

## Research Article

### Quality of Life in Congenital Adrenal Hyperplasia with Disorders of Sex Development: Case Series

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#### ABSTRACT

**Background:** Congenital adrenal hyperplasia is the most common cause of disorders of sex development with incidence being 1/15,000 live birth cases. Children with ambiguous genitalia appearance can affect their quality of life.

**Aim:** To evaluate the quality of life in children with disorders of sex development.

**Case Description:** We have five patients aged 6, 7, 8, 12, and 15 years with atypical external genital appearance that their parents complained since toddler. In addition to find abnormalities on physical examination, we also found abnormalities on karyotyping, ultrasound, blood sex hormones, and MRI examinations. We determined their quality of life using the PedsQL 4.0 General Score. Of the four items of questionnaire, emotional items showed the lowest score in five patients, respectively 25, 25, 50, 31.25, and 25.

**Conclusion:** Disorders of sex development influenced the patient's quality of life, especially in emotional items. It may lead to their psychological impacts because they feel sad, afraid, and worried with their ambiguous genitalia.

**Keywords:** Quality of life, congenital adrenal hyperplasia, disorders of sex development, ambiguous genitalia

#### INTRODUCTION

Disorders of sex development (DSD) are a heterogeneous group of rare conditions.<sup>1</sup> DSD is an umbrella term for a variety of conditions that encompass various aetiologies and presentations. DSD refer to congenital conditions in which development of chromosomal, gonadal, or anatomical sex is atypical as proposed by 2006 Consensus statement on management of intersex disorders.<sup>1,2</sup> However, more specific conditions occur at a rate of 1:100,000 births or fewer. DSDs are broadly classified into male (XY), female (XX) DSDs and sex chromosomal DSDs. Sex chromosomal DSDs are further divided into 45, X (Turner syndrome and variants), 47, XXY (Klinefelter syndrome and variants), 45, X/46, XY (Mixed Gonadal Ddevelopment/ovotesticular DSD), and 46, XX/46, XY (chimeric, ovotesticular DSD).<sup>3,4</sup> Congenital adrenal hyperplasia is the most common cause of DSDs in the newborn babies, incidence being 1 case/15,000 live births while MGD/ovotesticular DSDs ranks the second.<sup>5,6</sup>

The long-term psychological, physical, and social outcomes for young people with DSD are unclear. Recent reports have raised concerns regarding early corrective surgery and decisions for determination of sex rearing, which are matched by concerns expressed by patient advocacy groups.<sup>7,8</sup> Nevertheless, health-related quality of life measures are an adequate endpoint by which to evaluate outcomes in this group of patients because they take into account multiple dimensions of the patient's wellbeing.<sup>9</sup>

Sex ambiguity was one of social problem in Indonesia and affected by local culture, which is some patients feel embarrass, and many people think as a disgrace. These factors would affect the quality of life in patient with sex ambiguity beside the limited resources in Indonesia for the comprehensive treatment for patients with DSD. The resources in health care facilities among developing countries are also limited. This is a challenging for such

management of DSD in developing countries during pandemic covid-19. The data about QoL in DSD during Covid-19 is very limited.

The limitations of social activity, fear of infections, lack of medicine due to disruption in distribution during Covid-19 pandemic, influence the quality of life in chronic illness, such as DSD. Moreover, the QoL in DSD outside Pandemic has already disrupted. Study in Germany highlight the significant mental health burden of German children and adolescents during the COVID-19 pandemic. They allow conclusions to be drawn enabling health policy, prevention and clinical practice to provide suitable support in the present crisis and comparable future situations.<sup>10</sup> To the best of author knowledge, this paper is the first to report quality of life in DSD patients in Indonesia as limited resources country, during pandemic covid-19.

## CASE SERIES REPORT OBJECTIVE

The objective of this case series report was to report the psychological effect of DSD to patient and parent by reporting PedsQL profile score in Indonesian DSD patient with limited resources during pandemic covid 19.

## MATERIALS AND METHOD

We collected Peds QoL data of DSD patients aged between 2 and 18 years ( $n = 5$ ) who attended the paediatric endocrine clinic at the Soetomo Hospital Surabaya during 30 March 2020 to 30 Juli 2020. Written informed consent was obtained during a clinic visit from the parents or legal guardians of all the patients before participation. Consenting participants received a questionnaire booklet that they were asked to complete by the end of the clinic visit. The protocol was approved by the ethical committees of Soetomo Hospital, Surabaya. The data were obtained from medical interview (complications of adrenal crisis, if any ; history of medication given, and socio-economic data), physical examination ( pubertal development, degree of virilization) and medical records (including age at diagnosis, gender assigned, clinical and biochemical data at presentation including degree of virilization, number and nature of surgical procedures performed, karyotype, and pubertal status).

