

21-Hydroxylase Deficiency: Newborn Screening in Iran?

Nejat Mahdieh^{1,2}, PhD; Bahareh Rabbani¹, PhD;
Ali Rabbani^{*1,3}, MD

1. Growth and Development Research Center, Tehran University of Medical Sciences, Tehran, Iran
2. Faculty of Medicine, Ilam University of Medical Sciences, Ilam, Iran
3. Pediatrics Center of Excellence, Tehran University of Medical Sciences, Tehran, Iran

21-hydroxylase deficiency (21-OHD) accounts for the cause of 90-95% of congenital adrenal hyperplasia (CAH) cases. The world incidence of 21-OHD is 1:20,000 to 1:10,000 live births^[1]. Prevalence of CAH trends to be high due to frequent consanguineous and first cousin marriages and underestimation because of stigmatization^[2,3]. A range of clinical phenotypes including salt-wasting, simple virilizing and non-classic forms is emerged due to the variable residual 21-hydroxylase enzyme activity in CAH. Enzymatic defects in steroid biosynthesis pathway leads to accumulation of the metabolic precursors and shifting to androgen synthesis. Ambiguous genitalia appear in infant girls^[4]. Basically, salt-wasting form occurs between first and third week after birth^[4]. Because of nonspecific symptoms, an accurate diagnosis is often delayed so that males with classic form are at serious risk of morbidity (including neurological damage or intellectual disability) and mortality^[4,5].

Newborn screening (NBS) for 21-OHD was performed for the first time in Alaska in 1977 and it is currently done in many European countries, USA, Canada and Japan^[1,6,7]. The time-resolved, dissociation-enhanced, lanthanide fluorescence immunoassay (DELFLIA) is used for 21-OHD NBS in most countries^[8].

Specificity and sensitivity of 21-OHD NBS are more than 99.5% and 92-100%, respectively^[9]. Decreased morbidity and mortality associated with salt-wasting crises is the main objective of 21-OHD NBS ^[8]. Other important objectives are decreasing the time of sex assignment for infants with a virilized 46,XX karyotype, preventing precocious puberty and decreased final height in the simple virilizing form, and health improvement for the afflicted families^[7]. 21-OHD NBS is usually performed before most babies with salt-wasting became symptomatic, so that it provides time for appropriate replacement therapy with hydrocortisone and fludrocortisone^[8]. Molecular testing is currently performed in this country, but early detection would significantly decrease the costs, although no data is available worldwide on the cost-effectiveness of screening for this condition. Decreased hospitalization and decreased time to correct sex assignment have been documented in the screened populations. Liquid chromatography-tandem mass spectrometry, however, is more reliable and less costly than molecular testing^[8].

In conclusion, CAH has all criteria for NBS^[10]: 1) if undetected, it leads to high morbidity and mortality; 2) if detected early, an effective cheap treatment exists for the patients; 3) the 21-OHD NBS test would be efficient and reliable; and 4) the incidence of CAH is also high in our country^[11]. However, a pilot study including approximately 10,000 infants is recommended to decipher incidence of disease and cost-effectiveness of the test; so that health professionals decide whether to perform 21-OHD NBS or not.

Key words: 21-hydroxylase Deficiency; Congenital Adrenal Hyperplasia; Screening

* **Corresponding Author; Address:** Gharib St., Pediatrics Center of Excellence, Children's Medical Center Hospital, Tehran University of Medical Sciences, Tehran, Iran, P.O.Box:14155-6386

E-mail: rabania@tums.ac.ir

References

1. Speiser PW, Azziz R, Baskin LS, et al. Congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2010;95(9):4133-60.
2. Ramazani A, Kahrizi K, Razaghiazar M, et al. The frequency of eight common point mutations in CYP21 gene in Iranian patients with congenital adrenal hyperplasia. *Iran Biomed J* 2008;12(1):49-53.
3. Rabbani B, Mahdih N, Haghi-Ashtiani MT, et al. Molecular diagnosis of congenital adrenal hyperplasia in Iran: Focusing on CYP21A2 gene. *Iran J Pediatr* 2011;21(2),139-15.
4. Riepe FG, Sippell WG. Recent advances in diagnosis, treatment, and outcome of congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *Rev Endocr Metab Disord* 2007;8(4):349-63.
5. Ghayee HK, Auchus RJ. Basic concepts and recent developments in human steroid hormone biosynthesis. *Rev Endocr Metab Disord* 2007;8(4):289-300.
6. Dietzen DJ, Rinaldo P, Whitley RJ, et al. National academy of clinical biochemistry laboratory medicine practice guidelines: follow-up testing for metabolic disease identified by expanded newborn screening using tandem mass spectrometry; executive summary. *Clin Chem* 2009;55(9): 1615-26.
7. Wu JY, Sudeep, Cowley DM, et al. Is it time to commence newborn screening for congenital adrenal hyperplasia in Australia? *Med J Aust* 2011;195(5):260-2
8. White PC. Neonatal screening for congenital adrenal hyperplasia. *Nat Rev Endocrinol* 2009;5(9):490-8
9. Van der Kamp HJ, Noordam K, Elvers B, et al. Newborn screening for congenital adrenal hyperplasia in the Netherlands. *Pediatrics* 2001;108(6):1320-4.
10. Therrell BL. Newborn screening for congenital adrenal hyperplasia. *Endocrinol Metab Clin North Am* 2001; 30(1):15-30.
11. Rabbani B, Mahdih N, Haghi Ashtiani MT, et al. Mutation analysis of CYP21A2 gene in Iranian population. *Genet Test Mol Biomarkers* 2012;16(2): 82-90.

Archive of SID