

# Challenges of the management of cancer in pregnant women during the COVID-19 pandemic

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## ABSTRACT

Cancer during pregnancy is a rare occurring, explained maybe by the fact that most of pregnant women are young patients. Unfortunately, if cancer appears during pregnancy it is many times diagnosed in advanced stages because of its symptoms similar with the pregnancy's and may have devastating effects on both the mother and the newborn. Because of the COVID-19 pandemic many patients with cancer withdraw from or delay cancer treatment. Pregnant women with cancer need special attention provided by a multidisciplinary medical team with a close follow-up even during COVID-19 pandemic, beyond all restrictions.

**Keywords:** cancer, COVID-19 pandemic, pregnancy

## INTRODUCTION

During the female reproductive years, cancer represents the second cause of death and it is diagnosed in 1-2 per 1,000 pregnant women [1,2]. In developed countries women delay childbearing and it is known that cancer incidence increases with age, these aspects explaining perhaps why the incidence of cancer during pregnancy increases [1,3]. At the same time, in developing countries, the age of women who procreate is lower than in developed countries, 95% of adolescent mothers residing in low and middle-income countries [4,5].

The possibilities of diagnostic and treatment of cancer during pregnancy are increasing and the management strategies have changed. Fewer women need the pregnancy terminated prematurely with the purpose to initiate maternal oncologic treatment [1,6]. Cancer during pregnancy is recommended to be managed by a multidisciplinary team consisting of an obstetrician, an oncologist, a neonatologist and a psychotherapist. They need to decide over the best moment of delivery and the tim-

ing of treatment depending on prematurity and fetal exposure.

The diagnostic of cancer during pregnancy may be difficult due to its occult symptoms or because many types of cancer may have symptoms similar to pregnancy, like headaches in glioblastoma, fatigue, severe anemia or thrombocytopenia in advanced cancers or digestive symptoms in digestive cancers. Due to all these aspects and because the incidence of cancer during pregnancy is increasing any unexplained sign or symptom that cannot be associated to pregnancy should be rigorously considered [7,8].

Diagnosing cancer during pregnancy is difficult due to the need to choose less invasive tests that are not harmful to the fetus and this seems to delay diagnosis which impacts the overall survival rate [7,9]. An integrative review shows that pregnancy does not accelerate the progression of cancer and the poor prognosis is because of the diagnose of cancer in an advanced stage [7,10].

Studies suggest that the treatment for cancer during pregnancy should be as the one for non-preg-

nant women and it should not be delayed [7,11]. Of course, there should be done a balance of benefits and risks for both the mother and the newborn, including toxicity and premature delivery risk or other side effects associated with cancer treatments, especially chemotherapy.

The COVID-19 pandemic had a negative impact on cancer patients, because the compliance of these patients was lower in this period. It is known that cancer patients are more vulnerable to the infection with SARS-CoV-2 virus because of their immunosuppressed state [12,13].

## MATERIAL AND METHODS

We analyzed pregnant women with cancer who delivered at the University Emergency Hospital of Bucharest, on a period of one year when there was no COVID-19 pandemic (January 1<sup>st</sup>, 2019 – December 31<sup>st</sup>, 2019) and on a period of one year during COVID-19 pandemic (October 1<sup>st</sup>, 2020 - September 30<sup>th</sup>, 2021).

The information regarding the pregnancy, investigations for cancer, delivery outcome, neonatal data, follow-up consultations and the oncological treatment were retrieved from patients records and from the database of the University Emergency Hospital in Bucharest.

The oncological diagnostic was established after numerous clinical and paraclinical investigations.

The delivery was defined as the expulsion of the gestational product after completing 24 weeks of gestation.

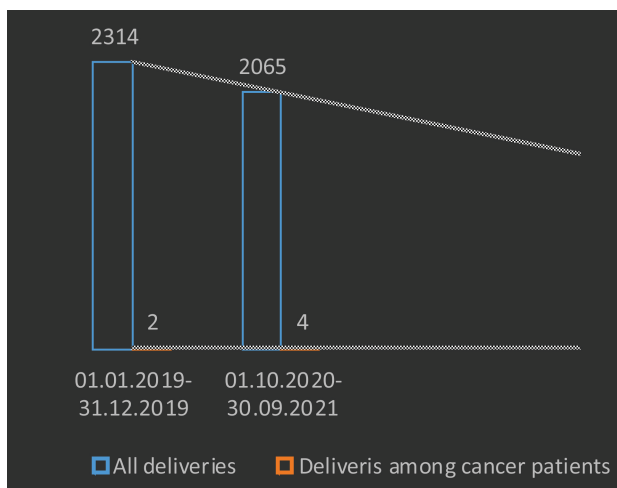
We evaluated and compared the types of cancer during the two periods analyzed, the moment when it was diagnosed, the moment of delivery and the oncological follow-up and treatment. The outcome of the newborn was assessed base on Apgar score at 1 minute and birth weight.