The tool used in these case series was the Pediatric Quality of Life Inventory™ Version 4.0 (PedsQL) Generic Core Scales questionnaire [17, 18]. The Peds QoL was translated to Indonesian language (approved by certified English translator). There were 4 core dimensions of health evaluate in Peds QoL, which are physical, social, emotional, and school function. The total questions were 23. We used the parent questionnaires version, which are age appropriate, with a modified version for each age group (5–7, 8–12, 13–18 years). For each question the parents were asked to score the answer on a scale of 0–4. Subsequently, this score was linearly transformed into a 0–100 scale so that a higher score would indicate a better quality of life (0–100, 1–75, 2–50, 3–25, 4–0). To create scores for each dimension, the mean of the scores was computed. The higher score indicated a better quality of life in each of the four dimensions. Psychosocial health summary score was taken from emotion, social, schooling functions, whether physical health summary score was taken from physical functioning.

## RESULT

First case, A, 7-year-old child, with chief complain of bilateral undescended testis (referral from urology surgery). From physical examination, patient had a phallus with chordae, the right and left gonad were palpable 1 cm near the phallus. Urology USG revealed intrainguinal right testis in right inguinal with size 0.9 cm x 0.46 cm x 1.32 cm, and left testis in left inguinal with size 0.8 cm x 0.4 cm x 1.2 cm. The karyotyping was 46, XX. The working diagnosis was 46 XX testicular DSD. The PedsQL score showed mean of physical functioning 100, emotional functioning 25, social functioning 83 and school functioning 83.

Second case, B, 12-year-old child was consulted due to elongated phallus and delayed puberty (referred from the Department of Obstetrics and gynecology). Initially, the child was reared as a girl. Parents also reported that patient had not experienced breast enlargement yet. On examination, the child had fully developed vagina and elongated phallus(1.5cm). However, there were no skin hyperpigmentation, labioscrotal fusion, nor palpable

gonads observed. The Tanner stage was A1M1P1. The USG showed that testis were observed in the right inguinal with size 1 cm x 0,9 cm x 1.4 cm, and left testis in left inguinal with size 1,1 cm x 0.9 cm x 1.2 cm; about 1,5cm near the phallus. The uterus was not visualized. Karyotyping was 45,X/46, XY. Laboratory results showed high testosterone level and low FSH. The working diagnosis was 45,X/46XY testicular DSD. The PedsQL score show mean of physical functioning 95, emotional functioning 31.25, social functioning 66.6 and school functioning 100.

Third case, C, 6 years old child was consulted due to undescended testis bilaterally. Patient had girl's name, but the parents treated as a boy since he was 3 years old. Parents noted that patient preferred to play cars with boys, instead of playing dolls with the girls. With regarding this preference, parents then started to seek for help the many general practitioners, until at the age of 6 year old; patient was consulted to pediatric endocrinology OPC at Dr Soetomo Hospital. From physical examination there were undescended testes bilaterally. USG result showed no uterus observed. The right testis was in right inguinal, the size was 0.7 cm x 0.4 cm x 0,9 cm, and left testis was not observed. Abdominal MRI was performed which showed right testis in inguinal and left testis in abdomen. Karyotyping showed 46, XY. The working diagnosis was 46 XY, DSD testicular and undescended testis bilaterally. The PedsQL score show mean of physical functioning 100, emotional functioning 25, social functioning 100 and school functioning 100.

Forth case, D, 8 years old boy was consulted with Congenital Adrenal Hyperplasia (CAH) for routine control. He was diagnosed as CAH since 6 month years old of age, with history of acute diarrhea and severe dehydration, electrolyte imbalance and adrenal crisis at the first admission. The diagnosis was confirmed by high level of 17-OHP serum and Karyotype was 46,XY. He got hydrocortison and fludocortison therapy routinely. The PedsQL score show mean of physical functioning 100, emotional functioning 50, social functioning 91.6 and school functioning 75.

The fifth case, E, 15-year-old female patient was consulted with Congenital Adrenal Hyperplasia (CAH) for routine control. She was diagnosed as CAH since she was one month old. She was brought up as a girl. Karyotype was 46,XX. 17-hydroxyprogesterone was 200 (> 37.8 ng/mL). An uterus with endometrial lining was found on USG examination. MRI examination showed a uterus and enlargement of bilateral adrenal glands consistent to CAH. Bone age study at 11 years old was consistent with an 15-year-old female. The PedsQL score show mean of physical functioning 100, emotional functioning 25, social functioning 100 and school functioning 100.

