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INFLUENCE OF LISTENING TO AL-FATIHA ON BLOOD PARAMETERS AND COGNITIVE FUNCTIONS IN PATIENTS WITH CEREBRAL PALSY

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ABSTRACT

Background of the Study: Cerebral Palsy also referred as CP is a neurodevelopmental disorder that disturbs balance, blood parameters, cognition, movement, muscle coordination, oral health, and various other functions. Many studies have demonstrated that Quranic verses have therapeutic effects on several diseases. This study explored the influence of listening to Al-Fatiha on blood parameters and cognitive functions in patients with CP.

Methodology: This first phase clinical trial was conducted from February 1st to March 30th, 2021 after obtaining ethical permission from the Institutional Bioethics Committee (IBC-2017) and the rehabilitation centre. Inducted pparticipants were assigned randomly into control (11 males and 1 female; age in years 14±5) and Al-Fatiha groups (11 males and 5 females; age in years 14±4.5). The Al-Fatiha group participants received thirty-one structured sessions of listening to Al-Fatiha. Blood analyses encompassed a spectrum of parameters, including blood urea nitrogen, calcium, creatinine, electrolytes, liver function tests, protein levels, and random blood sugar. Cognitive functions were evaluated using 5 Lumosity software games. Paired t-tests and descriptive statistics were performed using SPSS v28.

Results: The findings indicated a significant improvement in cognition however, blood parameters remained within normal levels. Alpha brain waves, various hormones, the parasympathetic nervous system, the prefrontal cortex, and the neurotransmitter serotonin have been suggested as potential contributors to improving patients.

Conclusion: The findings imply that Al Fatiha can be a therapeutic, non-pharmacological, cost-effective, and miracle approach for the overall improvement of CP patients.

Keywords: *Blood parameters, brain waves, cerebral palsy, cognition, neurodevelopmental disorder, childhood development.*

Introduction

Cerebral Palsy also referred as CP is a neurodevelopmental disorder characterized by motor dysfunction. It arises due to brain lesions sustained prenatally, during infancy, or in the early stages of childhood development. It is the most common and noticeable type of motor disability, affecting 2-3 births per 1,000[1] but unfortunately, the burden of CP in Pakistan is unknown yet[2]. It predominantly affects males, unlike females[2]. Furthermore, it disturbs balance, blood parameters, cognition, movement, muscle coordination, oral health, and various other functions[1,4]

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Blood tests have revealed that individuals with CP may exhibit abnormalities in blood sugar, chloride, potassium, and total protein[5,7]. While several reduced blood markers have been identified in CP-inflicted individuals[8], research on changes in these biomarkers due to interventions is limited. Cognition involves various processes in the brain, like learning and remembering information. In almost half of patients with CP, cognitive functions are affected, which can impact their education and vocational achievement. Brain lesions in CP can change early experiences, affecting overall cognitive development[9,10]. Lumosity, a company, created games to measure cognitive skills. Research suggests assertive effects of cognitive training on the mental health of healthy adults[11] and early-stage Alzheimer's[12]. Likewise, computer-based cognitive training can also be adapted for patients with CP. Enriched environment techniques are intended to upgrade at least one of the motor, sensory, cognitive, or social aspects of one's environment with apparent motor or cognitive deficits. Such techniques have shown modulation of behavior, spasticity, and cognitive outcomes in 3 spastic diplegic CP children[13]. The administration of Al-Fatiha can be a part of enriched environment techniques for CP. Dhikr and Quran have a very significant role in the life of Muslims. A study by El-Saleh et al., affirmed that the Holy Quran improved some psychological and physical variables in the listeners[14]. Surah Al-Fatiha, the opening chapter of the Quran, comprises seven verses and is regarded as a holistic remedy for physical, societal, and spiritual issues, providing comprehensive treatment for a variety of problems[15]. Al-Fatiha has been reported to ameliorate behavioral, physical, social, and spiritual calamities[16]. Based on reported studies, it is anticipated that the verses of Allah, specifically from Surah Al-Fatiha, can provide comfort and hope to believers, promoting patience and inspiring them to seek Allah's cure, mercy, and relief. This study explored the influence of listening to Al-Fatiha on blood parameters and cognitive functions in patients with CP.