## RESULTS

In the first analyzed period the number of pregnant women with cancer who delivered in our hospital was two out of 2,314 deliveries (0.08%). In the period of the COVID-19 pandemic the number of patients with cancer who delivered in our hospital was double representing 0.19% of all deliveries. Even if the percentage is not high, we can see an accelerated ascending trend, and this can be an alarming thing.

It's important to mention that the number of pregnancies decreased between the two analyzed periods, while, as said before, the number of patients diagnosed with cancer during pregnancy increased (Figure 1).

In the first analyzed period there were two patients with cancer and both of them were diagnosed



**FIGURE 1.** The incidence of all deliveries and the incidence of deliveries among cancer patients in the two analyzed periods

with breast cancer during pregnancy. They were 35, respectively 37 years old. They delivered in our hospital at 38 weeks of pregnancy by caesarean section – one for invasive ductal carcinoma and the other for the high risk of rupture of uterine scar after caesarean section. Both newborns where around 3,000 grams with Apgar scores of 8, respectively 9. Both mothers followed-up the oncologic treatment after childbirth having a good prognostic.

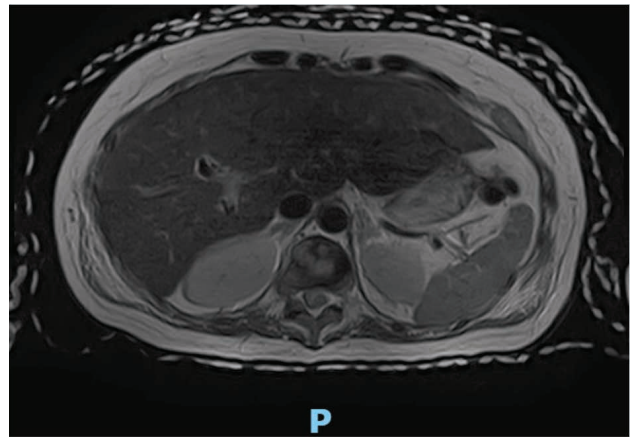
In the second analyzed period there were four patients diagnosed with cancer during pregnancy. They all had been transferred from other hospitals for aggressive symptomatology and signs that could not be pregnancy related and they were diagnosed with cancer in our hospital. One patient was 33 years old, 24 weeks pregnant and was transferred for severe anemia with thrombocytopenia. The patient had previously done all routine investigations and the only abnormal finding was a minor anemia in the first trimester of pregnancy. She had a birth two years earlier with no complications and she had no remarkable personal or familial medical history. She was admitted in our department where she underwent multiple investigations – blood samples, including tumor markers, transabdominal echography, superior endoscopy with biopsy and abdominal magnetic resonance imaging (MRI) (Figure 2). After corroborating the results of all the above, the diagnostic of stage IV gastric adenocarcinoma was established. The patient followed all recommendations, including the chemotherapeutic treatment. She delivered at 31 weeks of gestation by caesarean section for severe preeclampsia; the newborn weighting 1,550 grams had an Apgar score of 4. The patient continued the oncologic treatment as far as she could. The newborn had a favorable evolution and was released after one moth. Unfortunately, the mother died 3 months later.



**FIGURE 2.** MRI showing the gastric tumor and the vertebral metastases

The second patient was 37 years old and 24 weeks pregnant. She was transferred in our hospital for hypoxic respiratory failure. Because of her deteriorate health condition we could not determine if she had any relevant personal or familial medical history. Multiple clinical and paraclinical investigations were done including tumoral markers and MRI which raised the suspicion of breast cancer with multiple metastases (Figure 3, Figure 4). After breast biopsy, the diagnosis was mixed ductal and lobular carcinoma. After three days of hospitalization in the intensive care unit the patient suffered a cardiac failure. An emergency caesarean section was done and was extracted a newborn who weighted 640 grams and had an Apgar score of 3. In the same day both the mother and the newborn died.

