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Unusual Lifespan of Edwards' Syndrome in COVID-19 Era

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Abstract

Edwards' syndrome is caused by an extra chromosome on the 18th chromosome. Patients with this diagnosis have median survival of only 3–14.5 days, with the majority of infants with full trisomy 18 type die before or shortly after they are born. There is only supportive treatment available for Edwards' syndrome. During the COVID-19 pandemic, providing health services was challenging, leading to less than optimum treatments added by patients' reluctance to visit healthcare facilities due to the fear of COVID-19 transmission. This case study presented an infant with Edwards' syndrome with major malformation. The patient had several organ problems, was admitted to the NICU, and continued with home care for monitoring for 6 months. Patient then died at 9 months of age. Maintaining the best quality of life for this patient was very challenging for parents and healthcare providers. Since the management for this type of sydnome is more palliative, good education, information, and psychosocial supports for the parents are needed to prepare them with the worst conditions, which was especially more challenging during the COVID-19 pandemic.

Keywords: Covid 19, full trisomy, survival, trisomy 18

Introduction

Edwards' syndrome or trisomy 18 was discovered by John H. Edwards in 1960, also known as autosomal aneuploidy chromosomal disorder. It is caused by an extra chromosome on the 18th chromosome and is the second most common genetic disorder after trisomy 21.[1,2] Patients with Edwards' syndrome have some characteristics in physical appearance, which may be accompanied by congenital heart defects, and abnormalities in the brain, gastrointestinal, and kidney.[3,4] The incidence varies from 1/2500 to 1/7000 live births, more often in girls (about 80%) compared to boys.[1,2]

Children with trisomy 18 present with a range of congenital abnormalities, including mild to severe physical deformities, psychomotor impairment, cognitive deficits, and a high risk of intrauterine or postnatal death.[5] This current study reports a median survival of 3 to 14.5 days for infants with full trisomy 18, with the majority dying before or shortly after birth..[2,5]

Management is multidisciplinary based on the clinical manifestations, the decision of parents to care for the baby, ethical issues related to the high mortality rate, and the disabilities that arise if the baby survives.[2] The most common cause of death in these cases is heart problems and respiratory disorders.[2]

The COVID-19 pandemic situation has had an impact on restrictions in all routine health services, including the maternal and newborn health service sector. The impacts include a decrease in visits by pregnant women to healthcare facilities, issuance of recommendations for postponing pregnancy check-ups and classes for pregnant women, and limited health resources both in terms of personnel and facilities. Maternal and newborn health services are one of the services affected in terms of access and quality.[6]

In this case, we are about to discuss a baby with Edwards' syndrome who was born in the era of the COVID-19 pandemic, there are restrictions in various aspects of life including access to health services. The real impact of the COVID-19 pandemic, in this case, is that the health services provided to patients are not optimal. However,

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this patient's life span can still last longer.

Case

A 33-day-old baby boy was referred to Dr. Hasan Sadikin General Hospital (RSHS) as a tertiary health care for West Java, Indonesia located in Bandung, with the diagnosis of pneumonia, ventricular septal defect, patent ductus arteriosus, heart failure, 36 weeks preterm infant, low birth weight, intrauterine growth restriction, cholestasis jaundice, bacterial conjunctivitis oculi sinister and microcephaly. The baby was given supplemental oxygen therapy at 0,5 liters per minute due to respiratory distress.

