Attitudes towards COVID-19 vaccination in patients with cancer: A cross-sectional study of 12 oncology centers

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Abstract. Patients with cancer are a high-priority population for COVID-19 vaccination, as per guideline recommendations. The present cross-sectional study was performed to assess the perception of patients with cancer from Romania regarding COVID-19 vaccines. The study included 932 patients with solid and hematologic malignancies. This was a multicenter study including 12 oncology centers located in Western and Northwestern Romania. Between December 2021 and January 2022, patients with cancer completed an individual paper questionnaire regarding acceptance of the SARS-CoV-2 vaccination, type of vaccine, side effects and source of information. During the first year of the vaccination campaign in Romania, 58.05% (541/932) of the investigated patients received COVID-19 vaccines. The vaccination rate was highest in the 61-70 year age group (61.22%). The most frequently used vaccine was Pfizer-BioNTech (72%). There was a statistically significant association between the rate of vaccination and the area of residence and level of education (P<0.001), with rural residence and a lower level of education being predictive factors for COVID-19 vaccination hesitancy. Patients living in rural areas used non-medical sources (e.g. mass media, social platforms) as their main source of information (53.40%, 204/382), whereas patients living in urban areas (64.90%, 357/550) used predominantly medical sources (e.g. recommendations from oncologists and general practitioners). The main source of information among non-vaccinated patients was mass media (e.g. television, radio); 72.38% vs. 29.67% among vaccinated patients. For the latter, the primary source of information was the recommendations made by oncologists (59.70%) and general practitioners (56.76%). The most commonly reported side effect was injection site pain (20-33% for the first dose and 5-27% for the second dose). In conclusion, the present study confirmed that patients with cancer may be reluctant to receive a COVID-19 vaccine, mainly due to the fear of its potential side effects. Although there is scientific evidence to support the efficacy and safety of vaccines, the primary source of information for patients may affect vaccine uptake, thus affecting the efforts to stop the pandemic. Furthermore, the

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present study revealed that non-vaccinated patients preferred mass media as their main source of information, whereas vaccinated patients relied on the recommendations made by oncologists or general practitioners.

Introduction

Throughout human history, infectious diseases have been the leading cause of death, especially during pandemics (1). As expected, the COVID-19 pandemic had a major impact on humanity. Vaccination has been shown to reduce morbidity and mortality, particularly among vulnerable populations; cancer patients are one of the most vulnerable groups both due to the disease itself and more frequent hospital presentations. They also have an increased risk of developing severe complications and even die due to the infection (2).

Cancer patients have a higher risk of mortality as compared to non-cancer patients. Consequently, mortality rates were high among patients with active cancer who developed COVID-19 during the first wave of the pandemic. In the United Kingdom, mortality in hospitalized cancer patients with COVID-19 was 40.5% vs. 28.5% for non-cancer patients (HR 1.62; p <0.001) (3), while in the German LEOSS registry, COVID-19-related mortality in cancer patients was 22.5% vs. 14% for non-cancer patients (p <0.001) (4).

Vaccination campaigns were launched less than a year after the pandemic outbreak. In studies, the vaccine demonstrated more than 90% efficacy in the general population (5). Cancer patients were shown to have a variable, higher risk of developing COVID-19, and were considered a target population for vaccination (6). Therefore, COVID-19 prevention is crucial for cancer patients, with vaccination being the most effective method to achieve this goal.

Vaccines have always been surrounded by controversy and polarized the wide public into two opposing camps: those in favor of vaccination and those against it. The most common reasons for vaccination refusal include negative opinions about the need of vaccination, fear of side effects and fear of needles (7,8). Although the infection caused by SARS-CoV-2 spread around the world, in Romania a large part of the population denied the very existence of the disease, the need of vaccination and the use of prevention methods such as wearing a mask or social distancing (9). Immediately after the beginning of the pandemic, major research centers focused on the discovery of a vaccine. The relatively brief time interval needed for the development of vaccines raised suspicions among the general population, while doubts about the long-term side effects, effectiveness and safety of the vaccine were the main concerns of cancer patients (10). Furthermore, the use of non-scientific sources of information led to misconceptions about vaccination (11).

The main purpose of our study was to assess the acceptance of the COVID-19 vaccine among cancer patients undergoing immunosuppressive therapy from 12 oncology centers in Western and Northwestern Romania by means of administration of an adapted questionnaire and to understand which factors are associated with COVID-19 vaccine acceptance.

Since according to GLOBOCAN 2020 (12), there were approximately 260,000 cancer patients in Romania, we calculated a statistically representative sample for this population of 384 respondents by sample size determination test. Normality analyses were performed and the results and statistical tests were adjusted accordingly. This means at least 384 measurements/surveys were needed to have a confidence level of 95% that the real value is within +/- 5% of the measured/surveyed value.

To the best of our knowledge, no study has been performed to date to investigate the perception regarding COVID-19 vaccination among cancer patients considering their reason for acceptance, educational level and source of information. In our opinion, such an assessment is of extreme importance in this specific group of patients, therefore we conducted this pilot study in Romania.

