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Research

# Evaluation of Adult Patients with Childhood-onset Chronic Disease Admitted to the Intensive Care Unit

## Yoğun Bakım Ünitesine Başvuran Çocukluk Çağı Başlangıçlı Kronik Hastalığı Olan Erişkin Hastaların Değerlendirilmesi

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## ABSTRACT

**Objective:** Many patients with childhood-onset chronic disease (CCD) can reach adulthood with improvements in medical treatments. They may require intensive care unit (ICU) admission for various reasons throughout their lives. The aim of this study was to evaluate the reasons for hospitalization and treatment processes of patients with CCD in the adult ICU.

**Methods:** The files of 69 patients with CCD who were treated in the adult ICU between June 1, 2010 and May 31, 2020 were retrospectively evaluated. Demographic characteristics, CCD and coexisting diseases, ICU admission diagnosis, treatment processes, and results were recorded.

**Results:** The patients were median age 24 (21-30.5) years 43.5% of whom were female. The most common CCD, comorbid disease, and diagnosis of ICU admission were cerebral palsy (27.5%), epilepsy (23.2%), and pneumonia (40.6%), respectively. Ten (52.6%) of 19 patients who died were lost due to sepsis. Mortality rates were significantly higher in patients with comorbid diseases, such as chronic lung disease or mental retardation ($p<0.005$).

**Conclusion:** We believe that the life expectancy of patients with childhood chronic illnesses is increasing, necessitating the development of adult ICUs to cater to these patients. Furthermore, it is essential to provide training to doctors and nurses working in ICUs for special patient care.

**Keywords:** Chronic childhood disease, cerebral palsy, intensive care

## ÖZ

**Amaç:** Çocukluk çağında başlayan kronik hastalığı (ÇKH) olan birçok hasta, tıbbi tedavilerdeki gelişmelerle yetişkinliğe ulaşabilmektedir. Bu hastaların yaşamları boyunca çeşitli nedenlerle yoğun bakım ünitesine (YBÜ) yatışları gerekebilmektedir. Çalışmamızın amacı, erişkin YBÜ'lerde çocukluk çağında başlayan kronik hastalığı olan hastaların yatış nedenlerini ve tedavi süreçlerini değerlendirmekti.

**Gereç ve Yöntem:** 1 Haziran 2010 ve 31 Mayıs 2020 tarihleri arasında erişkin YBÜ'lerde tedavi edilen, ÇKH olan 69 hastanın dosyaları retrospektif olarak değerlendirildi. Demografik özellikler, ÇKH ile eşlik eden sistemik hastalıkları, YBÜ'ye yatış tanıları, tedavi süreçleri ve sonuçları kaydedildi.

**Bulgular:** Hastalar ortanca 24 (21-30,5) yaşındaydı ve %43,5'i kadındı. En sık görülen ÇKH, eşlik eden sistemik hastalık ve YBÜ'ye yatış tanısı sırasıyla serebral palsi (%27,5), epilepsi (%23,2) ve pnömoni (%40,6) idi. Ölen 19 hastanın 10'u (%52,6) sepsis nedeniyle kaybedilmişti. Kronik akciğer hastalığı veya mental retardasyon gibi yandaş hastalığı olanlarda ölüm oranları anlamlı olarak daha yüksekti ($p<0,005$).

**Sonuç:** ÇKH olan hastaların ortalama yaşam sürelerinin uzamakta olduğunu ve bu hastalara yönelik yetişkin YBÜ'lerin hazırlanması gerektiğini düşünmekteyiz. Ayrıca YBÜ'lerde çalışan doktor ve hemşirelere özellikli hasta bakımı için eğitim verilmesi gereklidir.

