Original Article

Baseline Parameters in Untreated Ovarian and Breast (Symptomatic and Asymptomatic Covid-19) Cancer Patients

Untreated Ovarian and Breast Cancer Patients

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ABSTRACT

Objective: To evaluate the effect of covid-19 on CBC, LFT's, RFT's and TMR's in cancer patients.
Study Design: A prospective study
Place and Duration of Study: This study was conducted at Multan Institute of Nuclear Medicine and Radiotherapy (MINAR) from April 2019 to December 2020.
Materials and Methods: This study was performed on 3772 untreated cancer patients (includes bladder, bone, brain, breast, colon, larynx, leukemia, liver, lung, ovary and other cancer types with age ranging from 8-87 years (49.59±15.27) of 2019 and 2020 (50% of COVID attack) at MINAR hospital, Multan. Chi-square Mann Whitney, Independent T- test and Spearman correlation analysis were performed to calculate results.
Results: The incidence of bone cancer (p value-0.02), brain cancer (p value-0.03), breast cancer (p value-0.00001) liver cancer (p value-0.006), and ovarian cancer (p value-0.0001) was higher in 2020 patients. All cancers, data indicated that Creatinine (p=0.004) and CA 125(p=0.04) were in higher ranges in COVID 19 cancer patients. There observed significant change in creatinine levels of breast (p=0.02) and ovarian cancer patients (p=0.04) and also higher level of CA-125(p=0.04) was indicated in ovarian cancer patients along with covid-19. There observed strongly significant positive association of CA- 125 with creatinine (r=0.34, p=0.02), and CEA with Bilirubin Total(r=0.57, p=0.04) in ovarian cancer. MCV (p=0.00), HGB (p=0.01), HCT (p=0.04), MCH (p=0.001), and MCHC (p=0.02) were decreased in breast cancer patients. CA-125 showed a strongly significant negative association with LY %(r= -0.305, p=0.03) and MO %(r= -0.299, p=0.049) in ovarian cancer.
Conclusion: Our findings suggest that incidence of ovarian cancer and breast cancer was very high during COVID pandemic attack. Association of CA 125 with creatinine in breast cancer and with LY% and MO% in ovarian cancer serve as the prognostic factor during viral attack. MCV and Creatinine are diagnostic factors in both cancers.
Key Words: COVID 19, Breast cancer, Creatinine, CA 125, MCV.

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INTRODUCTION

In 2019 WHO announced that out of 183 countries in 112 countries, cancers are the first or second cause of death, but in 23 further countries, it is the third or fourth cause of death. Breast cancer is the fifth leading cause of death worldwide, in 159 countries out of 185, one in four cancer patients has breast cancer [(1)]. In Pakistan, in every nine women one develops breast cancer some time in her life[(2)].

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Ovarian cancer (OC) is the seventh most commonly diagnosed cancer among women in the world [(3)]. Asian Indians/Pakistanis had the highest incidence, whereas Koreans had the lowest of ovarian cancer[(4)]. In the United States, in 2019 approximately 5930 new cases were diagnosed and 1500 patients were dying[(5)]. For the diagnosis of cancer, baseline parameters which are important to test include CBC, LFTs and RFTs. If there is no change in these parameters we can stop wasting our time with an ineffective method. Because chemotherapy and radioactive rays can fluctuate their concentration in blood and show some harmful effects on liver and kidney functions[(6)]. We also use TMRs (tumor markers) which are some sort of protein found in the blood and act as biomarkers for cancerous cells should be monitored along radiology tests[(7)].

LFTs (AST, ALT, ALP, and Total Bilirubin) are the blood tests used as screening tool which give information about the state of the liver. Via RFPs (renal function parameters) tests we calculate biochemical like serum creatinine and urea level whose increased level is toxic for whole body functioning and also indicate kidney dysfunction or cancer[(8)]. The tumor markers used for cancer diagnosis and treatment control are

CA19-9, CA 125, AFP and CEA.CA 19-9 detects cancer masses related to pancreases. CA 125 is beneficial for ovary cancer detection in pelvic masses.

Complete Blood Picture (CBC) is one of the most common tests that are recommended by every physician in every cancer. Different parameters of CBC including WBC, RBC, HBG, HCT, MCV, MCH, MCHC, RDW-CV, PLT MPV PDW, PCT, NE, LY (Lymphocytes), MO (Monocytes) and EO (Eosinophils) are observed.

