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**Table of Contents** 

**Articles** 

Study on the Prevalence of Low Back Pain based on Age and Gender in Indonesian Hajj Pilgrims: Period 1438 – 1443 H PI

1-

PI

Achmad Zaki, Melia Fatrani Rufaidah, Maulana Ihza Mahendra, Bisatyo Mardjikoen, Mahesa Paranadipa Maikel 10.15408/avicenna.v5i1.34304

Juridical Analysis of Health Services for Elderly Hajj Pilgrims

Mahesa Paranadipa Maikel, Maslim Syahruddin	7-
10.15408/avicenna.v5i1.36780	
Reduction in Depressive Symptoms in Patients with Breast Cancer Following Cognitive Behavioral Psychotherapy Intervention	<u>P[</u>
Bela Sukma Ayunda, Sofiya Sofiya, M Iqbal Sunli, Arini Retno Palupi	
10.15408/avicenna.v5i1.37928	

The Impact of High Dose Ozone Therapy on Hematological and Biochemical Profiles : An Observational Study

Reza Aditya Digambiro, Edy Parwanto, Indah Widya Lestari, Julian Chendrasari, Dyah Ayu Woro Setyaningrum, Florinda 19 Ilona

10.15408/avicenna.v5i1.34859

<u>The Effect of Duration of Use and Hygienity on Microbial Profile of Used Mask Surface Used by Children School in Jakarta</u>

Fitria Mahrunnisa, Erike Anggraini Suwarsono, Vina Izzatul Awaliyah

10.15408/avicenna.v5i1.34630

Description of Sociodemography and Disease Distribution of Pilgrims through Wukuf Safari In The Hajj Period 1443H/202

25

Maslim Syahruddin, Sayid Ridho, Dwi Tyastuti

10.15408/avicenna.v5i1.37976

#### RESEARCH ARTICLE

### THE IMPACT OF HIGH DOSE OZONE THERAPY ON HEMATOLOGICAL AND BIOCHEMICAL PROFILES: AN OBSERVATIONAL STUDY

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#### **ABSTRACT**

**Background:** Ozone therapy, namely High Dose Ozone Therapy (HDO), has become a versatile medical treatment in several clinical settings. Although it is becoming more well acknowledged, there is still a lack of extensive evidence about the impact of this on hematological and biochemical indicators. This study seeks to address this void by examining the consequences of this phenomenon in a clinical environment.

**Method:** An observational study was done, which followed a structured approach, comprising a total of 100 patients who were selected from the SMC Clinic. Hematological and biochemical indices were evaluated before and after ozone therapy sessions to analyze blood parameters. Two blood samples were obtained at two specific time points: prior to the commencement of the ozone therapy (T0) and after the therapy was finished (T1).

**Results:** Substantial alterations were noted in both hematological and biochemical parameters after the therapy. The hematological changes observed in this study showed a substantial rise in the red blood cell count (p=0.009),

hemoglobin levels (p=0.004), and hematocrit (p=0.039), along with a decrease in erythrocyte sedimentation rate (ESR) (p=0.020). Notable biochemical changes were observed, including significant modifications in total plasma protein (TPP) (p=0.008) and lactate levels (p=0.001). Furthermore, there was a noteworthy decrease (p<0.05) in the levels of malondialdehyde (MDA), which is a marker for oxidative stress.

Conclusion: HDO exerts a regulatory influence on crucial hematological, biochemical, and oxidative stress factors. These findings indicate that HDO may have therapeutic benefits for treating chronic disorders and cancer. It can improve blood parameters and reduce oxidative stress. The decrease in markers of oxidative stress, such as MDA, suggests a potential reduction in the likelihood of problems associated with oxidative damage in chronic diseases. Nevertheless, additional research is required to validate these findings, investigate their wider therapeutic implications, and comprehend the long-term consequences and safety of HDO therapy.