Methodology

Figure 1 depicts a schematic overview of the study protocol. This first phase clinical trial was conducted from February 1st to March 30th, 2021 in Karachi, Pakistan after obtaining ethical permission from the Institutional Bioethics Committee (IBC-2017) and the rehabilitation center i.e., 'Al umeed rehabilitation association' where intervention trial was performed. The rules of the Helsinki Declaration were taken into consideration. Parents of participants voluntarily gave consent for the inclusion of their children in the study. Due to a limited number of consents, participants were chosen without regard for age, gender, GMFCS levels, muscle tone, mode of transition, topographic presentation, or other additional impairments.

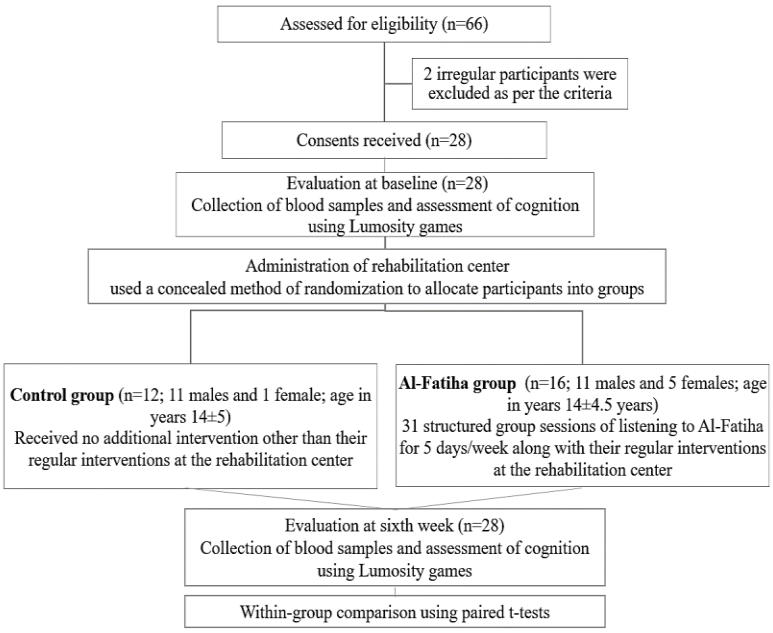

Fig 01: Study protocol

Study design
The administration of rehabilitation centre used a concealed randomization method to assign twenty-eight CP-inflicted participants to one of two groups: the control group or the Al-Fatiha group. Participants in both groups continued their regular physical and speech therapies during the study period.

Administration of Al-Fatiha
Sixteen participants assigned to the Al-Fatiha group were randomly distributed across four classrooms, each accommodating four individuals. The purpose of this arrangement was to minimize disruptive activities such as crying, laughing, playing, shouting, and unnecessary chattering during listening to Al-Fatiha. A pre-recorded recitation by 'Mishary Rashid Alafasy' was played over a loudspeaker during the twelve-minute-long Al-Fatiha listening sessions A total of thirty-one structured Al-Fatiha sessions were conducted five days a week for six weeks, all conducted within the premises of rehabilitation centre.

Inclusion criteria of the study
Participants with no vision or hearing issues.
Participants who can understand the given instructions to play games.
Participants who can skillfully hold a computer mouse.
Participants with no photosensitive epilepsy.

Exclusion criteria of the study
Participants who were not allowed by the parent institute.

Evaluation
a. Blood analyses
Blood analyses encompassed a spectrum of parameters, including blood urea nitrogen, calcium, creatinine, electrolytes, liver function tests, protein levels, and random blood sugar. The collection of blood samples was carried out by a proficient phlebotomist. The serum extraction was performed using 'Labofuge 400R centrifuge'. Quantitative assessments for blood urea nitrogen, calcium, creatinine, liver function, protein, and random blood sugar in the serum were conducted using the 'Cobas 6000 c 501' operating on photometric method. Additionally, electrolyte levels in the serum were determined through the 'nova biomedical 4^{+}', operating on ion-selective electrode technique.

b. Cognition
The Lumosity games software, developed by Lumos Labs located in San Francisco, California, was purchased online for the study. Professionals at rehabilitation center selected 5 Lumosity games appropriate for study participants. Each selected game helped in testing a specific cognitive skill: lost in migration game for testing selective attention, highway hazards game for information processing, tidal treasure game for working memory, space trace game for spatial fluency, and masterpiece game for spatial reasoning respectively. Each participant underwent training sessions before baseline and sixth week assessments, during which they played the games using their hands or feet. All participants (n=28) were evaluated for both blood parameters and cognitive functions at baseline and sixth week.

