agreement for surgery. Most middle-aged Saudi people have a sedentary life style. Social and economic factors led to the availability of immediate help at home in the form of family members or hired domestic help. These factors, when combined with the slow and chronic nature of OA, lead many patients to accept their symptoms and physical limitation as part of the natural aging process. Lack of knowledge and misunderstanding of the disease and the treatment options as well as misinformation regarding TKR lead many patients to become reluctant to accept it. With careful patient selection, TKR has been shown to diminish pain and decrease disability more efficiently than commonly used nonsurgical treatments. Modern TKR is safe, effective and carries a risk rate comparable to other surgical disciplines. Gill et al,[7] reported on the 5-8 years follow-up (mean 10 years) of TKR in patients less than 55 years old. In that series, only 2 of 72 knees required revision, and function was good or excellent in all knees. Other studies found similar results in the older age group.[8]

While it is quite possible that other factors such as the specific institute and the specific surgeon might influence the patient's decision to undergo TKR, our report still showed a high refusal rate (67%) among local patients. No specific influencing factor could be identified in our study group. Pain and disability as measured by the WOMAC OA index score did not seem to be a factor. A thorough Medline search failed to produce any similar reports. Patient education about the disease process and the contemplated surgery are crucial in helping them to make an informed and reasonable decision.

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From the Department of Surgery, King Fahad National Guard Hospital, Riyadh, Kingdom of Saudi Arabia. Address correspondence and reprint requests to Dr. Yaser Behairy, Department of Surgery, King Fahad National Guard Hospital, PO Box 53118, Riyadh 11583, Kingdom of Saudi Arabia. Tel. +966 (1) 2520088 Ext. 4119. Fax. +966 (1) 2520088 Ext. 4138. E-mail: ybehairy@yahoo.com

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Congenital adrenal hyperplasia due to 3 beta-hydroxysteroid dehydrogenase type II deficiency in 4 Saudi children. *Long term follow up*

Bassam S. Bin-Abbas, *MD, FAAP,*
Nadia A. Sakati, *MD, FAAP,*
Abdullah A. Al-Ashwal, *MD, FRCPC.*

Classical 3 beta-hydroxysteroid dehydrogenase type II (HSD_3B_2) deficiency is a rare type of congenital adrenal hyperplasia that impairs steroidogenesis in both the adrenals and the gonads, resulting from mutations in the HSD_3B_2 gene. The clinical spectrum of this inherited disease is heterogeneous and ranges from the severe salt-wasting form with or without ambiguous genitalia to the non salt-wasting form, with ambiguous genitalia and premature puberache in young children or both, and hirsutism and menstrual disorders in older females.[1] Congenital adrenal hyperplasia secondary to 21 hydroxylase and 11 hydroxylase deficiencies have been described in Saudi children, however, there are no published reports on HSD_3B_2 deficiency. We report here our long term experience with 4 Saudi siblings who were diagnosed with HSD_3B_2 deficiency based on the revised hormonal diagnostic criteria.[2] The patients are 3 brothers and one sister. Parents are first degree relatives who had another 3 normal children. The oldest brother is 20 years old. He presented at the second week of life with vomiting and dehydration. He was found to have penoscrotal hypospadias and palpable testes within the bifid scrotum. Electrolytes profile, showed hyperkalemia (potassium level of 10.7 mmol/L), hyponatremia (Sodium level of 115 mmol/L) and acidosis. He had normal male karyotypes and absent mullerian structures on pelvic ultrasound. Three beta-hydroxysteroid dehydrogenase type II deficiency was suspected based on elevated adrenocorticotropic hormone (ACTH) level of 257 pmol/L (0-10.2), low serum cortisol (F) level of 0.058 mmol/L and low testosterone (T) level of <0.3 nmol/L (0.4-0.7). He was started on hydrocortisone 5mg twice a day and fludrocortisone 0.1mg once a day. Adrenocorticotropic hormone stimulation test

was performed at the age of 18 years (after stopping hydrocortisone for 2 days) by giving 0.25mg intravenous cortrosyn, which showed a baseline ACTH level of 237 pmol/L, a baseline F level of 0.028 mmol/L, a stimulated F level of 0.04 mmol/L, a baseline 17 hydroxypregenolone (Δ5-17P) level of 360 nmol/L (HSD_3B_2 genotype proven male patients >159), a stimulated Δ5-17P level of 419 nmol/L (HSD_3B_2 genotype proven male patients >289), a baseline ***Δ5-17P/F*** ratio of 12857 (HSD_3B_2 genotype proven male patients >1943), a stimulated Δ5-17P/F ratio of 10475 (HSD_3B_2 genotype proven male patients >4010). His baseline 17 hydroxyprogesterone (17OHP) was 152 nmol/L (0.8-6), which increased to 161 nmol/L on stimulation. His dehydroepiandrosterone (DHEA) was 107 nmol/L (5-27), which increased to 180 nmol/L at 60 minutes of stimulation. His androstenedione (Δ4-A) was 10.8 nmol/L (0.8-7.2) at baseline and increased to 12.2 nmol/L on stimulation. He was followed closely and maintained normal electrolytes and suppressed Δ5-17P throughout his life on a hydrocortisone dose of 10-15 mg/m^2/day and fludrocortisone 0.1mg/day. He had a surgical repair of the external genitalia at the age of 2 years and achieved normal puberty with normal development of secondary sexual characters. He had now a stretched penile length of 7.5cm, tanner stage V testicular size and a final height of 155cm. His T level was 28 nmol/L (9.9-27) and Δ4-A level was 10.8 nmol/L. Semen analysis was normal with normal sperm count.

