

## Effect of COVID-19 pandemic on children undergone percutaneous endoscopic gastrostomy due to neurologic diseases

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### ABSTRACT

**Aim:** To investigate the effects of SAR-CoV-2 infection on nutritional status in patients who underwent percutaneous endoscopic gastrostomy (PEG) for neurological disorders.

**Methods:** The clinical and laboratory follow-up data of the patients who underwent PEG in our clinic between 2002 and 2018 were evaluated before and during the pandemic. The results were analyzed statistically.

**Results:** Twenty patients were included. They were 70.9±64.4 months old at the time of PEG, 97.9±67.8 months before the pandemic, and 105.5±60.8 months during the pandemic ( $p=0.048$ ). Weight for age at the time of PEG increased from 10.7±4.6 kg to 15.6±7.2 kg before the pandemic. Hemoglobin was 12.3±1.4 g/dl at the time of PEG, 13.5±1.6 g/dl before the pandemic ( $p=0.045$ ). Vitamin D was 24.1±8.9 ng/ml at the time of PEG and increased to 45.7±9.7 ng/ml during the pandemic ( $p=0.018$ ). The annual number of visits before the pandemic was 9.8±5.7 and decreased to 2±1.7 during the pandemic ( $p=0.003$ ). Twelve (%60) of the patients developed PEG complications, 6(30%) had their PEG replaced. Those who had developed PEG complications had low levels of albumin (3.3±0.4 vs 4±0.4 g/dl,  $p=0.022$ ) and vitamin B12 (578±199 vs 1299±533 pg/ml,  $p=0.007$ ).

**Conclusions:** Even if PEG is applied late, it provides a partial improvement in patients, but the COVID-19 pandemic reversed these benefits and caused an increase in PEG complications. In order for the patient to get the maximum benefit from PEG, close follow-up is essential.

**Key words:** COVID-19, percutaneous endoscopic gastrostomy, neurologic disease, follow-up, child.

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### Introduction

Nourishment is the intake of adequate and balanced nutrients to maintain healthy growth

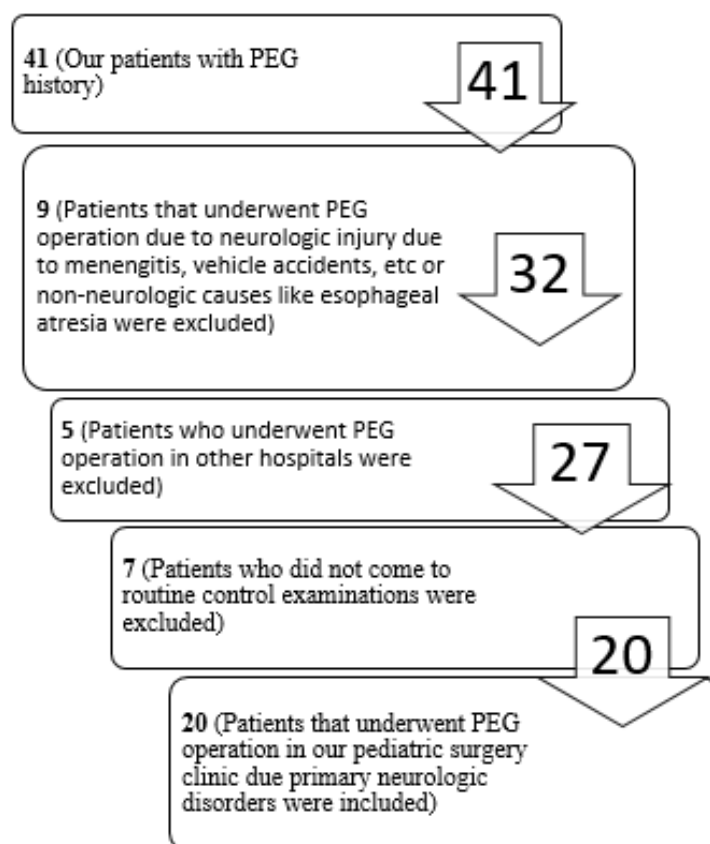
and development. If the required energy and nutrients are not provided or provided inadequately, malnutrition may occur with high mortality and morbidity. When physiological oral nutrition is not possible, alternative ways should be sought. The alternative way is chosen based on the time required until the physiologic oral feeding can be established again. If the time interval is shorter than 3 months, nasogastric or orogastric feeding, if longer