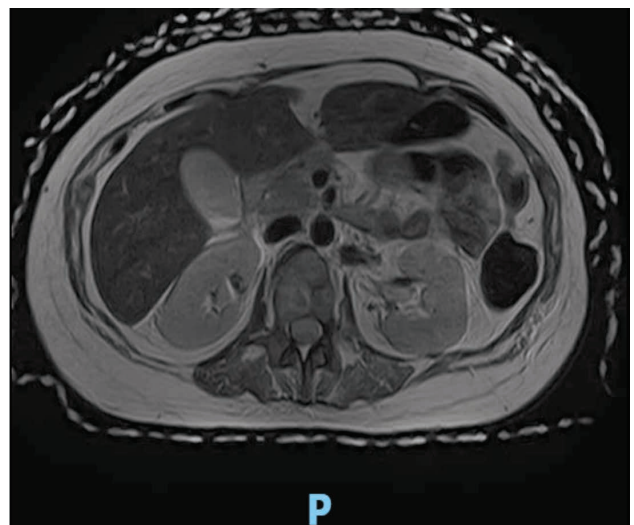
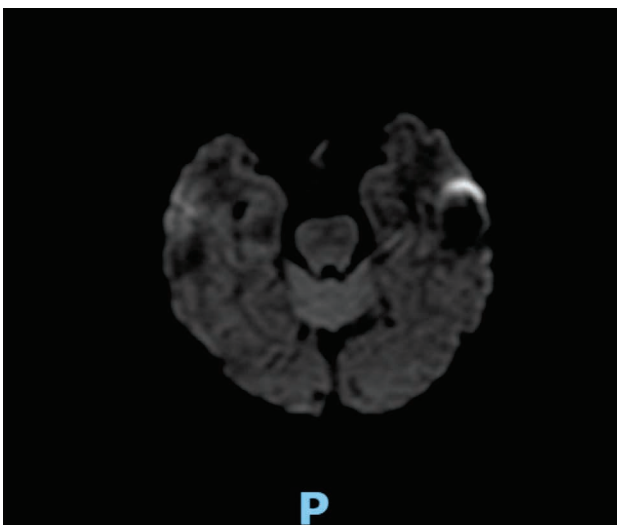
The third patient was transferred to our hospital for a massive frontotemporal tumor diagnosed in the same day. The patient was 25 years old, 36 weeks pregnant and her only symptomatology consisted of a headache that started two weeks earlier. Prior to admission she underwent all routine pregnancy related consults. She had not any notable personal or familial history. We performed cerebral MRI (Fig-



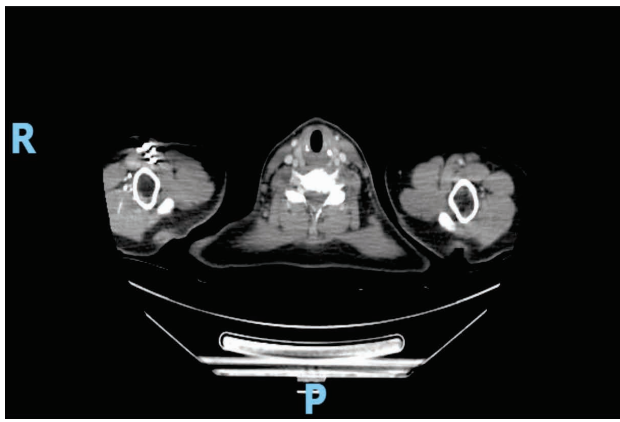
**FIGURE 4.** MRI showing vertebral metastases

ure 5). Next day a caesarean section was performed and was extracted a 2,860 grams newborn with an Apgar score at 1 minute of 8. At the same time a neurosurgery was performed and the anatomopathological result was glioblastoma. The mother's and the newborn's evolutions were favorable, and they were released after 10 days. The mother needed oncologic treatment after 30 days from the surgery and she is still under oncological monitoring.

The fourth patient had a presumptive diagnostic of acute myeloid leukemia attributed 5 days prior the admission in our hospital. She was 33 years old and 28 weeks pregnant. She underwent all pregnancy consults indicated by her obstetrician and she was positive for hepatitis B virus. She had no significant family health history. The patient was clinically and paraclinically evaluated including bone marrow aspiration and biopsy which established the certain diagnostic – acute promyelocytic leukemia. After a multidisciplinary evaluation was established the need for pregnancy termination with immediate start of chemotherapy. The patient underwent a cesarean section trough which was ex-



**FIGURE 3.** MRI showing cerebral metastases (left) and hepatic metastases (right)



**FIGURE 5.** Computed tomography noting cervical adenopathy

tracted a newborn who weighted 1,200 grams and had an Apgar score of 3. Two days after the surgery were performed a thoracic radiography and a thoraco-abdominal computed tomography which showed multiple cervical adenopathies (Figure 5).