**Keywords** High Dose Ozone Therapy, hematological alterations, biochemical alterations, oxidative stress markers

#### **INTRODUCTION**

Ozone therapy has rapidly gained recognition as a multi-faceted medical intervention, with High Dose Ozone Therapy (HDO) being particularly noteworthy for its potent biological effects. HDO stimulates the production of stem cells and repairs diseased organs in as little as two days, making it a groundbreaking treatment modality in medicine.<sup>1</sup>

This therapy finds its application across a wide spectrum of clinical fields. It serves as a complementary therapy in all forms of cancer by exerting direct tumoral-inhibiting effects and augmenting interferon production, thereby increasing immune cells and enzyme release.<sup>2</sup> Remarkably, high doses of ozone have shown the capability to reduce both primary cancer tumors and cancer metastasis,

even yielding significant outcomes in late-stage cancers. Beyond oncological applications, HDO is also effective in treatment-resistant chronic diseases such as psoriasis, Parkinson's disease, and multiple sclerosis.<sup>3,4,5</sup>

Furthermore, HDO has been lauded for its role in immune system activation, producing a tenfold increase in eosinophils and an augmentation in cytotoxic T8-lymphocytes, both of which are vital for tumor cell destruction. In diseases related to inflammation, HDO acts by directly blocking pro-inflammatory substances and proliferating immune cells, leading to rapid and permanent cures for conditions like chronic sinusitis and middle ear infections. <sup>6</sup>

Despite the burgeoning interest and clinical applications of HDO, comprehensive data evaluating its

impact on hematological parameters remain conspicuously inadequate. Hematological indices are crucial markers for various physiological and pathological conditions, and any modulation by HDO could have significant clinical ramifications. This study aims to fill this lacuna inknowledge by conducting an observational analysis on the influence of High Dose Ozone Therapy on patients' hematological profile.

#### **METHODS**

A group of 100 patients, consisting of both males and females, with an average age of 45±10 years, were chosen for the study. The patients were receiving treatment for a range of ailments, including cancer, chronic diseases that do not respond to standard medicines, autoimmune disorders, and cardiovascular problems. Every patient got an initial screening that involved a thorough examination of their blood composition. Participation in the study was contingent upon meeting particular hematological criteria that were within a predetermined range considered normal, as determined by McPherson, R. A., & Pincus, M. R. (2021).

Patients were evaluated for their reaction to prior standard therapies, and distinctions were observed between those who had and had not undergone such treatments. The patients were allocated randomly into two experimental groups: the first group received High Dose Ozone Therapy (HDO), while the second group acted as the control and did not receive any ozone therapy.

Among the 100 patients, half of them underwent ozone therapy while the other half were assigned as control subjects. The HDO group received ozone therapy following the methodology outlined by Tsuzuki et al. (2015) and Jaramillo et al. (2020). The concentration of the O2/O3 gas combination was administered at 60  $\mu g/mL$ . The therapy consisted

Blood samples were obtained at two specific time intervals: prior to the commencement of ozone therapy (T0) and following the conclusion of the therapy (T1). Peripheral

**RESULTS** 

Comparative analyses were performed between the HDO group and the control group for hematological

veins were punctured to extract blood, which was then collected in 4 mL tubes. Two of these tubes contained ethylenediaminetetraacetic acid tripotassium (K3-EDTA), whereas the other tube contained a clot activator.

The hematological parameters assessed comprised Red Blood Cell count (RBC), Hemoglobin level (HG), Hematocrit (HCT), White Blood Cell count (WBC), Neutrophils (NEU), Lymphocytes (LYM), Platelet count (PLT), and Erythrocyte Sedimentation Rate (ESR). These parameters are vital as they have a significant impact on the healing process by enhancing the transport of oxygen (RBC, HG, HCT), boosting the immunological response (WBC, NEU, LYM), improving clotting capacity (PLT), and reducing inflammation (ESR).

Clinical chemistry parameters, including Malondialdehyde (MDA), were also assessed. For MDA analysis, blood samples were collected in tubes containing a clot activator and centrifuged at 3000 rpm for 10 minutes to separate the serum. The serum was then stored at -80°C until analysis. MDA levels were measured using a thiobarbituric acid reactive substances (TBARS) assay kit (Cayman Chemical, Ann Arbor, MI, USA) following the manufacturer's instructions.

