	JURNAL INTERNATIONAL BERPUTASI TERAKREDITASI Q4
JUDUL ARTIKEL	Ethical aspects of gender assignment in ambiguous genitalia-congenital adrenal hyperplasia: A case report
JURNAL	Paediatrica Indonesiana
PENULIS	Nur Rochmah, Muhammad Faizi, Adwina Nurlita Kusuma Wardhani
No	**Perihal**
1	BUKTI SUBMIT
2	BUKTI REVIEW 1
3	BUKTI REVIEW 2
4	BUKTI PUBLISH

Surabaya, 7 Agustus 2023

Dr. NUR ROCHMAH dr., Sp.A(K)

1. BUKTI SUBMIT

Gmail **UNIT KERJA ENDOKRIN ANAK <endokrin.ilmiah@gmail.com>**

Fwd: [PI] New notification from Paediatrica Indonesiana

1 pesan

nur rochmah <drnurrochmah@gmail.com> 6 Agustus 2023 pukul 14.29
Kepada: endokrin ilmiah PPDS <endokrin.ilmiah@gmail.com>

---------- Forwarded message ---------
Dari: **Partini Pudjiastuti Trihono** <paediatr.indones@gmail.com>
Date: Rab, 3 Nov 2021 16.01
Subject: [PI] New notification from Paediatrica Indonesiana
To: nur rochmah <drnurrochmah@gmail.com>

You have a new notification from Paediatrica Indonesiana:

You have been asked to review copyedits for "Ethical aspects of gender assignment in ambiguous genitalia - congenital adrenal hyperplasia".

Link: https://www.paediatricaindonesiana.org/index.php/paediatrica-indonesiana/workflow/access/2376

Anna Dewiyana

** If you wish to stop receiving this notification, please edit your **notifications** preferences under View Profile. **

The following message is being delivered on behalf of PAEDIATRICA INDONESIANA.

_____

Gmail 2. BUKTI REVIEW

UNIT KERJA ENDOKRIN ANAK <endokrin.ilmiah@gmail.com>

Fwd: Perbaikan Makalah 2376

1 pesan

nur rochmah <drnurrochmah@gmail.com> 6 Agustus 2023 pukul 14.30
Kepada: endokrin ilmiah PPDS <endokrin.ilmiah@gmail.com>

---------- Forwarded message ---------
Dari: **Paediatrica Indonesiana** <enquiry@paediatricaindonesiana.org>
Date: Sel, 21 Sep 2021 14.17
Subject: Perbaikan Makalah 2376
To: <drnurrochmah@gmail.com>
Cc: <dr.fayzi@gmail.com>, <adwinanurlita@gmail.com>

Yth. Penulis,

Pada 10 September 2021 kami telah mengirimkan notifikasi melalui sistem, seharusnya perbaikan sudah kami terima sebelum 17 September 2021.

Harap lakukan perbaikan sesuai dengan komentar pada file terlampir.

Hasil perbaikan kami tunggu sebelum 28 September 2021.

Atas perhatian dan kerjasamanya kami ucapkan terima kasih.

Salam,

Anna Dewiyana, MD
Journal Manager
Paediatrica Indonesiana

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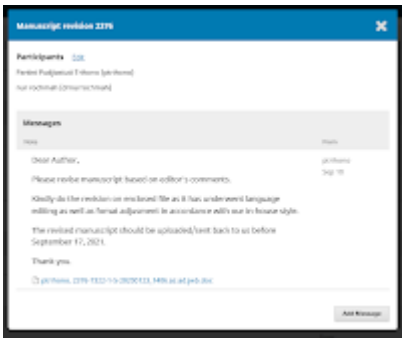
3 lampiran



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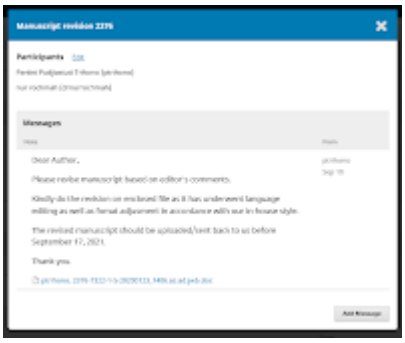

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456K

Gmail 3. BUKTI REVIEW 2 **UNIT KERJA ENDOKRIN ANAK <endokrin.ilmiah@gmail.com>**

Fwd: [PI] Editor Decision

1 pesan

nur rochmah <drnurrochmah@gmail.com> 6 Agustus 2023 pukul 14.29
Kepada: endokrin ilmiah PPDS <endokrin.ilmiah@gmail.com>

---------- Forwarded message ---------
Dari: **Partini Pudjiastuti Trihono** <paediatr.indones@gmail.com>
Date: Rab, 3 Nov 2021 16.02
Subject: [PI] Editor Decision
To: nur rochmah <drnurrochmah@gmail.com>

nur rochmah:

We have reached a decision regarding your submission to Paediatrica Indonesiana, "Ethical aspects of gender assignment in ambiguous genitalia - congenital adrenal hyperplasia".

Our decision is to: accept submission.

