## ORIGINAL PAPERS

# Haemoglobin and red cell distribution width levels in internal medicine patients indicate recurrent hospital admission during COVID-19

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A – Study Design, **B** – Data Collection, **C** – Statistical Analysis, **D** – Data Interpretation, **E** – Manuscript Preparation, **F** – Literature Search, **G** – Funds Collection

**Summary** **Background.** The novel coronavirus pandemic (COVID-19) has caused significant change in the daily life of humans, as well as in access to medical care.

**Objectives.** We aimed to compare the general characteristics, medical diagnoses and laboratory data of patients referred to the outpatient internal medicine clinics of our institution and to observe relevant factors that correlate with the number of hospital admissions in this population.

**Material and methods.** Patients who visited our outpatient clinics of internal medicine between March 2020 and June 2020 were enrolled. Age, gender, medical diagnoses, number of admissions, cause of admission and laboratory parameters on first admission were recorded. Patients who visited outpatient clinics only once were grouped as group I, and patients admitted more than once were grouped as group II. General characteristics and laboratory data of groups I and II were compared.

**Results.** Patients with cancer were more common in group II compared to group I ($p < 000.1$). Haemoglobin (Hb) ($p = 0.001$) was significantly lower, and red cell distribution width (RDW) ($p = 0.007$) was significantly higher in group II compared to group I. RDW was positively ($r = 0.23$, $p < 0.001$) correlated, and Hb inversely ($r = -0.19$, $p < 0.001$) correlated, with the number of hospital admissions in the study population.

**Conclusions.** We think that decreased Hb and increased RDW values in patients during the pandemic should alert physicians for possible recurrent hospital admissions in the near future and may promote taking measures to reduce multiple medical admissions.

**Key words:** COVID-19, red cell distribution width, hemoglobin, internal medicine.

## Background

The novel coronavirus infection (COVID-19), which first emerged in China and rapidly disseminated throughout the entire world, effects the daily living of humans [1]. Patients with COVID-19 may present with fever, cough, myalgia and sore throat [2], which are common symptoms of patients in internal medicine clinics, which physicians deal with in everyday practice. During the COVID-19 outbreak, there were changes in habits, lifestyle and economic life, as well as a reduction in hospital admissions due to other causes [3].

Patients referring to internal medicine outpatient clinics have a wide variety of diagnoses. Patients with haematological, oncological, gastroenterological, nephrological, rheumatological or endocrinological diagnoses are among those that visit internal medicine clinics. Individuals who also want to have a check-up initially apply to these outpatient clinics. However, the COVID-19 pandemic may have also caused changes in the characteristics and the number of patients who referred to internal medicine clinics. For instance, daily access to outpatient internal medicine clinics in our institution was also reduced (more than 200 patients before the pandemic to 60–70 patients during the pandemic).

## Objectives

To address this question, we retrospectively analysed the subjects were admitted to the internal medicine outpatient clinics of our institution during the COVID-19 outbreak. We aimed to compare the general characteristics, medical diagnoses and laboratory data of these patients and to find the factors that correlated with the number of hospital admissions in this population.

## Materials and methods

### Study design and setting

After obtaining ethical approval from the local ethics committee (date: 07.07.2020 number: 2020/164), patients visiting our outpatient clinics of the internal medicine department between March 2020 and June 2020 were enrolled to the study. Age, gender, medical diagnoses, number of admissions, cause of admission (diabetes mellitus, hypertension, endocrinological, nephrological, haematological, oncological, rheumatological, check-up or others) and laboratory parameters on first admis-

sion, including: white blood cell count (WBC), neutrophil count (Neu), lymphocyte count (Lym), eosinophil count (Eos), basophil count (Bas), haemoglobin (Hb), mean corpuscular volume (MCV), red cell distribution width (RDW), platelet count (PLT), aspartate and alanine transaminases (AST and ALT), serum creatinine, blood urea, estimated creatinine clearance (eGFR), fasting plasma glucose (FPG), c-reactive protein (CRP), erythrocyte sedimentation rate (ESR), ferritin, vitamin $B_{12}$, folic acid, vitamin D and thyroid stimulating hormone levels, were obtained from patients' files and the database of the institution and were recorded. Type of cancer was also recorded in subjects with oncological conditions. Patients with incomplete descriptive or laboratory data were excluded from the study.

