Current Status of DSD Indonesia

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Short Communication

Current Status of Disorders of Sexual Development in Indonesia

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Abstract

Disorders of Sex Development (DSD) rise challenges in various aspects of life due to the abnormalities in the patients' sex chromosomes, gonads or reproductive organs. Its causes are often due to genetic and environmental factors. Considering the complexity of the condition, the patients require comprehensive management and an interdisciplinary approach. The delayed intervention may reduce the quality of life in patients, implying the significance of early detection and diagnosis. There is only little data present on the incidence and characteristics regarding DSD patients in Indonesia. This review wished to provide insight into the current status of DSD in Indonesia.

Keywords: Disorders of Sex Development, DSD, Indonesia, Status

Introduction

When a mother gives birth to a baby, usually we can know the baby's gender by examining the external genitalia. However, it can be complicated when the baby has a congenital disorder called Disorders of Sex Development (DSD).[1] People with DSD would have abnormal anatomical development of the sex chromosomes, gonads or reproductive organs.[2] DSD can be identified immediately at birth or sometimes later at the adolescence stage.[3] Individuals with DSD have several types of manifestation, like genital ambiguity to phenotypes that can go unnoticed or appear normal. Genetic, hormonal and environmental factors during prenatal and postnatal development are likely responsible for DSD manifestations.[4] The incidence of DSD is estimated to be 1 in every 4500–5500 births.[5]

Stigma is inseparable in the life of children with DSD because of the poor understanding and awareness about the condition.[6] The same situation applies in Indonesia, where knowledge and awareness about DSD are still lacking, even among health practitioners. The limited diagnostic and treatment facilities may have played a role in it.[7] Currently, the research centre providing molecular examinations needed to diagnose DSD is still limited in big cities. Thus, it could lead to delay in establishing diagnosis and access to early treatment for DSD patients.[8] These limitations made the patients had not received proper medical care and were still in doubt about their gender identity.[9]

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The importance of knowledge about a disease or condition in a country is pivotal, especially for the health practitioners responsible for educating the patients and their families. It is no exception to DSD. Health practitioners in Indonesia need to be well informed about it; its natural courses, the clinical manifestations, the pattern of inheritance, the expected physical and psychological challenges, the available diagnostic methods and the possible management. There are several studies about DSD in Indonesia, namely in Semarang, Palembang and Bandung. This review provides the current status of DSD in Indonesia from the prevalence, types and other attribution based on existing studies in that three big cities.

Characteristics of Disorders of Sex Development in Indonesia

Based on the studies in Palembang, Semarang and Bandung, the majority of the birth gender in DSD patients were male (84.4% in Palembang, 70% (children and adolescents), and 59% (adults) in Semarang, and 91.42% in Bandung.[2,7,10] There are no nation's incidence rates of DSD in Indonesia

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to this date.[2] However, some studies were revealing the incidence of DSD in some places in Indonesia. In Semarang, from May 2004 to December 2015, there were 617 DSD patients (426 patients with 46, XY DSD (69.04%); 117 patients with 46, XX DSD (18.96%), and 74 patients with sex chromosome DSD (12%). These data were collected from the record at the Centre for Biomedical Research Faculty of Medicine Diponegoro University.[8] In 2019, also from Semarang, there were 118 patients with DSD (60 children, 24 adolescents and 34 adults) that had participated in Ediati *et al*. studies. From a total of 118 patients, there were 77 patients with 46 XY DSD, 26 patients with 46 XX DSD and 14 patients with sex chromosome DSD.[9] In Palembang, Maritska *et al*. found 173 patients with clinical manifestations of DSD from the medical records in Mohammad Hoesin Hospital Palembang (2013–2017).[10,11] In Bandung, from January 2017 to December 2019, there were 70 patients with DSD (90.62% patients with 46, XY DSD; 4,68% patients with 46, XX DSD; 3,12% patients with 45, XO–46, XY, and 1,56% patients with 47, XXY.[2]

Early detection of DSD is a challenge, including in Indonesia, where many patients first come from as early as 2-year-old to preschool and even late childhood (6–12 years).[2,11-13] Not many patients came when they were still newborns or in their early childhood. There were various clinical findings of DSD found in Indonesia.[13] Hypospadias was the most commonly found manifestation of DSD in Indonesia. In Palembang, 59,06% of DSD patients had hypospadias during 2013–2017.[11] In Semarang, 91% of DSD patients had severe hypospadias during 2004–2009.[3] Unfortunately, there is no data about the most clinical manifestations in Bandung.[2]

Indriasari *et al*., in their study, showed that the most common type of DSD found in their center Universitas Padjajaran is 46, XY DSD followed by sex chromosome DSD and 46, XX DSD, respectively.[2] The same results were delivered by studies in Semarang. It revealed 46, XY DSD as the most common type found, followed by 46, XX DSD, and sex chromosome DSD.[7-9,14] However, owing to no chromosomal analysis available in their centre, the study in Palembang did not declare types of DSD based on the Chicago Consensus 2006. Instead, they use clinical findings and hormonal profiles to screen for DSD.[10,13]

