ORIGINAL RESEARCH ARTICLE

Diponegoro International Medical Journal 2024 December, Vol 5, No.2: 36-43
e-ISSN: 2745-5815

Disorders of Sex Development: A Review of Medical and Psychosocial Aspects

Fanti Saktini[1*], Widodo Sarjana A.S.[1,2], Hang Gunawan Asikin[2], Agustini Utari[3]
[1]*Department of Psychiatry, Diponegoro National Hospital, Diponegoro University, Semarang, Indonesia*
[2]*Department of Psychiatry, Faculty of Medicine, Diponegoro University, Semarang, Indonesia*
[3]*Department of Pediatric Endocrinology, Faculty of Medicine, Diponegoro University, Semarang, Indonesia*

Keywords:

DSD
Disorders of sex development
Gender Identity
Multidisciplinary care
Psychosocial aspects

*) Correspondence to:
fantisaktini@fk.undip.ac.id

Article history:

Received 21-11-2024
Accepted 03-12-2024
Available online 10-12-2024

ABSTRACT

Background: Disorders of Sex Development (DSD) refer to a spectrum of congenital conditions involving atypical chromosomal, gonadal, or phenotypic development. Although recent studies have improved our understanding of the medical management of DSD, the psychosocial impact and the role of multidisciplinary care in addressing these challenges remain less well known.
Objective: This review aims to examine the classification, diagnostic approaches, and medical and psychosocial challenges associated with DSD, while also highlighting the importance of multidisciplinary support.
Methods: A narrative review was conducted to explore the current research and clinical guidelines on DSD, including studies on medical management and psychosocial interventions.
Results: The review found that early diagnosis and management are essential to reducing life-threatening risks and psychosocial distress in individuals with DSD. The impact of societal stigma, gender identity complexities, and increased rates of anxiety and depression were observed to contribute to body image concerns. A multidisciplinary care team, involving psychiatrists, endocrinologists, and other specialists, was highlighted as critical for holistic patient care.
Conclusion: The findings underscore the importance of a multidisciplinary approach in addressing both the medical and psychosocial aspects of DSD. While collaborative decision-making and individualized care strategies showed positive outcomes, further research is needed to optimize long-term health and quality of life for individuals with DSD.

DIMJ, 2024, 5(2), 36-43 DOI: https://doi.org/10.14710/dimj.v5i2.25084

1. Introduction

Disorders of Sex Development (DSD) refer to a group of congenital conditions resulting in atypical development of chromosomal, gonadal, or anatomical sex. The incidence of DSD is approximately 1 in 4,500 to 5,500 live births, although specific subtypes vary in prevalence.[1] The 2006 Chicago Consensus proposed classifying DSD into three main categories: (1) sex chromosome DSD, (2) 46,XY DSD, and (3) 46,XX DSD.[2] Sex chromosome DSD includes Turner syndrome (45,X), Klinefelter syndrome (47,XXY), mixed gonadal dysgenesis (45X/46XY), and chromosomal ovotesticular DSD.[2] Among 46,XX DSD, congenital adrenal hyperplasia (CAH) is the most common, particularly 21-hydroxylase deficiency, which leads to cortisol deficiency and excess androgen production, resulting in virilization of female infants.[3] For 46,XY DSD, conditions include disorders of gonadal development and androgen synthesis or action, such as androgen insensitivity syndrome (AIS).[4]

Atypical genitalia in newborns, often referred to as a "social emergency," can generate significant psychological distress for families, leading to challenges related to gender identity, sexuality, and fertility.[5] Parents may face societal pressure and anxiety in navigating the uncertainty surrounding their child's gender, which can have long-lasting psychosocial effects.[6] Early diagnosis and management are critical, as conditions like CAH can pose life-threatening risks due to adrenal insufficiency.[7] Newborn screening in developed countries aids in the early detection of CAH, though in other regions, clinical symptoms may present later in life.[8,9]

Individuals with DSD often experience ongoing medical and psychosocial challenges, including anxiety, depression, and body image concerns.[7] Support from a multidisciplinary DSD team, including mental health professionals, is vital in addressing these issues.[6,10] This review will explore the medical and psychosocial aspects of DSD, focusing on the role of psychiatrists in the multidisciplinary care of affected individuals.