## Study population

The study population was grouped according to the number of admissions. Patients who visited the outpatient clinics only once were grouped as group I, and patients admitted more than once were grouped as group II. General characteristics and laboratory data of the groups were compared.

## Statistical analyses

Statistical analyses were conducted with SPSS software (SPSS 15.0 for Windows, IBM Co., Chicago, Il, USA). The Kolmogorov-Smirnov test was used to observe whether the study parameters had normal distribution among the study groups or not. Variables without normal distribution were compared with the Mann-Whitney U test and expressed as median (min–max), while variables with normal distribution were compared with the independent samples $t$-Test and expressed as mean ± standard deviation (SD). Categorical variables were compared with the Chi-square test and expressed as percentage. Pearson's correlation analysis test was used to observe any possible correlation between study parameters. Statistical significance was considered when the $p$-value was lower than 0.05.

## Results

After the exclusion criteria applied, the remaining 510 subjects were enrolled in the study. There were 321 and 189 patients in groups I and II, respectively. The mean age of the patients in group I and II was 52 ± 16 and 54 ± 14 years, respectively ($p = 0.13$). 161 (50.2%) of the subjects in group I were

women, and 160 (49.8%) were men, while 102 (54%) of the subjects in group II were women, and 87 (46%) were men ($p = 0.41$). The number of admissions in group I and II were 1 (1–1) and 3 (2–12), respectively ($p < 0.001$).

Some of the diagnoses of the participants include diabetes mellitus in 53 of those in group I and 17 of those in group II, hypertension in 19 of group I and 4 of group II, cancer in 52 of group I and 113 of group II, inflammatory bowel disease in 9 of group I and 5 of group II, thyroid conditions in 16 of group I and 8 of group II, rheumatoid arthritis in 9 of group I and 2 of group II, chronic kidney disease in 9 of group I and 1 of group II, dyspepsia in 37 of group I and 7 of group II, and myalgia in 10 of group I and 3 of group II.

The median base ($p = 0.13$), MCV ($p = 0.43$), plt ($p = 0.25$), AST ($p = 0.28$), blood urea ($p = 0.67$), FPG ($p = 0.07$), CRP ($p = 0.1$), folic acid ($p = 0.08$), vitamin D ($p = 0.18$), ferritin ($p = 0.27$) and ESR ($p = 0.18$), levels of the group I and II were not statistically different. On the other hand, WBC ($p = 0.001$), neu ($p = 0.003$), lym ($p = 0.01$), eos ($p = 0.002$), Hb ($p = 0.001$), RDW ($p = 0.007$), ALT ($p = 0.02$), serum creatinine ($p < 0.001$), GFR ($p = 0.04$), vitamin $B_{12}$ ($p = 0.03$) and TSH ($p = 0.007$) levels of the subjects in group I were significantly different from those in group II. Table 1 shows the characteristics and the laboratory parameters of the study groups.

Reasons for admission were diabetes mellitus in 53 (16.5%) in group I and 17 (9%) in group II, hypertension in 19 (5.9%) in group I and 4 (2.1%) in group II, oncological causes in 52 (16.2%) in group I and 113 (59.8%) in group II, gastrointestinal causes in 61 (19%) in group I and 17 (9%) in group II, rheumatological causes in 25 (7.8%) in group I and 9 (4.8%) in group II, endocrine causes in 28 (8.7%) in group I and 13 (6.9%) in group II, nephrological causes in 11 (3.4%) in group I and 1 (0.5%) in group II, haematological causes in 16 (5%) in group I and 8 (4.2%) in group II, infection in 7 (2.2%) in group I and 1 (0.5%) in group II, routine check-up in 29 (9%) in group I and 1 (0.5%) in group II, and miscellaneous causes in 20 (6.2%) in group I and 5 (2.6%) in group II ($p < 0.001$). Gastrointestinal disorders, diabetes mellitus and oncological disorders were the most common reasons for admission in group I, while oncological pathologies were by far the most common reason for admission in group II.