gastrostomy operation is preferred. A type of gastrostomy, percutaneous endoscopic gastrostomy (PEG) is the most preferred long-term feeding way nowadays because it takes short time for the procedure, has low morbidity, is economic, and is relatively safe [1]. PEG allows for easier feeding of patients with upper gastro-intestinal anatomical defects, or with neurologic or oncologic conditions [2]. For children, the most common indication for PEG operation is the neurological disorders that cause difficulty in swallowing, and cerebral palsy is on the top of this list of disorders [3]. Coronavirus disease 2019 (COVID-19) pandemic is one of the greatest threats to the health of humankind. Against all the precautions taken globally, and the quarantine, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection continues to spread rapidly throughout the world. After 15 months of the emergence of the SARS-CoV-2 virus, 113.467.303 cases were infected, and 2.520.550 people died [4]. SARS-CoV-2 infection increases the rate of mortality and morbidity of infected people, especially of those with chronic diseases [5]. One of the best preventive method from this infection is the isolation of ones' self. Therefore, including the patients with neurologic disorders, patients with chronic diseases to decrease the likelihood of contracting COVID-19 have stayed out of hospitals where the spread of infection is the highest. This approach caused patients to miss their routine examinations. On the other hand, preventive measures taken to protect people from SARS-CoV-2 infection harmed the socioeconomics of people and this limited the sources for patients with chronic diseases who need long-term care. In this study, we aim to analyze the effects of SARS-CoV-2 infection on patients' undergone PEG operations due to neurologic disorders.

## Materials and methods

The study was approved by the Bolu Abant Izzet Baysal University Clinical Researches Ethic Committee and Ministry of Health (Date and number: 2021/105) and was conducted in compliance with the principles of the Helsinki Declaration.

In this study, the data of patients who are followed due to primary neurological disorders that have undergone PEG operation in pediatric surgery clinics between 2002 and 2018 were analyzed retrospectively. The PEG operation was performed after 4-8 hours of fasting under general anesthesia with pull technique. For this operation PEG kit (EndoVive standard PEG kit No: 20-24 F) was used. Before the procedure consent was obtained from the patient relatives. The selection method of the patients included in this study is shown in figure 1.



**Figure 1.** The overview of flow of patient population selection. PEG: Percutaneous endoscopic gastrostomy.

Demographic information, birth details, underlying diseases, growth parameters, reasons for PEG replacement, complications of PEG, time of follow-up, number of hospital visits, and biochemical parameters were obtained and recorded from patient files.

Information obtained from patients were categorized into 3; time of PEG operation, before COVID-19 pandemic, and during COVID-19 pandemic. The causes of PEG complications were evaluated.

### Statistical analysis

For statistical analysis, Statistical Package for Social Sciences version 22.0 software was used. Numerical variables were expressed as descriptive statistics, mean  $\pm$  standard deviation, for categorical values numbers and percentages. For the comparison of double groups, Chi-square test for parametric values, and Mann-Whitney U test for non-parametric test were used. To compare triple groups ANOVA test was used. For significant difference Bonferroni test was used. *p* value smaller than 0.05 ( $p < 0.05$ ) was evaluated as statistically significant.

## Results

Patients included in the study underwent PEG operation due inability to meet the metabolic requirements through oral feeding and the long-

term nasogastric tube usage was not appropriate. 10 (50%) of the patients were male and 10 (50%) were female. Gestation age mean was  $35 \pm 3.5$  weeks. Eleven (55%) of the patients were pre-term babies. Weight at birth mean was  $2202 \pm 795$  gr where 10 (55%) had low birth weight. Eleven (55%) of the patients had cerebral palsy, 6 (30%) had refractory epilepsy and 3 (15%) had neurodegenerative diseases. Those patients who had cerebral palsy, 7 (63.6%) were pre-term babies, 5 (45.4%) were low birth weight.