Normal Sex Development and The Concept of Gender

Sexual development is crucial for maintaining genetic diversity in mammals and occurs through two key processes: sex determination and sex differentiation**.** In sex determination, the bipotential gonad differentiates into either testes or ovaries. The presence of the Y chromosome, particularly the SRY gene, triggers the formation of testes, while its absence leads to the development of ovaries.[11] During sex differentiation, fully formed testes or ovaries secrete hormones that influence the development of internal and external genitalia and extra-gonadal tissues.[11] In males, testes produce testosterone and dihydrotestosterone (DHT), resulting in the formation of male genital structures (e.g., penis and scrotum) and the regression of the Müllerian ducts, which develop into female reproductive organs in the absence of male hormones.[11] In females, the ovaries secrete estrogens, promoting the development of female genitalia and the persistence of the Müllerian ducts.[11]

While biological sex is determined through these developmental processes, the concept of gender introduces a distinct, psychosocial perspective. Gender development is shaped by a dynamic interplay of genetic, hormonal, and environmental factors.[12] For instance, exposure to androgens can significantly influence sexual behavior and orientation. The relationships between patients, their families, and medical professionals also play a vital role in shaping individuals' feelings about their gender identity.[12,13]

Recognizing gender dysphoria**,** characterized by discomfort with one's anatomical sex, is crucial in medical contexts.[12] The Diagnostic and Statistical Manual of Mental Disorders (DSM) identifies two subtypes of gender identity disorder (GID): one for children and another for adolescents and young adults, each with specific diagnostic criteria.[13] Additionally, there is a subclinical diagnosis known as gender identity disorder not otherwise specified (GID NOS) for individuals who meet some, but not all, diagnostic criteria. Gender identity encompasses observable behaviors, attitudes, personality traits, and cognitive abilities, and its expression can vary significantly across different cultures and time periods.[14] As psychologist John Money articulated, gender distinctly separates the psychosocial and psychological aspects of individuals from the biological differences associated with sex.[14]

Disorders of Sex Development (DSD)

Disorders of Sex Development (DSD) refer to congenital conditions where chromosomal, gonadal, and anatomical sex development is atypical. This term encompasses a range of conditions resulting from genetic lesions that manifest as various gonadal phenotypes, such as gonadal dysgenesis and ovotestis, as well as diverse genital presentations, including mild hypospadias and ambiguous genitalia.[11] The term "DSD" has gained preference among medical practitioners, although some advocacy groups prefer terms like "differences" or "variations." The previous term "intersex" is still debated, while outdated terms like "hermaphroditism" are no longer used.[5]

According to the Chicago Consensus Meeting in 2005, DSD can be classified into three major groups.[2]

Table 1. Types of DSD

Type of DSD	Key Characteristics
Sex Chromosome DSD	Includes Turner syndrome (45,X) and Klinefelter syndrome (47,XXY), presenting with unique physical features and fertility issues.
46,XY DSD	Involves conditions like complete/partial androgen insensitivity syndrome (cAIS/pAIS) and gonadal dysgenesis, often resulting in female phenotypes despite male karyotype.
46,XX DSD	Includes congenital adrenal hyperplasia (CAH), leading to masculinization of external genitalia and presenting with varying degrees of ambiguity.

Although consideration of karyotype is useful for classification, unnecessary reference to karyotype should be avoided; ideally, a system based on descriptive terms (eg, androgen insensitivity syndrome) should be used wherever possible. StAR indicates steroidogenic acute regulatory protein.

In conditions like Turner and Klinefelter syndromes, patients often present with distinct physical characteristics tied to their chromosomal anomalies.[15] Turner syndrome (45,X) typically results in short stature, webbed neck, and other features, while Klinefelter syndrome (47,XXY) causes male individuals to develop with some feminizing features like gynecomastia and infertility.[15] Mixed gonadal dysgenesis and ovotesticular DSD often lead to ambiguous genitalia with internal reproductive structures reflecting both male and female development.

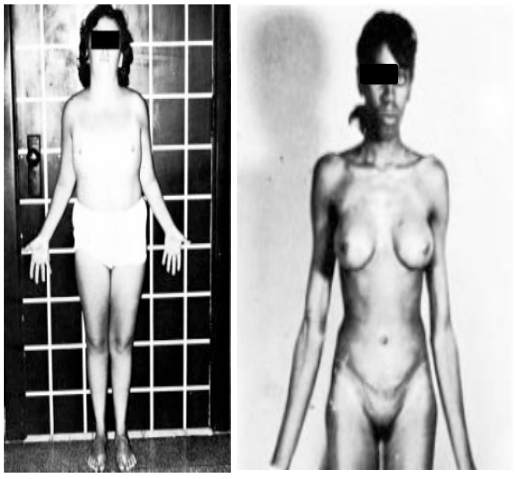

Figure 1. [Left] Patient with Turner syndrome and a 45,X karyotype. Note the absence of sexual maturity signs. [Right] Patient with androgen insufficiency syndrome.[15]

Figure 1 shows that individuals with 46,XY DSD, such as complete or partial androgen insensitivity syndrome (cAIS/pAIS), may have external female genitalia but lack internal female reproductive organs like a uterus.[15] Testes are often located internally or in atypical positions, and there may be a significant risk of gonadal tumors later in life. In cases like 5α-reductase deficiency, masculinization

can occur at puberty, often leading to gender identity changes.[5]