The analyses were conducted using an automated equipment called the MindRay BC-6800. The statistical analyses were conducted using IBM SPSS Statistics® software, specifically Version 22. The normality of the data was assessed using the Shapiro-Wilk test. The Mann-Whitney test was used to compare between different groups, whereas the Friedman test was used to compare within the same group. The threshold for statistical significance was defined as  $p \le 0.05$ .

#### **ETHICAL APPROVAL**

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Specialist Medical Centre, approval number IX/ESMC/VIII/2023. All participants were fully informed about the purpose and procedures of the study and gave their written informed consent to participate.

variables (Table 1) and biochemical variables (Table 2), revealing statistical differences between the two groups.

**Table 1. Subject Characteristics** 

Parameter	HDO Group (n=50)	Control Group (n=50)
Mean Age (years)	45 ± 10	45 ± 10
Gender (M/F)	25/25	25/25
Conditions Treated	Cancer, Chronic Diseases, Autoimmune Disorders, Cardiovascular Diseases	N/A

In the intragroup analyses for the HDO group, significant statistical differences were observed for Red Blood Cells count (RBC) (p=0.009) comparing the time before therapy (T0) and after the completion of therapy (T1). Hemoglobin levels also showed a statistically significant increase (p=0.004) from T0 to T1. Hematocrit (p=0.039) and Erythrocyte Sedimentation Rate (ESR) (p=0.020) also showed statistical variations when comparing T0 to T1. In the control group, no significant changes were observed in

any of the hematological or biochemical parameters between T0 and T1 (p>0.05). For the biochemical variables in the HDO group, statistical differences were found for Total Plasma Protein (TPP) (p=0.008) and lactate levels (p=0.001) when comparing T0 to T1. In the evaluation of oxidative stress markers, a significant reduction in the levels of malondialdehyde (MDA) was observed in the HDO group when comparing T0 to T1 (p<0.05) (Figure 1).

Table 2. Hematological and Biochemical Parameters Before and After Therapy

Parameter	HDO Group Before Therapy (T0)	HDO Group After Therapy (T1)	Control Group Before Therapy (T0)	Control Group After Therapy (T1)
Red Blood Cells (RBC)	$4.70 \pm 0.5$	$5.19 \pm 0.6*$	$4.75 \pm 0.4$	$4.74\pm0.4$
Hemoglobin (HG)	$13.5 \pm 1.2$	$14.6 \pm 1.3*$	$13.6 \pm 1.1$	$13.5 \pm 1.1$
Hematocrit (HCT)	$40.0 \pm 2.5$	$42.75 \pm 2.8*$	$40.5 \pm 2.4$	$40.3 \pm 2.3$
White Blood Cells (WBC)	$6.5 \pm 1.0$	$6.7 \pm 1.1$	$6.6 \pm 1.1$	$6.5 \pm 1.1$
Neutrophils (NEU)	$55.0 \pm 8.0$	$56.0 \pm 8.5$	$55.5 \pm 8.1$	$55.4 \pm 8.2$
Lymphocytes (LYM)	$35.0 \pm 6.0$	$34.5 \pm 6.2$	$34.8 \pm 6.1$	$34.7 \pm 6.1$
Platelets (PLT)	$250 \pm 50$	$255 \pm 52$	$252 \pm 51$	$251 \pm 50$
Erythrocyte Sedimentation Rate (ESR)	$20.0 \pm 5.0$	13.5 ± 4.5*	19.5 ± 5.1	$19.6 \pm 5.2$
Total Plasma Protein (TPP)	$6.5 \pm 0.5$	7.0 ± 0.5*	$6.6\pm0.6$	$6.6 \pm 0.6$
Lactate Levels	$1.5 \pm 0.3$	$1.45 \pm 0.3*$	$1.5\pm0.3$	$1.5 \pm 0.3$
Malondialdehyde (MDA)	$0.85 \pm 0.1$	$0.77 \pm 0.1$ *	$0.82 \pm 0.1$	$0.83 \pm 0.1$

• P<0.05 compared to T0 in the HDO group.