Statistical analysis
The collected data was analyzed using a statistical package for social sciences (version 28.0). To examine the demographical characteristics of the inducted CP-inflicted patients, descriptive statistics was used for calculating the frequencies as shown in Figure 1. The demographic characteristics data encompassed GMFCS levels, muscle tone, topographical presentation, mode

of transition, and additional impairments. For the blood parameters, the mean, standard deviation, standard error, and 95% confidence were determined. For cognitive functions, the mean and standard deviation were determined. The data was parametric so, paired t-test was applied to measure the within-group mean differences for each blood parameter and cognitive function at baseline and the sixth week.

Results

Figure 2 shows the physical characteristics of the inducted participants by gender, GMFCS levels, muscle tone, mode of transition, topographical distribution, and additional impairments

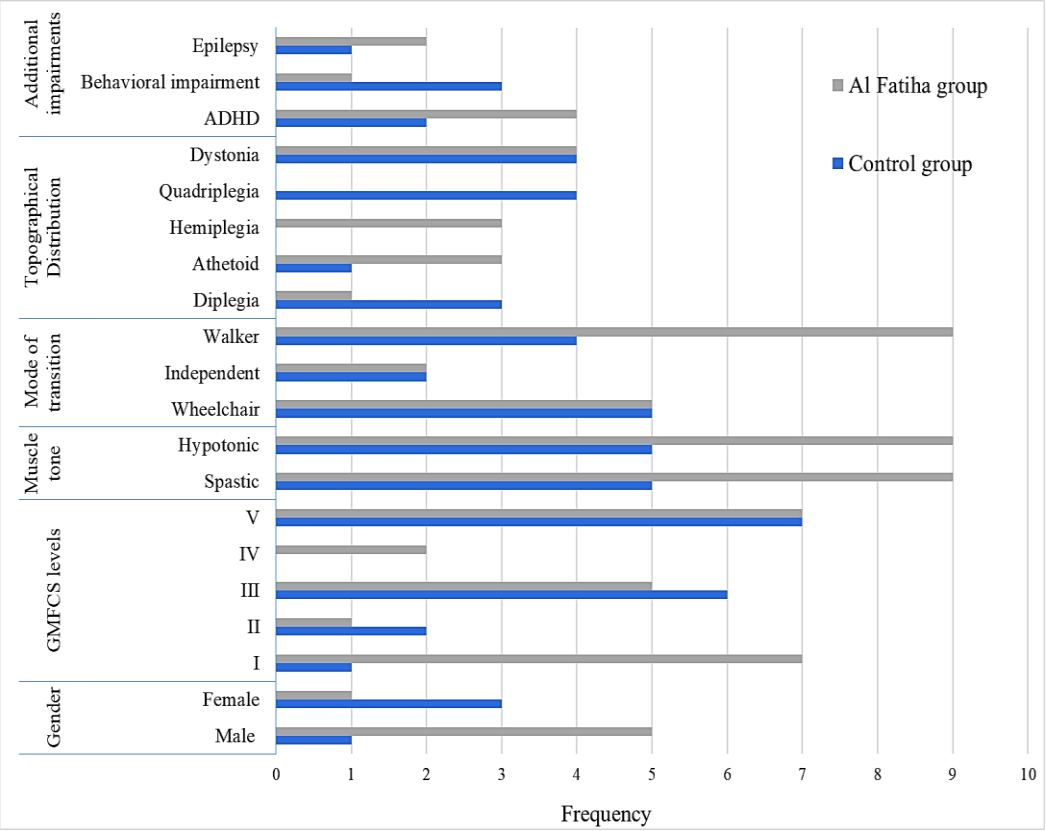

Fig 02: Physical characteristics of the inducted participants (n=28)

a. Blood analyses

Paired t-tests revealed significant increases in chloride ($p<.001$), creatinine ($p<.01$), direct bilirubin ($p<.01$), sodium ($p<.001$), and urea nitrogen ($p<.01$) within the control group. Conversely, the Al-Fatiha group exhibited significant increases in γ-glutamyl transpeptidase ($p<.05$), chloride ($p<.01$), creatinine ($p<.01$), random sugar ($p<.05$), sodium ($p<.001$), and total proteins ($p<.05$), along with significant decreases in alanine aminotransferase ($p<.05$) and bicarbonate ($p<.05$) (refer to Table 1-4). Importantly, all observed alterations in both groups remained within the normal range for the respective parameters under consideration.