Conditions like congenital adrenal hyperplasia (CAH) result in varying degrees of genital masculinization in individuals with a 46,XX karyotype (Figure 2). This can range from mild clitoromegaly to genital ambiguity resembling male genitalia.[15] CAH can also involve life-threatening salt-wasting conditions, requiring urgent intervention. Genetic screening and hormonal assessments play key roles in early diagnosis and management.[5]

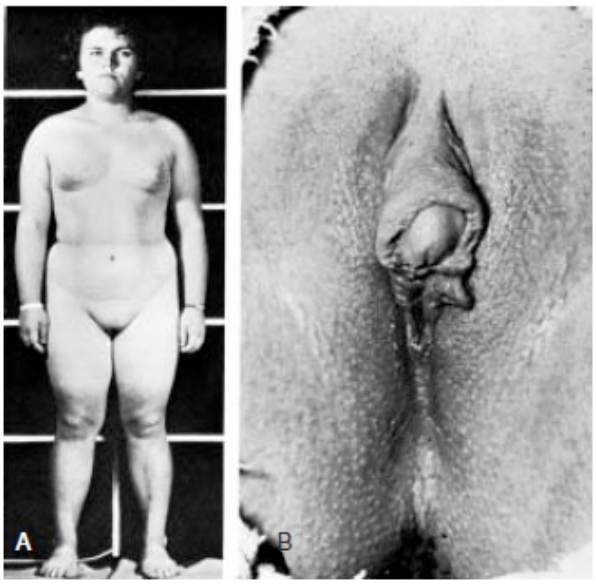

Figure 2. A. Patient with congenital adrenal hyperplasia. B. External genital showing labial fusion and clitoromegaly.[15]

DSD associated with genital ambiguity is rare, occurring in about 1 in 4,500 to 5,500 live births. Turner syndrome and Klinefelter syndrome have higher prevalence rates, affecting approximately 1 in 2,500 females and 1 in 450–600 males, respectively.[1] Understanding these disorders is crucial for guiding families through complex decisions regarding gender identity, medical interventions, and long-term management strategies.[5]

DSD present with varying clinical pictures based on the patient's age at diagnosis.[16] Newborns with DSD often display ambiguous genitalia, which can include clitoromegaly, posterior labial fusion, or undescended testes.[16] Early diagnosis is critical, as infants with ambiguous genitalia usually receive specialized care in well-resourced countries within hours of birth, while those in resource-limited settings may face delays of months or years, leading to poorer outcomes.[5]

Figure 3 illustrates a practical diagnostic framework tailored for healthcare providers. This framework emphasizes the critical first steps in evaluation and management, highlighting the importance of early recognition and intervention in newborns. By outlining common diagnostic pathways and potential underlying conditions, the figure serves as a vital tool for clinicians, ensuring that timely and appropriate care is provided to optimize patient outcomes.

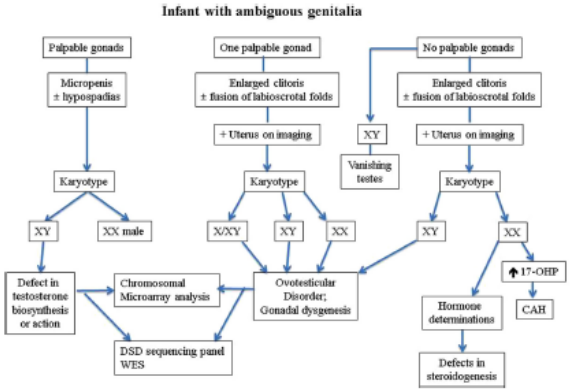

Figure 3. Practical Diagnostic Approach to Infant with Ambiguous Genitalis[17]

Common diagnoses in newborns include congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency and 45,X/46,XY partial gonadal dysgenesis.[5] Cultural taboos and stigma can prevent timely medical attention, exacerbating virilization and impacting psychological development.[17] In adulthood, DSD may be identified when individuals with 46,XX non-salt-losing CAH present with significant virilization, often having been raised as males.[18] This leads to a higher prevalence of gender confusion and dysphoria among adolescents with DSD.[19] Additionally, intra-abdominal gonadal cancer can sometimes be the first indication of an underlying DSD.[5] Given the complex presentation of DSD, thorough diagnostic evaluations are essential.

