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ORIGINAL ARTICLE

Effect of Plasma Rich Protein Use in Post (COVID 19) Anosmic Patients

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ABSTRACT

Background: Olfactory neural epithelium and olfactory filae can regenerate, making them potential candidates for therapeutic intervention in individuals with olfactory impairment. Platelet-rich plasma (PRP) is an autologous biologic product made from freshly obtained whole blood that has a high platelet content. In a variety of therapeutic contexts, it has been utilized as a secure and effective treatment for peripheral neuropathies, inflammation, and wound healing. The aim of this study was to assess the potential therapeutic effect of platelet-rich plasma (PRP) in the treatment of post-COVID-19 anosmic patients.**Methods:**This prospective study was conducted in the Otorhinolaryngology Department outpatient clinic at Zagazig University. Included 36 patients all of them were complaining of complete loss of smell (anosmia) post (COVID 19). Experimental group: included 18 patients Platelet-rich plasma preparation. Control group: included 18 patients received placebo. **Results:** Incidence of complete anosmia improvement in experimental group was 77.8% versus 11.1% in control group with relative improvement seven times, $p<0.05$. There was no significant difference of VAS score between groups in after first dose, $p>0.05$. There was no significant difference of VAS score in control group up to (6 weeks) follow $p>0.05$. Yet, there was significant decrease of VAS score in control group after (8 weeks) follow up, $p<0.05$. There is significant and inverse association between platelet count, and mean anosmia score in both group, $p=0.0001$. **Conclusions:** An injection of platelet-rich plasma into the olfactory cleft may be beneficial for patients with post-COVID-19 olfactory anosmia who did not respond to traditional conservative treatment.

Keywords: Olfactory dysfunction; Platelet-rich plasma; COVID-19

INTRODUCTION:

Olfactory dysfunction associated with the coronavirus disease 2019 (COVID-19) is a new issue that has a big influence on the quality of life for those who are affected. Various therapy approaches have been tried, with different degrees of success **[1].** The population's prevalence of olfactory dysfunction (OD) increased because of the coronavirus disease pandemic of 2019 (COVID-19). One of the most prevalent signs of the illness is olfactory impairment, which affects 30% to 86% of patients, depending on variations. Most patients regain their sense of smell during the weeks following the infection, while a small percentage experience mid- to long-term olfactory dysfunction, such as parosmia, phantosmia, hyposmia, or anosmia **[2]**. The COVID-19 virus's functional receptor has been identified as angiotensin-converting enzyme 2 (ACE2). Moreover, TMPRSS2, a priming protease, promotes viral uptake. Numerous organs, including the heart, lungs, kidneys, skeletal muscles, respiratory cells, and central nervous system (CNS), have been shown to contain this receptor. This suggests that the COVID-19 virus can impact up to three organ systems

simultaneously in the human body, leading to multisystem diseases.27, 30 Since the respiratory system's epithelium serves as the major site of coronavirus attachment, the effects of the virus on taste and smell have been expected **[3]**. Possible mechanisms include olfactory cleft syndrome, epithelial olfactory injury, damage to microglial cells, early olfactory cell apoptosis, changes in olfactory cilia and odor transmission, and impact on olfactory bulbs, and damage to olfactory neurons and stem cells **[4]**. Anosmia, the inability to identify smells, can have serious psychological repercussions, including feelings of social and physical victimization. Furthermore, anosmics may experience distress due to the loss of their capacity to recognize delicious food odors, which could lead to eating issues. These severe consequences result from a condition that can develop quickly and have a very low chance of recovery **[5]**. To treat persistent COVID-19-related smell loss, this study assessed the use of platelet-rich plasma (PRP), an autologous blood product with supraphysiologic quantities of growth factors. PRP is commonly utilized in various therapeutic domains and has shown promise in the regeneration of peripheral nerves by regulating the inflammatory response in the microenvironment and stimulating vascular and axonal regeneration using growth factors **[6]**. Platelet-rich plasma (PRP) is an autologous biologic product made from recently taken whole blood that has a high platelet content. One of PRP's anti-inflammatory and pro-regenerative properties is the overexpression of growth factors, such as insulin-like growth factor, transforming growth factor, vascular endothelial growth factor, and epidermal growth factor. In a variety of therapeutic contexts, it has been utilized as a secure and effective treatment for peripheral neuropathies, inflammation, and wound healing **[7]**. PRP has been shown to aid in both axon regeneration and neurodegeneration. In animal tests, anosmia has been treated with growth factors and stem cells, which also help regenerate olfactory neurons in the presence of neurodegenerative processes **[8]**. The purpose of the current study was to evaluate PRP's possible therapeutic impact in the management of patients who had become anosmic after COVID-19.