Tests (normal range with units)	Group	Evaluation Phase	Mean±SD	Std. Error	95% Confidence Interval for Mean		*p*-value
					Lower Bound	Upper Bound	
Albumin (3.2-4.5 G%)	Control	Baseline	4.6±0.3	0.09	4.48	4.89	0.07
		Sixth week	4.8±0.3	0.10	4.58	5.02	
	Al-Fatiha	Baseline	4.5±0.2	0.06	4.45	4.71	0.07
		Sixth week	4.7±0.2	0.06	4.61	4.87	
Globulin (1.9-2.8 G%)	Control	Baseline	2.9±0.2	0.07	2.74	3.06	0.30
		Sixth week	3.0±0.2	0.05	2.87	3.12	
	Al-Fatiha	Baseline	2.9±0.4	0.11	2.70	3.19	0.09
		Sixth week	3.1±0.4	0.10	2.90	3.34	
A/G ratio (1.1-2.2)	Control	Baseline	1.6±0.2	0.05	1.49	1.75	0.75
		Sixth week	1.6±0.1	0.04	1.51	1.70	
	Al-Fatiha	Baseline	1.5±0.1	0.04	1.48	1.68	0.40
		Sixth week	1.5±0.2	0.05	1.42	1.64	
Total proteins (6.6-8.7 G%)	Control	Baseline	7.6±0.3	0.11	7.35	7.84	0.09
		Sixth week	7.8±0.4	0.12	7.53	8.08	
	Al-Fatiha	Baseline	7.5±0.6	0.16	7.19	7.90	0.03
		Sixth week	7.8*±0.4	0.11	7.62	8.11	

Table 01: Paired t-tests performed for proteins (n=28)

Tests (normal range with units)	Group	Evaluation Phase	Mean±SD	Std. Error	95% Confidence Interval for Mean		*p*-value
					Lower Bound	Upper Bound	
Bilirubin total (0.1-1.2 mg%)	Control	Baseline	0.38±0.19	0.05	0.25	0.50	0.20
		Sixth week	0.45±0.18	0.05	0.33	0.57	
	Al-Fatiha	Baseline	0.36±0.15	0.03	0.28	0.44	0.67
		Sixth week	0.34±0.23	0.05	0.22	0.47	
Direct bilirubin (0.1-0.4 mg%)	Control	Baseline	0.14±0.05	0.01	0.10	0.17	0.001
		Sixth week	0.19**±0.05	0.01	0.15	0.22	
	Al-Fatiha	Baseline	0.13±0.04	0.01	0.10	0.15	0.10
		Sixth week	0.15±0.07	0.01	0.11	0.19	
Aspartate transaminase (upto 46 U/L)	Control	Baseline	25.9±11.1	3.22	18.8	33.0	0.43
		Sixth week	23.5±5.85	1.68	19.7	27.2	
	Al-Fatiha	Baseline	25.7±5.83	1.45	22.6	28.8	0.35
		Sixth week	25.0±5.17	1.29	22.2	27.7	
Alanine aminotransferase (upto 49 U/L)	Control	Baseline	22.9±18.3	5.30	11.2	34.5	0.27
		Sixth week	17.0±6.06	1.74	13.1	20.8	
	Al-Fatiha	Baseline	20.3±7.50	1.88	16.2	24.3	0.04
		Sixth week	17.9*±7.5	1.89	13.9	21.9	
γ-glutamyl transpeptidase (7-32 U/L)	Control	Baseline	12.4±4.64	1.33	9.46	15.3	0.15
		Sixth week	13.1±4.70	1.35	10.1	16.1	
	Al-Fatiha	Baseline	13.2±6.02	1.50	10.0	16.4	0.04
		Sixth week	14.0*±5.98	1.49	10.8	17.2	
Alkaline phosphatase (<300 U/L)	Control	Baseline	178.4±90.5	26.1	120.9	235.9	0.85
		Sixth week	176.1±78.1	22.5	126.5	225.8	
	Al-Fatiha	Baseline	245.4±162.0	40.5	159.0	331.8	0.30
		Sixth week	234.5±146.5	36.6	156.4	312.5	

Table 02: Paired t-tests performed for liver function tests (n=28)