The number of admissions to outpatient internal medicine clinics during the COVID-19 outbreak was significantly and positively correlated with RDW ($r = 0.23$, $p < 0.001$) and inversely correlated with blood Hb level ($r = -0.19$, $p < 0.001$). Figures 1 and 2 show the correlation between the number of admissions and Hb and between the number of admissions and RDW, respectively.

| Table 1. Characteristics and laboratory parameters the study groups | | | | |
|---|---|---|---|---|
| | | **Group I** | **Group II** | **p** |
| Gender | women (*n*, %) | 161 (50.2) | 102 (54) | 0.41 |
| | men (*n*, %) | 160 (49,8) | 87 (46) | |
| | | **Mean ± SD** | | |
| Age (years) | | 52 ± 16 | 54 ± 14 | 0.13 |
| | | **Median (min–max)** | | |
| Admissions (*n*) | | 1 (1–1) | 3 (2–12) | < 0.001 |
| WBC (k/mm³) | | 7 (1.16–20) | 6.7 (2–37) | 0.001 |
| Neu (k/mm³) | | 4.5 (0.1–17) | 4.1 (0.6–33) | 0.003 |
| Lym (k/mm³) | | 1.86 (0.15–11) | 1.79 (0.24–12) | 0.01 |
| Eos (k/mm³) | | 0.16 (0.01–1.5) | 0.12 (0.01–1.97) | 0.002 |
| Hb (g/dL) | | 13 (5–18) | 12.4 (7.3–17.8) | 0.001 |
| RDW (%) | | 14.9 (12–22) | 16.9 (12–28) | 0.007 |
| ALT (u/L) | | 23 (6–81) | 19 (6–213) | 0.02 |
| Creatinine (mg/dL) | | 0.82 (0.13–9) | 0.79 (0.3–6.7) | < 0.001 |
| GFR (%) | | 88 (5–131) | 90 (8–135) | 0.04 |
| Vitamin $B_{12}$ (ng/L) | | 315 (118–793) | 374 (83–616) | 0.03 |
| TSH (uIU/mL) | | 1.5 (0.001–45) | 2 (0.001–71) | 0.007 |
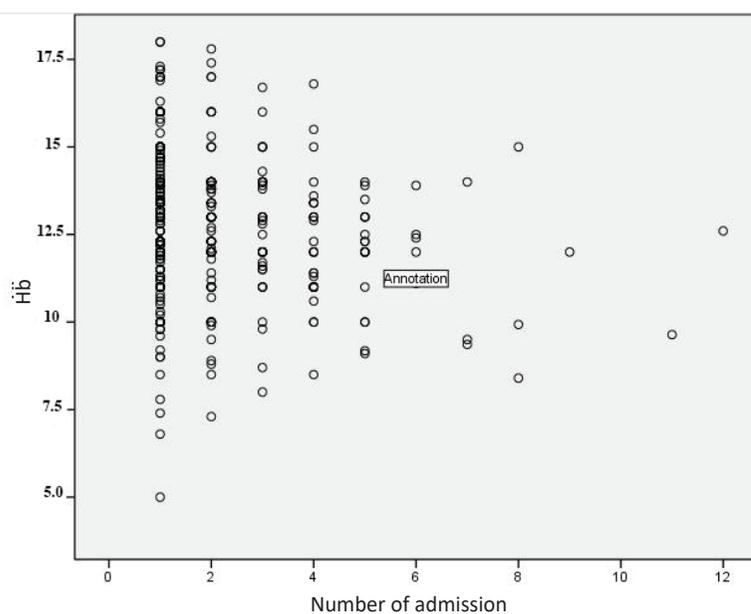
**Figure 1.** Relationship between Hb level and the number of hospital admissions
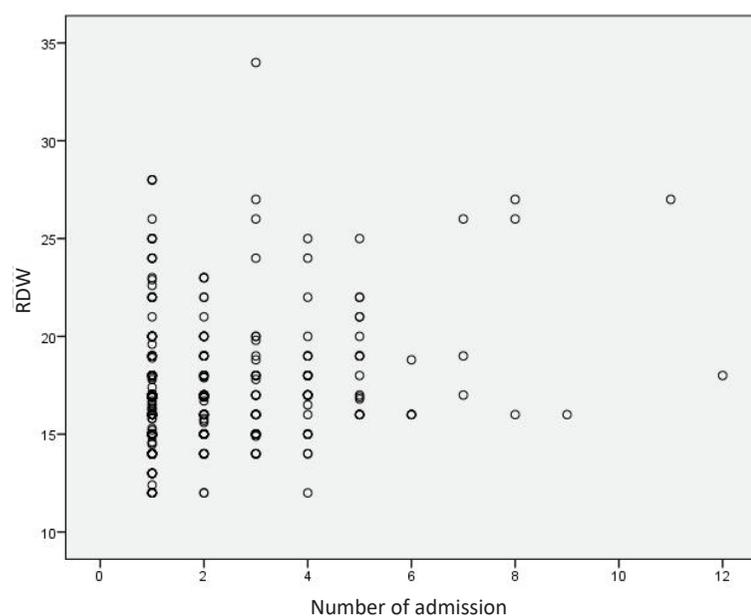