The evolution of the newborn was favorable in the neonatal intensive care unit and the newborn was released after two months. Also, the mother underwent oncological treatment in our hospital, her health status improved, and she was released after one month. The patient is still under oncologic monitoring.

All the patients were tested for SARS-CoV-2 by RT-PCR test and they were negative. None of them knew to ever have had the COVID-19 infection.

Regarding newborns statuses, from October 1<sup>st</sup>, 2020 until September 30<sup>th</sup>, 2021, 75% of patients associating cancer delivered premature newborns who needed neonatal intensive care, while in the first group of analyzed patients none of the newborns were premature, nor needed neonatal intensive care.

## DISCUSSION

Cancer during pregnancy is a rare condition [7,9]. Studies show that the most frequent types of cancer diagnosed during pregnancy are breast cancer, cervical cancer, leukemia, melanoma and lymphoma [7,10,14]. In our paper we showed that any type of cancer can appear during pregnancy from aggressive breast cancer or stage IV gastric adenocarcinoma to glioblastoma or leukemia. We diagnosed various types of cancer in pregnant women in the second group, while in the first group the patients had only breast cancer, this being consistent with other studies.

It is known that the diagnose of cancer can be delayed because its signs and symptoms may mimic those of pregnancy and fatigue, anemia, nausea or breast changes may not raise any suspicion [15]. This is the reason why in most cases a cancer asso-

ciated with pregnancy is diagnosed after delivery [2,15]. In both groups, patients were diagnosed before delivery, and in some cases, we even did invasive tests, giving that we considered the benefits to have weighted more than the risks implied for the mother and the fetus. Because of all the investigations we did, the patients were diagnosed in a better time for the oncological treatment.

As it is known, newborns from mothers with oncological pathology during pregnancy have a high risk of preterm births [16-20]. Also, studies show that there is an increased risk for small weight for gestational age for the newborns from mothers who were diagnosed with cancer during pregnancy, the explication may be laying in the changes that occur because of the cancer physiopathology or the side effects of the oncological treatment [16]. It is important to mention that the newborns who survived had a good neurological and cognitive development.

Regarding the follow-up of patients, we note that in the first group patients had a suitable oncologic monitoring with a favorable evolution, while in the second group the patients had a poor oncological follow-up care. It is difficult to say if this happened due to the pandemic or the reticence of the patients confronting this type of pathology. It is important that oncologic treatments have a continuation even in the COVID-19 time. The evolution of the patients in the second group may be attributed to the advanced stages and the aggressiveness of the types of cancer that we diagnosed.

## CONCLUSIONS

We can conclude that, even if it's a rare occurring during pregnancy, cancer can have devastating effects on both the mother and the fetus. Nowadays we see that the incidence of pregnancies complicated with cancer is increasing and this is why we have to pay attention to any suspicious signs or symptoms that cannot be explained by the pregnancy. In present, there are no extended studies done for oncological therapies in pregnant women, but the reported cases show that they can be carefully administered during pregnancy.

It is important to use any available investigations, even invasive tests, being aware at the same time of the fetal risks. There should not be any delay in the diagnose and treatment for these patients even if we are confronting the COVID-19 pandemic, because pregnant patients represent a special category with multiple implications.

In case of pregnancy associating cancer is important to balance the risks and the benefits for the mother and for the fetus and to have a multidisciplinary medical team deciding the most suitable treatment.