Diagnostic Approach

Diagnosis of DSD involves a series of evaluations. A comprehensive history taking is essential, considering antenatal maternal virilization, potential drug exposures, and family history of DSD or related features.[5,16] Physical examination involves assessing dysmorphic features, growth parameters, and genital morphology.[5] Special attention should be given to the size and structure of the penis or phallus, the presence of labial-scrotal folds, and the location and size of gonads.[5] Standardized virilization charts, like Prader staging chart (Figure 1), aid in documenting findings.[20]

Laboratory examinations prioritize ruling out life-threatening conditions, such as salt-losing congenital adrenal hyperplasia (CAH).[5] Key tests include serum 17-hydroxyprogesterone (17-OHP), electrolytes, and hormone levels (FSH, LH, testosterone).[5] A Human Chorionic Gonadotropin (HCG) stimulation test can help assess testosterone production.[5] Genetic testing for associated genes is crucial for accurate diagnosis.[5] Imaging examinations like pelvic ultrasound or MRI confirm anatomical structures, identifying the presence of a uterus and the type and location of gonads.[5] Surgical exploration may be necessary for further evaluation.[5] Genetic and molecular examinations start with chromosome analysis and may include Comparative Genomic Hybridization (CGH) arrays or Multiplex Ligation-dependent Probe Amplification (MLPA) to detect genetic abnormalities.[5] Multiple Parallel Sequencing (MPS) targeting candidate genes has shown increased diagnostic coverage for DSD.[21–

[23] Once diagnosed, management of DSD requires a multifaceted approach.[5]

Management of DSD

Therapy includes sex assignment, the need for hormone replacement therapy (adrenal and sex steroid hormones), and the requirement for surgical correction of genital and/or gonadal structures (if there is a risk of malignancy),

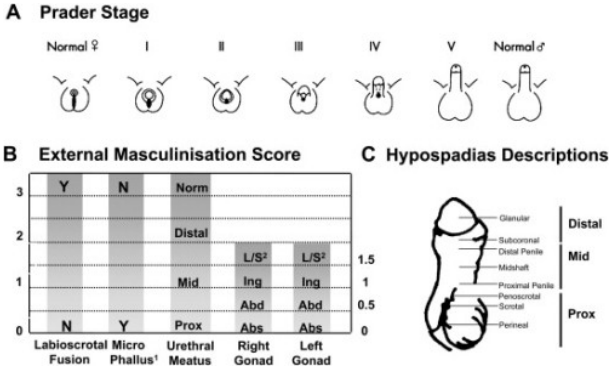

Figure 4. A. Scoring of External Genitalia. External genitalia can be objectively measured using the Prader staging system, which provides a comprehensive score for the appearance of the external genitalia. B. Each component of the genitalia (phallus size, labioscrotal fusion, gonad location, and urethral meatus) can be individually scored using the External Masculinization Score (EMS)[17]

psychosocial support needs, and managing the transition from childhood to adulthood (entering puberty).

Sex assignment in individuals with DSD involves complex decision-making influenced by a multidisciplinary team (including pediatricians, surgeons, psychiatrist, and psychologists) and should consider cultural and familial perspectives. Early sex assignment, historically focused on achieving a cosmetically normal appearance, is now shifting towards allowing individuals to participate in decisions about their gender identity as adults.[24] This approach aims to foster social integration and minimize potential psychological issues such as gender dysphoria and dissatisfaction with genital appearance.[5]

Effective medical management includes hormone replacement therapy to address adrenal insufficiency (using glucocorticoids and mineralocorticoids) and to induce puberty (administering testosterone for males and estrogen for females).[24,25] Regular monitoring of growth and hormonal levels is critical to ensure optimal development and to prevent complications associated with untreated DSD.[26]

Surgical interventions may be considered based on factors such as assigned sex, risk of malignancy, and gonadal function.[27–29] Decisions should involve the patient and a multidisciplinary team to ensure informed consent and alignment with the individual's long-term needs and identity.[30] Surgical options may include phalloplasty, vaginoplasty, and other procedures aimed at facilitating normal anatomical and functional development.[27–29]

Psychological support is essential for both individuals with DSD and their families, helping to navigate the emotional and social challenges associated with DSD.[5,10] Counseling can aid in addressing parental concerns, managing societal stigma, and facilitating open communication about the condition.[10] A collaborative, multidisciplinary approach fosters a supportive environment that promotes the individual's well-being and autonomy.[9,31,32] The psychosocial implications of DSD require special attention to ensure overall well-being.[31,33,34]

Psychosocial Impact of DSD

Individuals with DSD face a range of psychosocial challenges, with emotional disturbances being common across various conditions. Feelings of shame, stigma, difficulties in building self-esteem, and body image concerns are central to these experiences. Around 55%-70% of individuals with DSD are reluctant to disclose their condition to others, which reinforces feelings of shame and exacerbates mental health problems, particularly in those with Turner syndrome (TS) and Klinefelter syndrome (KS), where depressive symptoms are strongly correlated with feelings of shame.[35] Body image dissatisfaction, especially in conditions like TS and KS, is often tied to physical characteristics like short stature or infertility. Dissatisfaction with genital appearance and gender characteristics is also common, particularly among those with atypical genitalia or those undergoing gender transition, intensifying the risk of psychological distress.[35]