Table 1 Six Months Monitoring

Variable	Medical Problems
1st Month Chronological age: 4 months, 9 days Correction age: 3 months, 9 days	**Medical Problems,** The patient was unresponsive to calls, still using oxygen and fed by OGT sucking. Anthropometric status was underweight and short stature, developmental screening suspected intellectual disability. The patient had not been immunized. The parents were worried about the patient's growth and development and the COVID-19 pandemic. The parents were being educated about their concerns and how to stimulate development.
2nd Month Chronological age: 5 months, 9 days Corrected age: 4 months, 9 days	**Medical Problem,** Patient sometimes turned towards the sound. The patient began side-turning. Body weight has increased, the development began to progress. Oromotor training was done and OGT was replaced, advised to control polyclinics including ENT, eye, nutrition, neuropediatrics, social development and pediatrics, cardiology, endocrinology.
3rd Month Chronological age: 6 months, 9 days Corrected age: 5 months, 9 days	**Medical Problems,** The weight has increased; The patient received oromotor training and OGT nutritional fulfillment, OGT replacement, and monitoring oxygen therapy at home
4th month Chronological age: 7 months, 19 days Correction age: 6 months, 19 days	**Medical evaluation,** The patient responded to calls, sometimes smiled. The patient made a cooing sound. The patient paid attention to the sounding rattle. The patient has not received DPT, HiB, hepatitis B, and Polio immunization. The patient was no longer underweight but still short stature Patient received 135 ml/3-hour formula milk (723 kcal) Control to pediatrician Nutrition: The weight has increased, however, not on target, body length increase was not significant, and short stature was suspected to be related to the syndrome. The development began to progress, the patient began to respond to the sound
5th Month Chronological age: 8 months 9 days Correction age: 7 months 9 days	**Medical evaluation** Weight has increased however, not on target, body length increase was not significant **Plans** Formula milk plan was increased to 150 ml/3 hours (804 kcal) Control to polyclinics Immunization of DPT, HiB, hepatitis B, and Polio 2. Chest X-ray and laboratory examination were planned
6th Month Chronological age: 9 months Correction age 8 months	**Medical Problem,** The patient was still using oxygen at 1 LPM nasal cannula and getting nutrition through OGT. The patient was still a short stature **Medical evaluation,** The patient-controlled to a pediatrician and was advised to undergo physiotherapy and eye and ear examinations

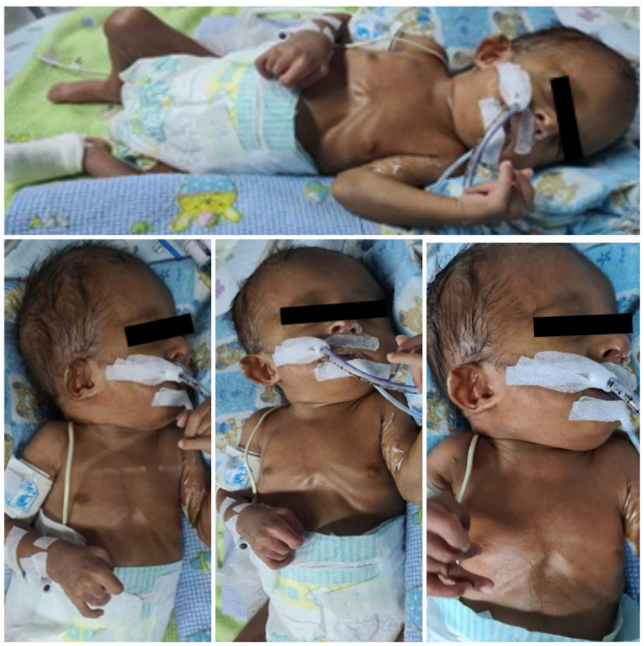

Figure 1 The Condition of the Baby at the Time of Being Treated at RSHS

Actual weight 2060 grams, length 45.5 cm with a head circumference of 32.5 cm. Physical examination showed facial dysmorphic micrognathia, strabismus, low-set ears, and hand clenched with abnormal fingers (Figure 1). On the fourth day of treatment, the patient experienced respiratory failure and was transferred to the Neonatal Intensive Care Unit (NICU).

The patient was born at a secondary healthcare hospital in Bandung, West Java, since the family resides in Bandung. The baby boy was born to a P4A0 mother by cesarean section with the indication of Intra Uterine Growth Restriction (IUGR) and high-risk mother (aged 42 years), birth weight of 2050 grams, birth length of 42 cm, head circumference 32 cm, APGAR score 1 minute and 5 minutes were 6/8 with no history of bluish at birth. The patient was referred to another secondary healthcare hospital in Bandung with more comprehensive tools for intensive care. On the 22nd day of treatment, the patient was referred to RSHS for further treatment.

Chest X-ray results showed right pneumonia

Figure 2 Patient at 8 Months of Age

with a differential diagnosis of right superior lobe atelectasis and cardiomegaly. Chest X-rays suggested bilateral pneumonia and cardiomegaly. The echocardiography showed a large perimembrane ventricular septal defect and a tiny patent ductus arteriosus. Ultrasound showed a right inguinal hernia and mild hepatomegaly. A head ultrasound examination revealed benign external hydrocephalus. An ultrasound examination of the testicles revealed a right inguinal hernia with a right hydrocele. Analyze of chromosomes that were 47XY + full trisomy 18.