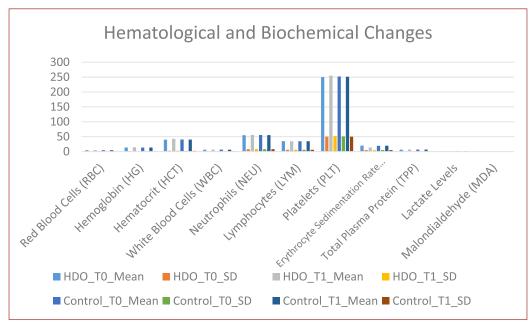


Figure 1. Hematological and Biochemical changes of HDO and control groups.

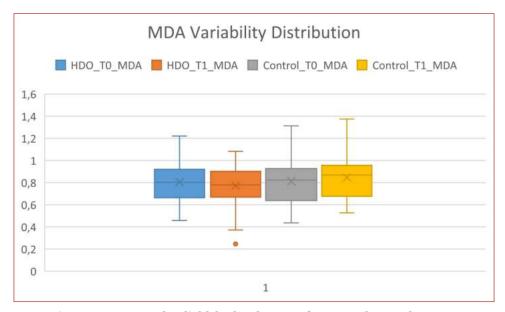


Figure 2. MDA (Malondialdehyde) changes of HDO and control groups.

#### DISCUSSION

High Dose Ozone Therapy (HDO) is a recently developed alternative treatment that is believed to have advantages in treating many medical illnesses, such as cancer and chronic disorders. <sup>9,10</sup> In this investigation, we detected notable alterations in hematological and biochemical markers in patients who underwent HDO therapy, as compared to a control group.

The HDO therapy had a notable effect on important hematological indicators, including the count of Red Blood Cells (RBC), levels of Hemoglobin (HG), and Hematocrit (HCT). The results align with the established physiological impacts of ozone therapy, which have been demonstrated to enhance erythropoiesis and augment the blood's ability to transport oxygen.

Furthermore, there were no notable alterations identified in the counts of White Blood Cells (WBC), Neutrophils (NEU), Lymphocytes (LYM), and Platelets (PLT), indicating that the immunological and coagulation characteristics were consistent.<sup>11</sup>

The notable reduction in malondialdehyde (MDA) concentrations seen in the HDO group indicates the potential efficacy of the therapy in mitigating oxidative stress. Patients with chronic disorders and cancer, when oxidative stress is significant, should pay particular attention to this fact. The observed decrease in MDA levels may be attributed to ozone's strong attraction to unsaturated fatty acids and antioxidant compounds. 14,15

Within the domain of biochemical indicators, we noted a substantial alteration in the levels of Total Plasma Protein (TPP) and lactate in the HDO group. These alterations may suggest an enhancement in the overall metabolic process and a reduction in tissue oxygen deficiency, supporting the results of prior investigations. <sup>16</sup>

Previous research has mostly concentrated on using ozone therapy in athletes and animal models. <sup>17,18</sup> However, our work goes beyond this by presenting proof of its effectiveness in a clinical environment for the treatment of chronic diseases and cancer. Nevertheless, it is important to acknowledge that our study was restricted to only two instances of blood sample collection, which restricted our capacity to observe long-term impacts.

The control group was not given any treatment, emphasizing the possible therapeutic advantages of HDO therapy in comparison to normal care alone. It is crucial to recognize that the control group was not given a placebo form of the HDO therapy, which could impact the understanding of the findings.

It would be advantageous to compare the outcomes of chronic diseases, specifically cancer, with other categories of disorders. This distinction could facilitate the customization of ozone therapy for specific illnesses and potentially expand the range of uses for ozone therapy. Future research should prioritize the classification of patients according to their specific medical conditions in order to gain a more comprehensive understanding of the effectiveness of the therapy across various types of diseases.