Materials and methods

Patients. This is a pilot cross-sectional study to investigate the attitudes of Romanian cancer patients towards the COVID-19 vaccination, based on a self-administered questionnaire. The survey questions were validated by the Institutional Ethics Committee of the 'Prof Dr Octavian Fodor' Regional Institute of Gastroenterology and Hepatology in Cluj-Napoca, Romania. The target group included patients meeting the following criteria:
   a) >18 years of age;
   b) Oncology patient defined as a patient with solid or hematologic tumours undergoing active systemic treatment or follow-up;
   c) Any level of education;
   d) Any status of COVID-19 vaccination;
   e) Any history of SARS-CoV-2 infection.

Patients were selected upon presentation to the oncologist from 12 hospitals (out of 14) in Northwestern Romania. We targeted these 12 hospitals because they include the largest and most representative oncology departments that provide treatment and follow-up to most cancer patients in Northwestern Romania. We enrolled patients who consented to enter the study on a presentation to their medical oncologist during active treatment or follow-up. The recruitment period lasted between December 2021-January 2022, during the fourth wave of the COVID-19 pandemic in Romania. We avoided a selection bias by indiscriminately offering the patients the opportunity to take part in the study and complete the questionnaire. The selection was based on their consent and all patients provided a written informed consent. During the mentioned period, 932 patients agreed to complete the survey.

The details were collected by means of an anonymous questionnaire including questions about age, the cancer diagnosis, disease stage and type of cancer treatment, place of residence (rural or urban) and formal education level (primary, secondary or university), history of COVID-19 infection, influenza vaccination status and COVID-19 vaccination status. Patients were further guided based on the answer to the question: 'Are you vaccinated against COVID-19?' Patients who answered 'yes' continued to questions regarding the type of vaccine chosen, side effects related to the first and second dose, drivers of the vaccination acceptance and the source of information about the vaccine. Patients who answered 'no' completed questions regarding the intention to get vaccinated, why they refused the vaccination and their main source of information about the vaccination.

Statistical analysis. This a cross-sectional study, so we selected a number of 932 patients out of the total 260,884 cancer patients

Table I. Characteristics of patient population.

Characteristics	All patients, n (%)	Vaccinated, n (% of all patients)	Not vaccinated, n (% of all patients)	P-value
Number of patients	932	541 (58.05)	391 (41.95)	
Age group, years				0.001
<30	22 (2.36)	8 (0.85)	14 (1.51)	
31-40	37 (3.97)	15 (1.60)	22 (2.37)	
41-50	124 (13.30)	73 (7.84)	51 (5.47)	
51-60	200 (21.46)	118 (12.67)	82 (8.79)	
61-70	361 (38.74)	221 (23.72)	140 (15.02)	
>71	188 (20.17)	106 (11.37)	82 (8.79)	
Residence				0.001
Rural	382 (40.97)	178 (19.09)	204 (21.88)	
Urban	550 (59.00)	363 (38.94)	187 (20.06)	
Education				0.001
Elementary school	416 (44.64)	193 (20.71)	223 (23.93)	
High school	303 (32.51)	184 (19.74)	119 (12.77)	
University	213 (22.85)	164 (17.59)	49 (5.26)	
Primary tumor				0.001
Breast cancer	210 (22.53)	116 (12.44)	94 (10.09)	
Gastrointestinal cancer[a]	277 (29.72)	179 (19.21)	98 (10.51)	
Genitourinary cancer[b]	109 (11.70)	68 (7.30)	41 (4.40)	
Gynecological cancer	77 (8.26)	35 (3.75)	42 (4.51)	
Hematology[c]	119 (12.77)	68 (7.29)	51 (5.48)	
Lung cancer	85 (9.12)	45 (4.83)	40 (4.29)	
Skin cancer[d]	19 (2.04)	13 (1.40)	6 (0.64)	
Other[e]	36 (3.86)	17 (1.71)	19 (2.15)	
Cancer treatment phase				0.03
Active treatment primary[f]	444 (47.64)	250 (26.83)	194 (20.81)	
Active treatment metastatic[g]	347 (37.23)	195 (20.93)	152 (16.30)	
Follow-up	141 (15.13)	96 (10.31)	45 (4.82)	
Previous COVID-19 infections	294 (31.53)	163 (17.48)	131 (14.05)	0.27
Previous influenza vaccine	384 (41.20)	278 (29.82)	106 (1.00)	0.001

[a]Including: colon, cholangiocarcinoma, gastric, GIST, hepatobiliary and pancreatic cancer; [b]including: renal, prostate, bladder and testicular cancer; [c]including: leukemia and lymphoma; [d]including: melanoma; [e]including: head and neck, brain cancer and sarcoma; [f]including: Chemotherapy, targeted therapy, hormonal therapy; [g]including: Chemotherapy, targeted therapy, hormonal therapy, checkpoint inhibitors, tyrosine kinase inhibitors.

in Romania (GLOBOCAN 2020) (12). To provide our study with statistical validity or significance/power (95% confidence level), we calculated that a sample of at least 384 patients was necessary. Vaccinated and non-vaccinated cancer patients were compared using Pearson χ^2 test.