METHODS

After the approval of the Institutional Review Board (IRB#10506-5-3-2023), this prospective study was performed on eighteen patients recruited from the ENT outpatient clinic in Zagazig University Hospital during the period from March 2023 to September 2023; the mean age was more than 18 years old. All of them were complaining of complete loss of smell (anosmia) post-COVID-19, and eighteen apparently healthy age- and sex-matched controls. Written consent was obtained from each patient before to their involvement in the research. The Helsinki Declaration, the World Medical Association'scode of ethics for human subject's research, was adhered to by the study's protocol. **Inclusion criteria:** age; range >18 years old. Sex: males and females. Patients have anosmia lasting 3 months or more with a history of COVID-19 infection. There are no other reasons for anosmia. I received medical treatment without a response.

Exclusion criteria: age <18 years, infection (Influenza, Atrophic Rhinitis, Sinusitis ….), previous nasal trauma. previous nasal surgery, pathological illness of the nose (Benign& malignant tumors….) and nasal polyps. In the study, patients were divided into two groups. Group I (case group): It included 18 patients with anosmia post-covid 19; the mean age was more than 18 years old and treated with (PRP). Group II (control group): It included 18 apparently healthy people; the mean age was more than 18 years old mean±SD45.33±13.44, The study participants underwent a protocol of evaluation that included obtaining their histories. An analysis of the chief symptoms of the patient was obtained. The main symptom was a loss of smell. Routine examination of the ears, nose, and throat, with an emphasis on thorough nasal examination, every patient underwent anterior rhinoscopy and a nasal flexible fiberoptic nasopharyngeal endoscope, noting any visible congestion,

discharge, polyps, adhesions, or nasal masses. A visual analog scale with a range of 0 to 10 was used to subjectively evaluate the degree of anosmia. On the visual analog scale, a score of 0–1 indicates a total improvement. On the VAS, a score of five indicates a slight improvement, and a score of ten indicates total anosmia.

Platelet-rich plasma preparation for group (1):

The procedures outlined by **Perez et al. [9]**were carried out on each patient with minor adjustments following sterilization. A venipuncture was used to extract 8.5 ml of whole blood from the cubital vein using a wide pore canula, and the blood was collected into a vacutainer that contained acid citrate dextrose (ACD). The blood did not cool before or during platelet separation. To create a "soft" spin, the gathered tubes on the (ACD) were centrifuged by (Hitachi himac CT6E made in Taiwan) centrifuge at 1000 round per minute (RPM) for 15 minutes on Sterile syringes was used to Place the platelet-containing supernatant plasma (without anticoagulant) in another sterile, clean tube. After PRP preparation, the platelet count was evaluated to guarantee sufficient platelet yielding using xn 330 sysmex CBC analyzer made in USA.

Placebo (Normal saline) for group (2):

Normal saline Using a nasal endoscope, normal saline was injected into the olfactory region after a local anesthetic solution made by combining decongestant nasal drops with 10% Xylocaine spray was placed in the nose on a cotton piece for 10 minutes in the nasal septum at the upper level of middle turbinate approximately every 1 cm^2 bilaterally using a 1- ml syringe and 30-G needle. Injection was carried out 1 time.

Outcomes of both groups:

The primary outcome of the study was to assess a patient's post treatment score for anosmia two weeks after the first injection. The second outcome was to assess it two weeks after the second injection. The third outcome was to assess it two weeks after the third injection. The fourth outcome was to assess it regarding the degree of improvement one month after the cessation of the last injection.

STATISTICAL ANALYSIS:

All data were collected, tabulated, and statistically analyzed using IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp. Quantitative data were expressed as the mean ± SD & (range), and numerical and percentage data were used to express the qualitative data. T: Student t test was utilized to compare normally distributed variables between two groups. To compare two groups which are not normally distributed variables the Mann-Whitney U test was employed. The Wilcoxon sign rank test was employed to assess differences between non-normally distributed pairs of variables. When appropriate, the Fisher Exact test or the Chi square test was used to compare the percentage of categorical variables. Every test had a two-sided design, with a p-value of less than 0.05 deemed statistically significant.

