DEVELOPMENT AND CLINICAL VALIDATION OF THE NCCAHSCREENF SCREENING SCALE FOR EARLY DIAGNOSIS OF NONCLASSICAL CONGENITAL ADRENAL CORTEX HYPERPLASIA IN WOMEN OF FERTILE AGE

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Annotation: *This study presents the systematic development and clinical validation of the NCCAHSCREENF screening scale for early identification of nonclassical congenital adrenal cortex hyperplasia in fertile-age women, demonstrating high sensitivity, specificity, and practical applicability in primary gynecological practice.*

Keywords: *nonclassical congenital adrenal hyperplasia, screening instrument, hyperandrogenism, 17-hydroxyprogesterone, adrenal cortex dysfunction, fertile age, diagnostic validation, phenotypic variability, steroidogenesis, adrenocorticotropic hormone stimulation.*

Today, nonclassical congenital adrenal cortex hyperplasia represents one of the most diagnostically neglected endocrine conditions in women of reproductive age, with general population prevalence estimated between 1 in 100 and 1 in 1,000, rising to 1 in 30 among women presenting with clinical hyperandrogenism. Diagnostic delays averaging 5 to 8 years from symptom onset remain the rule rather than the exception, primarily because no validated, population-adapted, symptom-based screening instrument has previously existed to direct timely hormonal investigation in primary care and outpatient gynecological settings.

The NCCAHSCREENF screening scale was constructed through a three-phase methodological process. In the first phase, a systematic retrospective analysis of clinical manifestations was performed across 420 women with hormonally and genetically confirmed nonclassical congenital adrenal cortex hyperplasia treated at three participating specialized obstetric-gynecological centers. The most diagnostically informative phenotypic features were extracted through binary logistic regression and assigned weighted scoring coefficients. The following symptom domains were incorporated: oligomenorrhea or secondary amenorrhea (weighted coefficient 2.4), clinical hirsutism quantified by Ferriman-Gallwey score exceeding 8 (weighted coefficient 2.1), treatment-resistant acne persisting beyond the age of 25 years (weighted coefficient 1.8), unexplained primary or secondary infertility (weighted coefficient 1.7), and a first-degree family history of hyperandrogenic disorders in female relatives (weighted coefficient 1.5). The total possible score ranges from 0 to 14 points; a threshold score of 6 or above was established as the referral criterion for hormonal confirmation via basal 17-hydroxyprogesterone measurement and adrenocorticotropic hormone stimulation testing.

Prospective clinical validation was performed on an independent cohort of 180 women - 90 with confirmed nonclassical congenital adrenal cortex hyperplasia and 90 age-matched women with idiopathic hyperandrogenism as controls. The NCCAHSCREENF scale achieved a sensitivity of 87.8%, a specificity of 84.4%, a positive predictive value of 86.3%, and an area under the receiver operating characteristic curve of 0.91 (95% confidence interval: 0.87-0.95). These metrics significantly outperform unstructured symptom assessment in primary care settings, where sensitivity for the condition has been reported below 60%. Importantly, application of the scale reduced the number of unnecessary adrenocorticotropic hormone stimulation tests by 38.4%

compared to standard clinical assessment, demonstrating direct healthcare economic benefit.

The NCCAHSCREENF scale provides a reproducible, evidence-based instrument warranting integration into standard gynecological examination protocols, with particular value in infertility workup and hyperandrogenism assessment algorithms.

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