Results

Patient population. A total of 932 cancer patients undergoing active treatment or follow-up who completed the questionnaire were included in the study. The analyzed patient population characteristics are listed in Table I. The age of the patients ranged between 25 to 82 years; 541 (58.05%) accepted vaccination while 391 (41.95%) rejected it. Only 22 patients were under the age of 30; of these, 8 (36.36%) were vaccinated and 14 (63.64%) were not vaccinated. The age group where the vaccination rate was highest ranged between 61-70 years and included 361 patients, 221 (61.22%) of which were vaccinated and 140 (38.78%) not vaccinated.

Place of residence. According to the place of residence (Fig. 1), in patients from rural areas the immunization rate reached 46.06% (178/382), well below the urban population rate of 66% (363/550). This difference was statistically significant (P<0.001).

Level of education. The impact of the level of formal education on the vaccination status is shown in Fig. 2. 416 of the
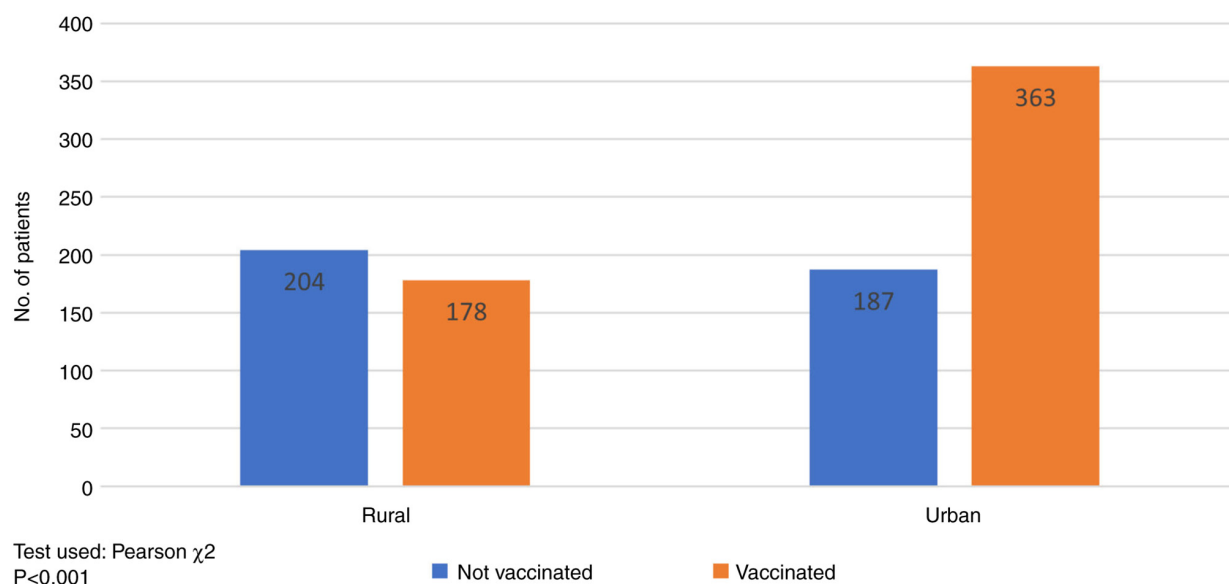
Figure 1. Distribution of subjects regarding vaccination status and area of residence. Test used: Pearson χ^2, P<0.001.
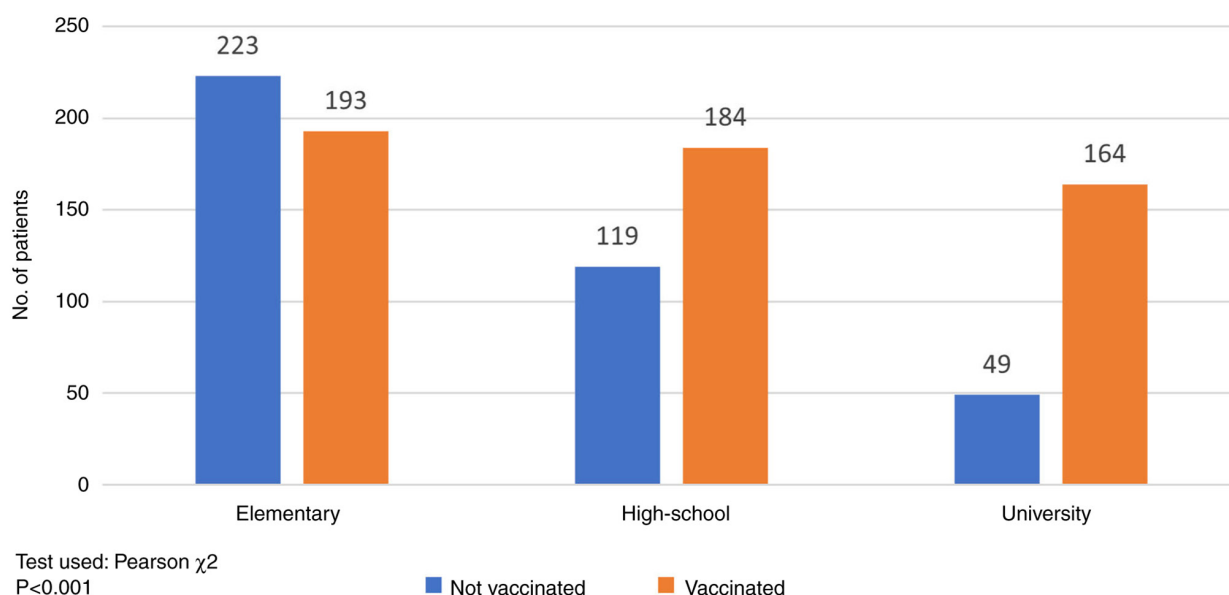

Figure 2. Distribution of subjects regarding vaccination status and level of education. Test used: Pearson χ^2, P<0.001.

total number of patients had primary education; 193 (46.39%) were vaccinated and 223 (53.61%) non-vaccinated. The rate of vaccination was higher in the secondary education group (60.72%, 184/303) and in the post-secondary (university) education group (76.99%, 164/213) (P<0.001).