Partini Pudjiastuti Trihono
Department of Child Health, University of Indonesia Medical School/Dr. Cipto Mangunkusumo, Jakarta
partinipt@yahoo.com

The following message is being delivered on behalf of PAEDIATRICA INDONESIANA.

Ethical aspects of gender assignment in ambiguous genitalia - congenital adrenal hyperplasia: a case report

Nur Rochmah[1,2], Muhammad Faizi[1,2], Adwina Nurlita Kusuma Wardhani[2]

Comment [ad1]: Kasus ini bisa lebih membantu jika penulis menjelaskan lebih spesifik apay g penulis lakukan, apa yg salah, apa yg benar, dan bagaimana memperbaikinya. Karena masalah kultur yang sensitive, dokter anak mungkin memerlukan penjelasan yang lebih spesifik sebagai panduan dalam membantu anak-anak yg memiliki masalah serupa dan orangtuanya.

Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder commonly caused by mutation of the CYP21A2 gene, resulting in deficiency of an enzyme required for cortisol synthesis in the adrenal cortex. In 90-95% of cases, the deficient enzyme is 21-hydroxylase (21-OH), with an incidence ranging from 1 in 5,000 to 15,000 live births across various ethnic and racial backgrounds. In classical 21-OH deficiency (21-OHD) CAH, excessive androgen exposure in the fetus results in virilization at birth.[1]

The management of ambiguous genitalia in children with CAH presents a unique and ethically challenging decision-making dilemma for the medical team. Insensitive and poorly informed statements made in the delivery room may cause long-term psychological problems for the families. It is important to refrain from assigning gender until sufficient diagnostic information can be gathered. Parents, as guardians, and the supporting medical team must make decisions on behalf of the child, with the goal of enabling the child to grow into a healthy and happy adult with his or her assigned gender.[2,3] We report a case of a child with CAH, focusing on the ethical challenges in management of ambiguous genitalia.

Keywords: *ethical approach; congenital adrenal hyperplasia; child; ambiguous genitalia; gender identity*

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The Case

A 14-month-old girl who had been diagnosed with salt-wasting CAH since the age of three months was brought to Dr. Soetomo General Hospital, Surabaya, Indonesia, with complaints of

vomiting at every feeding, about four times per day, for the previous three days. The child's body weight was 7.4 kg, body length was 66 cm, and head circumference was 37 cm. Her routine medications were hydrocortisone, fludrocortisone, and salt supplementation.

On physical examination, her vital signs were normal. She had craniosynostosis and ambiguous external genitalia with enlarged clitoris, partly fused and rugated labia majora, and no palpable gonads (**Figure 1**).

Figure 1. CAH female patient with ambiguous genitalia

Laboratory examination revealed a 17-hydroxyprogesterone (17-OHP) level of 73.00 ng/mL (reference value 0.11-1.70 ng/mL) and a karyotype of 46XX, supporting the diagnosis of CAH. Thyroid function tests showed a free thyroxine (FT4) level of 2.19 ng/dL (reference value 0.9-2.3 ng/dL) and a thyroid-stimulating hormone (TSH) level of 14.68 uIU/mL (reference value 1.7-9.1 uIU/mL), consistent with compensated hypothyroidism. As shown in **Figure 2**, her bone age was appropriate for age, based on Greulich and Pyle.REF? The patient was

Comment [ad2]: Tambahkan referensi

diagnosed with 46XX classical salt-wasting CAH, with microcephaly, craniosynostosis, and severe stunting.

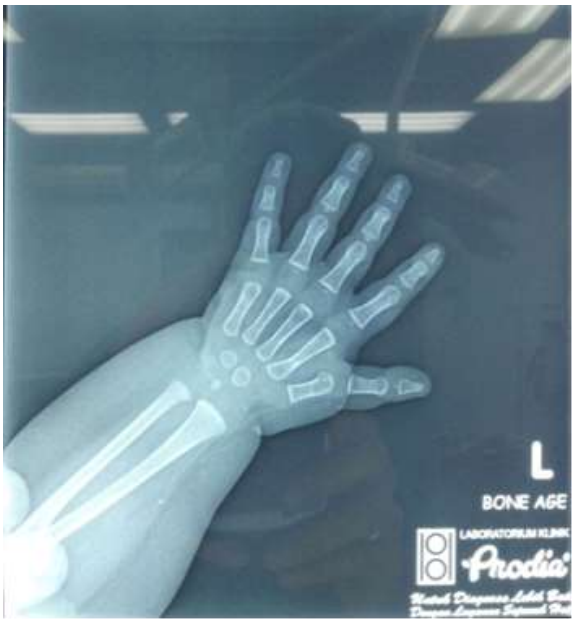

Figure 2. An x-ray revealed a bone age appropriate for a 14-month-old girl

Discussion

Congenital adrenal hyperplasia (CAH) is the most common cause of genital ambiguity due to 21-OHD in cortisol synthesis. Females with classic 21-OHD have ambiguous genitalia at birth: clitoromegaly, fused and rugated labia majora, and a common urogenital sinus consisting of the urethra and the vagina,[1] as was present in this patient.

