

COVID-19 and Cervical Cancer: Analysis of the Hospital Cancer Registry of the National Cancer Institute in Rio de Janeiro

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Covid-19 e Câncer do Colo do Útero: Análise do Registro Hospitalar de Câncer do Instituto Nacional de Câncer no Rio de Janeiro
COVID-19 y Cáncer del Cuello Uterino: Análisis del Registro Hospitalario de Cáncer del Instituto Nacional del Cáncer de Río de Janeiro

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ABSTRACT

Introduction: Cervical cancer remains a public health problem despite the possibility of screening and early diagnosis. **Objective:** Comparative analysis of 2,486 analytical and non-analytical patients referred to INCA only for treatment, with follow-up at the hospital of origin, admitted with cervical cancer between January 2017 and December 2021 at *Hospital do Câncer II (HCII/INCA)*, using the Hospital-based Cancer Registry as database. **Method:** Quantitative and observational study divided into four groups: pre-pandemic analytical, pandemic analytical, pre-pandemic non-analytical and pandemic non-analytical. Five selected variables were analyzed descriptively: time between diagnosis and hospital admission, first treatment received at the hospital, disease status after first treatment, reason for non-treatment and staging. Pearson's chi-square test was utilized to verify the association of frequency variations between the pre-pandemic and pandemic periods. **Results:** Among analytical patients during the pandemic, there was a 34.1% increase in the proportion of patients admitted more than 61 days after diagnosis, 4.6% in referrals for therapeutic support and a 6.3% reduction in cases with complete remission of the disease after treatment. Among non-analytical patients during the pandemic, there was a 20.6% increase in the proportion of patients admitted in stage IV, 23.3% of patients who did not submit to any treatment due to disease progression or lack of clinical conditions and 12.1% of referrals for therapeutic support. **Conclusion:** The COVID-19 pandemic had a negative impact on the disease and access to the health system.

Key words: Uterine Cervical Neoplasms; Early Diagnosis; Patient Admission; COVID-19.

RESUMO

Introdução: O câncer do colo do útero continua sendo um problema de saúde pública apesar da possibilidade de rastreamento e diagnóstico precoce.

Objetivo: Análise comparativa de 2.486 pacientes analíticas e não analíticas, encaminhadas ao INCA apenas para tratamento, com acompanhamento no hospital de origem, admitidas com câncer do colo do útero, entre janeiro de 2017 e dezembro de 2021, no Hospital do Câncer II (HCII/INCA), utilizando como base de dados o Registro Hospitalar de Câncer.

Método: Estudo quantitativo e observacional dividido em quatro grupos: analíticos pré-pandemia, analíticos pandemia, não analíticos pré-pandemia e não analíticos pandemia. As cinco variáveis selecionadas foram analisadas de forma descritiva: tempo entre diagnóstico e admissão hospitalar, primeiro tratamento recebido no hospital, estado da doença após primeiro tratamento, razão para o não tratamento e estadiamento. Utilizou-se o teste chi-quadrado de Pearson para verificar a associação das variações das frequências com os períodos pré-pandemia e pandemia. **Resultados:** Entre as pacientes analíticas, na pandemia, houve aumento de 34,1% na proporção de pacientes admitidas com mais de 61 dias após o diagnóstico, 4,6% de encaminhamentos ao suporte terapêutico e redução de 6,3% de casos com remissão completa da doença pós-tratamento. Entre as não analíticas, na pandemia, houve aumento de 20,6% da proporção de pacientes admitidas em estágio IV, 23,3% de pacientes submetidas a nenhum tratamento por avanço da doença ou falta de condições clínicas e 12,1% de encaminhamentos ao suporte terapêutico. **Conclusão:** A pandemia da covid-19 teve impacto negativo sobre a doença e o acesso ao sistema de saúde.

Palavras-chave: Neoplasias do Colo do Útero; Diagnóstico Precoce; Admissão do Paciente; COVID-19.

RESUMEN

Introducción: El cáncer de cuello uterino sigue siendo un problema de salud pública a pesar de la posibilidad de realizar exámenes de detección y diagnóstico temprano.

Objetivo: Análisis comparativo de 2486 pacientes analíticas y no analíticas, remitidas al INCA únicamente para tratamiento, con seguimiento en el hospital de origen, ingresadas con cáncer de cuello uterino, entre enero de 2017 y diciembre de 2021, en el Hospital Oncológico II (HCII/INCA), utilizando como base de datos el Registro Hospitalario de Cáncer.