Vaccine distribution. In this cancer population, the most widely used vaccine was Pfizer-BioNTech (72%, 329 patients), followed by Johnson & Johnson, (14%, 75 patients), AstraZeneca (8%, 43 patients), and Moderna (6%, 33 patients) (Fig. 3).

Source of information. As shown in Fig. 4, the main source of information in non-vaccinated patients was the mass-media (TV, radio), 72.38% vs. 29.67% in vaccinated patients, respectively, while for vaccinated patients the primary source of information was the recommendation by the oncologist (59.70%)
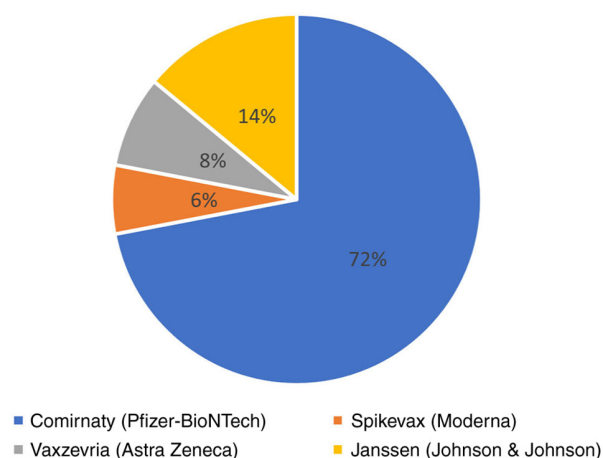

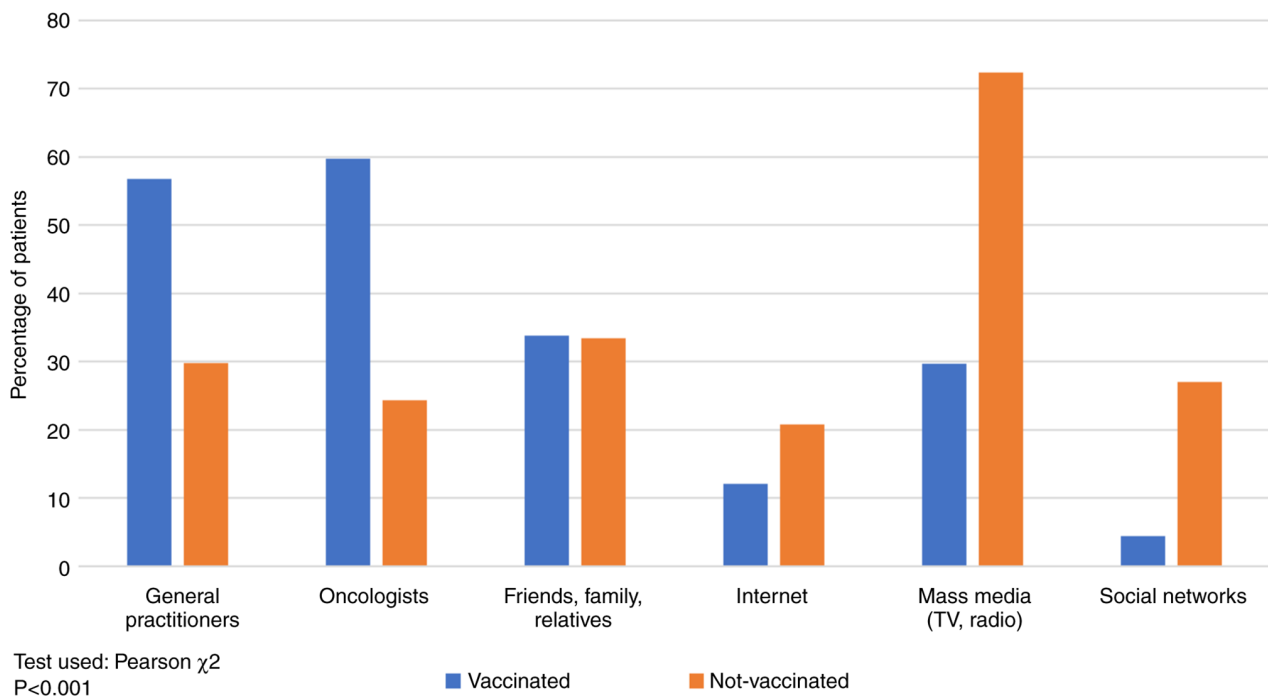Figure 3. Vaccine distribution in patients with cancer.