The age of patients at the time of PEG operation was  $70.9 \pm 64.4$  months old, before the COVID-19 pandemic during their last visit the mean age was  $97.9 \pm 67.8$  months old and during COVID-19 pandemic examinations were done when they were  $105.5 \pm 60.8$  months old. The weight of patients at the time of PEG operation was  $10.7 \pm 4.6$  kg, during their last examination before the Covid-10 pandemic the mean weight rose to  $15.6 \pm 7.2$  kg. This increase in weight was statistically significant ( $p = 0.048$ ). During COVID-19, the mean weight dropped to  $14.2 \pm 4.6$  kg, however, this decrease was not statistically significant ( $p > 0.05$ ). The increase in head circumference and the decrease in Body Mass Index (BMI) of the patients in all three-time intervals were not statistically significant ( $p > 0.05$ ) (Table 1).

**Table 1.** The anthropometric values of the patients.

Characteristics	At the time of PEG <sup>1</sup>	Pre COVID-19 <sup>2</sup>	During COVID-19 <sup>3</sup>	<i>P</i> value
Age (months)	70.9 $\pm$ 64.4	97.9 $\pm$ 67.8	105.5 $\pm$ 60.8	0.33
Weight for age (kg)	10.7 $\pm$ 4.6	15.6 $\pm$ 7.2	14.2 $\pm$ 4.6	<b>0.048<sup>1-2</sup></b>
Weight Percentile	11.4 $\pm$ 27.7	13.6 $\pm$ 28.7	10.1 $\pm$ 10.7	0.85
Height for age (cm)	82.1 $\pm$ 20.2	97.3 $\pm$ 19.9	103.5 $\pm$ 13.6	0.12
Height Percentile	1.5 $\pm$ 2.2	6.9 $\pm$ 16.3	3.5 $\pm$ 1.7	0.49
BMI	15.9 $\pm$ 4.1	14 $\pm$ 3.3	13.5 $\pm$ 3.6	0.42
BMI percentile	39.4 $\pm$ 40.4	23.4 $\pm$ 37.6	17.9 $\pm$ 35.7	0.54
Head circumference (cm)	43.7 $\pm$ 4.6	44.4 $\pm$ 4	44.6 $\pm$ 4.2	0.84
Head circumference percentile	2.7 $\pm$ 8.3	3.6 $\pm$ 10.4	3.7 $\pm$ 7.9	0.71

PEG: Percutaneous endoscopic gastrostomy, BMI: Body mass index.

The hemoglobin level of patients at the time of PEG operation was  $12.3 \pm 1.4$  g/dl rose to  $13.5 \pm 1.6$  g/dl during their last examination before the COVID-19 pandemic. This rise in hemoglobin levels was statistically significant ( $p=0.045$ ), on the other hand, hemoglobin levels drop to  $13.4 \pm 1.3$  g/dl during the COVID-19 pandemic, but this was not statistically significant ( $p>0.05$ ) (Table 2).

( $p=0.016$ ). The glomerular filtration rate (GFR) value of patients at the time of PEG operation was  $160.5 \pm 26.4$  ml/min/1.73m<sup>2</sup>. This value was found to be  $137.6 \pm 31.1$  ml/min/1.73m<sup>2</sup> in their last examination before the COVID-19 pandemic and  $113.2 \pm 23.6$  during the COVID-19 pandemic. This decrease in the value of GFR was found to be statistically significant ( $p=0.041$ ) (Table 2). Serum vitamin D values