Método: Estudio cuantitativo y observacional dividido en cuatro grupos: analíticos prepandemia, analíticos pandemia, no analíticos prepandemia y no analíticos pandemia. Se analizaron descriptivamente cinco variables seleccionadas: tiempo entre el diagnóstico y el ingreso hospitalario, primer tratamiento recibido en el hospital, estado de la enfermedad después del primer tratamiento, motivo de no tratamiento y estadificación. Se utilizó la prueba de ji al cuadrado de Pearson para verificar la asociación de las variaciones de frecuencia con los períodos prepandémico y pandémico. **Resultados:** Entre las pacientes analíticas, durante la pandemia, hubo un aumento del 34,1% en la proporción de pacientes ingresadas más de 61 días después del diagnóstico, del 4,6% en las derivaciones hacia soporte terapéutico y una reducción del 6,3% en los casos con remisión completa de la enfermedad después del tratamiento. Entre los casos no analíticos, durante la pandemia hubo un aumento del 20,6% en la proporción de pacientes ingresados en estadio IV, un 23,3% de pacientes sin tratamiento por progresión de la enfermedad o falta de condiciones clínicas y un 12,1% de derivaciones hacia apoyo terapéutico.

Conclusión: La pandemia de COVID-19 tuvo un impacto negativo en la enfermedad y el acceso al sistema de salud.

Palabras clave: Neoplasias del Cuello Uterino; Diagnóstico Precoz; Admisión del Paciente; COVID-19.

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INTRODUCTION

Cervical cancer remains a public health issue, especially in middle- and low-income countries. In Brazil, this pathology is more common in the North and Northeast regions and, despite advances in detection and treatment, it is still one of the main causes of cancer death in women.

For each year of the triennium 2023-2025, the National Cancer Institute (INCA) estimated that 17,010 new cases of cervical cancer will be diagnosed, with an estimated risk of 15.38 cases in each 100 thousand women, with cervical cancer being the third most common type in women. In 2020, the mortality rate for cervical cancer in Brazil adjusted by the world population was 4.6 deaths per 100 thousand inhabitants¹.

Persistent human papillomavirus (HPV) infection is the main cause of cervical cancer development, the target of the virus is the basal epithelial cell or metaplastic cell, whose proliferation is necessary for viral replication. Cervical cancer is preceded by cellular abnormalities in the epithelium known as cervical intraepithelial neoplasms (CIN) mainly in the squamous junction when the columnar epithelium becomes squamous epithelium, constituting the so-called transformation zone (TZ)².

The most common histopathological types are spinocellular and adenocarcinoma. Among invasive tumors, non-keratinizing large cell squamous cell carcinoma is the most frequent associated with HPV infection.

In Brazil, several government initiatives to encourage cervical cancer control have taken place since the 1980s³. Cervical cancer screening through cytopathological examination is a public health strategy capable of reducing the incidence and mortality of the disease.

The World Health Organization (WHO) establishes coverage between 80% and 85% of the female population aged 25 to 64 years old to reflect morbimortality statistics⁴. However, in order to achieve this high population coverage, it is necessary to implement an active mechanism for the search and recruitment of women, a form of organized screening, because isolated actions of information and education mobilize more women naturally motivated than those that are not up to date with screening⁵.

In 2021, the WHO began to recommend that screening be done through the HPV-DNA test, which identifies the deoxyribonucleic acid (DNA) of HPV every five years in women between 25 and 64 years old, accompanied or not by cytology. In Brazil, this is done through the pap smear exam until HPV screening is established. Periodicity may vary, but for women with two consecutive tests and with a normal one-year interval, the examination may be performed every three years. Priority should be for women between 30 and 49 years old⁶.

The path to treatment is estimated to be a long one. Patients start at the Primary Healthcare Units (PHC), passing through the colposcycological examination, colposcopy, biopsy, complementary tests for diagnosis and staging, such as ultrasound and computed tomography, and are then sent to the reference hospital where they will be treated and followed up. Patients will face a considerable waiting time in the Regulation System flow, which is a process responsible for ensuring access to hospital beds, procedures and consultations or specialized treatments⁷.