**Figure 2.** Relationship between RDW level and the number of hospital admissions

## Discussion

The striking results of the present study indicated that patients with oncological conditions make up the majority of subjects with multiple hospital admissions during the pandemic era. Another important outcome of our study was that initial Hb and RDW levels could predict repeat hospital admissions during the COVID-19 outbreak.

Health facilities are the front line of the war against COVID-19. Therefore, patients with chronic conditions are hesitant to make regular clinical visits, as they previously would have done. This reduction in healthcare services is mainly due to the fear of becoming infected [4]. Studies during previous coronavirus epidemics have shown that seeking health care by inpatient and outpatient patients remained low almost 4 years after the resolution of the epidemic [5]. Similar results have been reported during the novel coronavirus pandemic, too. Garcia et al. reported that the activity of the cardiac catheter laboratory was reduced during COVID-19 pandemic [6]. The study by De Rosa et al. reported similar results, which indicated a nearly 50% reduction in hospital admissions due to acute myocardial infarction in Italy during the novel pandemic [7]. In another study in literature, it has been reported that hospital admissions due

to ischemic stroke were reduced by 36% during the pandemic compared to the same time period in 2019 [8]. Not only access to medical care for cardiovascular conditions but also access to surgery for surgical conditions has been reduced in the COVID-19 era. The authors reported that surgical interventions for aortic dissection decreased by 76.5% [9]. Similar to literature, daily access to outpatient internal medicine clinics was reduced to 60–70 patients during the study period from more than 200 patients in pre-pandemic times.

The negative impact on general health caused by reduced access to health care is a well-established issue [10]. Indeed, a recent study reported that the death rate caused by cardiac arrest in the pandemic era has increased fivefold compared to the same time period in 2019 [11]. This situation could be a consequence of delayed or postponed access to medical care, possibly due to the fear of transmission of infection. Despite the extensive anxiety among public to hospital admission, patients with certain conditions had to have access to medical care more than once during the COVID-19 pandemic. In the present study, a majority of the subjects referring to our outpatient clinics had cancer. This was mostly because they had to receive chemotherapy treatments, which are repeated every 3 or 4 weeks.

The second important outcome of our study was the inverse correlation between the number of medical care access and Hb

level and positive correlation between the number of medical care access and RDW level. Decreased levels of Hb were suggested to be associated with a worse outcome in various clinical conditions, such as cancer, heart failure or chronic kidney disease [12–14]. Moreover, better survival has been reported in older and frail nursing home residents with higher Hb levels [15]. In accordance with literature, multiple admissions to hospital were required for the subjects with lower Hb levels in our study.

Many studies in literature have reported the association between RDW and inflammatory status in various conditions [16–23], which is also associated with morbidity and mortality in certain diseases [24–26]. Therefore, the increased necessity of hospital admissions in subjects with higher RDW values reported in our study is similar to that in literature.

### Limitations of the study

The retrospective design and narrow period of time (3 months) are limitations of our study. The single centre nature of the study could be a third limitation that is worth mentioning. This is the first study to reveal that most of the patients who need to be admitted to the hospital more than once during the COVID-19 epidemic are patients with oncological diseases. Moreover, this is also the first report that established a significant negative correlation between the number of hospital admission and Hb levels and a positive correlation between the number of hospital admission and RDW levels.

## Conclusions

We suggest that patients with cancer were more likely to visit outpatient clinics of health institutions multiple times during the outbreak of the novel coronavirus. Moreover, decreased Hb and increased RDW values in a patients during the pandemic should alert physicians to possible recurrent hospital admissions in the near future and may promote taking measures to reduce multiple medical admissions.

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