**Table 2.** Laboratory results of the patients.

Variables	At the time of PEG <sup>1</sup>	Pre COVID-19 <sup>2</sup>	During COVID-19 <sup>3</sup>	p value
Hgb (g/dl)	12.3±1.4	13.5±1.6	13.4±1.3	<b>0.045</b> <sup>1-2</sup>
Glucose (mg/dl)	102±54.8	92.5±16.4	97.6±30.2	0.75
BUN (mg/dl)	24.1±12.2	22.1±14.1	32.5±13.7	0.25
Creatinine (mg/dl)	0.43±0.09	0.45±0.07	0.55±0.06	<b>0.016</b> <sup>1-3</sup>
GFR (ml/min/1.73m <sup>2</sup> )	160.5±26.4	137.6±31.1	113.2±23.6	<b>0.041</b> <sup>1-3</sup>
AST (IU/l)	78.1±92.9	54.1±57.9	43±24.1	0.48
ALT (IU/l)	64.2±104.7	34.2±39.6	27.5±16.9	0.36
GGT (IU/l)	161.2±233.9	244.6±139.9	81.3±118.3	0.53
Albumin (g/dl)	3.8±0.5	3.5±0.4	4±0.4	0.21
Sodium (mEq/l)	137.7±4.4	139.6±4.1	141±4.4	0.18
Potassium (mEq/l)	4.5±0.6	4.2±0.5	4.1±0.6	0.3
Phosphorus (mg/dl)	4±1.1	4.9±0.8	3.8±1.4	0.12
Calcium (mg/dl)	9.3±0.8	9.4±0.5	9.2±0.2	0.75
Magnesium (mg/dl)	1.8±0.3	2.1±0.2	2.2±0.2	0.1
Vitamin D (ng/ml)	24.1±8.9	32.7±14.4	45.7±9.7	<b>0.018</b> <sup>1-3</sup>
Vitamin B12 (pg/ml)	818.6±484.6	847±163	532±127.2	0.26
Ferritin (ng/ml)	67.8±61.5	32.7±22.1	172±285	0.16
Folate (ng/ml)	12±4.7	12.5±3.5	10.5±5.2	0.78
PTH (pg/ml)	32.9±42.4	43.6±24.8	68.1±41.2	0.39

PEG: Percutaneous endoscopic gastrostomy, Hgb: Hemoglobin, BUN: Blood urea nitrogen, GFR: Glomerular filtration rate, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, GGT: Gamma Glutamyl Transferase, PTH: Parathyroid hormone.

The serum creatinine levels of patients at the time of PEG operation were  $0.43 \pm 0.09$  mg/dl creatinine value before the COVID-19 pandemic was  $0.45 \pm 0.07$  mg/dl and during the COVID-19 pandemic was found to be  $0.55 \pm 0.06$  mg/dl. The increase in value between the time of PEG operation and during the COVID-19 pandemic was statistically significant

of patients at the time of PEG operation were  $24.1 \pm 8.9$  ng/ml. Vitamin D values increased to  $32.7 \pm 14.4$  ng/ml before the pandemic and  $45.7 \pm 9.7$  during the pandemic. This increase in the value of vitamin D was statistically significant ( $p=0.018$ ). The change in other lab results of these patients given in table 2 was not found to be statistically significant ( $p>0.05$ ).

The number of visits to the hospital was  $19.2 \pm 16.6$  before the pandemic, this number dropped to  $5 \pm 4.2$  during the pandemic. The yearly visit number before the COVID-19 pandemic was  $9.8 \pm 5.7$  dropped to  $2 \pm 1.7$ . These changes in the number of visits were found to be statistically significant ( $p=0.009$  and  $p=0.003$ , respectively).

Seven (35%) of our patients had peristomal wound infection, 3 (15%) had to leak, 1 (5%) had obstruction, and 1 (5%) had its PEG dislocated, 4 of them developed before the pandemic and 8 of them developed during the pandemic. Six (30%) of these patients had their PEGs replaced, 2 of them were done before the pandemic and 4 of them were done during the pandemic. It was seen that PEG complications and PEG replacements were determined mostly during the COVID-19 pandemic, but these changes were not statistically significant ( $66.7$  vs  $50\%$ ,  $p=0.54$  and  $66.6$  vs  $33.3\%$ ,  $p=0.69$  retrospectively). Three (15%) had a home-type mechanic ventilator and 5 (25%) had a tracheostomy.

Those who developed PEG complications had their serum values of albumin and vitamin B12 decreased statistically significantly when compared to those patients who did not develop complications. ( $3.3 \pm 0.4$  vs  $4 \pm 0.4$ ,  $p=0.022$  and  $578 \pm 199$  vs  $1299 \pm 533$ ,  $p=0.007$ ). Patients who had their PEG replaced had a statistically significant drop in their serum albumin levels ( $3.6 \pm 0.4$  vs  $4.2 \pm 0.5$ ,  $p=0.028$ ). When compared the parameters of patients with home typing mechanic ventilator and without as well as those with tracheostomy and without, the difference was not statistically significant ( $p>0.05$ ).