Figure 4. Sources of information in vaccinated and non-vaccinated patients with cancer.
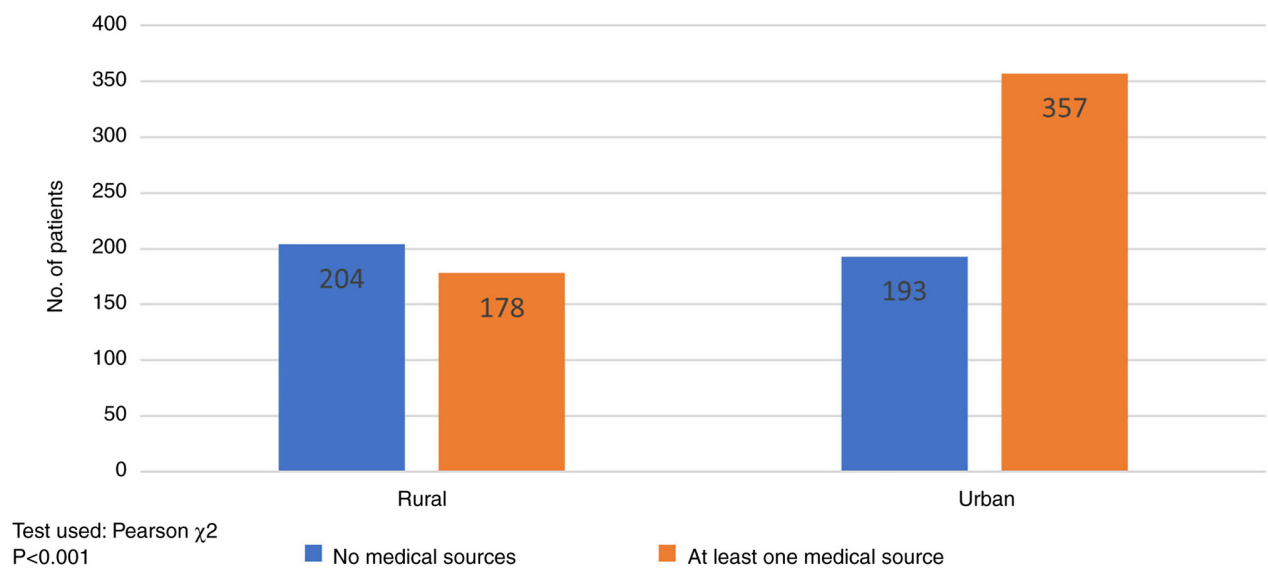

Figure 5. Distribution of subjects in terms of sources of information and area of residence. Test used: Pearson χ^2, P<0.001.

and the general practitioner (56.76%). Recommendations by general practitioners and oncologists are considered in medical sources, while mass-media, internet, social platforms and friends'/family/relatives' advice are non-medical sources.

Since statistically significant differences were observed in terms of the patients' place of residence and vaccination status, we further investigated the main source of information based on the former. As shown in Fig. 5, patients (53.40%, 204/382) from rural areas relied on a non-medical main source of information (mass-media, social platforms, friends'/family advice), while in urban areas medical sources of information predominated (64.09%, 357/550) (recommendation by the oncologist and general practitioner) (P<0.001).

A statistically significant association between the level of education and the rate of vaccination was also noticed, therefore we explored the preferred sources of information according to the level of education. Fig. 6 shows that high-school (60.06%, 182/303) or university (76.05%, 162/213) graduates relied on a medical source of information (oncologist, general practitioner recommendation), while primary education patients (54.08%, 225/416) were influenced by non-medical sources in particular (mass-media, social platforms or friends'/family advice) (P<0.001).

