Red cell distribution width, a predictive factor in immunocompromised patients with COVID-19: A comparison retrospective study between cancer and kidney transplant patients

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Abstract

We aimed to review the records of cancer and kidney transplant patients of out of 1135 COVID-19 patients, who were referred to our hospital (Valiasr) in Zanjan, from March 16th, 2020, to June 11th, 2020. This was single-center, historical cohort study. Patients were divided into different subgroups and compared of disease outcomes. The only predictor of death was lactate dehydrogenase (LDH). The rate of red cell distribution width (RDW) in patients with active cancer was higher than kidney transplant patients and was statistically significant. There was no statistically significant difference in mortality between active and non-active cancer groups. Female sex and low SpO2 has increased the chances of ICU admission. Patients with active cancer generally have severe and more complicated disease and RDW can be a predictable option.

Key Words: COVID-19; kidney transplantation, cancer, immunocompromised patient.
susceptibility to infection. Therefore, we aimed to review the records of cancer and kidney transplant patients of out of 1135 COVID-19 patients, who were referred to our hospital (Valiasr) in Zanjan, Iran.

**Materials and Methods**

**Study design**

This was a single-center, historical cohort study. We reviewed the records of cancer and kidney transplant patients with COVID-19 were referred to our hospital (Valiasr) in Zanjan, from March 16th, 2020, to June 11th, 2020 (Figure 1). The most prevalence between SOT patients that referred to our system was kidney transplant. Cancer (solid tumor and hematologic malignancy) and kidney transplant patients with positive COVID-19 RT-PCR (reverse-transcriptase polymerase chain reaction) were included.

This study was approved by the institutional ethics review boards of our university (approval number IR.ZUMS.REC.1399.265 date: Oct 15th, 2020). The Research Ethics Committee waived the requirement informed consent before the study started because of the urgent need to collect epidemiological and clinical data. We analyzed all the data anonymously.

**Diagnostic methods**

The method of diagnosis is RT-PCR assay test using throat swab specimens collected from upper respiratory tracts. All patient aged was more than 18. Patients with a radiological or clinical diagnosis of COVID-19, without a positive RT-PCR test were not included in this analysis.

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**Fig 1. Statistics of patients suspected to COVID-19: Cancer and kidney transplant patients with positive COVID-19 RT-PCR were included.**

**Fig 2. Division algorithm of patients with COVID-19, including two groups 1: Patients with cancer, 2: Patients with renal transplant. Patients with cancer were studied in two groups: active cancer and inactive cancer. Cancers were studied in 3 groups: blood malignancy, gastrointestinal cancer and non-gastrointestinal cancers.**
Patients with non-invasive cancers including non-melanomatous skin cancer, in-situ carcinoma, or precursor hematological neoplasms were excluded from this analysis. Patients with room air oxygen saturation (SpO2) < 90% were considered as severe COVID-19, and ≥90% were considered moderate COVID-19. Clinical data of each patient were collected, which included age, gender, and known comorbidities (diabetes mellitus (DM), hypertension (HTN)). Other underlying diseases were not included in the study due to their lower prevalence. Cancer stage was not chosen for the multivariable analysis as this variable was only collected in solid tumors. Patients with cancer were studied in two

Table 1. Description of patients on admission.

| Variables          | Cancer patient’s N (%) | Graft patients N (%) |
|--------------------|------------------------|----------------------|
| Sex                | Male 16(57.1)          | 4(80)                |
|                    | Female 12(42.9)        | 1(20)                |
| Age                | M ± SD 62.54±14.78     | M ± SD 48.60±15.14   |
| Severity           | severe 11(39.3)        | 2(40)                |
|                    | Non-severe 17(60.7)    | 3(60)                |
| Comorbidity        | DM 3(10.7)             | 1(20)                |
|                    | HTN 6(21.4)            | 4(80)                |
| Cancer activity    | Active 22(78.5)        |                      |
|                    | Non-active 6(21.4)     |                      |
| Type of cancer     | Hematologic 5(17.9)    | N/A                  |
|                    | GI 8(28.6)             |                      |
|                    | Non-GI 15(53.6)        |                      |
| Total              | 28(100)                | 5(100)               |

GI: Gastrointestinal; Non GI: Non Gastrointestinal; HTN: Hypertension; DM: Diabetes Mellitus; N: Number; SD: standard deviation