Mental health issues such as anxiety, depression, and suicidal ideation are more prevalent in individuals with DSD compared to the general population.[36] In males with KS, psychiatric conditions are more frequent, with rates of autism (13.8%), attention difficulties (13.8%), and lifetime depression (59%) significantly higher than the general population.[35] Similarly, in individuals with congenital adrenal hyperplasia (CAH), studies have shown an increase in affective distress, with rates of autistic symptoms (6.7%) being higher than in the adult population (1%). These mental health challenges are often linked to the psychosocial impacts of DSD, such as poor self-esteem, stigma, and negative healthcare experiences.[35]

Psychosexual development in DSD is complex, particularly regarding gender identity and sexuality. Gender dysphoria is a common challenge, especially when the sex assigned at birth does not align with the individual's internal perception.[37] Adolescents and adults with DSD may experience confusion about their gender identity, leading to emotional distress.[38] Additionally, societal pressures around marriage and fertility, particularly in cultures where these milestones are crucial, add another layer of difficulty.[38] In India, for instance, 55.2% of patients with DSD do not consider marriage due to fears of rejection, while 85% of parents still hope their children with DSD will marry.[39] Infertility is especially distressing, with women often facing greater social consequences than men, particularly in cultures where childbearing is highly valued.[38]

Parents of children with DSD also face significant psychological strain. Studies indicate that the stress levels experienced by these parents are comparable to those of parents of children with cancer, with 15%-30% reporting symptoms of anxiety and depression.[35] The complex decision-making process regarding early surgical interventions can lead to feelings of guilt and shame, particularly when parents feel pressured to conceal their

child's condition.[6] This emotional strain is compounded by societal ignorance about DSD, making it difficult for parents to access appropriate medical care and emotional support for their child. Research has shown that late healthcare seeking is common in countries like Indonesia, where individuals with DSD are often misperceived as transgender, delaying necessary interventions.[40]

Additionally, healthcare experiences play a crucial role in the mental health of individuals with DSD. Negative interactions with medical personnel, a lack of knowledge about DSD, and insufficient support contribute to emotional distress.[31] Studies have shown that satisfaction with healthcare services is associated with better mental health outcomes, particularly when individuals and their families feel informed and involved in decision-making.[41] However, ignorance and stigma in healthcare settings often leave DSD patients feeling isolated, underscoring the need for more specialized and sensitive healthcare services.[42]

The Role of a Multidisciplinary Team

DSD is a complex condition requiring a biopsychosocial approach, and optimal care involves a multidisciplinary team, as outlined by the Chicago Consensus. This team typically includes pediatricians, endocrinologists, surgeons, mental health professionals, and social workers, among others. Each member plays a specific role in ensuring comprehensive care, addressing medical, psychological, and social needs. For effective collaboration, communication must be clear, consistent, and culturally sensitive, especially when counseling families and involving them in decision-making.

Moran and Karkazis provided a six-step process and tools for forming such a team. The steps are: (1) identifying and selecting potential team members with shared interests, (2) assessing the team's capacity, (3) evaluating resources, (4) interviewing potential team members, (5) analyzing interview responses, and (6) developing tools and reporting findings. The 2006 Intersex Consensus mentioned that the ideal team members include "a pediatric endocrinologist, surgeon or urologist, psychologist/psychiatrist, gynecologist, geneticist, neonatologist, and, if available, a social worker." The team should be coordinated by a committed leader. In assessing team capacity, it is important to determine how much time each member can commit weekly, any special skills or expertise they possess, short-term plans, and willingness to develop a team program. In evaluating resources, collaboration with the hospital's business development department is necessary, considering the potential for research grants, incentive programs, or facilities for team members, external consultants if needed, and estimating the time for periodic meetings. During the interview, the current practice activities, vision, and role within the team should be discussed.[43]

In Indonesia, six public hospitals, including RSUP Dr. Kariadi (RSDK) in Semarang, provide DSD services. Since 1989, the hospital's Gender Assignment Team (GAT) has evolved into a comprehensive team with various specialists, including psychiatrists and psychologists. Most patients come from low-income families, and while the government funds basic medical care, expenses for specialized tests remain a challenge.[44]

To ensure comprehensice care for patients with DSD, specific protocols are established for both inpatient and outpatient settings (Table 2 and 3).