Requests for low and medium complexity consultations should be made by the Municipal Regulation (SISREG) and, for high complexity consultations (cardiac surgery, neurosurgery and oncology), by the State Regulation System (SER), in the case of the State of Rio de Janeiro⁷.

Although the disease is easily preventable and early detected, patients continue to be admitted to INCA in advanced stages (III and IV)⁸.

In March 2020, the WHO recognized COVID-19 as a pandemic, with subsequent restrictive sanitary guidelines, causing a limitation of care in basic health units and a substantial drop in demand for health services in general⁹.

The present study aims to elucidate the main changes in the profile of patients diagnosed with cervical cancer, admitted to HCII/INCA, located in Rio de Janeiro, when comparing the periods from January 2017 to December 2019 (pre-pandemic period), with the period from January 2020 to December 2021 (during the pandemic).

METHOD

Descriptive, observational, retrospective and quantitative study conducted at HCII/INCA, located in the Center Region of the City of Rio de Janeiro. The database of the Hospital II Hospital-based Cancer Registry (RHC-HCII)¹⁰ was used as source from 2017 to 2021, including all records of patients admitted with code C53 (malignant cervical neoplasm) of the tenth revision of the International Classification of Diseases and Related Health Problems (ICD-10)¹¹ in the analyzed period.

The patients were initially divided into two groups: Patients admitted in the years 2017, 2018 and 2019, called the pre-pandemic group; and patients admitted in the years 2020 and 2021, called the pandemic group. Subsequently, each group was divided into two more subgroups: Pre-pandemic analytical (PPA); Pandemic analytical (PA); Pre-Pandemic non-analytical (PPNA); and Pandemic non-analytical (PNA).

The cases are considered analytical when received with diagnosis to be staged, treated and followed in the HCII itself, while the non-analytical ones are those whose diag-

nosis and staging were made in another hospital reference unit and later referred to INCA for some treatment modality (radiotherapy, brachytherapy and chemotherapy). The objective of separating the cases into analytical and non-analytical is the differentiated follow-up of the analytical ones, a priority in the evaluation of results that depend on the assistance provided specifically by the hospital¹².

The sum of the analytical and non-analytical cases made it possible to observe the profile of all patients serviced by the institution.

In order to describe in detail, with representativeness of the patients admitted to HCII with cervical cancer, all 2,486 patients registered in the RHC database under ICD C53 of January 1, 2017, and December 31, 2021, were included, therefore, the calculation to determine the sample size or power calculation were not applied. Patients with incomplete data, marked as no information, for a given variable, at the date of collection, were thus described in the results.

At the time of data collection of the present research, RHC-HCII was updated until December 2021. Data was collected from RHC-HCII on December 1, 2022, under approval number 5.712.339 (CAAE (submission for ethical review): 63059622.4.0000.5274), which was favorable in the submission to the Research Ethics Committee (CEP) of this hospital, and under the opinion of the co-participant institution number 5.770.455 (CAAE (submission for ethical approval): 63059622.4.3001.5284). The study followed all the recommendations of Resolution n°. 466/2012¹³ of the National Health Council.

The data were analyzed in a descriptive way. The results were presented in the form of frequencies obtained by simple tabulations between variables. Pearson's Chi-square test¹⁴ was used to verify the association of frequencies variations of the categories with the pre-pandemic periods, from 2017 to 2019, and the pandemic, between 2020 and 2021, both in the analytical and non-analytical groups. The objective was to test the relationship between the

period (pre-pandemic and pandemic) and each variable, independently. The software used was SPSS¹⁵ v. 22 (IBM, USA). *P* values below 0.05 were considered statistically significant. The results will be detailed in the next section, with emphasis on the variables that presented Pearson's chi-square test with a *p* value less than 0.05.

RESULTS

The distribution of the total number of patients throughout the study period and the four groups is detailed in Table 1. The data presented shows a gradual decrease in the number of patients with cervical cancer admitted to HCII/INCA, considering the two studied periods.

In the pre-pandemic period, the decrease in admissions stood at around 20% between 2017 and 2018 and 10% the following year. When the proportion of drops in admissions between 2019 and 2020 was evaluated, the first year of the coronavirus pandemic, there was an approximate value of 32%; and 51% when the proportional drop in 2021 was evaluated, compared to 2019. The distribution between analytical and non-analytical patients remained stable throughout the study period, maintaining around 35% to 40% of non-analytical patients. Graph 1 shows the evolutionary drop in admissions of both analytical and non-analytical cases throughout this period.