**Anahtar Kelimeler:** Çocukluk çağı kronik hastalıkları, serebral palsi, yoğun bakım

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## INTRODUCTION

Today, many patients with chronic diseases, such as congenital heart disease, cystic fibrosis, and cerebral palsy (CP), starting in childhood can reach adulthood with improvements in medical treatments (1-5). These patients, who are treated in pediatric intensive care units (ICUs) during the growing period, may require ICU hospitalization for various reasons (heart failure, epileptic seizure, aspiration pneumonia, etc.) when they reach adulthood. While pediatricians may not be adequately equipped to treat the adult medical needs of these patients, healthcare professionals and hospitals specializing in the care of adult patients may have insufficient expertize to manage adult symptoms of conditions emerging in childhood (6).

In our country, the Ministry of Health considers individuals under the age of 18 as children. The Ministry recommends that pediatric patients should be treated in pediatric ICUs; however, if there is no space available, they should be admitted to adult ICUs (7). In routine practice, children taken to adult ICUs are transferred to pediatric ICUs as soon as possible because of the conditions. However, when children with childhood-onset chronic disease (CCD) reach the age at which they should be accepted as adults, they are admitted to the adult ICU due to the payment terms of "Social Health Insurance". However, despite the increasing age of these children, some of them are still considered children in terms of physical development. In these patients, physiological and developmental differences require different approaches in drug and fluid therapies, drug doses, cardiopulmonary resuscitation, and safety. The characteristics of these patients who are admitted to ICUs should be well known to prepare for the increase in the number of adults with chronic diseases starting in childhood. However, very few studies have focused on adults living in spite of CCD and hospitalized in the ICU (8,9). Until now, there has not been any study conducted in our country on the status of these patients treated in ICUs managed by physicians and nurses specialized in adult patient treatment.

The aim of this study was to evaluate the demographic characteristics of patients with CCD admitted to the adult ICU, the reasons for admission to the ICU, treatment processes, and treatment results.

## METHODS

After the approval of the University of Health Sciences Türkiye, Bursa Yüksek İhtisas Training and Research Hospital Ethics Committee (decision no: 2011-KAEK-25 2020/06-24, date: 24.06.2020), the files of patients who were hospitalized in the adult ICU between June 1, 2010 and May 31, 2020 were scanned in electronic records. Chronic diseases that started in childhood were identified using the International Statistical Classification of Diseases and Related Health Problems 10 codes. Demographic data of the patients, chronic diseases diagnosed in childhood, coexisting diseases, ICU admission diagnosis, ICU hospitalization place (emergency room, clinic, operating room), Glasgow coma score, Acute Physiology and Chronic Health Evaluation (APAHCE) II score, and status of ICU hospitalization before were recorded.

Treatments applied to patients in the ICU and their durations mask-nasal oxygen, noninvasive/invasive mechanical ventilation (NIMV/IMV), endotracheal intubation, opening tracheostomy, extracorporeal treatments [renal replacement therapy (RRT), plasmapheresis, selective bilirubin apheresis, extracorporeal membrane oxygenation (ECMO)], route of nutrition administration (oral/nasogastric, gastrostomy, parenteral), length of ICU stay, and treatment outcome (death, discharge) were saved.

The basic life conditions of the patients (not dependent, partially dependent and fully dependent) and the presence of contractures were evaluated.

### Statistical Analysis

The IBM SPSS ver. 22.0 (SPSS Inc.; Armonk, NY, USA) program was used for statistical evaluation. The Shapiro-Wilk test was used to examine whether the data were compatible with the normal distribution. Descriptive statistics for numerical variables are expressed as mean ± standard deviation or median ± interquartile range for quantitative data, frequency and percentage (%) for qualitative data. The t-test was used to evaluate the significance of variations and to compare quantitative variables, and the Mann-Whitney test was used to compare quantitative variables with abnormal distribution. Qualitative variables were evaluated using the chi-square ($\chi^2$) test. Results were evaluated at 95% confidence interval and $p<0.05$ was considered significant.