Tests (normal range with units)	Group	Evaluation Phase	Mean±SD	Std. Error	95% Confidence Interval for Mean		*p-value*
					Lower Bound	Upper Bound	
Blood urea nitrogen (7-21 mg%)	Control	Baseline	10.4±3.23	0.93	8.36	12.4	0.004
		Sixth week	11.9**±3.72	1.07	9.54	14.2	
	Al-Fatiha	Baseline	10.4±2.65	0.66	9.02	11.8	0.70
		Sixth week	10.6±1.85	0.46	9.70	11.6	
Calcium (8.1-10.4 mg%)	Control	Baseline	9.83±0.30	0.08	9.63	10.0	0.79
		Sixth week	9.85±0.35	0.10	9.63	10.0	
	Al-Fatiha	Baseline	9.48±0.60	0.15	9.16	9.80	0.39
		Sixth week	9.58±0.58	0.14	9.26	9.89	
Creatinine (0.6-1.3 mg%)	Control	Baseline	0.55±0.17	0.04	0.44	0.66	0.003
		Sixth week	0.65**±0.17	0.04	0.54	0.76	
	Al-Fatiha	Baseline	0.48±0.18	0.04	0.37	0.57	0.003
		Sixth week	0.53**±0.20	0.05	0.42	0.64	
Random sugar (upto 180 mg%)	Control	Baseline	83.9±11.9	3.44	76.3	91.4	0.46
		Sixth week	87.5±15.4	4.47	77.6	97.3	
	Al-Fatiha	Baseline	87.0±8.22	2.05	82.6	91.3	0.01
		Sixth week	98.8*±15.9	3.97	90.3	107.2	

Table 03: Paired t-tests for blood urea nitrogen, calcium, creatinine, and random sugar (n=28)

Tests (normal range with units)	Group	Evaluation Phase	Mean±SD	Std. Error	95% Confidence Interval for Mean		*p-value*
					Lower Bound	Upper Bound	
Sodium (136-149 M Eq/L)	Control	Baseline	139.1±0.90	0.26	138.5	139.6	0.000
		Sixth week	144.5***±2.24	0.64	143.1	145.9	
	Al-Fatiha	Baseline	139.2±1.46	0.36	138.4	140.0	0.000
		Sixth week	144.1***±2.53	0.63	142.8	145.5	
Potassium (3.8-5.2 M Eq/L)	Control	Baseline	4.5±0.3	0.11	4.34	4.84	0.19
		Sixth week	4.3±0.3	0.09	4.18	4.60	
	Al-Fatiha	Baseline	4.5±0.3	0.09	4.34	4.73	0.12
		Sixth week	4.5±0.3	0.09	4.13	4.54	
Chloride (98-107 M Eq/L)	Control	Baseline	102.9±1.00	0.29	102.3	103.6	0.000
		Sixth week	105***±1.55	0.44	104.0	106.0	
	Al-Fatiha	Baseline	102.8±2.41	0.60	101.5	104.1	0.001
		Sixth week	105**±2.27	0.56	103.8	106.2	
Bi-carbonate (25-29 M Eq/L)	Control	Baseline	28.4±1.0	0.31	27.7	29.1	1
		Sixth week	28.4±1.6	0.48	27.3	29.4	
	Al-Fatiha	Baseline	28.5±1.6	0.40	27.6	29.3	0.04
		Sixth week	27.6*±1.7	0.42	26.7	28.5	

Table 04: Paired t-tests performed for electrolytes (n=28)

b. Cognition

In the paired t-test comparisons depicted in Figure 3:

i. Lost in migration game: The participants in the control group presented no significant improvement in the scores ($p>.05$).
The participants in the Al-Fatiha group presented a significant improvement in the scores($p<.01$).

ii. Highway hazards game: Neither the participants in the control group nor the participants in the Al-Fatiha group presented significant improvement in the scores ($p>.05$).

iii. Tidal treasure game: The participants in the control group presented no significant improvement in the scores ($p>.05$).
The participants in the Al-Fatiha group presented a significant improvement in the scores ($p<.001$).

iv. Space trace game: Neither the participants in the control group nor the participants in the Al-Fatiha group presented significant improvement in the scores ($p>.05$).

v. Masterpiece game: The participants in the control group presented a significant improvement in the scores ($p<.05$).
The participants in the Al-Fatiha group presented no significant improvement in the scores ($p>.05$).