Fig 3. Comparison of cancer type with mortality. GI: Gastrointestinal, Non GI: Non Gastrointestinal
groups: active cancer (for which anticancer treatment (chemotherapy) had been administered in the past 6 months; or hematological cancer that is not in complete remission) and inactive cancer. Also cancer patients were studied in 3 groups: blood malignancy, gastrointestinal cancer and non-gastrointestinal cancers (Figure 2).
Indicators measurements and analysis

The main outcome was patient survival during hospitalization. Measurements included RDW (elevated RDW defined as greater than 14.5%), Lymphocyte count (ALC < 1,000 cells/mm3 was defined as lymphopenia) and Platelet (PLT < 150,000 platelets/mm3 was defined as thrombocytopenia) at first day admission in hospital. Secondary outcomes were: a composite of severe illness (death, severe illness, admission to an intensive care unit (ICU), or a combination of these). Statistical analysis carried out using SPSS version 22. Significance level considered 0.05.

Results

We retrospectively enrolled 28 cancer (2.4%) and 5 kidney transplant patients of the 1135 patients admitted to Valiasr hospital for treatment of COVID-19. Demographic, clinical feature and underlying diseases of the patients are shown in Table 1. The mean age was 62 for cancer and 48 for kidney transplant patients (Mann-Whitney sig=0.053). The sex distribution in patients was not significantly different between cancer and kidney transplant patients (Exact sig=0.625). The most types of cancer patients were Gastric (3 patients), lung (3 patients), Breast (3 patients). Gastrointestinal cancer was the most frequent type of cancer (28.6%). The patient

| Table 3. Cancer and Graft patients |
|-----------------------------------|
| **ICU admission** | **Days of hospitalization** | **Mortality** | **ICU admission** | **Days of hospitalization** | **Mortality** |
|                  | N (%)                       | (Med ±IQR)    | N (%)            | (Med ±IQR)                  | N (%)        |
| Sex              | Male                        | 4(25)         | 7±5              | 5(31.3)                     | 1(25)        |
|                  | Female                      | 5(41)         | 5.5±5            | 4(33.3%)                    | 0            |
| Severity         | Severe                      | 4(36.4%)      | 6±6              | 4(36.4%)                    | 1(50)        |
|                  | Non-severe                  | 5(29.4%)      | 7±7              | 5(29.4%)                    | 0            |
| Cancer activity  | Active                      | 7(31.8%)      | 6±5              | 8(36.4%)                    | N/A          |
|                  | Non-active                  | 2(33.3%)      | 7±13             | 1(16.7%)                    | N/A          |
|                   | Total                       | 9(32)         | 6.50±6           | 9(32.1)                     | 1(20)        |

IQR: Inter Quartile Range, N: Number, Med: Medium

| Table 4. Main Laboratory Findings according to clinical situation |
|---------------------------------------------------------------|
| **Cancer patients**                                           | **Graft patients** |
|---------------------------------------------------------------|-------------------|
| PLT count<150,000                                            | RDW>14.5%         |
| N (%)                                                        | N (%)             | N (%)            |
| Sex                                                          | Male              | Female           |
|                                                             | 11(68%)           | 7(63.6%)         |
|                                                             | 11(68.8%)         | 6(50%)           |
| Exact sig                                                    | 1.00              | 0.441            |
| Severity                                                     | Severe            | Non-severe       |
|                                                             | 8(72.7%)          | 10(62.5%)        |
|                                                             | 8(72.7%)          | 9(52.9%)         |
| Exact sig                                                    | 0.692             | 0.435            |
| Cancer activity                                              | Active            | Non-active       |
|                                                             | 15(71.4%)         | 3(50%)           |
|                                                             | 15(68.2%)         | 2(33.3%)         |
| Exact sig                                                    | 0.305             | 0.174            |

PLT: Platelets, RDW: Red Distribution Width, N: Number
findings, two variables of sex and \( \text{O}_2 \) saturation were entered the Logistic regression model. Female sex and \( \text{SpO}_2 < 90\% \) increased the chances of admission in ICU. None of the variables could estimate the number of days a patient will spend in the hospital based on clinical conditions and laboratory results at the time of patient admission using linear regression. Comparing active cancer and kidney transplant patients, interesting results were obtained that are shown in Table 5. Mortality and the need for hospitalization in ICU were higher in patients with active cancer, although the difference was not statistically significant (exact sig=0.05). RDW in patients with active cancer was higher than kidney transplant patients (exact sig=0.01).