## RESULTS

During the study period, 75 patients with CCD were admitted to the adult ICU. Six patients were admitted to the ICU on different dates. Only the first hospitalizations of these patients were included in the study, and evaluation was performed for 69 patients. The patients were a median age of 24 (21-30.5) years, and 43.5% of them were women. The most common CCD was CP (27.5%) and the most common comorbid disease was epilepsy (23.2%). Patients were frequently admitted to the ICU with more than one

diagnosis, and the most common ICU diagnosis was pneumonia (40.6%) and status epilepticus (18.8%). Forty (58%) patients were admitted from the emergency room, 19 (27.5%) from in-hospital clinics, 8 (11.6%) from the operating room, and 2 (2.9%) from the pediatric ICU. APACHE-II was calculated as the prognostic ICU hospitalization score in all patients, and the expected mortality was found to be 32.65±3.96% with a mean score of 16.59±5.24. The actualized ICU mortality was 27.53% (n=19). The difference between the expected and actual mortality rates was statistically significant (p=0.004). Demographic data, ICU admission data, and clinical characteristics are given in Table 1.

Endotracheal intubation was performed in 45 patients. Difficult intubation was encountered in 4 of them. Video laryngoscopy was used in 3 of these patients, and fiberoptic bronchoscopy was used in 1 patient. A total of 18 patients underwent tracheostomy. Of these, 14 underwent percutaneous tracheostomy and 4 underwent surgical tracheostomy, which was performed by otolaryngologists. Three patients had a tracheostomy cannula when they were admitted to the ICU. IMV was applied to 48 patients for follow-up. During ICU treatment RRT was administered to 15 patients. Bilirubin apheresis was also applied to 2 of the patients who underwent RRT, and plasmapheresis was also applied to 1 of them. Bilirubin apheresis was performed to treat acute liver failure. Continuous RRT had to be applied to 4 patients with unstable hemodynamics. In addition, ECMO support was provided to 3 patients, one of whom had continuous RRT during ECMO. The treatments applied to the patients and their durations are shown in Tables 2 and 3.

The nutrition of the patients was mostly provided by a nasogastric tube (47.5%). Four patients underwent percutaneous endoscopic gastrostomy (PEG) on admission to the ICU; one of them had to be removed because of infection. PEG was performed in three patients during their treatment in the ICU (Table 2).

In the ICU routine, while family members' visits were limited to once a day, the families of these patients were allowed to visit at least three times a day.

Patients were discharged to in-hospital clinics most frequently (60%) after ICU treatment. Ten (52.6%) of 19 patients who died were lost due to sepsis (Table 4). There was no significant relationship between CCD and ICU mortality (p=0.1). The mortality of the patients whose reasons of hospitalization were pneumonia, sepsis, and post-cardiac arrest was found to be significantly higher than the other hospitalization diagnoses (p<0.05, p<0.05, p<0.01, respectively).

**Table 1. Demographic data of patients and disease diagnosis**

| | ICU patients (n=69) |
|---|---|
| Gender (F/M), (n), (%) | 30/39 (43.5/56.5) |
| Age (year) (median) (IQR) | 24 (21-30.5) |
| APACHE-II score (mean ± SD) | 16.59±5.24 |
| GCS (median) (IQR) | 10 (8.5-14) |
| **Diagnosis of admission to ICU n (%)*** | 100 (100) |
| Pneumonia | 28 (40.6) |
| Status epilepticus | 13 (18.8) |
| Acute respiratory failure | 12 (17.3) |
| Renal failure | 11 (15.9) |
| Post-cardiac arrest | 11 (15.9) |
| Diabetic ketoacidosis | 8 (11.6) |
| Post-operative respiratory failure | 5 (7.2) |
| Sepsis | 5 (7.2) |
| ARDS | 2 (2.9) |
| Post-operative bleeding | 3 (4.3) |
| Others | 2 (2.9) |
| **Childhood-onset chronic disease n (%)** | 69 (100) |
| Cerebral palsy | 19 (27.5) |
| Diabetes mellitus type I | 11 (15.9) |
| Chromosomal genetic abnormality | 9 (13) |
| Immune deficiency | 8 (11.6) |
| Cystic fibrosis | 5 (7.2) |
| Epilepsy | 3 (4.3) |
| Congenital muscular dystrophies | 3 (4.3) |
| Familial Mediterranean fever | 2 (2.9) |
| Primer sclerosing cholangitis | 2 (2.9) |
| Congenital cardiac disease | 2 (2.9) |
| Lymphoma | 2 (2.9) |
| Meningomyelocele | 1 (1.4) |
| Thalassemia major | 1 (1.4) |
| **Comorbidity n (%)*** | 60 (100) |
| Epilepsy** | 16 (26.6) |
| Mental retardation | 12 (20) |
| Chronic renal failure | 10 (16.7) |
| Hypertension | 6 (10) |
| Chronic lung disease | 6 (10) |
| Other | 10 (16.7) |