The following variables were selected from the tumor record sheet: Time between diagnosis and the first hospital visit (days); staging; first treatment received at the hospital; disease status after the first treatment. With the intention of elucidating the variable first treatment received at the hospital, the variable reason for not getting treatment was later included. The results are represented in Table 2.

As observed, in the group of analytical patients, during the pandemic, there was an increase of 34.1% in the proportion of patients admitted over 61 days after diagnosis, a

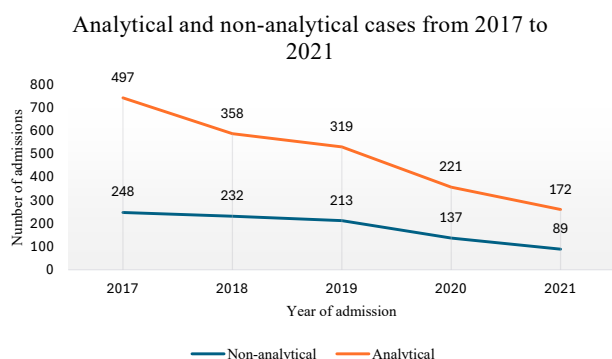
Table 1. Distribution of 2,486 admitted cases of HCII/INCA (2017-2021)

Year	Analytical		Non-analytical		Total per year
	Number	(%)	Number	Non-analytical	n
2017	497	66.70	248	33.30	745
2018	358	60.67	232	39.33	590
2019	319	59.96	213	40.04	532
2020	221	61.73	137	38.27	358
2021	172	65.90	89	34.10	261
Total	1,567	63.03	919	36.97	2,486

Source: Adapted from RHC/HCII¹⁰.



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Graph 1. Analytical and non-analytical cases (2017-2021)

Source: Adapted from RHC/HCI¹⁰.

Note: The four groups showed no difference regarding the sociodemographic profile of the studied population in terms of race, color, education, age group and tobacco consumption.

reduction of 6.3% in cases with complete remission of the disease after the first treatment, and an increase of 4.6% in referrals to therapeutic support. Although the study pointed to the absence of statistical significance for staging variables, the first treatment received in the hospital and the reason for not getting treatment, the *p* values were higher than 0.5 (0.987 – 0.065 – 0.890, respectively). The admission staging for most patients in the analytical group remained at stage III, the recommended treatment is still the association of radiotherapy and chemotherapy, so patients are submitted to specific treatment, which makes the option – not applicable – the most frequent for the variable reason for not treating, however, the outcome for treatment was different, as mentioned earlier. For the other results mentioned, all *p* values were lower than 0.05.

Among non-analytical patients, during the pandemic period, there was an increase of 20.6% in the proportion of patients admitted with stage IV, a reduction of 23.1% of cases that presented complete remission of the disease, with a decrease of 15.7% of cases referred to radiotherapy alone, 23.3% more patients submitted to no treatment due to disease advance or lack of clinical conditions, and 12.1% of referrals to therapeutic support.

DISCUSSION

In 2017, the Oncology Care Network of the State of Rio de Janeiro was composed of 25 High-Complexity Oncology Care Units (Unacon) and High-Complexity Oncology Care Centers (Cacon), respectively, three isolated radiotherapy services and two cancer surgery hospitals, distributed in 12 municipalities in eight of the nine State Regions. Currently, according to data from the Brazilian Society of Radiotherapy, there are 30 radiotherapy devices in the State of Rio de Janeiro, with eight of them outside the city of Rio¹⁶.

The Oncological Plan¹² of the State of Rio de Janeiro, approved in July 2017 and in force between 2017 and 2021, estimated a deficit of 49 units for the care of cancer patients throughout the State and established a special budget, as well as co-financing of the State for the accreditation and qualification of new Unacon to cancer patients. This Oncological Plan was renewed in 2022.

The strategy, which foresees the increase in funding and investment in new Cacon and Unacon, can be one of the reasons for the consecutive drop in the number of patients with cervical cancer treated by HCII/INCA observed even before the COVID-19 pandemic in 2020. However, the present study does not have enough elements to evaluate this possibility.

Similarly, the world literature¹⁷⁻²⁰, during the period of the COVID-19 pandemic, observed a variable drop in both colposcycological tests and biopsies and surgeries for the treatment of cervical cancer.