Management of Disorders of Sex Development in Indonesia

Diagnosis of DSD is established by taking a history of symptoms, physical examination, imaging examinations, gonadal biopsy, karyotyping, endoscopy or laparoscopy and hormonal assays.[6] Most primary physicians in peripheral centres would be able to pick up DSD cases with provisional diagnoses and send them to tertiary centres for proper counselling and care if they used the clinical clues and diagnostic workup indicated here. Increasing the awareness of DSD among the medical community in Indonesia becomes more and more significant. Many health-care providers are unaware of the availability of such laboratory testing, let alone the fact that it is not offered in all regent hospitals (Type B hospitals).[15] Genetic testing is still not covered by BPJS (Government Health Insurance in Indonesia) because it is still not a prime concern by the government.[6,15]

There is an interdisciplinary team in Semarang that provides thorough services for DSD patients. This team is called the Gender Adjustment Team, a collaborative team from Diponegoro University and Dr Kariadi Hospital Semarang. The patients who needed molecular and chromosomal analysis will be referred to the Centre for Biomedical Research in the Faculty of Medicine of Diponegoro University.[15] Unfortunately, there is no such interdisciplinary team in Palembang and Bandung or any other cities yet.[2,10]

In Palembang, descriptive research was undertaken on people who were clinically diagnosed with DSD between 2013 and 2017. A total of 22 patients, from 173 DSD patients, had their hormones tested. A total of thirteen hormone variations were tested in DSD patients. Among DSD patients, the testosterone profile was the most sought hormonal profile (54.54%). The most examined hormone was testosterone (n = 12;17.6%), followed by TSH (n = 9;13.2%). Other hormones include free T4 (11.8%), LH and FSH (10.3%), blood beta-hCG, estradiol and prolactin (7.4%), free hormones T3 and cortisol (4.4%), progesterone (2.9%) and total T3 and T4 hormones (1.5%).[11]

The management of children with DSD is determined by the discord between chromosomal, gonadal, and phenotypic sex. Gender identity, gender role and sexual orientation are three aspects of psychosocial development in DSD patients that may not always be in sync.[4,6,7] Thus, there are substantial modifications in sex assignment that occurred in recent years. The main purpose is gender identification with sex assignment and decreases gender dysphoria.[6,7]

There are limited options for medical and surgical management for patients with DSD in Indonesia. In managing infants, children, and adolescents with DSD, a multidisciplinary team of geneticists, neonatologists, pediatric endocrinologists, pediatric radiologists, paediatric ob-gyn/urologists/surgeons specialists, behavioural health professionals and pediatric nurse educators should be involved.[8,16] The Sexual Adjustment Multidisciplinary Team (SAT) from Semarang is the only DSD multidisciplinary team in Indonesia. SAT team consists of several departments, such as endocrinology, gynaecology, andrology, genetics, urology, anaesthesiology, legal medicine, plastic surgery, psychiatry, psychology, social-medical staff and also religion. The purpose of this team is to provide thorough care for DSD patients and their families.[8]

Many things hinder the progress of the management of DSD in Indonesia. Lack of experience, unstandardized laboratory facilities, lack of financial support, and most importantly, lack of awareness from medical personnel and community play a role in it. For some ethnic groups, it appears that disclosing a

genital anomaly to family and medical workers is culturally taboo. A nationwide general guideline for DSD management should be defined and standardised, allowing for adaptability.[8]

Pharmacological Therapy

The examination effort to establish the diagnosis of DSD according to its classification includes giving hormone therapy. Hypogonadism is frequently found in people with gonadal dysgenesis, and hormonal puberty induction may be required.[3] Among the goals of hormone replacement therapy are the induction and maintenance of secondary sex traits and another aspect of pubertal development, such as growth. Hormone replacement therapy has a good impact on psychosocial and psychosexual development, as well as general well-being. The administration of hormone therapy in DSD is based on the need for sex hormones to initiate pubertal maturation.[3]

Hormonal therapy can start when patients with DSD reach the age of puberty.[3] DSD patients commonly have a decrease in androgen activity or production. The purpose of hormone replacement therapy for DSD male patients at the age of 10–12 years old is to increase the development of masculinity and to decrease feminisation.[8,15] Low-dose estrogen replacement therapy is used for DSD female patients aged between 9 and 11 years old. The health practitioners must adjust the dose of estrogen replacement therapy every 6 months. Delaying hormone therapy for too long might cause delays in genital development, reproductive function, and sexual function, as well as affecting their quality of life. Glucocorticoids and hormones for salt retention are administered to people with congenital adrenal hyperplasia (CAH).[8,17] CAH is the frequent type of 46, XX DSD that needs to be treated as soon as possible because of the life-threatening issue. Unfortunately, the majority of CAH medications are not available in Indonesia.[8]