Table 2. Inpatient Care Protocol for DSD Patients

Stage	Action
First 24 Hours	1. Neonatologist contacts endocrinologist and DSD liaison. 2. First responders (neonatologist, pediatric endocrinologist, etc.) provide psychosocial support. 3. Endocrinologist requests hormone testing (within 24 hours). 4. Team coordinator prepares summary and schedules team meeting (within 24-48 hours).
First Week	1. DSD team meets with patient and family within 48-72 hours. 2. Offer support and provide information gradually. 3. Referral to psychiatrist. 4. Complete imaging exams and plan for gender assignment.
First Month	1. Patient discharged (if stable) and follow-up scheduled for 2-3 weeks. 2. Social worker assesses family needs, reiterates information. 3. Discuss patient's condition with family in a supportive, non-alarming manner.
Next Steps	1. Annual follow-up coordinated by social worker. 2. Address body-related topics based on patient's age. 3. During adolescence, discuss dating, sexual relationships, and gender assignment.

Table 3. Outpatient Care Protocol for DSD Patients

Stage	Action
First Week	Assess privacy concerns, family's perception, and required support.
Week 1-4	1. Diagnosis established and discussed with family. 2. Ensure access to peer support, medical records, and genetic counseling.
First Six Months	1. Follow-up visits planned for puberty and surgical options. 2. Seek patient input on surgical options. 3. Provide peer support and coordinator acts as a hotline for the family.

Psychiatrists play a crucial role in managing the psychosocial aspects of DSD care. They support patients and families in coping with the emotional impact of the condition, facilitating acceptance, and addressing complex gender-related issues. Their role includes educating families on sex and gender concepts, providing guidance on gender identity and assignment, and offering ongoing psychological support. Psychiatrists also address psychiatric comorbidities through therapy and pharmacological treatment, helping patients navigate medical decisions and social challenges.

Psychosocial screening is integral to improving the quality of life for patients and families. Tailored psychosocial, medical, and surgical interventions, based on thorough assessments, can empower patients, reduce emotional distress, and enhance long-term outcomes. The Indonesian context highlights the need for better resources and financial support for comprehensive DSD management, emphasizing the importance of a well-functioning multidisciplinary team in overcoming these challenges.[44]

Published by Universitas Diponegoro.

Available online at: https://ejournal2.undip.ac.id/index.php/dimj

Table 4. Psychosocial Screening Protocol

Tool	Assessed Aspects	Respond-ents	Follow-up
Psycho-social Assessment Tool[a]	Family structure/support, parental stress	Parents	1 year
Support and Resource Assessment[b]	Access to support systems, education	Parents	1 year
Patient Health Questionnaire-4[c]	Anxiety, depression symptoms	Parents	1 year
Knowledge of Condition[d] *Caregiver Report Self-Report*	Diagnosis understand-ing (parent/child perspective)	Parents and patients	1 year
Child Behavior Checklist[e]	Activities, social skills, behavior issues	Parents	1 year
Self-Perception Profile[f]	Self-esteem, social/work competence	Patients	1 year
Body Image Scale[g]	Satisfaction with sex traits, body image	Patients	2 years
Multidimen sional Gender Identity Scale[h]	Gender uniqueness, dissatisfactio n, stereotypes	Patients	2 years
Youth Self-Report[e]	Behavior, social skills, school performance	Patients	1 year

2. Conclusion

Disorder of sex development (DSD) is a group of disorders in sexual development that is highly complex in terms of diagnosis and management. The medical and psychosocial issues faced by patients and their families present challenges for clinicians. A multidisciplinary team approach and parental involvement in decision-making are highly recommended. Mental health practitioners are essential in preparing patients and families to navigate the decision-making process related to diagnosis and management, raising the child according to gender, and addressing any psychiatric issues that may arise.

Ethical Approval

There is no ethical approval.

Conflicts of Interest

The authors declare no conflict of interest.

Funding

No specific funding was provided for this review.

Author Contributions

The authors contributions to this review are as follows: conceptualization, collecting literature, writing draft: Fanti Saktini, Agustini Utari; review and editing: Widodo Sarjana A.S.; Supervision: Hang Gunawan Asikin.

Acknowledgments

This work was supported by Department of Psychiatry, Faculty of Medicine, Diponegoro University.