His sister is 16 years old. She was born with normal external genitalia. However, on the second week of life, she presented with hyperkalemia (K level of 7.7 mmol/L) and hyponatremia (Na level of 129 mmol/L). She was diagnosed with HSD_3B_2 deficiency based on her strong family history of this disease. She had elevated ACTH level of 276 pmol/L and low cortisol level of 0.034 mmol/L. She had normal female karyotypes and a T level of < 0.1 nmol/L. She was started on hydrocortisone 5mg twice a day and fludrocortisone 0.1mg once a day. At the age of 14 years, hydrocortisone was stopped for 2 days and she had an ACTH stimulation test which showed a baseline ACTH level of 217 pmol/L, a baseline F level of 0.04 mmol/L, a stimulated F level of 0.04 mmol/L, a baseline Δ5-17P level of 98 nmol/L (genotype normal females with hirsutism/menstrual disorder <45), a stimulated Δ5-17P level of 98.4 nmol/L (genotype normal females with hirsutism/menstrual disorder <150), a baseline Δ5-17P/F ratio of 2450 (genotype normal females with hirsutism/menstrual disorder <43), a stimulated Δ5-17P/F ratio of 2460 (genotype normal females with hirsutism/menstrual disorder <151). Her baseline 17OHP was 23 nmol/L, which did not rise on stimulation. Dehydroepiandrosterone was 45 nmol/L at baseline, which increased to 52 nmol/L on stimulation. Androstenedione was 1.3 nmol/L, which increased to 1.5 nmol/L. She was maintained on hydrocortisone dose of 10-15 mg/m^2/day and fludrocortisone 0.1mg/day with normal electrolytes. Her Δ5-17P was ranging from 6.6-10 nmol/L on substitutive therapy. She had mild hirsutism and menstrual irregularities, although her T level and Δ4-A was suppressed. She had normal puberty with normal development of secondary sex characters at the age of 14 years with a follicular stimulating hormone level of 8 iu/L, luteinizing hormone level of 8 iu/L and an estradiol level of 159 pmol/L (>100). Her final height was 150cm.

The younger brother is 12 years old. He was born with micropenis, bifid scrotum and descended palpable testes. He was observed until the second week of life when he developed hyperkalemia (K level of 7.7 mmol/L and hyponatremia (Na level of 129 mmol/L). His ACTH level was 207 pmol/L and F level was 0.02 mmol/L. Three beta-hydroxysteroid dehydrogenase type II deficiency was suspected and he was started on the same replacement therapy. He had a monthly injection of 50 mg testosterone for 3 months for micropenis. His last stretched penile length was 8cm. Adrenocorticotropic hormone stimulation test was performed at the age of 10 years which showed a baseline ACTH level of 233 pmol/L, a baseline F level of <0.028 mmol/L, a stimulated F level of <0.028 mmol/L, a baseline Δ5-17P level of 59.8 nmol/L (HSD_3B_2 genotype proven children >26.4), a stimulated Δ5-17P level of 211 nmol/L (HSD_3B_2 genotype proven children >165), a baseline Δ5-17P/F ratio of >2107 (HSD_3B_2 genotype proven children >94), a stimulated Δ5-17P/F ratio of >7535 (HSD_3B_2 genotype proven children >216). His baseline 17OHP was 29 nmol/L, which increased to 35 nmol/L on stimulation. His DHEA was 38 nmol/L, which did not rise on stimulation. Androstenedione was 0.4 nmol/L, which increased to 0.9 nmol/L.

