigated in the clinical sample, correlated with the building process of prenatal attachment, with higher levels of negative mood states, and with PTSD symptoms.

Our results showed that women with past cancer diagnosis had significantly higher levels of PTSD symptoms, confirming the results reported in literature [40, 41, 42]. Moreover, those women perceived pregnancy as more central to their identity and life history. This result may provide insight in the meaning of maternity for women that experience cancer and subsequent pregnancy. Becoming mother after cancer may be considered as a chance of redemption from the illness. It is interesting to notice that the extent to which the cancer diagnosis is considered central for these women's life story and identity is not associated with psychological aspects, such as the building process of prenatal attachment, mood states and PTSD symptoms.

Results also showed that women of the clinical sample reported lower levels of quality of life, specifically in the domain related to their life environment, which measures aspects related to safety and security, health and social care availability, as well as information and activity accessibility. Generally, women who have experienced cancer before pregnancy have to deal with a state of uncertainty regarding the effects of the oncological treatment and the fear of recurrence, and this can accentuate their fears and worries about their own safety and survival.

Moreover, women with past cancer diagnosis, compared with control sample, had lower intensity of prenatal attachment, in terms of behaviors that indicate interaction and affiliation with their fetus. These aspects of prenatal interaction are fundamental for the construction of the maternal representation and for the future mother-child relationship in the post-partum period [43, 44]. These women might be unable to create a mental space for the progressive relationship with their child, as some space is used to elaborate their experience of the illness. These preliminary results suggest that a past cancer diagnosis can influence the mother's psychological functioning and the development of the relationship with their child.

*Resilience: a protective factor*



Although few studies have explored the psychological aspects of cancer during pregnancy [45] it is plausible that a diagnosis of cancer might interfere with factors that are necessary to deal positively with an ongoing or future gestation. For this purpose, we investigated if resilience could be considered a protective factor in the construction of the mother-foetus relationship. Resilience can be defined as the ability to positively deal with adverse conditions to overcome stress and difficulties while maintaining relatively good psychological and physical health [46]. It is a protective factor for prenatal attachment and for negative moods during pregnancy.

For this study [47], 26 pregnant women (25 with breast cancer and 1 with hepatic pecoma) were enrolled during the last trimester of pregnancy. Of these women, 20 has a pregnancy after cancer diagnosis, while 6 had a cancer occurring during pregnancy. Analyses showed positive correlations between resilience factors and prenatal attachment and negative correlations between resilience factors and negative mood states. In particular, there was a significant correlation between Social resources and the quality of prenatal mother-fetus relationship and intensity of attachment. Moreover, there was a correlation between Planned Future and anxiety and fatigue; a correlation between Family cohesion and anxiety, depression and anger. Finally, there was a correlation between Social resources and anxiety. These data indicate that, it is important to asses resilience and family support in pregnant women with current or past experience of oncological diagnosis.

### *Psychological dynamics and maternal representations*

In order to have a deeper understanding of the psychological dynamics that, starting from the first stages of pregnancy, help women with cancer diagnosis to develop the maternal identity and maternal representations, we conducted a qualitative study on the transition to motherhood [48].

In this qualitative study, we investigated maternal representations in pregnant women with diagnosis of Breast Cancer and those with any oncological history. For this study, only patients with breast cancer were recruited, in order to reduce confounding variables, as cancer management and treatment are different depending on tumor type. We choose to include in the clinical sample both women who become pregnant after an oncologic disease and those who received a diagnosis during pregnancy. A total of 38 women were recruited, 19 women who had received a breast cancer diagnosis and 19 who had not. The Interview of Maternal Representations [25] administered in the last trimester of pregnancy, asks the mothers-to-be to narrate the experience of their pregnancy and of becoming mothers. It allows to explore pregnant woman's mental representations, focusing on the woman's past experiences, impressions and emotions related to pregnancy and maternity, and on how she builds an

image of the foetus and of the future child. Analysis of interviews allows to identify four main themes related to the fear and concerns about pregnancy, meaning of motherhood, mother-foetus relationship and fears and concerns to postpartum and breastfeeding.

#### Fear and concerns about pregnancy

Women with breast cancer diagnosed during pregnancy expressed fears connected to their health and expressed concerns regarding the child's health as possibly affected by their treatments. These women described the decision process related to treatment as colored with negative feelings: the benefits and harms for both women and their child have to be weighted and the choice is often difficult to do.