### Discussion

It was surprising for us that mortality and the need for ICU care were not significantly difference between active and inactive cancer patients. Liu study showed that the anti-tumor treatment did not lead to poorer prognosis in patients with solid tumors diagnosed with COVID-19. Lee study showed that chemotherapy in the past 4 weeks had no significant effect on COVID-19 mortality. In our study, although the rate of mortality and admission in the ICU were higher in patients with active cancer, but there were not statistically significant.

Active hematologic malignancies with COVID-19 had a similar risk of death versus non active hematologic patients. In Shoumariyeh study no significant difference was observed between solid tumor and hematological malignancy in overall survival. Our study shows same result (between GI cancer, non GI cancer and hematologic cancer) but mortality was higher in GI malignancy without statistical significance. In this study among the cancer patients, gastrointestinal was the most frequent type of cancer.

It is noteworthy that in the Ma study; the most common cancer was colorectal (29.7\%), some studies indicated that lung cancer patients were the most common to be infected. Elevated LDH have been observed in the blood of patients with COVID-19, and levels of this enzyme correlate with disease severity. The findings of this study also confirmed this point. Men have a much greater risk of severe acute COVID-19 than women. While in our study, woman had increased risk of admitted to the ICU.

COVID-19 is an immunosuppressant disease. An important question that has not yet been properly answered is: which patient with immunosuppression is more sensitive to COVID-19? Compared with active cancer and kidney transplant patients, interestingly high RDW was significant between the two groups, although the mortality rate was not statistically different, but it was higher in the active cancer group. In Sharma et al. study RDW in COVID-19 patients, was found to be higher than normal patients; however, it had no significant

### Table 5. Comparison of active cancer patients with kidney transplant patients

|                | Active Cancer | Kidney Transplant | p-value |
|----------------|---------------|-------------------|---------|
| ICU admission  | 7(31.8\%)     | 1(20\%)           | 0.52    |
| Mortality      | 8(36.4\%)     | 1(20\%)           | 0.44    |
| RDW>14.5%     | 15(68.2\%)    | 0                 | 0.01    |

ICU: Intensive Care Unit; RDW: Red Distribution Width.
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association with disease severity. In our study, the proportion of severe COVID-19 with active cancer was 31.8% which was also significantly higher than that of the Iranian general population with severe COVID-19 (11%). It seems cancer patients were more likely to be immunosuppressed than kidney transplant patients included in our study and are more susceptible to COVID-19, but why there isn’t a statistical difference between mortality in active cancer and kidney transplant patients? One of the reasons is the presence of associated underlying disease (hypertension and diabetes) that more predispose patients to COVID-19 in most kidney transplant patients. However, we cannot ignore the limitations of our study, the most important of which is the small number of immunosuppressed patients in each group and don’t enrolled other immunocompromised condition.

In conclusion, our data suggest that patients with active cancer generally have severe and more complicated disease. But in our study, there was no higher mortality among patients with active versus inactive cancer in COVID-19. Therefore, it seems logical not to deprive cancer patients who need chemotherapy as basic treatment. The severity of COVID-19 varies in different types of immunosuppressed patients. RDW can be a predictor in these patients, but for clearer results, studies with larger statistical populations should be evaluated.

List of acronyms
ALC - Lymphocyte count
ARDS - acute respiratory distress syndrome
CBC - complete blood count
CLL - Chronic Lymphocytic Leukemia
DM - diabetes mellitus
GBM - Glioblastoma Multiform
GI - Gastrointestinal;
Hb - Hemoglobin
HTN - hypertension
ICU - intensive care unit
LDH - lactate dehydrogenase
Non GI - Non Gastrointestinal
PLT - platelet
RCC - Renal Cell Carcinoma
RDW - red cell distribution width
ROC - receiver operating characteristic
RT-PCR - Reverse transcription polymerase chain reaction
SCC - Squamous Cell Carcinoma
SOT - solid organ transplant
SpO2 - oxygen saturation
WBC - white blood cell

Contributions of Authors
Conceptualization: MM and KK; Methodology: MM, KK and MJ; Data Curation: MJ, SPS and SVAP; Analysis: NJ; Writing, MM and KK; Reviewing and Editing: MM, KK and NJ. All authors have read and agreed to the published version of the manuscript.

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Ethical Publication Statement
We confirm that we have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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