The main source of information in non-vaccinated patients was mass-media (TV, radio) at a rate of 72.38% as compared to 29.67% among vaccinated patients. In vaccinated patients
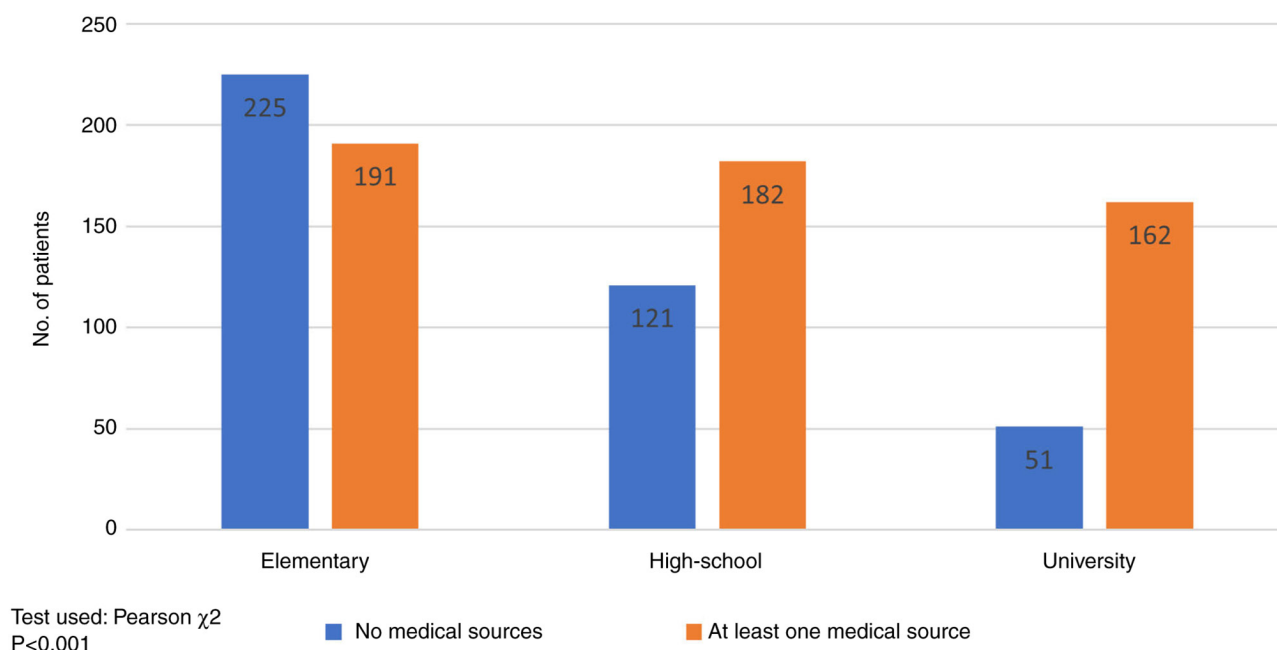
Figure 6. Distribution of subjects regarding sources of information and level of education. Test used: Pearson χ^2, P<0.001.
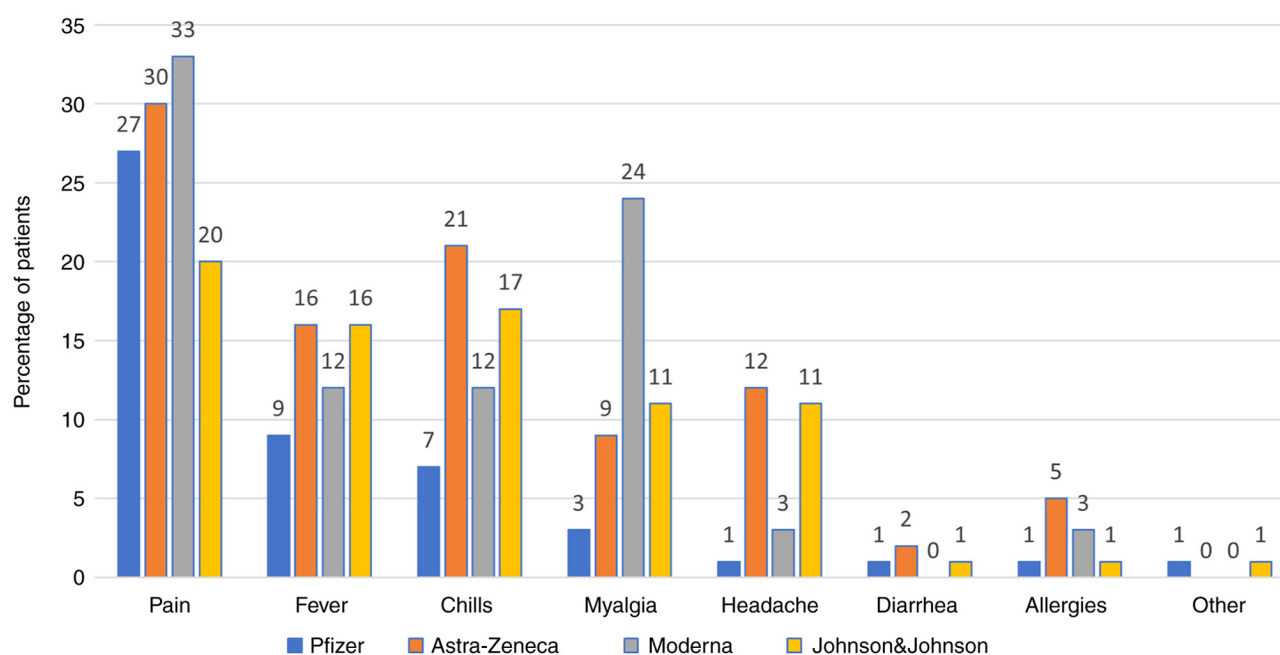

Figure 7. Side effects reported after the first dose.

the primary source of information was the recommendation by the oncologist (59.70%) and the general practitioner (56.76%).

Side effects. The most commonly reported side effect was pain at the injection site after the first (Pfizer vaccine, 27.04%) and the second dose (Pfizer vaccine, 4.85%). All the side effects are shown in Figs. 7 and 8.

Discussion

COVID-19 vaccination hesitancy rates vary in the general population worldwide (13). This attitude towards COVID-19

vaccines among cancer patients was reported in other papers as well (14,15,16). According to the findings of this study, the Romanian cancer patients also need more comprehensible information regarding this issue.