## Discussion

Preterm birth or low birth weight are the etiologic risk factors for neurological diseases

where the most common condition is cerebral palsy. This being said, these causes are the reasons the PEG candidate number increase. In our study, 55% of all cases and 63.6% of those who had cerebral palsy were preterm babies. Again, 50% of all cases and 45.4% of cerebral palsy patients had low birth weight. Especially, when the feeding conditions of cerebral palsy patients were considered, Wang et al [6] in their study showed that 54.1% of all their cases were pre-term babies and 43.8% were born with low birth weight. When compared with the current literature, both our total cases and cerebral palsy cases in terms of preterm birth and low birth weight following the literature.

The most common indications for PEG operation are neurologic disorders (84.6%) and metabolic disorders (10.2%) [7]. Children who suffer from neurologic disorders have difficulty with feeding, the most common disorder being cerebral palsy [8]. Studies show that most of the patients who have undergone PEG operation had cerebral palsy [7, 9]. In our study, this ratio was found to be 55%. The main reason for this percentage in our study is that all of our cases suffer neurologic disorders. Childhood neurologic disorders along with their complications cause feeding difficulty. This difficulty increases mortality and morbidity by adding malnutrition to the table. Malnutrition can be due to many causes, the most important of those causes are as follows; choking during feeding, prolongation in feeding time, hyperactive gag reflex, for those children who suffer seizures if the sleeping period after a seizure is prolonged, low energy intake due to medication and recurrent vomiting and gastroesophageal reflux disorder (GERD) [8,10]. The emergence of malnutrition depends on the type of disease, duration, and grade. The best way to prevent malnutrition is the regular visits to the hospital. Regular visits to the

hospital allow for the close follow-up of anthropometric measurements and if there is any deviation from the standard ranges they can be easily intervened. Regular visits to the hospital decrease the number of hospital admission, quicken the wound healing, and allow for cognitive and neurologic conditions to be corrected [10,11].

Cerebral palsy is where cerebral motor cortex is affected and a non-progressive disorder that limit movement of the patient and is a permanent motor function disorder [12]. The incidence in world is 2-3 in 1000 live births, but in Turkey, the incidence of cerebral palsy is 4.4 in 1000 live births [13, 14]. Feeding difficulty is a condition seen throughout the lives of cerebral palsy patients. This difficulty causes malnutrition in 56% -73% of the cases [15, 16]. In cerebral palsy, difficulty in feeding causes inadequate nutrition intake [17]. In addition, neurologic damage to muscle structure, endocrinologic factors, sedentary and general health condition contribute to feeding in these patients [18]. PEG is an important tool that can prevent malnutrition, but the operation must be decided on whether the PEG will better the life quality of the patient or not [19]. Another point that must be kept in mind for the PEG operation is the timing of the procedure. After the diagnosis of primary neurologic disorder when the oral feeding is insufficient within the first 6 months, feeding through tube is shown to affect the linear growth positively [20]. However, in our study the mean age of our patients was  $70.9 \pm 64.4$  months, and they were older compared to previous studies. Between the time of PEG operation and before the COVID-19 pandemic, patients were intervened to correct the weight for age which had positive effect on their overall health, but this intervention was not for height for age or BMI and the main reason for that is the late operation of PEG procedure. On

the other hand, we have seen that COVID-19 pandemic disrupted and nullified the positive effect we had on the patients.

It is shown that 50% of cerebral palsy patients have low iron intake [22]. In these cases, the prevalence of anemia ranged from 7.5% - to 33.3% [23, 24]. From this, it was evident that anemia not only leads to loss of appetite and malnutrition but also has negative effects on learning. In cerebral palsy patients, defect in absorption along with used medicines such as anti-convulsions, diuretics or corticosteroids create a clinical presentation with low levels of vitamins and minerals [25]. In a study done by Hillesund et al [26], 8.3% of cerebral palsy cases had low levels of serum vitamin B12 and 22.2% of cases had low levels of folate. Contrary to this study, Papadopoulos et al [24], stated none of the children with cerebral palsy had low serum vitamin B12 or folate levels. In our study, an adequate and balanced diet was maintained after PEG operation and as a result, the increase in weight for age and hemoglobin levels was statistically significant. After PEG operation, we did not observe any changes in vitamin and mineral levels, this result was considered to be due to refractory epilepsy and neurodegenerative diseases in the population. It should be noted that the findings of normal vitamin B12 and folic acid levels were consistent with the study of Papadopoulos et al [24].