RESULTS:

Table 1; showed that there was no difference between in both groups regarding gender distribution, age, $p>0.05$.

Platelet count used in treatment patients in experimental group ranged from 114-659 with mean 462.1±168.8 and WBCs ranged 0.1 to 8.7 with mean 1.94±2.42 **Table 2**.

Visual Analogue Scale (VAS) score anosmia before intervention was matched in both groups **Table 3**.

Incidence of complete anosmia improvement in experimental group was 77.8% versus 11.1% in control group with relative improvement seven times, $p<0.05$ **Table 4**.

Table 5; showed that there was a significant high platelet count in complete improvement patients compared to mild improvement patients, $p<0.05$, While there was no difference in WBCs in complete improved versus mild improved patients, $p>0.05$.

Table 6; showed that there was no significant difference of VAS score between groups in after first dose, $p>0.05$. After that there was significant gradual improvement of anosmia according to (VAS) score in experimental

group compared to control group during study time, p<0.05.

Table 7; showed that there was no significant difference of VAS score after first dose, p>0.05. Then there was significant gradual improvement of anosmia vas score in experimental during intervention time, p<0.05.

Table s1; showed that there was no significant difference of VAS score in control group up to (6weeks) follow p>0.05. Yet, there was a significant decrease of VAS score in control group after (8 weeks) follow up, p<0.05.

Table s2; showed that there is significant and inverse association between Platelet count and mean anosmia score in both groups, p=0.0001.

Table (1): Demographic characters of studied groups

Parameters	Experimental Group n.18	Control Group n.18	t-test	p-value
Gender n (%) **Males** **Females**	 6(33.3%) 12(66.7%)	 9(50.0%) 9(50.0%)	1.029c	0.31
Age per years **Mean ±SD.** **(range)**	 45.33±13.44 (24-66)	 42.89±12.92 (20-61)	0.556	0.58

t: student t test. **χ 2: Chi**-square test **(c)** ***P value ≥ 0.05: no significant***

Table (2): Platelet count and WBCs of in experimental group

Parameters	Experimental Group n.18
Platelet count (x10^3/cc) **Mean ±SD.** **(range)**	 462.1±168.8 114-659
WBCs (x10^3/cc) **Mean ±SD.** **(range)**	 1.94±2.42 0.1-8.7

Table (3): Anosmia score post COVID19 infection of studied groups before treatment

Material used for detecting anosmia	Experimental Group n.18	Control Group n.18
Pre anosmia score for Coffee **Mean ±SD.** **range**	 10±0 10-10	 10±0 10-10
Pre anosmia score Perfume **Mean ±SD.** **range**	 10±0 10-10	 10±0 10-10
Pre anosmia score Onion **Mean ±SD.** **range**	 10±0 10-10	 10±0 10-10
Pre anosmia score Garlic **Mean ±SD.** **range**	 10±0 10-10	 10±0 10-10

Table (4): Incidence of anosmia improvement of studied groups

Outcome	Experimental Group n.18	Control Group n.18	χ 2	p-value
Outcome n (%) **Complete improvement** **Mild improvement** **Complete anosmia**	 14(77.8%) 4(22.2%) 0.0	 2(11.1%) 3(16.7%) 13(72.2%)	22.14	0.0001*

Table (5): Comparison Platelet count and WBCs according to improvement of anosmia in experimental group

Parameters	Experimental group		u-test	p-value
	Complete improvement n.14	Mild improvement n.4		
Platelet count (x10^3/cc) **Mean ±SD.** **(range)**	 529.7±99.8 244-659	 255.5±149.5 114-430	2.774	0.006*
WBCs (x10^3/cc) **Mean ±SD.** **(range)**	 2.33 ±2.6 0.25-8.7	 0.61±0.8 0.1-1.8	1.812	0.070

u: Mann Whitnney u test ***P value < 0.05: Significant P value ≥ 0.05: no significant***