Cancer is one of the most common comorbidity of people in covid-19 and cancer patients are the most vulnerable people in the pandemic[9].So, they need some intensive care as their immune system is already at high risk due to the continuous use of immune suppressants, it is better to stop the chemotherapy if possible[10].

MATERIALS AND METHODS

We studied 3772 cancer patients' data from MINAR hospital, Multan, from April 2019 to December 2020. They include 1626 cancer patients of 2019 and 2146 cancer patients also suffering from covid-19. We have mentioned only 10 of cancer data for incidence study. Blood samples were collected in K2 -BD vacutainers(11). LFTs and RFTs were measured by the kinetic method in Selectra junior. After collection, (within 15 minutes) testing of all samples for CBC was performed on NIHON KOHDEN. For statistical analysis, SPSS version 22.0 (SPSS Inc., Chicago, IL, USA) was used. First of all we applied chi-square test to check the incidence of different cancers in covid-19 cancer patients. After checking the normality of data, results for CBC, LFTs and RFTs were assessed by Mann Whitney test and Independent T test. Finally, the relationship of TMRs with bio- chemical parameters was assessed by Spearman correlation analysis. The level of statistical significance was set at $P<0.05$.

RESULTS

We have calculated two year cancer incidence rate of southern Punjab region of Pakistan to some extent with the help of Chi square test in IBMSPSS 22.0 version. The data have been shown in table no. 1.

Our data indicated that the breast and ovarian cancer incidence was very high during COVID -19 outbreak. All cancer patients were untreated in both years, while in 2020, 50% of them were symptomatic and asymptomatic covid-19 along with cancer. Table No. 2 showed that creatinine levels was decreased significantly in breast cancer and increased in ovarian cancer patients along with COVID 19. There was a positive relationship of creatinine with CA125 in 2020 data. It shows that creatinine level have a close relationship with CA125 in ovarian cancer patients. There is also an indication of increased CA125 level in ovarian cancer patients with COVID 19.In ovarian cancer the tumor marker CEA also have a significant relationship with bilirubin total value. MCV was significantly lower in breast (p=0.00) and ovarian (p=0.03) cancers. HGB(p=0.01), HCT(p=0.04), MCH (p=0.001), MCHC(p=0.02),and PDW(p=0.01) showed significant decrease and PCT(p=0.00) and MPV(p=0.00), RDW-CV(p=0.00) MO%(p=0.00) and EO%(P=0.02) were significantly increase in the patient having breast cancer along with covid-19. CA-125 showed a strongly significant negative association with LY% (r= -0.305, p=0.03) and MO% (r= -0.299, p=0.049) and positive association with PCT in ovarian cancer patients along with COVID 19 as shown in Table no.3.

Table No 1: Incidence of cancers during COVID-19 outbreak

Different cancer sites	Year 2019		Year 2020		P value	Total (2019 & 20)	
	No. of patients	%	No. of patients	%		No. of patients	%
Bladder	18	1.1	41	1.9	0.05	59	1.56
Bone	12	0.7	34	1.58	0.02	46	1.2
Brain	20	1.2	12	0.55	0.03	32	0.84
Breast	236	14.5	109	5.07	0.00001	345	9.1
Colon	20	1.2	31	1.4	0.58	51	1.35
Larynx	20	1.2	16	0.74	0.13	36	0.95
Leukemia	20	1.2	14	0.65	0.06	34	0.9
Liver	20	1.2	54	2.51	0.005	74	1.96
Lung	20	1.2	41	1.9	0.11	61	1.6
Ovary	20	1.2	69	3.2	0.0001	89	2.35
Other cancer types	1220	75	1725	80	0.17	2945	78
All cancer patients	1626		2146			3772	

Table No. 2: Biochemical parameters & their association with tumor markers during covid-19 outbreak