The increase in the time necessary to reach HCII/INCA after diagnosis can be explained by the temporary suspension, for the period of 90 days, of the consultations and procedures scheduled by SISREG, established by Decree Rio n°. 47.282²¹, which maintained the procedures related to cancer, was succeeded by the Resolutions SMS n°. 4.330²² and n°. 4.334, which, in turn, did not include colposcopy, cervical biopsy and home consultations for oncological patients that were not high-risk, as procedures to be maintained during the pandemic. This fact impairs not only patients of accessing the health system but also the evolution of the cervical cancer line of care for timely diagnosis and treatment.

Decree n°. 46.983²³ and n°. 47.012²⁴ of the State Government also temporarily interrupted inter-municipal transport. This fact becomes extremely important when considering that more than 50% of analytical patients come from another city in the State of Rio de Janeiro. In addition to the Resolutions of the Ministry of Health, the Government of the State of Rio de Janeiro and the Crisis Committee, the collection flow of the pap smear exam, the result and the follow-up for colposcopy, biopsies and consultations in the specialized care units are in person, which, at the time of the pandemic, may have contributed to delay the process, as the population was instructed to avoid healthcare services so they could focus on COVID-19 patients.

Although the staging is recorded in the Tumor Registration Form according to the Classification of Malignant Tumors (TNM)²⁵ for cervical cancer, the classification used for staging is that of the 2018 International Federation of Gynecology and Obstetrics (FIGO)²⁶.

According to data from INCA¹, by 2019, about 35% of the analytical cases were diagnosed with advanced stag-

Table 2. Analytical and non-analytical pre-pandemic and pandemic clinical data

Characteristics	Analytical			Non-analytical		
	Pre-pandemic (%)	Pandemic (%)	p	Pre-pandemic (%)	Pandemic (%)	p
Time between diagnosis and 1st consultation (days)			< 0.001*			< 0.001*
Less than 30	34.6	13.5		20.6	12.4	
Between 30-60	36.5	25.7		17.2	19.0	
Between 61-120	15.7	40.7		14.7	31.0	
Between 121-180	3.3	10.2		8.2	8.4	
More than 180	4.0	6.6		32.9	18.1	
Invalid	5.9	3.3		6.3	11.1	
Staging			0.987			< 0.001*
0	9.8	9.2		7.2	7.1	
I	21.7	21.6		6.6	1.3	
II	28.7	28.0		15.4	4.0	
III	33.0	34.1		32.6	24.3	
IV	5.5	6.1		21.9	42.5	
No information	1.3	1.0		16.2	20.8	
First treatment received at the hospital			0.065			< 0.001*
None	0.1	0.5		60.9	71.2	
Surgery	27.4	27.7		0.3	0	
Radiotherapy	12.8	8.7		33.8	18.1	
Chemotherapy	2.0	1.3		3.0	6.6	
Radiotherapy + chemotherapy	57.7	61.8		2.0	4.0	
Condition of the disease after the end of this treatment			< 0.001*			< 0.001*
Complete remission	68.6	62.3		27.1	4.0	
Stable disease	3.2	6.1		2.3	1.8	
Disease in progression	6.4	3.3		0.6	0	
Therapeutic support	8.4	13.0		1.2	13.3	
Death	12.9	9.7		7.5	9.3	
Not applicable	0.3	4.1		60.9	71.7	
No information	0.2	1.5		0.4	0	
Reason for not treating			0.890			< 0.001*
Treatment performed elsewhere	3.9	4.1		34.3	11.9	
Advanced disease/lack of Clinical conditions	11.0	11.7		27.1	50.4	
Abandoned treatment	0.2	0.3		1.2	0	
Refusal	0	0		0.3	0.4	
Death	0.6	1.0		25.4	31.9	
Other reasons	0.3	0.5		10.7	5.3	
Not applicable	84.1	82.4		1.0	0	

Source: Adapted from RHC/HCI¹⁰.

(*) significant p value.



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ing (III and IV). In the years 2020 and 2021, just over 39% of patients had advanced diagnosis. No data from a long series is available, however, for non-analytical cases. Nonetheless, when observing non-analytical patients, an increase of 20.6% in admissions in staging IV was found when comparing the years 2020 and 2021 to the pre-pandemic period, while there was a reduction of 5.3% and 11.4% in admissions in stages I and II respectively, in the same group.