References

1. Lee PA, Nordenström A, Houk CP, Ahmed SF, Auchus R, Baratz A, et al. Global Disorders of Sex Development Update since 2006: Perceptions, Approach and Care. Vol. 85, Hormone research in paediatrics. 2016. p. 158–80.
2. Consensus statement on management of intersex disorders. Pediatrics [Internet]. 2006;118(2):e488–500. Available from: www.sickkids.ca/childphysiology/cpwp/
3. Parsa AA, New MI. Steroid 21-hydroxylase deficiency in congenital adrenal hyperplasia. Vol. 165, Journal of Steroid Biochemistry and Molecular Biology. Elsevier Ltd; 2017. p. 2–11.
4. Ahmed SF, Bashamboo A, Lucas-Herald A, McElreavey K. Understanding the genetic aetiology in patients with XY DSD. Vol. 106, British Medical Bulletin. 2013. p. 67–89.
5. Raza J, Zaidi SZ, Warne GL. Management of disorders of sex development – With a focus on development of the child and adolescent through the pubertal years. Vol. 33, Best Practice and Research: Clinical Endocrinology and Metabolism. Bailliere Tindall Ltd; 2019.
6. Krege S, Eckoldt F, Richter-Unruh A, Köhler B, Leuschner I, Mentzel HJ, et al. Variations of sex development: The first German interdisciplinary consensus paper. J Pediatr Urol. 2019 Apr 1;15(2):114–23.
7. Falhammar H, Frisén L, Norrby C, Hirschberg AL, Almqvist C, Nordenskjöld A, et al. Increased mortality in patients with congenital adrenal hyperplasia due to 21-hydroxylase deficiency. Journal of Clinical Endocrinology and Metabolism. 2014 Dec 1;99(12):E2715–21.
8. Speiser PW, Arlt W, Auchus RJ, Baskin LS, Conway GS, Merke DP, et al. Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: An endocrine society* clinical practice guideline. Journal of Clinical Endocrinology and Metabolism. 2018;103(11):4043–88.

9. Ediati A, Maharani N, Utari A. Sociocultural Aspects of Disorders of Sex Development. Wiley Periodicals. 2016;108:380–3.
10. Parisi MA, Ramsdell LA, Burns MW, Carr MC, Grady RE, Gunther DF, et al. A Gender Assessment Team: Experience with 250 patients over a period of 25 years. Vol. 9, Genetics in Medicine. 2007. p. 348–57.
11. Arboleda VA, Sandberg DE, Vilain E. DSDs: Genetics, underlying pathologies and psychosexual differentiation. Vol. 10, Nature Reviews Endocrinology. Nature Publishing Group; 2014. p. 603–15.
12. 12. Reiner WG, Reiner DT. Thoughts on the nature of identity: How disorders of sex development inform clinical research about gender identity disorders. J Homosex. 2012 Mar;59(3):434–49.
13. Leibowitz SF, Spack NP. The Development of a Gender Identity Psychosocial Clinic: Treatment Issues, Logistical Considerations, Interdisciplinary Cooperation, and Future Initiatives. Vol. 20, Child and Adolescent Psychiatric Clinics of North America. 2011. p. 701–24.
14. Meyer-Bahlburg HFL. Psychoendocrinology of Congenital Adrenal Hyperplasia. In: Genetic Steroid Disorders. Elsevier Inc.; 2014. p. 285–300.
15. T.W. Sadler. Langman's Medical Embryology. 7th ed. Lippincott Williams & Wilkins, a Wolters Kluwer business; 2019.
16. Ahmed SF, Rodie M. Investigation and initial management of ambiguous genitalia. Vol. 24, Best Practice and Research: Clinical Endocrinology and Metabolism. 2010. p. 197–218.
17. Özbey H, Etker S. Disorders of sexual development in a cultural context. Vol. 11, Arab Journal of Urology. 2013. p. 33–9.
18. Jorge JC, Echeverri C, Medina Y, Acevedo P. Male gender identity in an XX individual with congenital adrenal hyperplasia. Journal of Sexual Medicine. 2008;5(1):122–31.
19. de Jesus LE, Costa EC, Dekermacher S. Gender dysphoria and XX congenital adrenal hyperplasia: how frequent is it? Is male-sex rearing a good idea? Vol. 54, Journal of Pediatric Surgery. W.B. Saunders; 2019. p. 2421–7.
20. Ahmed SF, Khwaja O, Hughes IA. The role of a clinical score in the assessment of ambiguous genitalia. BJU Int. 2000 Jun;85:120–4.
21. Eggers S, Sadedin S, van den Bergen JA, Robevska G, Ohnesorg T, Hewitt J, et al. Disorders of sex development: Insights from targeted gene sequencing of a large international patient cohort. Genome Biol. 2016 Nov 29;17(1).
22. Juniarto AZ. Disorders of sex development: insights from targeted gene sequencing of a large international patient cohort. 2018.
23. Yatsenko SA, Witchel SF. Genetic approach to ambiguous genitalia and disorders of sex development: What clinicians need to know. Semin Perinatol. 2017 Jun 1;41(4):232–43.
24. Guerrero-Fernández J, Azcona San Julián C, Barreiro Conde J, Bermúdez de la Vega JA, Carcavilla Urquí A, Castaño González LA, et al. Management guidelines for disorders / different sex development (DSD). An Pediatr (Engl Ed). 2018 Nov 1;89(5):315.e1-315.e19.
25. Speiser PW, Arlt W, Auchus RJ, Baskin LS, Conway GS, Merke DP, et al. Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: An endocrine society* clinical practice guideline. Journal of Clinical Endocrinology and Metabolism. 2018;103(11):4043–88.
26. Ankarberg-Lindgren C, Kriström B, Norjavaara E. Physiological estrogen replacement therapy for puberty induction in girls: A clinical observational study. Horm Res Paediatr. 2014;81(4):239–44.
27. Dangle PP, Lee A, Chaudhry R, Schneck FX. Surgical Complications Following Early Genitourinary Reconstructive Surgery for Congenital Adrenal Hyperplasia—Interim Analysis at 6 Years. Urology. 2017 Mar 1;101:111–5.
28. Fallat ME, Hertweck P, Ralston SJ. Surgical and Ethical Challenges in Disorders of Sexual Development. Vol. 59, Advances in Pediatrics. 2012. p. 283–302.
29. Vidal I, Gorduza DB, Haraux E, Gay CL, Chatelain P, Nicolino M, et al. Surgical options in disorders of sex development (dsd) with ambiguous genitalia. Vol. 24, Best Practice and Research: Clinical Endocrinology and Metabolism. 2010. p. 311–24.
30. Wang LC, Poppas DP. Surgical outcomes and complications of reconstructive surgery in the female congenital adrenal hyperplasia patient: What every endocrinologist should know. Vol. 165, Journal of Steroid Biochemistry and Molecular Biology. Elsevier Ltd; 2017. p. 137–44.
31. Ediati A. Disorders of Sex Development in Indonesia: The course of psychological development in late identified patients. GVO drukkers & vormgevers B.V.; 2014.
32. Joseph AA, Kulshreshtha B, Shabir I, Marumudi E, George TS, Sagar R, et al. Gender Issues and Related Social Stigma Affecting Patients with a Disorder of Sex Development in India. Arch Sex Behav. 2017 Feb 1;46(2):361–7.
33. Wisniewski AB, Sandberg DE. Parenting children with disorders of sex development (DSD): A developmental perspective beyond gender. Vol. 47, Hormone and Metabolic Research. Georg Thieme Verlag; 2015. p. 375–9.
34. Meyer-Bahlburg HFL, Reyes-Portillo JA, Khuri J, Ehrhardt AA, New MI. Syndrome-Related Stigma in the General Social Environment as Reported by Women with Classical Congenital Adrenal Hyperplasia. Arch Sex Behav. 2017 Feb 1;46(2):341–51.
35. De Vries ALC, Roehle R, Marshall L, Frisén L, Van De Grift TC, Kreukels BPC, et al. Mental Health of a Large Group of Adults with Disorders of Sex