High creatinine levels indicating disturbed renal function in patients with PEG are accepted as predictors of mortality [27]. Interestingly, the serum creatinine levels of our patients increased progressively after PEG operation and serum GFR levels dropped during the COVID-19 pandemic, these changes were statistically significant. Although the change was statistically significant, the values were not outside the normal ranges. The main

cause of this change is thought to be the feeding of concentrate to the patients for weight gain. This shows us the importance of monitoring renal functions after PEG operation.

Having direct contact with the outside environment of the gastrointestinal system brings complications along. In childhood, complications of PEG range from 42.9% – to 54.7% [28, 29]. Park et al [30], stated that when patients with PEG due only to the neurologic disorders are taken into consideration, the complication rate was found to be 47%. In our study, we found a complication rate of 60%, which is a high value compared to the literature. We believe that the main reason for this high rate is the low number of hospital visits due to the COVID -19 pandemic, as the number of annual visits decreased from  $9.8 \pm 5.7$  to  $2 \pm 1.7$ . The complications suffered by the patients were basic complications such as local infections, and leaks. The most common complications listed in the literature at PEG were granulation tissue formation, local erythema, leakage and obstruction [28, 31]. This high complication rate was the main cause of the high PEG replacement rate.

In developed countries, sepsis is observed in 4% of patients under 18 years of age admitted to hospital [32]. The mortality rate due to sepsis ranges from 10% to 18% depending on the severity of the underlying diseases, presence of risk factors, and geographical regions [33, 34]. Low levels of albumin are associated with sepsis and a high mortality rate [35]. In studies, hypoalbuminemia was found to be associated with a high mortality rate for patients with PEG, therefore hypoalbuminemia should not be allowed to develop under any circumstances [36]. Cerebral palsy patients may have low levels of serum albumin and prealbumin. However, these parameters should not be the only parameters to be considered when the

nutritional well-being of the patients is to be assessed [37]. In these patients, the main problem is not the lack of albumin but the low energy [38]. On the other hand, the relationship between hypoalbuminemia and inadequate nutrition has not yet been clarified [37]. This is because high levels of IL-6 and TNF-alpha-causing inflammation can cause hypoalbuminemia through decreased production and increased destruction of albumin [39]. Following the literature, in our study, we found low levels of serum albumin in patients who developed PEG complications and had their PEGs replaced.

These patients have a low intake of iron, zinc, copper, vitamin D, carnitine, folic acid, and vitamin B12 with other vitamins and minerals compared to healthy children [40]. Decreased vitamin C intake causes iron reabsorption defects, not getting enough sun time decreases vitamin D levels and increased antiepileptic medication usage decreases serum carnitine, vitamin B12, folate, calcium, and phosphorus levels. In these patients, low intake of calcium, phosphorus, magnesium, and vitamin D decreases muscle strength, bone density, and minimal injuries in bones causing fractures [41]. Feeding through PEG along with nutrition supplements prevents the lack of these vitamins and minerals, and is considered to be an important approach to these patients [26]. In our study, in all three-time intervals, the change in serum minerals, ferritin, folate and vitamin B12 levels was not statistically significant, but an increase in serum vitamin D levels was found to be statistically significant. Since there was a lockdown due pandemic, patients spent less time outside limiting their time spent in the sun, this increase in serum vitamin D levels must be due to the medications, the patients receive.

The main limitations in our retrospective study are the inability to assess the quality of the

nutritional products and the lack of GERD investigation.

### **Conclusions**

Childhood neurological disorders cause feeding difficulties in addition to disease-specific problems. When oral feeding is not possible for prolonged periods, PEG is an alternative method to prevent malnutrition. However, this procedure should not be delayed, as waiting will negate any benefits. Although our patients' procedures were delayed, there was a minimal benefit of PEG, but the quarantine conditions due to COVID-19 pandemic such as lockdown and socio-economic problems negated these minimal benefits and caused an increase in PEG complications. To benefit PEG maximally, patients must not skip their hospital visits under any circumstances, if they cannot visit the hospital, they should be visited in their home, but COVID-19 pandemic put an extreme amount of pressure on the health professionals either in hospitals or as filiation groups and prevented these visits.

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**Ethical Statement:** *The study was approved by the Bolu Abant Izzet Baysal University Clinical Researches Ethic Committee (2021/105).*

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