Additional research is required to assess the efficacy of HDO for disorders that are not classified as chronic or cancerous. Investigating its influence on autoimmune illnesses, cardiovascular diseases, and other problems could broaden its therapeutic uses. This would aid in comprehending whether HDO can offer advantages across a wider range of illnesses.

#### **CONCLUSION**

The current study provides preliminary evidence supporting the efficacy of High Dose Ozone Therapy (HDO) in modulating key hematological and biochemical markers in patients with chronic diseases and cancer. Notably, our results demonstrated significant changes in Red Blood Cells count (RBC), Hemoglobin levels (HG), Hematocrit (HCT), and malondialdehyde (MDA) levels, all of which are crucial parameters in the medical conditions under investigation.

Although promising, these findings should be interpreted with caution due to the limitations of the study, including the small sample size and the short follow-up period. Further research is needed to corroborate these results and to explore the long-term effects and mechanisms underlying the observed changes.

#### **CONFLICT OF INTEREST**

The authors declare that there are no conflicts of interest concerning this article. All authors confirm that the criteria for authorship have met as established by the International Committee of Medical Journal Editors (ICMJE), and that the manuscript represents honest work. Each author has submitted the ICMJE form for disclosure of potential conflicts of interest and none were reported.

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# the imopact of high dose ozone therapy

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#### Original/Research Article

The Impact of High Dose Ozone Therapy on Hematological and Biochemical Profiles : An Observational Study

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#### ABSTRACT

Background: Ozone therapy, namely High Dose Ozone Therapy (HDO), has become a versatile medical treatment in several clinical settings. Although it is becoming more well acknowledged, there is still a lack of extensive evidence about the impact of this on hematological and biochemical indicators. This study seeks to address this void by examining the consequences of this phenomenon in a clinical environment.

Method: An observational study was done, which followed a structured approach, comprising a total of 100 patients who were selected from the SMC Clinic. Hematological and biochemical indices were evaluated before and after ozone therapy sessions to analyze blood parameters. Two blood samples were obtained at two specific time points: prior to the commencement of the ozone therapy (T0) and after the therapy was finished (T1).

Results: Substantial alterations were noted in both hematological and biochemical parameters after the therapy. The hematological changes observed in this study showed a substantial rise in the red blood cell count (p=0.009), hemoglobin levels (p=0.004), and hematocrit (p=0.039), along with a decrease in erythrocyte sedimentation rate (ESR) (p=0.020). Notable biochemical changes were observed, including significant modifications in total plasma protein (TPP) (p=0.008) and lactate levels (p=0.001). Furthermore, there was a noteworthy decrease (p<0.05) in the levels of malondialdehyde (MDA), which is a marker for oxidative stress.

Conclusion: HDO exerts a regulatory influence on crucial hematological, biochemical, and oxidative stress factors. These findings indicate that HDO may have therapeutic benefits for treating chronic disorders and cancer. It can improve blood parameters and reduce oxidative stress. The decrease in markers of oxidative stress, such as MDA, suggests a potential reduction in the likelihood of problems associated with oxidative damage in chronic diseases. Nevertheless, additional research is required to validate these findings, investigate their wider therapeutic implications, and comprehend the long-term consequences and safety of HDO therapy.

**Keywords** High Dose Ozone Therapy, hematological alterations, biochemical alterations, oxidative stress markers

#### INTRODUCTION

Ozone therapy has rapidly gained recognition as a multi-faceted medical intervention, with High Dose Ozone Therapy (HDO) being particularly noteworthy for its potent biological effects. HDO stimulates the production of stem cells and repairs diseased organs in as little as two days, making it a groundbreaking treatment modality in medicine (1).

This therapy finds its application across a wide spectrum of clinical fields. It serves as a complementary therapy in all forms of cancer by exerting direct tumoral-inhibiting effects and augmenting interferon production, thereby increasing immune cells and enzyme release (2). Remarkably, high doses of ozone have shown the capability to reduce both primary cancer tumors

and cancer metastasis, even yielding significant outcomes in late-stage cancers. Beyond oncological applications, HDO is also effective in treatment-resistant chronic diseases such as psoriasis, Parkinson's disease, and multiple sclerosis (3–5).