Table (6): Post COVID19 Anosmia score during duration of study in both groups

Material used for detecting anosmia	Experimental Group n.18	Control Group n.18	u-test	p-value
Two weeks after first dose coffee **Mean ±SD.** **range**	9.33±1.45 5-10	9.83±0.51 8-10	1.374	.178
Two weeks after first dose perfume **Mean ±SD.** **range**	9.78±0.55 8-10	9.94±0.24 9-10	1.000	.324
Two weeks after first dose onion **Mean ±SD.** **range**	9.78±0.54 8-10	10±0 10-10	1.719	.095
Two weeks after first dose garlic **Mean ±SD.** **range**	9.28±1.7 5-10	10±0 10-10	1.794	.082
Two weeks after second coffee **Mean ±SD.** **range**	7±3.7 0-10	9.83± 10-10	3.223	.003*
Two weeks after second dose perfume **Mean ±SD.** **range**	8.67±2.1 5-10	9.94±0.24 9-10	2.582	.014*
Two weeks after second dose onion **Mean ±SD.** **range**	6.89±3.4 0-10	10±0 10-10	3.671	.001*
Two weeks after second dose garlic **Mean ±SD.** **range**	6.89 ±3.5 0-10	9.89±0.47 8-10	3.558	.001*
Two weeks after third dose coffee **Mean ±SD.** **range**	3.22±2.9 0-10	9.56±1.24 5-10	8.362	.0001*

Two weeks after third dose perfume Mean ±SD. range	7.72±2.2 5-10	9.67±1.19 5-10	3.342	.002*
Two weeks after third dose onion Mean ±SD. range	3.5±3.1 0-10	9.72±1.18 5-10	7.853	.0001*
Two weeks after third dose garlic Mean ±SD. range	3.9±3 0-10	9.67±1.19 5-10	7.441	.0001*
10 weeks after last dose coffee Mean ±SD. range	1.72±1.8 0-5	7.94±3.44 0-10	4.03	0.0001*
10 weeks after last dose perfume Mean ±SD. range	2±2.2 0-7	8.06±3.49 0-10	3.9	0.0001*
10 weeks after last dose onion Mean ±SD. range	1.67±1.87 0-5	8 ±3.46 0-10	4.07	0.0001*
10 weeks after last dose garlic Mean ±SD. range	1.61±1.91 0-5	8 ±3.46 0-10	4.09	0.0001*

u: Mann Whitnney u test
P value < 0.05: Significant
P value ≥ 0.05: no significant

Table (7): Anosmia score of experimental groups during intervention time

Material	Base Anosmia score	Anosmia score 2week	Anosmia score 4week	Anosmia score 6week	Anosmia score At follow up	P1	P2	P3	P4
Anosmia score for Coffee Mean ±SD. range	10±0 10-10	9.33±1.45 5-10	7±3.7 0-10	3.22±2.9 0-10	1.72±1.8 0-5	0.069	.003	.0001	.0001
Anosmia score Perfume Mean ±SD. range	10±0 10-10	9.78±0.55 8-10	8.67±2.1 5-10	7.72±2.2 5-10	1.89±2.03 0-5	0.331	.018	.006	.0001
Anosmia score Onion Mean ±SD. range	10±0 10-10	9.78±0.54 8-10	6.89±3.4 0-10	3.5±3.1 0-10	1.67±1.87 0-5	0.104	.002	.0001	.0001
Anosmia score Garlic Mean ±SD. range	10±0 10-10	9.28±1.7 5-10	6.89±3.5 0-10	3.9±3 0-10	1.61±1.91 0-5	0.091	.002	.0001	.0001

Wilcoxon Signed Ranks Test
P value < 0.05: Significant
P value ≥ 0.05: no significant
P1(**Base&**2week after first dose)P3(**Base&**2week after third dose)
P2(**Base&**2week after second dose)P3(**Base&**one month of follow up)

DISCUSSION:

The current study demonstrated that the age and sex differences between the two study groups were statistically negligible. These results were compatible with **Abo El Naga et al [10]**.who revealed that Regarding age and gender, there was no statistically significant difference between the two groups.

The present study found that Visual Analogue Scale (VAS) score anosmia before intervention was matched in both groups. This was in accordance with **Abo El Naga et al [10]**who revealed that Regarding the VAS for parosmia, there was no statistically significant difference between the two groups.