In Romania, the first dose of COVID-19 vaccine was administered on December 27, 2020 and all eligible individuals were encouraged to get vaccinated, cancer patients in particular. The European Society for Medical Oncology (ESMO) issued a statement recommending vaccination in cancer patients, monitoring of side effects and specific patient education. The European Medicines Agency (EMA)-approved RNA vaccines are safe and have no contraindications in
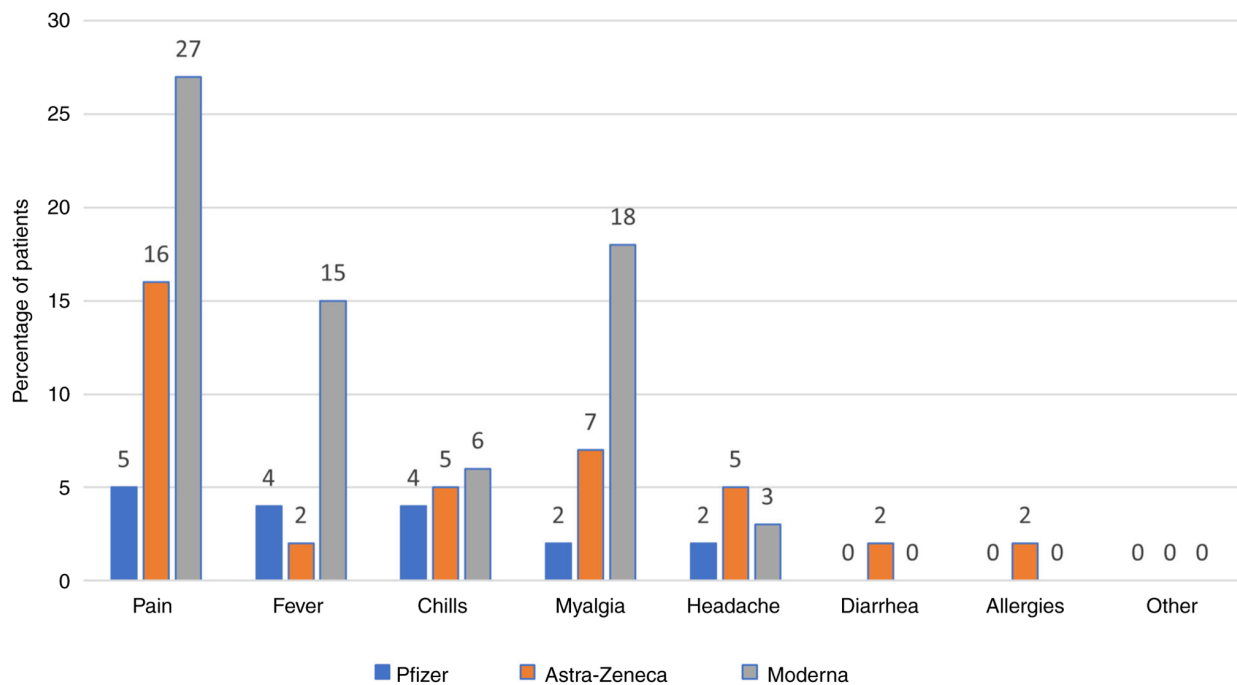
Figure 8. Side effects reported after the second dose.

patients with active cancer or in immunocompromised patients (17).

The study we conducted to investigate the attitudes of cancer patients regarding the COVID-19 vaccination, one year from the start of the vaccination campaign, was based on 932 analyzed patients: 58.05% were vaccinated and 41.95% not vaccinated. These results are comparable to data from the general population of Romania, where the rate of vaccination amounts to only 41.44% of the total population (18). Of the total number of patients enrolled in the study, 31.54% had a history of COVID-19 infection and 55.44% of these patients wanted to receive the vaccine. This finding is comparable to the data from a study published in *Vaccines* in 2022 regarding the general population of Romania, where 33% of participants had a history of SARS-CoV-2 infection with different degrees of severity (9).

As far as the influenza vaccination is concerned, 41.20% of the total number of patients analyzed in our study received such a vaccine, a higher rate as compared to the findings of another study conducted in the Romanian cancer population published in ESMO Open in 2021, before the start of SARS-CoV-2 vaccination campaign, where only 15.9% of patients had been vaccinated against influenza the previous year (19). Higher rates of influenza vaccination may be a useful by-product of the COVID-19 vaccination campaigns.

In Romania, 4 types of COVID-19 vaccine were available, all approved for use in cancer patients as well. Vaccinated cancer patients preferred Pfizer-BioNTech (72%), followed by Johnson & Johnson (14%). This finding is consistent with the general population, with a significantly higher number of Pfizer vaccines administered daily as compared to other vaccines (18). The drivers for this preference for Pfizer may be that it is EMA approved and shown to be 95% safe and effective in people 16 years of age and older (20).

To get a better understanding of attitudes towards vaccination in our study, the vaccinated patients were asked about how they made their decision while non-vaccinated patients about their arguments against vaccination. The reasons in vaccinated patients were the following: 63.96% observed the physicians' recommendations, 56.56% reported fear of the side effects caused by the SARS-CoV-2 infection, 53.05% wanted to protect their loved ones and 46.58% wanted their life to return to normal as soon as possible. These rates mirror the findings from the study published in *Vaccines* in 2022, conducted on the general population of Romania which assessed how much Romanians trusted physicians and the Romanian medical system and showed that 65% had confidence in the recommendations made by Romanian physicians, but only 26% trusted the Romanian health system (7). This low percentage of confidence results from problems encountered by the health system in recent years such as lack of medicines, medical equipment and modern facilities, as well as deadly hospital fires (21,22).