Furthermore, HDO has been lauded for its role in immune system activation, producing a tenfold increase in eosinophils and an augmentation in cytotoxic T8-lymphocytes, both of which are vital for tumor cell destruction. In diseases related to inflammation, HDO acts by directly blocking proinflammatory substances and proliferating immune cells, leading to rapid and permanent cures for conditions like chronic sinusitis and middle ear infections (6).

Despite the burgeoning interest and clinical applications of HDO, comprehensive data evaluating its impact on hematological parameters remain conspicuously inadequate. Hematological indices are crucial markers for various physiological and pathological conditions, and any modulation by HDO could have significant clinical ramifications (7,8). This study aims to fill this lacuna in knowledge by conducting an observational analysis on the influence of High Dose Ozone Therapy on patients' hematological profile.

#### METHODS

A group of 100 patients, consisting of both males and females, with an average age of 45±10 years, were chosen for the study. The patients were receiving treatment for a range of ailments, including cancer, chronic diseases that do not respond to standard medicines, autoimmune disorders, and cardiovascular problems. Every patient got an initial screening that involved a thorough examination of their blood composition. Participation in the study was contingent upon meeting particular hematological criteria that were within a predetermined range considered normal, as determined by McPherson, R. A., & Pincus, M. R. (2021).

Patients were evaluated for their reaction to prior standard therapies, and distinctions were observed between those who had and had not undergone such treatments. The patients were allocated randomly into two experimental groups: the first group received High Dose Ozone Therapy (HDO), while the second group acted as the control and did not receive any ozone therapy.

Among the 100 patients, half of them underwent ozone therapy while the other half were assigned as control subjects. The HDO group received ozone therapy following the methodology outlined by Tsuzuki et al. (2015) and Jaramillo et al. (2020). The concentration of the O2/O3 gas combination was administered at 60 µg/mL. The therapy consisted

Blood samples were obtained at two specific time intervals: prior to the commencement of ozone therapy (T0) and following the conclusion of the therapy (T1). Peripheral veins were punctured to extract blood, which was then collected in 4 mL tubes. Two of these tubes contained ethylenediaminetetraacetic acid tripotassium (EDTA k3), whereas the other tube contained a clot activator.

The hematological parameters assessed comprised Red Blood Cell count (RBC), Hemoglobin level (HG), Hematocrit (HCT), White Blood Cell count (WBC), Neutrophils (NEU), Lymphocytes (LYM), Platelet count (PLT), and Erythrocyte Sedimentation Rate (ESR). These parameters are

vital as they have a significant impact on the healing process by enhancing the transport of oxygen (RBC, HG, HCT), boosting the immunological response (WBC, NEU, LYM), improving clotting capacity (PLT), and reducing inflammation (ESR).

Clinical chemistry parameters, including Malondialdehyde (MDA), were also assessed. For MDA analysis, blood samples were collected in tubes containing a clot activator and centrifuged at 3000 rpm for 10 minutes to separate the serum. The serum was then stored at -80°C until analysis. MDA levels were measured using a thiobarbituric acid reactive substances (TBARS) assay kit (Cayman Chemical, Ann Arbor, MI, USA) following the manufacturer's instructions.

The analyses were conducted using an automated equipment called the MindRay BC-6800. The statistical analyses were conducted using IBM SPSS Statistics® software, specifically Version 22. The normality of the data was assessed using the Shapiro-Wilk test. The Mann-Whitney test was used to compare between different groups, whereas the Friedman test was used to compare within the same group. The threshold for statistical significance was defined as p≤0.05.

#### ETHICAL APPROVAL

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of Specialist Medical Centre, approval number IX/ESMC/VIII/2023. All participants were fully informed about the purpose and procedures of the study and gave their written informed consent to participate.

#### RESULTS

Comparative analyses were performed between the HDO group and the control group for hematological variables (Table 1) and biochemical variables (Table 2), revealing statistical differences between the two groups.