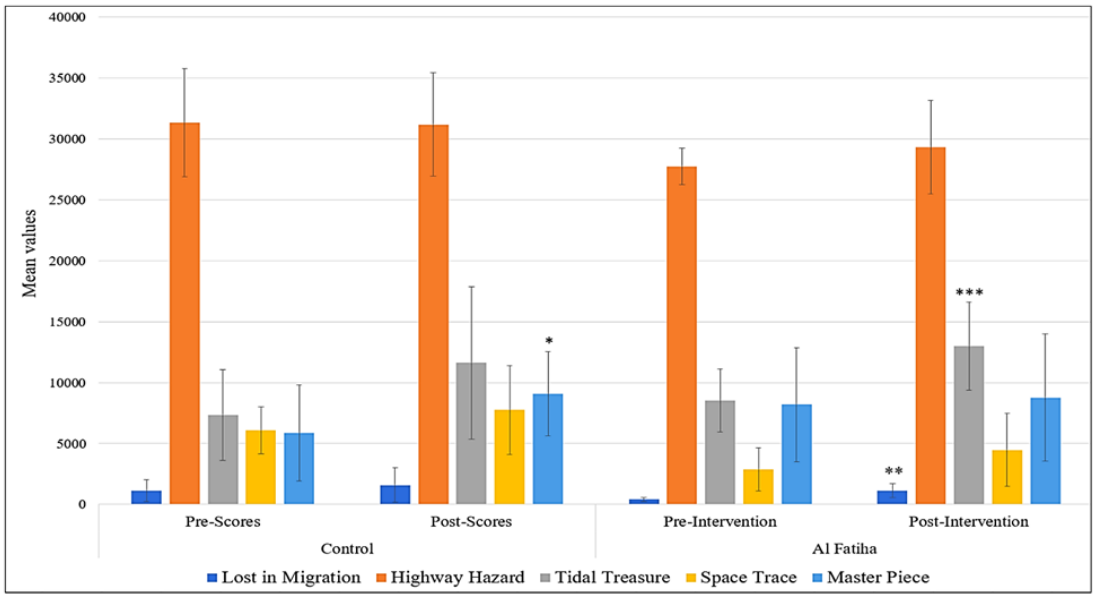

Fig 03: Significant mean values are denoted as $^{*}p<.05$, $^{**}p<.01$, and $^{***}p<.001$. Error bars are calculated standard deviations

Discussion

All participants with CP included in the study had normal blood parameters at the trial's initiation. Blood analyses in the participants in the Al-Fatiha group presented significant increases in γ-glutamyl transpeptidase, chloride, random sugar, creatinine, sodium, and total protein, on the other hand they presented decreases in bicarbonate and alanine aminotransferase (refer to Table 1-4). Importantly, all observed alterations in both groups remained within the normal range for the respective parameters under consideration. Listening to the recitation of the Quran has been found to generate alpha brain waves, contributing to a calming effect on listeners[14,17,18]. The ability to adjust our behavior, body, and mind (both due to internal and external factors) is essential for survival. A relaxed brain is noted to promote homeostasis in various physiological functions of the body systems. Studies emphasize the Quran's positive effects on behavioral, physiological, social, and spiritual aspects[14-18]. The relaxation induced by listening to Al-Fatiha is speculated to enhance the functioning of multiple systems, including circulatory, digestive, immune, lymphatic, nervous, respiration, reproductive, and urinary. Patients with CP may exhibit abnormal total proteins, which can lead to fatigue, inflammatory diseases, and weight loss[6]. The generation of alpha brain waves, induced through relaxation, plays a role in normalizing various physiological aspects, including appetite, blood circulation, blood pressure, heart rate, mood, sleep, and sugar levels contributing to optimal homeostasis. An increase in appetite leads to a higher dietary intake and therefore more muscle mass. Possibly the homeostasis restoration may have significantly improved creatinine (as indicated in Table 3) and total protein levels in the participants of Al-Fatiha group (as indicated in Table 1). Glucose serves as immediate energy for every cell in the