Our current findings clearly revealed that incidence of complete anosmia improvement in experimental group was 77.8% versus 11.1% in control group with relative improvement seven times. In agreement with our findings, **Abo El Naga et al [10]**revealed that three weeks of PRP injections in the olfactory cleft resulted in a noteworthy recovery in post-COVID olfactory parosmia, with a substantial difference favoring the case group over the control group. Upon reviewing the literature, some writers evaluated the potential of platelet-rich plasma in the treatment of anosmia, although they did not specify that the dysfunction was caused by post-COVID-19. In research by, five anosmia patients got injections of platelet-rich plasma **Mavrogeni et al [11]**.After the third and finally the fourth session, according to four patients, "their smell came back." Conversely, the final patient claimed to be able to smell "a lot, but not everything." According to the authors, a viable last-ditch therapy option for total anosmia would be to inject platelet-rich plasma into the olfactory region. In a test investigation, **Yan et al [12]**investigated the efficacy of platelet-rich plasma in treating olfactory dysfunction in seven patients who did not respond to topical budesonide rinses or olfactory training, had olfactory loss lasting longer than six months, and did not exhibit any symptoms of sinonasal inflammatory disease. They found that after injection, all patients reported a brief subjective improvement in smell, which then immediately stabilized. Three months following treatment, two patients with functional anosmia showed no discernible improvement. Five hyposmia patients showed improvement during the 3-month follow-up, and 60% of them reached normosmia.

This was consistent with **Goljanian Tabrizi et al[13]**researchreported that to assess the effectiveness of platelet-rich plasma as a postoperative treatment following endoscopic sinus surgery, 48 anosmic participants in a randomized controlled study included patients with sinonasal polyposis. According to their research, the capacity of sinonasal polyposis patients to restore their ability to smell was not immediately affected by PRP injection. A prospective trial with eighty individuals with different causes of anosmia was conducted by **Aboelmagd et al [14]**using plasma high in platelets. The researchers discovered 46 patients out of 80 (57.5%) reported that "their smell came back," whereas 34 patients out of 80 (42.5%) reported no change. Even though the patient and control groups did not differ statistically significantly from one another, all idiopathic anosmia patients demonstrated improvement.

According to the current study, following the first dosage, there was no discernible variation in the VAS scores

between the groups. After that there was significant gradual improvement of anosmia according to (VAS) score in experimental group compared to control group during study time. Recent evidence has supported the efficacy of PRP injection into the olfactory cleft by **Stefens et al [15]**. They noticed that, in comparison to patients who did not benefit from injection, patients treated with PRP injection for a chronic (>1 year) OD reported higher increases in threshold, discrimination and identification (TDI) test improvements one month following the PRP injection.

Similar findings were obtained by **Lechien et al [16]**who reported that when some patients underwent follow-up evaluations two months following their PRP injection, the olfactory dysfunction questionnaire showed notable changes (ODQ) and TDI ratings. 3.6 weeks following the injection, patients reported being able to smell again, which may support existing understanding of PRP's physiological effects. From a physiological perspective, The PRP pockets in the mucosa will release growth and transforming factors, insulin-like growth factor, vascular endothelial growth molecules, and epidermal growth factor gradually. This will cause the platelets' pro-regenerative and anti-inflammatory factors to be upregulated by the olfactory and nasal tissues' cells. Furthermore, it was proposed that PRP might encourage neurogenesis and axon regeneration. PRP's anti-inflammatory properties are especially important for COVID-19 OD patients, since OD patients may have a persistent virus in the olfactory region and associated neuroepithelial inflammation, according to a recent multicenter study, which could account for persistent or recurrent loss of smell. Theoretically, PRP's possible anti-inflammatory properties could lessen long-term inflammation and damage related to cells, encouraging the regeneration of the olfactory tissues.

Lechien et al [16]illustrated thatwith a mean procedure duration of 18.4 minutes, The PRP injection for olfactory cleft is a short procedure. The average duration of PRP extraction and injection in this investigation was consistent with other research that conducted PRP procedures for various otolaryngological causes. The average amount of PRP injected per side was 1.2 mL, which matched the findings of **Yan et al [12]**.

These results were compatible with **Yan et al [12]** who reported that PRP treatment resulted in a higher response rate and a larger improvement in olfaction at three months when compared to the placebo group. Compared to a placebo, there was a higher improvement in scent discrimination after PRP therapy, but there was no change in smell identification or threshold. Subjective scores did not differ between PRP and placebo. There were no side effects noted.