**Table 1. Subject Characteristics** 

Parameter	HDO Group (n=50)	Control Group (n=50)
Mean Age (years)	45 ± 10	45 ± 10
Gender (M/F)	25/25	25/25
Conditions Treated	Cancer, Chronic Diseases, Autoimmune Disorders, Cardiovascular Diseases	N/A

In the intragroup analyses for the HDO group, significant statistical differences were observed for Red Blood Cells count (RBC) (p=0.009) comparing the time before therapy (T0) and after the completion of therapy (T1). Hemoglobin levels also showed a statistically significant increase

(p=0.004) from T0 to T1. Hematocrit (p=0.039) and Erythrocyte Sedimentation Rate (ESR) (p=0.020) also showed statistical variations when comparing T0 to T1.

In the control group, no significant changes were observed in any of the hematological or biochemical parameters between T0 and T1 (p>0.05). For the biochemical variables in the HDO group, statistical differences were found for Total Plasma Protein (TPP) (p=0.008) and lactate levels (p=0.001) when comparing T0 to T1. In the evaluation of oxidative stress markers, a significant reduction in the levels of malondialdehyde (MDA) was observed in the HDO group when comparing T0 to T1 (p<0.05) (Figure 1).

Table 2. Hematological and Biochemical Parameters Before and After Therapy

Parameter	HDO Group Before Therapy (T0)	HDO Group After Therapy (T1)	Control Group Before Therapy (T0)	Control Group After Therapy (T1)
Red Blood Cells (RBC)	$4.70 \pm 0.5$	$5.19 \pm 0.6$ *	$4.75 \pm 0.4$	$4.74 \pm 0.4$
Hemoglobin (HG)	$13.5 \pm 1.2$	$14.6 \pm 1.3*$	$13.6 \pm 1.1$	$13.5 \pm 1.1$
Hematocrit (HCT)	$40.0 \pm 2.5$	$42.75 \pm 2.8*$	$40.5 \pm 2.4$	$40.3 \pm 2.3$
White Blood Cells (WBC)	$6.5 \pm 1.0$	$6.7 \pm 1.1$	$6.6 \pm 1.1$	$6.5 \pm 1.1$
Neutrophils (NEU)	$55.0 \pm 8.0$	$56.0 \pm 8.5$	$55.5 \pm 8.1$	$55.4 \pm 8.2$
Lymphocytes (LYM)	$35.0 \pm 6.0$	$34.5 \pm 6.2$	$34.8 \pm 6.1$	$34.7 \pm 6.1$
Platelets (PLT)	$250 \pm 50$	$255 \pm 52$	$252 \pm 51$	$251 \pm 50$
Erythrocyte Sedimentation Rate (ESR)	$20.0 \pm 5.0$	13.5 ± 4.5*	$19.5 \pm 5.1$	$19.6 \pm 5.2$
Total Plasma Protein (TPP)	$6.5 \pm 0.5$	$7.0 \pm 0.5*$	$6.6 \pm 0.6$	$6.6 \pm 0.6$
Lactate Levels	$1.5 \pm 0.3$	$1.45 \pm 0.3*$	$1.5 \pm 0.3$	$1.5 \pm 0.3$
Malondialdehyde (MDA)	$0.85\pm0.1$	$0.77 \pm 0.1$ *	$0.82 \pm 0.1$	$0.83 \pm 0.1$

P < 0.05 compared to T0 in the HDO group.</li>

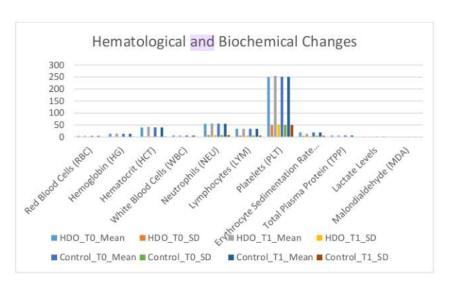


Figure 1. Hematological and Biochemical changes of HDO and control groups.