#### Meaning of motherhood

Despite the concerns about their and their baby health, the notice of pregnancy is positively received by women of clinical group. Women with cancer diagnosed during pregnancy and those with past oncologic pathology were charmed by the news of being a mother much more than healthy women. Creating a family for women of clinical group means reconstructing a positive dimension with their partner and taking their chance for redemption from the illness [49]. In particular, primiparous women with past breast cancer considered the gestation as an unexpected gift. This positive reaction was less manifested in healthy women, as the pregnancy was seen as a regular event in their lives, occurred without significant obstacles.

#### Partner role

Women of clinical group stress the role of the cancer diagnosis on the couple's relationship. Both women with past and actual cancer attributed to their partners a protective role and perceived heightened support from them. In particular, women with previous breast cancer recognized support and acceptance from their partners in desiring children and evaluating fertility options by sharing their doubts before the final decision. The significant role of partner during pregnancy expressed by women of clinical group [48] is in line with results of other studies conducted on oncological women [50]. The women perception of a good level of support from the partner during pregnancy, in fact, seems to constitute an important protective factor both for the psychological well-being and for the relationship built with the child-to-be. Expecting women who perceived their partner as more supportive, in fact, perceive the couple relationship as less difficult, but also feel more at ease in exercising their parental role [50].

### Mother- foetus relationship

According to previous literature, in our study women evidenced how the first ultrasound screening was seen as a crucial moment of developing a relationship with their unborn child and a start for feeling a bonding with their inside growing foetus. This development of bonding was conducted on different levels among the sample. Cancer survivors based this relationship on sensations that their body and medical screenings gave them, while the other women on concrete actions referred to the baby. Anyway, the perception of foetus activated the reflection on their maternal identity. Often, the women with cancer diagnosed during pregnancy believed that “they might not be good enough mothers, as treatments might force them to spend time away from their new-born and that they might feel tired or lack energy to take adequate care of their child” [48].

### After the birth: fears and concerns about breastfeeding

Women with breast cancer diagnosed during pregnancy expressed fears associated with breastfeeding. From one hand breastfeeding is perceived as relevant to strengthen the mother-child relationship; on the other side the possibility of not breastfeeding is experienced as challenging. Women with actual cancer who can choose to do or not, in fact, had to evaluate whether delaying even further the beginning of treatment because of breastfeeding might be deleterious for their health. Otherwise, expecting women with a previous history of cancer, who were unable to breastfeed were concerned about the negative consequences for the bonding with their infant. The impossibility to breastfeed for pregnant women with past breast cancer and the fear of not being able to breastfeed in those with actual breast cancer make them feel inadequate in their role as mothers so that their worries will obstacle the construction of a positive relationship with their child [1, 51]. The topic of breastfeeding in women with cancer history is actual because it is registered the lack of guidelines in this clinical population [52] conflicting with ongoing promotion of breastfeeding in general population. Specifically, the recommendations of the World Health Organization, encourage women to breastfeed emphasizing positive effects of breastfeeding for both mother and child [53]. Together to the positive impact on health, breastfeeding promotion is often accompanied by the message that it is a matter of “moral choice” associated to “optimal parenting” as opposed to potential risk in choosing formula [54]. As result, women with cancer experience who do not breastfeed may be exposed to unjustified stress, frustration and guilt which increase fatigue during the postpartum period. Analogue emotions of guilt and dissatisfaction have been found in normative sample of women who cannot breastfeed due to not fulfill the criteria of “optimal parenting” [55].

Moving from these considerations, we conducted another study aimed to explore the breastfeeding choice in women with a past oncological diagnosis. The questions that guided the study were:

Do women with previous oncologic history choose to breastfeed and for how long? How is the feeding method related to mother's mood states in women with cancer history?

To answer these questions, we selected a sample of women with previous oncological history and a control group of women without oncological diagnosis and we prospectively followed them from the third trimester of pregnancy to three months after childbirth.

We found that mothers with a cancer history choose to breastfeed significantly less than control sample at three months of age of the newborn, preferring more bottle-feed or using mixed feeding methods [56]. Moreover, among women with an oncological history, those who did not breastfeed reported higher levels of psychological distress and confusion compared to those who bottle-feed or use mixed feeding methods. Confusion related to feeding methods in women with past breast cancer may be due to the lack of target information, in line with the results of a previous study [52] Moreover, these emotions expressed by women with cancer are in line with the sense of guilt and the dissatisfaction that it has been found in the normative sample, in women who cannot breastfeed [55].

#### Cortisol: an objective indicator

It is well known that self-report questionnaires are subject to risk that respondents may not answer truthfully, because of social desirability and defense mechanisms. For this reason, we decided to combine self-report tools with measurement of cortisol concentration, that is a biological marker, free of risk of manipulation. Cortisol is a glucocorticoid hormone conventionally considered as a biomarker of stress, that rises steadily during the 40 weeks of gestation. Dysregulations in the rhythm of cortisol can lead to serious health and mental problems, that can negatively affect the mother-infant relationship [57].