The patient's respiratory function was supported with a mechanical ventilator. Multidisciplinary care involved several specialties, including Cardiology, Gastrohepatology, Respirology, Tropical Infectious Disease, Endocrinology, Neuropediatrics, Nutrition and Metabolic Disease, ENT, and Nutrition and Metabolic Disease.

The final diagnosis included Edwards syndrome, respiratory failure, pneumonia, suspected bronchopulmonary dysplasia, congenital CMV infection (manifesting as pneumonia, jaundice, microcephaly, failure to thrive, and intrauterine growth restriction), a large perimembranous ventricular septal defect (VSD), a tiny patent ductus arteriosus (PDA), mild heart failure, marasmus, short stature, and inguinal hernia.

After clinical improvement, the patient was discharged on the 43rd day of treatment using an orogastric tube (OGT) and oxygen 1 liter/ minute via nasal cannula.

The patient was visited by nurses for a home visit every 2 weeks, the monitoring results for 6 months are described in Table 1.

Monitoring for 6 months was carried out with home visits, parents did not bring their children for treatment control because they were worried about the increase in Covid-19 cases, therefore vision and hearing screening had not been carried out. During monitoring there was an increase in body weight, but still in short stature. The condition of the patient at 8 months of age is shown in Figure 2. At the age of 9 months, the patient was taken to the nearest hospital, and according to the doctor, the patient was death on arrival.

Discussion

The patient was the fourth child of four and was born by cesarean section. Since birth, the patient had shortness of breath and congenital heart disease. The patient was treated in NICU using a ventilator. Chromosomal analysis revealed Edwards' syndrome with full trisomy 18. The patient returned home with improvement, however, he was still on oxygen and OGT. Nurses made home visits to help care for patients every two weeks, the OGT was routinely changed. The family cared for and loved the patient with great affection.

Edwards' syndrome or trisomy 18 is caused by the presence of an extra chromosome on chromosome 18 and has various clinical manifestations with abnormalities on a scale of mild to severe.[5] Trisomy 18 has three types: full trisomy 18, partial trisomy 18, and mosaic trisomy 18, with 95% of all cases being full trisomy 18, where every cell in the body has an extra chromosome. Partial trisomy 18 and mosaic trisomy 18 are very rare.[7]

International guidelines for resuscitation and management of neonates with malformations recommend providing specialized palliative or supportive care and always emphasize that decisions must be made with the medical team and respect for parental autonomy.[8] The majority of infants with full trisomy 18 die before or shortly after they are born, some that survive will have severe cognitive impairment. Abnormalities include congenital heart defects, limb abnormalities, stunted fetal growth, and meningomyelocele.[9]

The clinical manifestations were facial dysmorphic micrognathia, low set ear, strabismus, hand clenched with abnormal fingers, ventricular septal defect, patent ductus arteriosus, right inguinal hernia, right hydrocele, and hydrocephalus. This patient had experienced severe clinical conditions at the beginning of life due to the abnormalities, nevertheless, after intensive treatment, clinical improvement was obtained, therefore, treatment could be continued at home. Parents were worried about home care but began to understand and accept the clinical condition after being explained slowly. They were willing to give the best to the patient; however, they were hampered by the pandemic.

A case report was obtained regarding 152 patients with Edward's syndrome. The male:female ratio was 1.3:1. More than half of the cases found that the parents' age was less than 30 years and were primigravida.[7] The most common disorders were cardiovascular, extremities, urinary tract, head, neck, GI tract, and genitalia. The most typical cardiovascular abnormalities

are VSD, atrial septal defect, and PDA. Common extremity abnormalities were abnormalities of the calcaneovalgus, hip abduction, and abnormalities of the fingers. The most common eye disorders were microphthalmos, epicanthal folds, and ocular hypertelorism. Regarding the ear, abnormalities were low set ear. Micrognathia and a short neck were also usual. In the GI tract, diaphragmatic hernia, umbilical hernia, and pyloric stenosis were often found. In the urinary tract often found hydronephrosis, hydroureter of the posterior urethral valve. In the testes, an undescended testis was often found.

Prenatal diagnosis using fetal DNA taken from maternal serum can identify abnormalities in the fetus at 10 weeks gestation. There is no actual data about the ratio of chosen termination compared to palliative care.[9] Congenital heart disease can be detected at the age of nine days, due to the poor prognosis, cardiology intervention was not performed.