The increase in the percentage of patients admitted to stage IV in the NAP group may justify the consequent increase in untreated patients due to disease advancement or lack of clinical conditions in this group, but it would be of great importance to know the time interval between diagnosis and the beginning of the proposed treatment, even as a way of assessing the service provided in the home hospital, the vacancies regulation system and the radiotherapy and brachytherapy care network. Thus, it is not known whether these patients are not treated because they are already in stage IV or if, in addition to arriving at a more advanced stage, they still wait longer in the Regulation System line for specific treatment.

A study carried out by the Brazilian Society of Radiotherapy²⁷ portrayed the radiotherapy services and devices in Brazil and the impact inflicted by the COVID-19 pandemic. In the country, there are 284 radiotherapy services, 52% of which are in the Southeast Region.

The deficit of devices or the percentage of obsolete devices is around 50%. During the pandemic, 15% of the services had a reduction of more than 50% in the number of daily visits and 46% of the patients chose to postpone this type of treatment for their cancer. It was estimated that, considering the five main tumors, there were at least 5 thousand deaths related to the lack of radiotherapy in one year²⁷.

The results presented by the study revealed a significant impact of the COVID-19 pandemic on the management and prognosis of cervical cancer in both analytical and non-analytical patients. In fact, the more limited infrastructure to access, diagnosis and treatment were already challenging before the pandemic. The importance of a resilient healthcare system, capable of protecting essential services even in global crises, is still evident. Thus, delays in the beginning of treatment and diagnosis reflect the vulnerability of the healthcare system and may affect the outcome.

The prevalence of cervical cancer and the stage of the disease at the time of diagnosis are determining factors. In populations whose screening is organized and comprehensive, and prevention is effective, there may be a higher proportion of early diagnoses, differing from the results found in this study.

Although the findings reflect a specific reality of HCII/INCA, generalization to other contexts depends on the similarities between the demographic, epidemiological and structural characteristics of the populations and health systems involved. Populations with significant differences in social health determinants may show variations in diagnostic times, accessibility to treatment and outcomes.

The limitations in the analysis of these results include the fact that cross-sectional studies, considering a single observation moment – in this case the data were observed on December 12, 2022 – should be identified as exploratory of a situation under study, and no analytical approaches for discussion about cause and effect are indicated.

Considering the inclusion of the entire sample of the period, the sample calculation or power calculation do not apply. However, it should be noted that the study selected the population of a single reference unit of the National Health System (SUS), patients admitted to HCII and, therefore, had access to the cervical cancer line of care. Due to the COVID-19 pandemic, the groups presented quite different components, a fact that may make less evident important characteristics in groups with fewer patients.

The study in question uses the RHC as a database, a secondary source. A secondary source is collected from a pre-existing source, in this case the tumor record. The advantages are lower cost and faster results than primary source research. However, there are other disadvantages, such as the absence of variables or important information for research. The possibility of errors in filling by the technical officer, delay of registration, among other limitations inherent to human work should also be considered²⁸.

CONCLUSION

Cervical cancer is a slow-growing tumor, with the possibility of early diagnosis when the population screening is done in an organized and wide way, however, the arrival of the coronavirus in Brazil in February 2020 brought numerous challenges to the country's already overloaded healthcare system.

It seems extremely important that special attention be paid to the improvement of the screening system, making it more effective and comprehensive, even in the context of sanitary emergencies, as was the COVID-19 pandemic. However, pointing out the stages of screening that offered the user the greatest difficulty was not the target of this study.

To make users seek primary care units, Community Health Agents (ASC) might need to use communication, dissemination and active search strategies in their in-home visits, affirming the safety and containment measures of

COVID-19 contagion, because many women still remain away for fear of coronavirus contamination.

With the increase in the number of patients referred directly to therapeutic support, it is necessary to think of palliative care and pain control clinics along with basic healthcare units to bring better quality of life and assistance to a population already so affected by the pandemic. Together with patient care, it is necessary to maintain support and guidance groups to family members. This would also prevent hospitals from having a large number of patients in therapeutic support and ensuring a better offer of beds available for those candidates for healing treatment.

CONTRIBUTIONS

Monique Villa Real Ayala has contributed to the study design, planning, data acquisition, analysis and interpretation, as well as wording. Maria Tereza Fonseca da Costa has substantially contributed to the study design, data acquisition, analysis and interpretation, and critical review. Both authors approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interest to declare.

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None.

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