ICU: Intensive care unit, F/M: Famele/male, IQR: Interquartile range, SD: Standard deviation, APACHE: Acute Physiology and Chronic Health Evaluation, GCS: Glasgow coma scale, ARDS: Acute respiratory distress syndrome, CPR: Cardiopulmonary resuscitation
*A patient may have more than one hospitalization diagnosis
**Childhood disease not diagnosed with epilepsy

High mortality was encountered in those with a diagnosis of cystic fibrosis (4 out of 5 patients=80%). It was found that these patients were admitted to the ICU due to respiratory failure and pneumonia, that 3 of them died from hypoxemia, and one of them died from heart failure in a median period of 6 days (minimum 2-maximum 10).

Mortality rates were significantly higher in patients with comorbid diseases such as chronic lung disease or mental retardation ($p<0.05$). The durations of ICU stay and respiratory support belonging to those who were discharged and those who died were similar ($p>0.05$).

When the basic life conditions of the patients during their hospitalizations were examined, it was found that 26 (37.7%) patients were completely dependent, 13 (18.8%) were partially dependent, and 30 (43.5%) patients were independent. There was no significant relationship between basic life situations and mortality. In addition, 6 (8.7%) patients had severe contractures of the extremities during ICU hospitalization.

**Table 2.** ICU supportive treatment of patients*

| | ICU patients (n=69) |
|---|---|
| **Oxygen therapy, n (%)** | 44 (100) |
| Mask | 39 (88.7) |
| Nasal cannula | 3 (6.8) |
| HFNO | 2 (4.5) |
| **Mechanical ventilation, n (%)** | 54 (100) |
| IMV | 48 (88.9) |
| NIMV | 6 (11.1) |
| **Nutrition, n (%)** | 69 (100) |
| NG | 33 (47.8) |
| Oral | 11 (15.9) |
| Oral + NG | 11 (15.9) |
| PN + NG | 8 (11.6) |
| PEG | 6 (8.7) |
| **Extracorporeal treatment, n (%)** | 21 (100) |
| RRT | 15 (71.4) |
| ECMO | 3 (14.3) |
| Bilirubin apheresis | 2 (9.5) |
| Plasmapheresis | 1 (4.8) |

ICU: Intensive care unit, IQR: Interquartile range, HFNO: High-flow nasal oxygen, IMV: Invasive mechanical ventilation, NIMV: Non-invasive mechanical ventilation, NG: Nasogastric tube, PN: Parenteral nutrition, PEG: Percutaneous endoscopic gastrostomy, RRT: Renal replacement therapy, ECMO: Extracorporeal membrane oxygenation
*More than one supportive treatment was applied to a patient

**Table 3.** Duration of supportive treatments and ICU length of stay

| | ICU patients (n=69) |
|---|---|
| Endotracheal intubation (day) median (IQR) | 12 (6-23) |
| **Oxygen therapy** | |
| Mask (day), median (IQR) | 3.5 (2-8) |
| Nasal (day), mean ± SD | 16.33±10.01 |
| HFNO (day), mean ± SD | 2±0 |
| NIMV (day), mean ± SD | 3.16±1.94 |
| IMV (day), median (IQR) | 19.5 (5.75-44) |
| ICU LOS (day), median (IQR) | 19 (6.5-45) |