Higher mortality rates were reported in the first week of life and the longest survival rate of most premature infants was 39 days. A case study mention that female carrier are more likely to survive longer, particularly with the mosaic type. Nonetheless, they had severe dependence and psychomotor retardation.[11] However, this study found an unusual pattern because the patient gender is male with full trisomy type and premature survived until 9 months.

The life expectancy of this case might increase due to the fast initial treatment since the baby was immediately given a mechanical ventilator when the respiratory failure happened. This is related to the three major causes of sudden death in Edwards syndrome: neurological instability, cardiac failure, and respiratory failure.[12]

The patient also receives a lot of attention in the tertiary healthcare hospital, where there is a Multidiscipline involved to treat the patient, such as Cardiology, Gastrohepatology, Respirology, Tropical Infectious Disease division, Endocrinology, Neuropediatric, Nutrition and Metabolic Disease, ENT, and Nutrition and Metabolic Disease division. This is similar to a case study mentioning that an 8-year-old girl with Edward syndrome and mosaic type has been treated by a multidisciplinary medical team due to musculoskeletal, joint, neurological, metabolic, and cardiovascular complications that have limited her quality of life.[13]

About 40-70% of Children with disabilities, including trisomy, have feeding problems. The factors include neurological status, anatomical problems, difficulty breathing, or motor disorders in the mouth. The interaction of one or more of these factors causes developmental delays or disorders that ultimately lead to feeding problems.[14] In this patient, feeding and breathing problems were also found. During home care, this patient used OGT to achieve nutritional needs and oxygen for his breathing problems.

The Denver II screening found delays in four aspects including gross motor, fine motor, language, and personal-social. The CAT CLAMS examination resulted in a suspected intellectual disability. This was suitable with the literature stating that developmental delays generally occur in patients with Edward's syndrome, both psychomotor disorders and intellectual disabilities. Most cases have expressive language disorder and gross motor disorder. Patients are unable to walk on their own, but a small proportion by using assistive devices. However, developmental delays are predictable, and developmental assessments are mandatory. Medical intervention and rehabilitation programs are recommended to reduce the progression of the delays that occur.[15]

The COVID-19 pandemic has caused a decline in the number of infants and toddlers that went to health facilities. Parents were worried that the patient would catch COVID-19. Furthermore, regarding the Large-Scale Social Restriction Policy (PSBB) to stay at home to prevent COVID-19, likewise limiting health service activities in health facilities.[16] Initially, the parents were concerned about managing the patient's condition in the hospital. After several counseling sessions, they agreed to continue with home care, including bi-weekly visits from nurses. A case study indicates that managing Edwards syndrome also requires counseling for parents regarding survival, frequent complications, and a risk-benefit assessment to be evaluated during the first year of life.[13]

The COVID-19 pandemic has also caused a decline in the number of infants and toddlers that immunized. Myths and misinformation about COVID-19 vaccine added to the doubts. Health workers were also adjusted for service hours or shifted to COVID-19 emergency health facilities and the lack of personal protective equipment (PPE). Vaccination officers were also concerned about the risk of transmitting COVID 19 that may occur during immunization services.[16] The decline in immunization visits was also found in the United States. The government-imposed social distancing and quarantine had an impact on immunization visits. The Michigan

Care Improvement Registry (MCIR) conducted a cohort study of changes in immunization coverage for children aged 1, 3, 5, 7, 16, 19, and 24 months during the pandemic and the result was a decrease in immunization coverage at every age, except the Hepatitis B vaccine.[17] In this case, the patient only received immunization once, this was also due to the worry to take the patient to healthcare facilities.

In this study, we found several limitations; firstly, our unique single case may not represent other cases, constraining our ability to extend these conclusions to a broader context. The lack of a control group in our study design significantly weakens the definitive cause-and-effect relationship. Lastly, considering the patient predominantly resided outside the hospital setting, numerous aspects of their condition remained beyond our observational scope. These limitations underscore the need for cautious interpretation of our results and suggest the value of further, more extensive studies in this area.

Edwards' syndrome, or trisomy 18, is characterized by numerous congenital abnormalities requiring palliative management. Essential aspects of care include immediate initial treatment, multidisciplinary involvement, ongoing evaluation of growth and development, and counseling with parents. These measures may improve life expectancy in individuals with Edwards syndrome. Additionally, social support and mental and psychological preparation for parents are crucial, particularly during the COVID-19 pandemic, to help them cope with challenging conditions.

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