Recent studies have focused on different factors that could represent a risk for the construction of the mother-child bonding both during pregnancy and in the early months post-partum [58, 59].

When pregnancy has to face the burden of cancer, women are at greater risk of experience high levels of distress [60] and negative emotional states (such as anxiety and depression), which contribute to modifications in the hormonal and biochemical status of pregnant women [61]

A sample of plasma cortisol and one of urinary cortisol (24 hours) have been collected for each participant over the last trimester of pregnancy. Plasma cortisol test was performed using a blood

sample (normal values for plasma cortisol samples in non-pregnant women are between 5 and 25 µg/dl). Urine samples collected over 24 hours provide an integrated measure of total free cortisol secretion.

Data were explored to examine the relationship between clinical variables (cortisol levels) and psychological variables, investigated by the questionnaires.

Sample were collected from 50 pregnant women, 8 belonging to the clinical group, 42 belonging to the control group. Both groups revealed a tendency of significance in the positive correlation between level of depression and concentration of urinary cortisol. Specifically, in the clinical group, a negative correlation has been found between both family cohesion (RSA) and structured lifestyle (RSA) and level of urinary cortisol. While in the control group, it has been found a significant positive correlation between level of depression and plasma cortisol. Results have also shown a significant negative correlation, in the control group, between social resources (RSA) and urinary cortisol. Similarly, a negative correlation has been found between planned future (RSA) and plasma cortisol.

In conclusion, when pregnancy is marked by the experience of cancer an increase in levels of depression occurs, that appears to be associated with higher level of cortisol. On the other hand, resilience resources seem to have a protective role against chronic distress experienced by pregnant women with a history of cancer.

From a practical point of view, level of cortisol can be used as a biomarker to identify women that are at greater risk of depression in the post-partum period, especially in those with a history of cancer.

### **BOX BRCA**

Hereditary breast-ovarian cancer (HBOC) is one of the most common hereditary cancer syndrome and it is associated with alteration in the BRCA1 and BRCA2 genes. This alteration confers a 72% risk of developing Breast Cancer and 17% of developing ovarian cancer.

There is a genetic test for the screening of the genetic mutation of BRCA 1/2 genes. However, the choice to undergo this test on one hand represents a better control of cancer, but, on the other hand, it has a deep emotional impact on women. The positive result may be associated with a sense of uncertainty, feelings of anger, anxiety, depression or guilt [62]. Indeed, BRCA1/2 tests may carry negative psychosocial consequences for women carriers and their families.

Since BRCA1/2 are usually transmitted as multiple generations, children of BRCA1/2 variant carriers have a 50% risk of receiving the genes and developing cancer in their life. For oncological women with BRCA 1 /2 mutation transition to motherhood could represent a challenge.

We have done a study to explore differences in prenatal attachment in a sample of 23 women with a history of cancer before pregnancy: 5 of them were BRCA1/2 variant carriers, while 18 were not.

Results showed a statistically significant difference between the two groups among the prenatal attachment dimension (PAI): BRCA1/2 variant carriers had lower levels of prenatal attachment. In other words, these women seem to have a lower disposal to anticipate emotionally and cognitively the child during the last trimester of pregnancy. This difficulty could be associated with the sense of guilt for the high possibility of transmission of the genetic mutation to the child, but also with the fear of leaving him prematurely orphaned [63].

It can be, therefore, concluded that clinicians should give pregnant BRCA1/2 variant women a particular attention and provide them psychological support.

### *Conclusion*

Our results clearly show that young women diagnosed by cancer, have a deep and rarely expressed desire to become mothers, which seems not to be weakened by cancer diagnosis. Thus, health care providers should inform patients about the possibility of motherhood despite cancer.

It is very important to give women with oncological history the adequate support during puerperium, with a particular focus on breastfeeding. It appears evident the need of a multidisciplinary team, able to consider and take care of the fragility of these women over different areas. The team should include Oncologists, Midwives, Gynaecologists, Psychologists, Radiologists and Paediatricians. Consequently, an adequate training is essential to help these health care professionals to manage and better support motherhood after cancer.

Furthermore, the substantial contribution of patients' associations should not be underestimated. In our project has been valuable the collaboration with "Salute Donna onlus" ([salutedonnaonlus.it](http://salutedonnaonlus.it)) , an association spread throughout the Italian Territory, founded by Anna Mancuso. From its foundation,

Salute Donna onlus actively promotes cancer patients' rights and needs. This partnership has allowed the extend our project all over Italy with the ambitious goal of establishing guidelines for the strengthening of health policies in support of oncofertility.

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