body, requiring a consistent supply of random sugar in blood for normal functioning. Amylin, insulin, glucagon, and somatostatin hormones play a crucial role in regulating blood glucose levels. Peterson et al. reported a 9.2% prevalence of diabetes in adults with CP[7]. However, in the current study, participants in the Al-Fatiha group exhibited normal levels of random glucose, as indicated in Table 3.Alanine aminotransferase is an enzyme responsible for converting food into energy. Emotional stress has the potential to harm the liver by influencing hepatic blood flow through vasospasm and centrilobular hypoxia. Liver damage prompts the release of alanine aminotransferase in substantial amounts, leading to symptoms such as fatigue, itchy skin, nausea, swelling, stomachache, vomiting, and changes in waste product color. In the present study, the decrease in the enzyme 'alanine aminotransferase' suggests that Al-Fatiha administration may have restored disrupted functions of liver by alleviating stress. Electrolytes are essential for preserving regular bodily functions because they control the amount of water in the body. Numerous organs including the lungs, kidneys, and liver, and hormones including antidiuretic, aldosterone, and parathyroid, controls the acid-base balance in body. Al-Fatiha may have helped to restore normal lung and kidney functions, pH levels, absorption of nutrients, and acid-base balance by inducing relaxation. As seen in Table 4, the participant's chloride and sodium levels significantly improved within normal ranges, indicating this rrestoration. The hydrogen ion concentration in body is regulated by bicarbonate, and any disruption in transport of bicarbonate can lead to formation of stones in the kidneys, brain damage, hypertension, or systemic acidosis. In study participants, bicarbonate test indicated normal levels. The reason for this normalcy is not entirely clear, suggesting that the interventions provided at the institute may have played a role, although the specific mechanism remains unexplained. The study reports enhanced cognitive function in the Al-Fatiha group. This is evidenced by a significant improvement in their selective attention and working memory as illustrated in Figure 3. The prefrontal cortex, located in the frontal lobe, governs high-order cognitive functions, including attention, decision-making, emotions, planning, memory, thinking, and reasoning but the exact process behind cognitive function execution through the prefrontal cortex remains unknown[19,20]. Working memory, a cognitive skill involving the temporary storage and manipulation of information, is regulated by the prefrontal cortex, particularly through the dorsal region's posterior and superior areas. Working memory and dopaminergic projections are linked in the brain. Neurotransmitter serotonin or 5-HT is essential for a number of physiological and cognitive processes[21]. The serotonergic system plays a regulatory role in behaviors with high cognitive demands. Serotonin receptors are known to be present in areas of the brain crucial for cognition, particularly the frontal cortex and hippocampus[22,23]. It is anticipated that perhaps Al-Fatiha may have stimulated hippocampus, dopaminergic projections (dopamine related pathways), prefrontal cortex, and the serotonergic system, leading to enhanced selective attention and working memory as observed in the participants. To the best of my knowledge, it is the first study of its kind that explored the influence of listening to Al-Fatiha on blood parameters and cognitive functions in patients with CP. While not all cognitive functions presented improvement in the Al-Fatiha group, it is suggested that prolonged continuation of listening to Al-Fatiha might improve all cognitive functions. At the time of induction in the trial, all inducted participants presented normal blood parameters, which could be attributed to the fact that participants were already receiving interventions at the rehabilitation center that helped maintain healthy blood parameters. Future research could explore the monitoring of blood alterations in naive patients with CP, as the present findings indicate improvement in certain parameters. Subsequent second and third-phase clinical trials could further validate these observed findings.

Conclusion

In conclusion, it can be stated that listening to Al-Fatiha precipitated no adverse effects on the inducted participants, both in terms of blood parameters and cognition. It is suggested that a prolonged continuation of listening to Al-Fatiha may lead to further progress. The findings imply

that Al Fatiha can be a therapeutic, non-pharmacological, cost-effective, and miracle approach for the overall improvement of CP patients.

AUTHORS' CONTRIBUTION:
The following authors have made substantial contributions to the manuscript as under:
Conception or Design: Ammara Rafique
Acquisition, Analysis or Interpretation of Data: Ammara Rafique
Manuscript Writing & Approval: Ammara Rafique
All authors acknowledge their accountability for all facets of the research, ensuring that any concerns regarding the accuracy or integrity of the work are duly investigated and resolved.

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INFORMED CONSENT: Written Informed Consent was taken from each patient.

CONFLICT OF INTEREST: The author (s) have no conflict of interest regarding any of the activity perform by PJR.

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ETHICS STATEMENTS: This first phase clinical trial was conducted from February 1st to March 30th, 2021 in Karachi, Pakistan after obtaining ethical permission from the Institutional Bioethics Committee (IBC-2017) and the rehabilitation center i.e., 'Al umeed rehabilitation association' where intervention trial was performed.

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