Parameters	Breast Cancer Mean ±SD		p value	Ovarian Cancer Mean ±SD		p value	R value (sig.) Ovarian Cancer		
	2019	2020		2019	2020		CA-125 2019	CEA 2020	CA-125 2020
Urea	33.32±16.84	32.89±13.27	0.71	43.83±24.99	45.86±56.70	0.88	-0.17 (0.56)	0.34 (0.20)	0.26 (0.64)
Creatinine	0.95±0.30	0.86±0.24	0.02	1.09±0.41	2.94±15.07	0.04	0.36 (0.18)	0.41 (0.12)	0.34* (0.02)
SGPT	37.66±56.66	36.41±28.97	0.42	22.88±14.79	29.72±24.82	0.46	0.03 (0.96)	0.39 (0.17)	-0.07 (0.67)
SGOT	51.55±116.95	38.59±29.60	0.12	34.12±15.78	37.88±31.30	0.67	0.14 (0.79)	0.25 (0.39)	0.13 (0.44)
BiT	0.71±1.92	0.48±0.43	0.21	1.15±1.98	3.50±19.75	0.9	0.31 (0.54)	0.57* (0.04)	0.31 (0.06)
ALP	124.67±75.43	135.62±113.22	0.3	163±114.17	130.88±122.63	0.42	0.09 (0.87)	0.14 (0.66)	0.10 (0.58)
CA-125	33.32±16.84	32.89±13.27	0.71	237.9±445.61	783.16±1080.77	0.04			

Table No.3: Significant variation of CBC parameters in ovarian and breast cancer patients

Parameters	Breast (Mean±S.D)		P-value	Ovary (Mean±S.D)		P-value	Ovary cancer			
							CEA		CA125	
	2019	2020		2019	2019		2019	2020	2019	2020
WBC	9.01±3.4	8.68±2.8	0.96	13.1±20.4	7.92±2.4	0.29	0.821* (0.023)	0.3 (0.433)	0.257 (0.354)	0.05 (0.729)
RBC	4.66±0.7	4.79±0.6	0.06	4.55±0.6	4.73±0.7	0.3	0.000 (1)	0.617 (0.077)	0.436 (0.104)	0.067 (0.642)
HGB	12.7±1.9	12±1.7	0.01	11.55±1.5	11.5±1.6	0.96	0.036 (0.939)	-0.083 (0.831)	0.068 (0.809)	-0.108 (0.452)
HCT	38.3±5.5	37.2±5.2	0.04	36.51±4.4	35.2±4.9	0.31	0.036 (0.939)	-0.05 (0.898)	0.154 (0.585)	-0.038 (0.793)
MCV	83.26±9.7	77.9±9.1	0.00	80.5±6.6	74.2±12.7	0.03	-0.036 (0.939)	-0.633 (0.067)	-0.25 (0.365)	-0.16 (0.264)
MCH	27.35±3.7	25.3±3.2	0.00	25.51±2.8	24.6±3.1	0.26	-0.143 (0.76)	-0.611 (0.081)	-0.279 (0.315)	-0.219 (0.123)
MCHC	32.79±1.5	32.4±1.9	0.02	31.63±1.4	32.8±2.3	0.01	-0.2 (0.667)	0.05 (0.898)	-0.109 (0.698)	0.09 (0.952)
RDW-CV	13.6±2.1	14.4±2.4	0.00	14.35±2.7	15.6±2.3	0.02	0.25 (0.589)	0.644 (0.061)	0.466 (0.08)	0.05 (0.752)
PLT	334.78±13.4	346.8±134.3	0.4	350.6±132.6	312.4±136.9	0.33	0.643 (0.119)	0.4 (0.286)	0.304 (0.271)	0.273 (0.052)
PCT	0.28±0.5	0.29±0.1	0.00	0.27±0.1	0.25±0.1	0.35	0.5 (0.253)	0.301 (0.431)	0.554* (0.032)	0.313* (0.025)
MPV	7.72±1.3	8.43±1.5	0.00	7.89±1	8.12±1.1	0.25	-0.214 (0.645)	0.075 (0.847)	0.404 (0.135)	0.108 (0.45)
PDW	17.79±1.2	17.1±2.9	0.01	17.91±1.3	16.7±2.5	0.05	-0.036 (0.939)	0.05 (0.898)	-0.011 (0.97)	-0.134 (0.347)
NE%	62.12±10.7	61.3±12.4	0.65	62.76±11.7	63.8±13.6	0.76	0.679 (0.094)	0.167 (0.668)	0.232 (0.405)	0.273 (0.053)
LY%	29.5±10.5	29.9±11.7	0.93	30.71±12.8	28.1±12.9	0.43	-0.821* (0.023)	-0.1 (0.798)	-0.254 (0.362)	-0.305* (0.03)
MO%	2.14±1.3	4±3.3	0.00	2.75±1.3	4.44±3.5	0.09	0.214 (0.645)	0.335 (0.417)	0.233 (0.403)	-0.299* (0.049)
EO%	1.21±1.9	2.42±3.2	0.02	0.6±0.5	1.72±1.9	0.06	-0.074 (0.875)	0.587 (0.126)	-0.404 (0.135)	0.006 (0.971)