ICU: Intensive care unit, IQR: Interquartile range, NIMV: Non-invasive mechanical ventilation, IMV: Invasive mechanical ventilation, HFNO: High-flow nasal oxygen, SD: Standard deviation, LOS: Length of stay

**Table 4.** Discharge and mortality status of patients

| | ICU patients (n=69) |
|---|---|
| **Mortality n (%)** | 19 (27.5) |
| **Cause of death n (%)** | 19 (100) |
| Sepsis | 10 (52.6) |
| Hypoxemia | 4 (21.1) |
| Multi-organ failure | 2 (10.5) |
| Acute liver failure | 2 (10.5) |
| Hearth failure | 1 (5.3) |
| **Discharge n (%)** | 50 (100) |
| Clinics | 30 (60) |
| Palliative service | 11 (22) |
| Home | 9 (18) |

ICU: Intensive care unit

## DISCUSSION

Our study on the treatment of CCDs in "adult ICUs" is the first study from our country on this subject. In our study, we found that these patients were most frequently admitted to the ICU with a diagnosis of pneumonia, that the most common CCD was CP, and that ICU treatments resulted in 27.5% mortality.

Nowadays, because more children with chronic diseases that start in childhood reach adult age, there is a need for healthcare professionals and hospitals that can manage both their CCDs and adult diseases that can occur with age. For example, cardiovascular diseases (CVDs), which we could not see in patients with CP years ago, are now seen today as they reach adulthood (2). In this case, the clinics where the patient is hospitalized should be sufficient for

the management of CVDs and CP. In addition, it is unclear in which clinics both such patients and patients situated between children and adults should be treated. Balancing subspecialty care with age-appropriate care is difficult. Goodman et al. (4) examined adult patients with CCD who were hospitalized in a children's hospital between 1999 and 2008 and found that 2.8% of all hospitalizations were over 18 years old [transitional (2.0%): 18-21, adult (0.8%): aged>21]. The authors reported that the most common reason for hospitalization was congenital heart disease, followed by malignant neoplasms. Loveday et al. (1) stated that when looking at adult and pediatric ICU admissions of teenagers aged 16-19, although those with congenital and neuromuscular disorders are hospitalized in pediatric ICU, admission diagnoses in adult ICU were trauma and diabetic ketoacidosis. In our study, we examined patients over 18 years of age with only a CCD diagnosis in the adult ICU. We determined that the 3 most common primary CCD diagnoses were CP, diabetes mellitus (DM) type I, and chromosomal/genetic diseases. While pneumonia was the most common cause of ICU admission, 11.6% of the patients were admitted to the adult ICU with the diagnosis of diabetic ketoacidosis.

It was reported that patients diagnosed with CP may have hospital and ICU admission requirements for reasons such as aspiration pneumonia, pressure sores, and status epilepticus until reaching adulthood and after. Similarly, in our study, we found that patients with the most frequent diagnosis of CP were admitted to the ICU with a diagnosis of status epilepticus and pneumonia (10). Mcphee et al. (11) in their systematic reviews based on 19 studies on adult CP patients showed some evidence that the prevalence of CVD increases with age in these patients and that there is an increased risk of death due to certain risk factors such as hypertension, obesity, and CVD. In our study, we found that 4 patients diagnosed of CP died because of ICU treatment. Although the relationship between deaths and CVD could not be determined, hypertension was in 3 patients as a concomitant disease.

The majority of patients diagnosed with cystic fibrosis reach adulthood today, and in a period of their lives, they may require ICU hospitalization because of pulmonary and gastrointestinal system problems (3,12). The median age of these patients is prolonged up to 40 years, and short-term ventilation support may be required after elective surgical operations such as opening a gastrostomy (12). Siuba et al. (13) found a mortality rate of 44.5% in adults with cystic fibrosis who required mechanical ventilation. In our study, 5 patients diagnosed with cystic fibrosis were admitted to the ICU. One of these patients was taken to the ICU postoperatively, and the other four patients were diagnosed with respiratory failure due to pneumonia. Unfortunately, 80% of our patients who received IMV support died.