We compared the reasons provided by non-vaccinated patients and 67.52% reported fear of vaccine-induced side effects, 28.13% did not consider the vaccine necessary and 20.46% did not trust the current scientific data about it. We asked them if they intended to get vaccinated and 50.38% promptly answered they were unwilling to get vaccinated, 20.97% considered getting vaccinated on completion of their oncological treatment, 18.93% expected more evidence of vaccine efficacy and 9.46% were willing to get vaccinated as soon as possible. This is how our results compare to the findings in French [53.7% reported the desire to get vaccinated, 29.7% considered they were not ready and 16.6% refused vaccination (14)], Portuguese [84% intended to get vaccinated, 16% had not yet decided or were reluctant (23)] and Serbian cancer patients, respectively [10% certainly rejected vaccination (24)].

The main reason the population continues to reject vaccination is the fear of side effects. Recent studies have begun to systematically examine the frequency and types of side effects (25,26). The authors highlight that the adverse events

reported (cerebral thrombosis, Guillain-Barré syndrome, myocarditis, pericarditis) are not COVID-19 vaccination-specific side effects as compared with their background rate in the general population.

In our study, the most common side effect was pain at the injection site after the first and the second dose (for the Pfizer vaccine, 27.04 and 4.85%, respectively). Other side effects include fever, chills, headache, diarrhea, allergies, however all with significantly lower rates (around 1.28-2.81% for Pfizer). For other side effects, patients mentioned chest pain, dizziness, finger numbness, but rates were low (0.51%). We have comparative data from the study conducted in cancer patients in London by Monin *et al* reporting a lower rate of side effects in cancer patients compared to vaccinated healthy patients (46% vs. 62% and 29% vs. 69%) after the first and the second dose, respectively (27). A study published in *The Breast* which included breast and gynecologic cancer patients receiving active treatment in Germany found that the COVID-19 vaccines were well tolerated while undergoing systemic cancer therapy with no additional side effects reported as compared to the general population (28). The data provide solid evidence of the effectiveness of vaccinating patients while receiving active treatment.

In our study, we found a statistically significant association between the vaccination rate and both the place of residence and the level of education, as independent factors. These findings are comparable to those of the study published in *Supportive Care in Cancer* regarding patients in Portugal which showed that lower levels of education and rural residence are predictive factors of COVID-19 vaccination hesitancy (23).

Multiple sources of information regarding the COVID-19 infection and vaccines are used. As shown in Figs. 5 and 6, patients opted for different sources of information, depending on their level of education and area of residence. It is a known fact that mass-media often promote misinformation, channeling the opinions of different experts instead of official recommendations, which leads to increased uncertainty, anxiety and confusion in the general population and especially among cancer patients (29). The effects of 'fake news' were evident in the study conducted on the general population of Romania, where 47% of participants believed that a secret organization that controls the world wants to decrease the global population by means of vaccination (7,9). In February 2022 in Romania, only 44.62% of the total population of 19.29 million had received a COVID-19 vaccine (30).

Our study suggests that the information on vaccines needs to be tailored based on the patients' educational level. Also, public information campaigns designed on different levels of complexity may prove more efficient in Romania. Future research including a larger population with various subpopulations would provide further validation to our study. Also, this pilot study which highlights a correlation between the formal education level and the rate of vaccine acceptance gives a cue that public awareness-raising campaigns worldwide should be tailored to the patients' level of understanding.

The large number of cancer patients and the number of oncology centers included is the main strength of our study. The fact that it is the first study of this kind in Romania is the second. The first limitation of our study is the heterogeneity of participants and the lack of information on their medical background which made it impossible to demonstrate if the surveyed population is representative for the cancer patient population as a whole. Also, a better stratification of patients as well as an analysis of comorbidities would have helped to further clarify the patients' attitudes. Another limitation of our study is that the survey included non-standardized questions and that it was a multicenter study, leading to differences in terms of the health care providers-patient communication. However, to the best of our knowledge, there are no globally validated questionnaires to appropriately reflect our patients' characteristics and serve the objective of our study.

This study demonstrates that Romanian cancer patients are reluctant to receive the COVID-19 vaccines. In summary, their hesitancy is mainly influenced by the fear of side effects; mass-media (TV, radio) and social platforms play the main role as source of information among non-vaccinated patients, while for vaccinated patients the primary source of information is the recommendation by the oncologists or the general practitioners.

Although scientific evidence to support the efficacy and safety of vaccines exists, patients are prone to misinformation. The residence in rural areas and the lower level of education were identified as predictors of vaccination hesitancy.

Also, there is a need for specific vaccination-related education of the general population, especially in the rural areas, to improve the success of preventive measures and information campaigns implemented by health care authorities.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

RV was involved in conceptualization and supervision. LMB, GM, LD, TTV, IC, DS, AI, LAT, SH, RC, AG, AH, AU, DP and LOU contributed to data collection. DV performed the statistical analysis, CMO, RL and RV were involved in data analysis and confirmed the authenticity of all the raw data. RL was involved in writing and preparing the original draft. CMO was involved in writing, reviewing and editing. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was conducted according to the guidelines of The Declaration of Helsinki and was approved by the Institutional Ethics Committee of the 'Prof. Dr. Octavian Fodor' Regional Institute of Gastroenterology and Hepatology (Cluj-Napoca, Romania; approval no. 1677/09.12.2021). All patients provided a written informed consent.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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