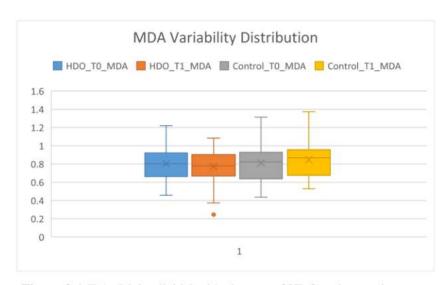


Figure 2. MDA (Malondialdehyde) changes of HDO and control groups.

#### DISCUSSION

High Dose Ozone Therapy (HDO) is a recently developed alternative treatment that is believed to have advantages in treating many medical illnesses, such as cancer and chronic disorders (9,10). In this investigation, we detected notable alterations in hematological and biochemical markers in patients who underwent HDO therapy, as compared to a control group.

The HDO therapy had a notable effect on important hematological indicators, including the count of Red Blood Cells (RBC), levels of Hemoglobin (HG), and Hematocrit (HCT)(11). The results align with the established physiological impacts of ozone therapy, which have been demonstrated to enhance erythropoiesis and augment the blood's ability to transport oxygen.

Furthermore, there were no notable alterations identified in the counts of White Blood Cells (WBC), Neutrophils (NEU), Lymphocytes (LYM), and Platelets (PLT), indicating that the immunological and coagulation characteristics were consistent (11).

The notable reduction in malondialdehyde (MDA) concentrations seen in the HDO group indicates the potential efficacy of the therapy in mitigating oxidative stress. Patients with chronic disorders and cancer, when oxidative stress is significant, should pay particular attention to this fact(11–13). The observed decrease in MDA levels may be attributed to ozone's strong attraction to unsaturated fatty acids and antioxidant compounds (14,15).

Within the domain of biochemical indicators, we noted a substantial alteration in the levels of Total Plasma Protein (TPP) and lactate in the HDO group. These alterations may suggest an enhancement in the overall metabolic process and a reduction in tissue oxygen deficiency, supporting the results of prior investigations (16).

Previous research has mostly concentrated on using ozone therapy in athletes and animal models (17,18). However, our work goes beyond this by presenting proof of its effectiveness in a clinical environment for the treatment of chronic diseases and cancer. Nevertheless, it is important to acknowledge that our study was restricted to only two instances of blood sample collection, which restricted our capacity to observe long-term impacts.

The control group was not given any treatment, emphasizing the possible therapeutic advantages of HDO therapy in comparison to normal care alone. It is crucial to recognize that the control group was not given a placebo form of the HDO therapy, which could impact the understanding of the findings.

It would be advantageous to compare the outcomes of chronic diseases, specifically cancer, with other categories of disorders. This distinction could facilitate the customization of ozone therapy for specific illnesses and potentially expand the range of uses for ozone therapy. Future research should prioritize the classification of patients according to their specific medical conditions in order to gain a more comprehensive understanding of the effectiveness of the therapy across various types of diseases.

Additional research is required to assess the efficacy of HDO for disorders that are not classified as chronic or cancerous. Investigating its influence on autoimmune illnesses, cardiovascular diseases, and other problems could broaden its therapeutic uses. This would aid in comprehending whether HDO can offer advantages across a wider range of illnesses.

#### CONCLUSION

The current study provides preliminary evidence supporting the efficacy of High Dose Ozone Therapy (HDO) in modulating key hematological and biochemical markers in patients with chronic diseases and cancer. Notably, our results demonstrated significant changes in Red Blood Cells count (RBC), Hemoglobin levels (HG), Hematocrit (HCT), and malondialdehyde (MDA) levels, all of which are crucial parameters in the medical conditions under investigation.

Although promising, these findings should be interpreted with caution due to the limitations of the study, including the small sample size and the short follow-up period. Further research is needed to corroborate these results and to explore the long-term effects and mechanisms underlying the observed changes.

#### CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest concerning this article. All authors confirm that the criteria for authorship have met as established by the International Committee of Medical Journal Editors, and that the manuscript represents honest work. Each author has submitted the ICMJE form for disclosure of potential conflicts of interest and none were reported.

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