The youngest brother is 3 years old. He was born with penoscrotal hypospadias, bifid scrotum and descended palpable testes within the scrotum. During the first week of life and before starting replacement therapy, he had an ACTH stimulation test which showed a baseline ACTH level of 813 pmol/L, a baseline F level of 0.075 mmol/L, a stimulated F level of 0.082 mmol/L, a baseline Δ5-17P level of 7636 nmol/L (HSD_3B_2 genotype proven children >26.4), a stimulated Δ5-17P level of 8666 nmol/L (HSD_3B_2 genotype proven children >165), a baseline Δ5-17P/F ratio of >101813 (HSD_3B_2 genotype proven children >94), a stimulated Δ5-17P/F ratio of >105682 (HSD_3B_2 genotype proven children >216). Seventeen hydroxyprogesterone was 468 nmol/L, which increased to 482 nmol/L on stimulation. Three beta-hydroxysteroid dehydrogenase type II was

confirmed and he was started on hydrocortisone and fludrocortisone. He had a corrective surgery and his stretched penile length post-operatively was 3.5cm.

Lutfallah et al,[2] recently revised the hormonal criteria of HSD3B2 deficiency, they showed that the baseline and the ACTH-stimulated Δ5-17P levels, and the baseline and the ACTH-stimulated Δ5-17P/F ratios have more accurate prediction of HSD3B2 deficiency. In their series, genotype proven children with ambiguous genitalia had baseline and ACTH-stimulated Δ5-17P levels of >26.4 nmol/L (>12SD) and >165 nmol/L (>35SD) and baseline and ACTH-stimulated Δ5-17P/F ratios of >94 (>15SD) and >216 (>23SD). For genotype proven adult males with ambiguous genitalia, the baseline and ACTH-stimulated Δ5-17P levels were >159 nmol/L (>74SD) and >289 nmol/L (>21SD) and the baseline and ACTH-stimulated Δ5-17P/F ratios were >1943 (>193SD) and >4010 (>221SD). For genotype normal females with hirsutism and menstrual disorder, baseline and ACTH-stimulated Δ5-17P levels were <45 nmol/L (<16SD) and <150nmol/L (<12SD) and baseline and ACTH-stimulated Δ5-17P/F ratios were <43 (<5SD) and <151 (<10SD). Our patients showed very high Δ5-17P levels and Δ5-17P/F ratios on ACTH stimulation test, which may represent a severe form of HSD3B2 deficiency, although they were not severely affected clinically.

The patients described in this report had neonatal ambiguous genitalia and salt losing secondary to HSD3B2 deficiency. However at puberty, they had normal development of the secondary sex characters with normal testosterone and estrogen levels. We believe that HSD3B2 deficient patients have normal ***HSD3B1*** activity, which is responsible for the extra-adrenal and extra-gonadal conversion of ***Δ5-hydroxysteroid*** precursors into the corresponding ***Δ4-ketosteroids***. This peripheral ***HSD3B*** activity could explain why some patients with HSD3B2 deficiency will have normal puberty.[3] Alos et al,[4] reported a 46xy patient with neonatal ambiguous genitalia, who had normal masculinization at puberty, but the patient was azoospermic. However, other reports described normal paternity in affected males with proven HSD3B2 deficiency.[5]

Male children with HSD3B2 deficiency may present with micropenis secondary to androgen deficiency. We believe that patients should be raised according to their genetic sex. Male patients who presumed to have a testosterone responsive microphallus may need one or more courses of intramuscular testosterone injection to achieve an adult penile length within the functioning range.

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From the Department of Pediatrics, King Faisal Specialist Hospital and Research Centre, Riyadh, Kingdom of Saudi Arabia. Address correspondence and reprint requests to Dr. Bassam S. Bin-Abbas, Section of Pediatic Endocrinology, Department of Pediatrics (MBC 58), King Faisal Specialist Hospital and Research Centre, PO Box 3354, Riyadh 11211, Kingdom of Saudi Arabia. Tel. +966 (1) 4427761. Fax. +966 (1) 4427784. E-mail: benabbas@kfshrc.edu.sa

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Risk factors for recurrent miscarriage in Sudanese women

Abubaker A. Ahmed, *MD, MBBS,*
Osman M. Ortashi, *MRCOG, MD,*
Amin H. Abdelmagied, *MBBS, MRCOG,*
Magdy S. Ramzi, *MD, MBBS.*

Recurrent miscarriage is defined as 3 or more consecutive miscarriages, its effects can be distressing and devastating. While the condition affects 1% of all women,[1] sporadic miscarriage is common, complicating 10-15% of all clinically diagnosed pregnancies.[2] This concludes that the statistical probability of having 3 consecutive miscarriages is 0.34%. Therefore, recurrent miscarriage is more complicated than a simple chance occurrence. Recurrent miscarriage is a multi-factorial condition, causes and associations include (chromosomal) genetic (thrombophilia), anatomical, endocrine and idiopathic factors.

While some causes of recurrent miscarriage remain difficult to treat such as, polycystic ovary syndrome and chromosomal abnormalities; the use of aspirin and heparin have proven to improve the outcome in cases of thrombophilia; namely, antiphospholipid (APL) syndrome.