**Table 1. The PedsQL scores in patients with DSD**

<b>Dimension</b>	<b>Case 1</b>	<b>Case 2</b>	<b>Case 3</b>	<b>Case 4</b>	<b>Case 5</b>	<b>Median</b>
Physical	100	95	100	100	100	100
Emotional	25	31.25	25	50	25	25
Social	83	66.6	100	91.6	100	91.6
Schooling	83	100	100	75	100	100
Psychosocial Health Summary Score	79.58	65.95	75	72.2	75	72.2
Physical Health Summary Score	100	95	100	100	100	100

The median of physical function was 100 (range 95-100), emotional function was 25 (range 25-50), social function was 91.6 (range 66.6-100) and school performance was 100 (range 60-100). The median score of psychosocial health summary score was 75 (range 65.95-79.58) and physical health summary score was 100 (range 93-100).

## DISCUSSION

In these case series, there were various diagnosis of DSD. The patient's ages were also varied. Four patients were sexual ambiguity with low score of psychosocial health summary score. The Peds QoL score in this case series during pandemic covid-19 showed impaired quality of life, which is the psychosocial health score, especially in the emotional dimension. Almost all the patients feel sad, fear and worry with their sex ambiguity.

These findings are in agreement with other studies that found a reduction in the quality of life of patients with DSD.<sup>11</sup> The results of a study on children with DSD conducted by Jürgensen et al. found a reduction in quality of life in the schooling, physical wellbeing, and self-esteem dimensions.<sup>12</sup> Health-related quality of life scores are important indicators of therapeutic outcomes in chronic conditions.<sup>10,11</sup> In patients with DSD, these scores can give an indication as to whether medical intervention has had a positive impact on their wellbeing.<sup>12,13,14</sup>

A variety of other factors may contribute to the impaired quality of life in children with DSD. Societal and peer pressure on the child and the family, parental support, and the patient's own personality are factors that should be accounted for.<sup>15,16</sup> Especially patient number 1,2,3 and 5 with sexual ambiguity, the condition will affect the patient's quality of life. In order to comprehensively assess quality of life we would have to evaluate relationships, family dynamics, and the patients' own perceptions by using quantitative methods of analysis.<sup>5</sup> Moreover, there are added difficulties given the fact that these patients live in a developing country. Poverty, ignorance, lack of accessibility to specialized medical care, and lack of psychological services may all contribute negatively to these patients' outcomes.<sup>17</sup> This score in childhood can be used to identify at-risk groups that may need counselling in adulthood.

During pandemic covid-19, there were many factors faced by the DSD patients to get proper treatment in fully resources hospital. Lockdown policy cause lacking the transportation of the patient to the hospital. In the other hand, patients and family also fear of being infected covid 19 because Soetomo hospital was referral hospital for covid 19 patients. The decreasing of socioeconomic condition of the parents also affects the hospital visit. All of the factors above may cause lack of health service. Study in Germany highlight the significant mental health burden of German children and adolescents during the COVID-19 pandemic. They experienced significantly lower HRQoL (40.2% vs. 15.3%), more mental health problems (17.8% vs. 9.9%) and higher anxiety levels (24.1% vs. 14.9%) than before the pandemic. Children with low socioeconomic status, migration background and limited living space were more affected.<sup>10</sup>

Limitations of these case series were few samples used. This can be explained that the disease is rare. Moreover, DSD itself is also still a negative stigma among the local people. In the other hand, we also faced pandemic, which cause multidimensional crisis, so these cause few patients would find the treatment properly. These case series could be the preliminary study for the next research concerning at the quality of life among DSD patient in limited resources country during covid 19 pandemic. More research on quality of life in DSD children during covid-19 pandemic is needed. Management of DSD patients' needs a skilled and multidisciplinary team.<sup>10,18</sup>

## CONCLUSIONS

Children with DSD have psychological impact, in the term of emotional affects, because they feel sad, afraid, and worried about their ambiguous genitalia. Lack of treatment due to limited resources and covid 19 pandemic also factors that affect the quality of life. Therefore, it is important to assess the quality of life in children with DSD, so they will receive proper treatment and psychological support immediately.

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## CONFLICT OF INTEREST

The authors declared no conflict of interest.

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