Development in Six European Countries. Psychosom Med. 2019 Sep 1;81(7):629–40.
36. Falhammar H, Claahsen-Van der Grinten H, Reisch N, Slowikowska-Hilczer J, Nordenström A, Roehle R, et al. Health status in 1040 adults with disorders of sex development (DSD): A European multicenter study. Endocr Connect. 2018 Mar 1;7(3):466–78.
37. Nock MK, Borges G, Bromet EJ, Alonso J, Angermeyer M, Beautrais A, et al. Cross-National Prevalence and Risk Factors for Suicidal Ideation, Plans, and Attempts. The British Journal of Psychiatry. 2008 Feb;192:98–105.
38. Ediati A, Juniarto AZ, Birnie E, Drop SLS, Faradz SMH, Dessens AB. Body image and sexuality in indonesian adults with a disorder of sex development (DSD). J Sex Res. 2015 Jan 2;52(1):15–29.
39. Gupta D, Bhardwaj M, Sharma S, Ammini AC, Gupta DK. Long-term psychosocial adjustments, satisfaction related to gender and the family equations in disorders of sexual differentiation with male sex assignment. Pediatr Surg Int. 2010 Oct;26(10):955–8.
40. Ediati A, Faradz SMH, Juniarto AZ, van der Ende J, Drop SLS, Dessens AB. Emotional and behavioral problems in late-identified Indonesian patients with disorders of sex development. J Psychosom Res. 2015 Jul 1;79(1):76–84.
41. Thyen U, Lux A, Jürgensen M, Hiort O, Köhler B. Utilization of health care services and satisfaction with care in adults affected by Disorders of Sex Development (DSD). J Gen Intern Med. 2014;29(SUPPL. 3).
42. Thyen U, Ittermann T, Flessa S, Muehlan H, Birnbaum W, Rapp M, et al. Quality of health care in adolescents and adults with disorders/differences of sex development (DSD) in six European countries (dsd-LIFE). BMC Health Serv Res. 2018 Jul 5;18(1).
43. Moran ME, Karkazis K. Developing a multidisciplinary team for disorders of sex development: Planning, implementation, and operation tools for care providers. Adv Urol. 2012;
44. Sandberg DE, Gardner M, Callens N, Mazur T. Interdisciplinary care in disorders/differences of sex development (DSD): The psychosocial component of the DSD—Translational research network. Am J Med Genet C Semin Med Genet. 2017 Jun 1;175(2):279–92.