Our current findings clearly revealed that platelet count used in treatment patients in experimental group ranged from 114-659 with mean 462.1±168.8 and WBCs ranged 0.1 to 8.7 with mean 1.94±2.42. There was a significant high platelet count in complete improvement patients compared to mild improvement patients, while there was notstatistically significant in WBCs in complete improved versus mild improved patients. PRP is useful and efficient treatment for post-COVID-19 anosmia unlike WBCs which showed no importance in treatment for

post-COVID-19 anosmia.

The present study illustrated that post anosmia score for coffee, onion and garlic were strong and effective as patients respond for their smell rapidly. However, post anosmia score for perfume was weak as patients do not respond for their smell. This finding may be explained by the fact that perfume receptors are in the olfactory epithelium, which is situated in the nose. The olfactory epithelium contains millions of chemical receptors that detect odors. When we sniff, chemicals in the air are dissolved in mucus. Odor receptor neurons in the olfactory these smells are detected by epithelium, which then notifies the olfactory bulbs. Olfactory neuro epithelium is disrupted during COVID-19 infection. Olfactory receptor neuron function may be impacted by inflammatory changes in the olfactory neuro epithelium, which may also promote further olfactory receptor neuron damage particularly for perfume receptors, which may take a long time to regenerate. As a result, the post anosmia score for perfume was low.

The current study stated revealed the mean anosmia score and platelet count had a strong and inverse relationship. This was consistent with **Yan et al [12]**who illustrated thatthere was statistically significantnegative association between platelet count and anosmia score. This means that as the platelet count decreases, the mean anosmia score tends to increase, and vice versa. However, it's important to note that this association does not imply causation. Further research is needed to understand the underlying mechanisms and potential implications of this relationship.

CONCLUSIONS

An injection of platelet-rich plasma into the olfactory cleft may be beneficial for patients with post-COVID-19 olfactory anosmia who did not respond to traditional conservative treatment. This strategy's main advantages are its safety and ease of use. Being an autologous biological product derived from the patient's blood, PRP carries no risk of disease transmission, rejection, or adverse blood events.

Recommendation:

Larger-scale research is required to validate the outcomes of this investigation, with a focus on the treatment line's long-term effects. The Threshold, Discrimination, and Identification (TDI) test and the Olfactory Disorder Questionnaire (ODQ) are used as assessment tools for anosmia since they are both proven methodologies that yield distinct but complementary olfactory findings.

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Table (S1): Anosmia score of control group during study time

Parameters	Base Anosmia score	Anosmia score 2week	Anosmia score 4week	Anosmia score 6week	Anosmia score at follow up	P1	P2	P3	P4
Anosmia score for Coffee Mean ±SD. range	10±0 10-10	9.83±0.51 8-10	9.83±0.51 8-10	9.56±1.24 5-10	7.94±3.44 0-10	.180	.180	.109	.017*
Anosmia score Perfume Mean ±SD. range	10±0 10-10	9.94±0.24 9-10	9.94±0.24 9-10	9.67±1.19 5-10	8.06±3.49 0-10	.317	1	.180	.038*
Anosmia score Onion Mean ±SD. range	10±0 10-10	10±0 10-10	10±0 10-10	9.72±1.18 5-10	8 ±3.46 0-10	1.000	1	.317	.026*
Anosmia score Garlic Mean ±SD range	10±0 10-10	10±0 10-10	9.89±0.47 8-10	9.67±1.19 5-10	8 ±3.46 0-10	1.000	.317	.180	.026*

Wilcoxon Signed Ranks Test ***P value < 0.05: Significant P value ≥ 0.05: no significant***

P1 (**Base&**2week after first dose)P3 (**Base&**2week after third dose)

P2 (**Base&**2week after second dose)P3 (**Base&**one month of follow up)

Table(S2): Correlation between Platelet count, WBCs, and anosmia score in experimental group

Variables	Anosmia score of experimental group	
	r	P
Platelet count	-0.601	0.008
WBCs (x10^3/cc)	-0.43	0.075

Spearman's correlation coefficient (r), Correlation is significant P<0.05, no significant, P>0.05.

Citation:

Abdelaziz, M., Taha, M., Mohamed ElToukhy, A., ElSayed, M. Outcome of Transforaminal Lumbar Interbody Fusion in Treatment of Single Level Spondylolisthesis. ***Zagazig University Medical Journal*****, 2024; (2910--2920): -. doi: 10.21608/zumj.2023.241547.2945**