Prenatal diagnosis should be performed in pregnant women who have previously given birth to a child with CAH. In such cases, the likelihood of bearing an affected girl is 1/8. Masculinization of the external genitalia begins at 8 weeks' gestation. Therefore, treatment must be started immediately after pregnancy is confirmed. Steroid treatment is commonly started at 6 weeks' gestation, using dexamethasone at a dose of 20 mg/kg/day, divided into three doses. Approximately 70% of prenatally treated females are born with normal genitalia or only a few male genitalia characteristics. Ethical gender assignment requires a multidisciplinary team.[4]

Prenatal preventive treatment remains controversial because dexamethasone consumption in early pregnancy influences fetal neural development.[1,4] In countries with limited resources, such as Indonesia, prenatal screening tests for CAH are not routinely done.[5]

The healthcare team and parents of newborns with ambiguous genitalia face an enormous challenge. Early conversations need to use positive terms like "your baby" rather than "it," to promote greater bonding and humanize the baby. Both parents and professionals need to use gender-neutral terms until the decision is finalized, to prevent misunderstanding and confusion.[2] The medical provider should emphasize the baby's potential to grow and develop into a healthy and happy adult if given appropriate treatment. In Indonesian society, parents may feel ashamed of having a child with ambiguous genitalia. Parents who seek help must be supported.[5]

The initial management of an infant diagnosed with ambiguous genitalia begins with gender assignment. There is agreement that patients should be assigned a gender as soon as clinical data are available. Factors influencing gender assignment include diagnosis, fertility potential, genitalia appearance, adult sexual function, surgical and hormone replacement options, family preferences, and cultural factors. Reduction of excess sex hormones and replacement of adrenal hormone deficiency remains the goal of CAH treatment. For severely virilized females, genital surgery may be necessary to produce successful development of gender which is programmed during the first few years of life through social conditioning.[2,3] A multidisciplinary team is important in the management of such cases and should be involved in discussions on sexuality, fertility, menstruation, and complementary surgery, as well as to provide information and options to families. The team should consist of pediatrician, gynecologist, and adult endocrinologists, geneticist, clinical psychologist, and pediatric surgeons/urologists.[3]

Comment [ad3]: Adult atau pediatric?

The medical and surgical management of children with disorders of gender development (DSD) require several major decisions on behalf of child. Parents as guardians have rights and responsibilities. Parental preference is the main factor in the ethics-based decision-making process to guide treatment for their child's fertility and sexual relations in the future, while minimizing health and psychosocial risks. The Halifax Resolution outlines the principles guiding decisions regarding the type and timing of surgery for children with DSD, including minimizing physical and psychological risks, preserving the capacity of satisfying

sexual relations, providing open options for the future, and respecting parents' wishes and beliefs.[2]

Ethics-based decision-making in the management of infants with ambiguous genitalia is challenging in terms of complexity, stigma, and implications on the child's future. Advancements in diagnostic technology and medicine cannot substitute for ethics-based decision-making. The multidisciplinary team should use ethics-based guidelines in communicating and educating parents, stabilizing mental health, developing treatment plans, and setting overall priorities to improve the well-being of individuals with DSD over their lifetime.[3]

We conclude that ethics-based guidelines for treatment plans by multidisciplinary team are the most important goal for improving the well-being of CAH patients with ambiguous genital over their lifetime.

Conflict of Interest

None declared.

Funding

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2. Gillam LH, Hewitt JK, Warne GL. Ethical principles for the management of infants with disorders of sex development. Horm Res Paediatr. 2010;74:412-8.
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5. Ediati A, Juniarto AZ, Birnie E, Okkerse J, Wisniewski A, Drop S, et al. Social stigmatisation in late identified patients with disorders of sex development in Indonesia. BMJ Paediatrics

Comment [ad4]: Most important goal atau most important factor?

Penulis tidak menjelaskan lebih banyak tentang pasien ini atau bagaimana mengimplementasikan ethics-based guideline

Tambahkan penjelasan mengenai:
1.Apa yg terjadi pada pasien tsb?
2.Akhirnya memilih jenis kelamin apa? Bagaimana orang tua/tim medis menentukan keputusan ini?
3.Terapi apa yg dijalani pasien? Informasi di hal. 2 hanya sampai diagnosis. Tidak menyebutkan konseling, terapi, dll
4.Tim multidisiplin utk kasus ini terdiri dari apa saja?
5.Bagaimana tim memandu orang tua. Ini harus spesifik supaya SpA lain bisa belajar dari pengalaman penulis
6.Bagaimana reaksi orang tua? Bgmana tim menghadapi reaksi orang tua?
7.Keputusan apay g diambil orant tua setelah konsultasi dng anggota tim?

Comment [ad5]: Tambahkan DOI untuk setiap artike yg berasal dari jurnal
Format penulisan seperti pada ref #1

Open. 2017;1:e000130.

Gmail 4. BUKTI ACCEPTED

UNIT KERJA ENDOKRIN ANAK <endokrin.ilmiah@gmail.com>

Fwd: [PI] Editor Decision

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Partini Pudjiastuti Trihono
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