In Palembang, hydrocortisone was given to CAH patients to decrease virilization. It is because the role of hydrocortisone that suppressed adrenocorticotropic hormone (ACTH) has a resemblance to the natural glucocorticoids. Moreover, the Centre in Palembang also used the combination of hydrocortisone and fludrocortisone to treat salt-wasting type CAH patients. Fluorohydrocortisone is known to maintain electrolyte balance. It also has a role in reducing plasma renin activity and helping suppress the ACTH. However, the use of hydrocortisone and fludrocortisone can cause salt retention and then increase the risk of hypertension in CAH patients.[10]

Surgical Procedures

The final sex assignment affects the surgical reconstruction of the external genitalia. Cosmetic enhancements and the maintenance of genital function or sensitivity should be the goals of the surgery. Another viewpoint is that dsd surgery should be delayed until a child is old enough to understand the condition and the consequences and make informed consent.[17] the goal of reconstructive surgery in women is to reshape the external female genitalia to a more normal shape and function. From the study overseas, the first part of this operation is to reduce the size of the clitoris, which is overly large, and the second stage is to reduce the shape of the vagina. CAH patients with feminising genital surgery already showed they decreased sexual function and sensitivity after vaginal reconstruction during childhood.[17] While feminising genitoplasty in infants may provide immediate physical improvements, some researchers believe it is ineffective in influencing gender identity or psychological development. As a result, only those with the most severe clitoromegaly should have clitoroplasty with neurovascular bundle preservation. Corrective surgery aims to fix the shape of the penis and urethra in men, usually with just one stage of surgery, unless the case is particularly complex. American Urological Association stated that there are several criteria for the surgery. For the men with hypospadias or undescended testes, the recommended age is 6–12-month-old, where then they can complete all stages of correction when the patient is 2-year-old. Infants with the risk of neoplasm will be suggested to do gonadectomy as quickly as possible.[17]

Due to a lack of knowledge, diagnostic facilities, and treatment options, clinical dsd management in Indonesia is fraught with difficulties. According to a study conducted by Ediati in Semarang, most DSD patients were not treated, and they had ambiguous genitals and uncertainties about their gender.[18] A 23-year-old patient with CAH in Jakarta, Indonesia, was a rare example of delayed diagnosis of DSD 46, XX. The patient, who suffered from genital ambiguity and primary amenorrhea, wished to be a man. The hormone levels were as follows: high dehydroepiandrosterone sulfate (937.8 g/dl); high testosterone (27.3 nml/l); and low estradiol (45 pg/ml), all of which corresponded to normal male levels. Long-term exposure to androgens causes the brain to become masculinized. As a result, she opted to transform into a boy rather than a girl. Her external genitalia was masculinized after a thorough laparoscopic hysterectomy and reconstruction surgery. In addition, the patient got psycho-adaptive counselling both before and after surgery.[19]

In Palembang, surgical intervention was the most common intervention for dsd patients (89,6%). Maritska *et al*. Stated that in dr. Mohammad hoesin hospital Palembang during 2013–2017, 156 DSD patients had surgical intervention (82% single surgery and 18% multiple surgeries). Urethroplasty with multiple approaches was the most common type of surgery in Palembang for dsd patients (41,9%) since its most clinical findings are hypospadias. Besides that, orchidopexy was also common for DSD patients with undescended testis manifestation (12,2%). Urethroplasty and orchidopexy are the types of corrective surgery.[10]

Psychosocial Aspect in Disorders of Sex Development Patient

Psychosocial care for children with DSD and their families is currently limited. Some challenges include the complexity of medical issues, genetic information, doubt about the patient's

gender identity, lack of explanation about gonadal tumour risk, the possibility of infertility and the complications of surgery. Diagnosing the patient at birth is an acute problem. Some parents explain that a high level of emotional distress and cognitive confusion often occurs at that time.[20]

Children diagnosed with DSD and their families are at risk of experiencing psychological challenges. Depression, anxiety, post-traumatic stress and uncertainty of the future are some things that might happen to them. Added to the fact that their condition is still considered taboo by the culture, the psychological challenges will get more challenging that parents often keep their child's condition secret and do not look for help.[5]

Health practitioners in Indonesia are not yet familiar with DSD. There are also only limited diagnostic and treatment facilities. The treatment is used to decrease the physical atypicality and to fix their sexual function. However, these interventions can affect the patient's life and are usually performed without their consent.[7]

Neonate is the best period in gender assignment in DSD patients. The longer it takes to assign the gender, can lead to greater the risk of rejection in children existence with DSD by the patient's parents. This can cause some problems in growth and development, especially in sexual organ development. Gender reassignment can be done at a maximum age of 18 months. If gender reassignment is done beyond 18 months, there is some development inhabits based on the new gender. Hopefully, better information management will make DSD patients understand its condition.[12]

Conclusion

Children with DSD are susceptible to both physical and mental health issues, owing to their condition. Delayed referral and intervention may reduce their quality of life. One of the causes of the current situation is the poor knowledge and awareness about DSD, even among health practitioners. Added to the fact that there are limited centers with facilities and multidisciplinary teams focusing on it, establishing and treating DSD is still a demanding problem in Indonesia.

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Conflicts of interest

There are no conflicts of interest.

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