DISCUSSION

Cancer is a major cause of death in the world. In clinical research, prognostic factors play important roles in cancer state. During treatments, the relatable prognostic factors show some changes in their values and guide the doctors to continue the treatment or to stop it. [12].

According to our study, breast cancer incidence rate is of 9.1% in two years (2019-2020). Global cancer observatory in Pakistan have also mentioned that breast cancer has the highest incidence in 2020. Our study also showed that in Karachi, adult female has breast cancer.

According to our study, breast cancer has shown the highest incidence rate of 9.1% in two years (2019-2020). This significant result was also found by global cancer observatory in Pakistan. They mentioned that breast cancer has the highest incidence in 2020. Death rates for females in breast cancer and cervical cancer were considered highest of all cancers[13].It has also been observed that in Karachi, adult female has breast cancer. [14].

Our study showed that significant increase in baseline parameters as creatinine and CA125 during 2020 (where 50% of patients have symptomatic and asymptomatic covid-19). So, we can say that Creatinine and CA125 were prognostic factors in untreated cancer patients during covid-19 attack. However, recent study of renal impairment in COVID 19 patients, 15.5% elevation in creatinine and 14.1% elevation in urea is observed[15].In other study, significant increase in CA-125 level is shown in Covid-19 patients[16] as study of Xiang, J., et al., of severe COVID 19, urea and creatinine has been shown significantly higher values [17].

In our study we observed, changes in other biochemical parameter during covid-19 like creatinine has decreased in breast cancer (p-0.02), conversely another laboratory tests of breast cancer in the study of Kent, R., et al., proved that the creatinine level towards higher (2.0 mg/dl) side [18].Creatinine also acts as a predictive value for the risk of death in covid-19, when elevated than normal value[19].Additional studies authenticate that Covid-19 patients have shown abnormal liver function tests. [20].

In ovarian cancer, both creatinine and CA-125 has been raised (p-0.04) in those cancer patients in which 50% were suffering from covid-19. Creatinine level is an independent prognostic factor of survival in ovarian cancer. 1.2% mg/dl or higher value of creatinine in patients indicated poor survival rate and found in 4.4% of patients[21]. Higher level of CA 125 is a positive test for ovarian cancer in 90% females. So, this TMR is a significant diagnostic factor at the clinical level[22]. There also found some association of TMRs with LFTs, as CA-125 has shown a significant positive association relationship with Creatinine (r-0.34, p-0.02) and CEA with bilirubin total (r-0.57, p-0.04) in ovarian cancer patients.

According to our research in asymptomatic covid-19 Breast Cancer patients, MCV was significantly decreased, while Akinbami et al., proved that MCV was decreased only in Breast cancer[23]. MCV was found to be decreased in symptomless covid-19 ovarian cancer as well as in symptomless covid-19 brain cancerous patients. But in the case of Ovarian cancer, MCV decreased[24] and in brain cancer, prognostic factor MCV increased[25].In Ovarian cancer, CA-125 Correlates negatively with LY% and MO% in covid19 Ovarian Cancer. On the other hand in ovarian cancer high or low CA-125 is positively correlate with Neutrophil to lymphocyte ratio[26]. So these tumor markers may be helpful with these CBC parameters in the prognosis of ovarian cancer.

CONCLUSION

Our findings suggest that in ovarian cancer and breast cancer patients MCV and Creatinine and serve as a diagnostic factor of COVID 19 during treatment. Association of CA 125 with creatinine in breast cancer serve as the prognostic factor of treatment in covid-19 patients. While LY% and MO% with CA-125 are prognostic factors in ovarian cancer during COVID attack.

Author's Contribution:

Concept & Design of Study:	Kainat Warraich
Drafting:	Shahida Parveen
Data Analysis:	Rubaida Mehmood
Revisiting Critically:	Kainat Warraich, Shahida Parveen
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Conflict of Interest: The study has no conflict of interest to declare by any author.

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