## REFERENCES

1. Wolters VERA, Lok CAR, Gordijn SJ, Wilthagen EA, Sebire NJ, Khong TY, van der Voorn JP, Amant F. Placental pathology in cancer during pregnancy and after cancer treatment exposure. *Placenta*. 2021 Aug;111:33-46.
2. Smith LH, Danielsen B, Allen ME, Cress R. Cancer associated with obstetric delivery: results of linkage with the California cancer registry. *Am J Obstet Gynecol*. 2003 Oct;189(4):1128-35.
3. Parazzini F, Franchi M, Tavani A, Negri E, Peccatori FA. Frequency of Pregnancy Related Cancer: A Population Based Linkage Study in Lombardy, Italy. *Int J Gynecol Cancer*. 2017 Mar;27(3):613-619.
4. Uzunov AV, Bohiltea RE, Munteanu O, Nemescu D, Cirstoiu MM. A retrospective study regarding the method of delivery of adolescents in a Romanian Hospital. *Exp Ther Med*. 2020 Sep;20(3):2444-2448.
5. Cook SM, Cameron S T. Social issues of teenage pregnancy. *Obstetrics, Gynaecology & Reproductive Medicine*. 2015 Sep;25(9):243-248.
6. de Haan J, Verheecke M, Van Calsteren K, Van Calster B, Shmakov RG, et al.; International Network on Cancer and Infertility Pregnancy (INCIPI). Oncological management and obstetric and neonatal outcomes for women diagnosed with cancer during pregnancy: a 20-year international cohort study of 1170 patients. *Lancet Oncol*. 2018 Mar;19(3):337-346.
7. Gomes JS, Sand ICPV, Girardon-Perlini NMO. Cancer during pregnancy: from the diagnosis to the repercussions on the family experience of maternity. *Rev Esc Enferm USP*. 2021 Sep 10;55:e20200518.
8. Slepicka PF, Cyrill SL, Dos Santos CO. Pregnancy and Breast Cancer: Pathways to Understand Risk and Prevention. *Trends Mol Med*. 2019 Oct;25(10):866-881.
9. Monteiro DLM, Nunes CL, Rodrigues NCP, Antunes CA, Almeida EM, Barmpas DBS, Magalhães ALC, Trajano AJB. Factors associated with gestational breast cancer: case-control study. *Cien Saude Colet*. 2019 Jun 27;24(6):2361-2369.
10. Brito EAS, Feitosa PWG, Vieira JG, de Oliveira IC, Sousa CMS, de Santana WJ. Cancer Diagnosis During Pregnancy: An Integrative Review. *Revista de Psicologia* 2020;14(49):150-161.
11. Raphael J, Trudeau ME, Chan K. Outcome of patients with pregnancy during or after breast cancer: a review of the recent literature. *Curr Oncol*. 2015 Mar;22(Suppl 1): S8-S18.
12. Rassy E, Khoury-Abboud RM, Ibrahim N, Kattan C, Assi T, Kattan J. What the oncologist needs to know about COVID-19 infection in cancer patients. *Future Oncol*. 2020 Jun;16(17):1153-1156.
13. Weinkove R, McQuilten ZK, Adler J, Agar MR, Blyth E, Cheng AC, et al. Managing haematology and oncology patients during the COVID-19 pandemic: interim consensus guidance. *Med J Aust*. 2020 Jun;212(10):481-489.
14. Bezerra NC, Martins VHS, Guisande TCCA, Santos TV, Carvalho MAB, Belfort LRM. Gestational cancer: a literature review. *Res Soc Dev*. 2019;8(6):e40861075.
15. Silverstein J, Post AL, Chien AJ, Olin R, Tsai KK, Ngo Z, Van Loon K. Multidisciplinary Management of Cancer During Pregnancy. *JCO Oncol Pract*. 2020 Sep;16(9):545-557.
16. Lu D, Ludvigsson JF, Smedby KE, Fall K, Valdimarsdóttir U, Cnattingius S, Fang F. Maternal Cancer During Pregnancy and Risks of Stillbirth and Infant Mortality. *J Clin Oncol*. 2017 May 10;35(14):1522-1529.
17. Peccatori FA, Azim HA Jr, Orecchia R, Hoekstra HJ, Pavlidis N, Kesic V, Pentheroudakis G; ESMO Guidelines Working Group. Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2013 Oct;24 Suppl 6:vi160-70.
18. Greene MF, Longo DL. Cautious Optimism for Offspring of Women with Cancer during Pregnancy. *N Engl J Med*. 2015 Nov 5;373(19):1875-6.
19. Van Calsteren K, Heyns L, De Smet F, Van Eycken L, et al. Cancer during pregnancy: an analysis of 215 patients emphasizing the obstetrical and the neonatal outcomes. *J Clin Oncol*. 2010 Feb 1;28(4):683-9.
20. Loibl S, Han SN, von Minckwitz G, Bontenbal M, Ring A, Giermek J, et al. Treatment of breast cancer during pregnancy: an observational study. *Lancet Oncol*. 2012 Sep;13(9):887-96.

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