In fact, in everyday medical practice, the answer to the question "Can adult ICUs adequately meet the care needs of pediatric-looking patients due to growth retardation with CCD?" is essential. Today, as increasing numbers of children with chronic diseases survive into adulthood, it is unclear whether pediatric or adult ICUs are the best place to meet the critical care needs of these patients or not. In a study, it was found that, 19-40 years-old adult patients with CCD, except for type I diabetes, were hospitalized more frequently in pediatric ICUs. The authors suggested that as the number of these patients increased, pediatric ICUs should gradually be prepared for older patients and/or adult ICUs should be able to meet the care needs of these patients (2). In another study by the same authors, it was found that those in their early 20s (20-22 years) were admitted to the pediatric ICU and 25-32 years old individuals were admitted to the adult ICU. In this study, it was observed that patients with CCD are mostly admitted to the pediatric ICU (5).

Because family dependency is high in patients with CCD, it should not be forgotten that the role of the family may be different in the treatment process in such patients in the ICU, and hospitalization in a separate child-oriented decorated unit should be considered in adult ICUs (14). In our study, a flexible visitation policy was applied to family members.

Patients with CCD may encounter some problems when they reach adulthood and are admitted to the adult ICU. Adult airway equipment (oral-nasal airway, laryngoscope blade, endotracheal tube, laryngeal mask airway, bronchoscope, etc.) may not be suitable for some of these patients who are adult in age and may be child-sized in terms of body surface area and development. Likewise, the doses of all drugs, including intravenous peripheral and central venous catheters, antibiotherapy and sedative-analgesic drugs, and fluid-electrolyte replacement, may differ from those in adult patients. Adult ICU nurses may have difficulties caring for adult patients with a childlike appearance (14,15). However, in a survey conducted by Suzuki et al. (15) about "transitional care" of adolescents and adults with CCD, they found that 73.6% of nurses had no awareness of "transitional care". In this study, both pediatrics and adult nurses stated that pediatricians would be the ideal coordinator for transiting CCD patients from child-focused to adult-focused health care. The improved survival of children with chronic illnesses has led to the necessity of transitioning from pediatric healthcare to adult care for adolescents and

young adults with special healthcare needs. Transfer of care from pediatric to adult providers is vital for young adults with complex health needs. Good communication and collaboration between the pediatric and adult care teams are crucial to reduce the rate of ICU morbidity and mortality (14-16).

It is retrospective and examines patients with a disease that only started in childhood and was treated in the adult ICU. However, these patients can sometimes be treated in the pediatric ICU by pediatricians who have followed the patient since childhood when the disease was diagnosed. Another limitation of this study is that we could not compare the data of patients with the same characteristics who were treated in the pediatric ICU.

## CONCLUSION

It should be kept in mind that the life expectancy of patients with CCD is prolonged, that adult ICUs should be prepared for these patients, and that physicians and nurses in the ICU should be trained in the care of patients.

### ETHICS

**Ethics Committee Approval:** University of Health Sciences Türkiye, Bursa Yüksek İhtisas Training and Research Hospital Ethics Committee approval was obtained (decision no: 2011-KAEK-25 2020/06-24, date: 24.06.2020).

**Informed Consent:** Retrospective study.

### Authorship Contributions

Concept: G.Ç., A.S., H.E.S., N.K.G., Design: G.Ç., A.S., H.E.S., N.K.G., Data Collection or Processing: G.Ç., A.S., H.E.S., N.K.G., Analysis or Interpretation: G.Ç., H.E.S., N.K.G., Literature Search: G.Ç., A.S., H.E.S., N.K.G., Writing: G.Ç., A.S., H.E.S., N.K.G.

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