Clitoral Length in Indian Newborn Girls: Need for Regional References

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Clinical assessment of a neonate is incomplete without proper genital examination. Anatomic abnormalities of the external genitalia may provide vital clues to underlying endocrine and genetic disorders. In the male, bilaterally descended testis in the completely fused scrotum, and a normal phallic length (for the ethnicity) with urethral opening at the tip clinically signifies normal androgenization. In the female, though etiology may vary, *in utero* exposure to a hyperandrogenic milieu leads to various degrees of masculinization of the external genitalia which have been graded by Prader [1]. The main clinical measures of this androgenization are clitoral enlargement and posterior labial fusion. Androgen exposure, very early *in utero*, causes both clitoromegaly and labial fusion whereas a delayed exposure (usually after the first trimester) generally leads to clitoromegaly alone [2]. In conditions like congenital adrenal hyperplasia (CAH) or other virilizing conditions in the mother during early pregnancy, the clitoral enlargement and labial fusion is so obvious along with hyperpigmentation (in CAH only) that exact measurements of clitoral length may not be required for clinical diagnosis. However, in lesser degrees of virilization (as in isolated clitoral enlargement), inter-observer variations may confound clinical decision making. In these clinical situations, exact measurement of the clitoral length and different indices of labial fusion may be highly relevant. Also, newly born preterm babies may have an apparently more prominent clitoris than term babies. In the study published in this issue of *Indian Pediatrics*, Mondal, *et al.* [3] assessed clitoral length, anogenital distance (AGD) and anogenital ratio (AGR) in a cohort of term and preterm newborns from Kolkata, East India. This normative data on clitoral length and anogenital distance and anogenital ratio is probably the first in Indian patients.

Based upon our previous study [4], the stretched penile length was found to vary not only between different ethnic groups but also between different regions of similar race and ethnicity. In addition to possible methodological differences, role of other factors (genetic or local environmental) cannot be ruled out. Even with the availability of a very sensitive measuring device as in the current study, measuring less than 3 mm in newborns in routine practice may have its own logistic difficulties. Kutlu, *et al.* [5] attempted to determine the regional reference standards for clitoral length and suggested a cut-off length of 4.69 mm below which the clitoris is covered by the labia majora when the child was held in a frog-leg like position. This definition has some practical significance as the availability of the digital calipers or other highly sensitive measuring instruments may be questionable in a resource constrained setting like India, more so in the primary health care set-ups. Further, this kind of very simple observation may act like a basic screening, and prompt the neonatal team for further investigation only in a subset of babies.

Interestingly, normative values for AGD and AGR in this study did not show any correlation with gestational age, and was in line with other Western studies [3]. This again would be useful in individualizing the endocrinological evaluation. Further, in cases of suspected maternal androgen exposure as a cause of virilization in the baby, AGD and AGR may help in timing of the exposure.

A recent multi-centric study conducted by the Indian Council of Medical Research (ICMR) has revealed that CAH is not uncommon, especially in South India with a reported prevalence of a little over 1 in 2000 [6]. With newborn screening for congenital hypothyroidism yet to pick up in a big way in India, screening for CAH with standardized 17-hydroxy-progesterone assay still has a long way to go. The basic idea of newborn screening for CAH is to identify the male baby with salt losing CAH as they do not have any genital ambiguity and cannot be picked up clinically. However, female babies with CAH may provide an opportunity for clinical diagnosis as the genitalia may reveal some degree of virilization. This

again stresses the importance of clinical examination of the genitalia and early identification of clitoromegaly which seems to be the pragmatic approach to pre-screen for CAH in our setting.

In summary, there is a need for more studies from different parts of India on clitoral length and anogenital distance. Neonatologists and Pediatric endocrinologists should be aware of local and regional references before subjecting the patients to detailed hormonal evaluation in otherwise asymptomatic newborns with suspected genital abnormalities.

Funding*: None;* Competing interest*: None stated.*

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Why Antibiotic 'Invisibility Day' is Better than 'Invisible Antibiotic' Future?

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Antibiotics provided the *vis-a-tergo* to "modern medicine" almost a century ago. The discoverer of antibiotics, Sir Alexander Fleming, had warned about penicillin resistance in many of his lectures, including in his 1945 Nobel Prize lecture where he said "It is not difficult to make microbes resistant to penicillin in the laboratory by exposing them to concentrations not sufficient to kill them, and the same thing has occasionally happened in the body…there is the danger that the ignorant man may easily under-dose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant." What Fleming had envisioned did come true. It is estimated that for the seven major classes of known antibiotics, resistance has developed within a span of about one to four years from the time of clinical introduction of the drug [1].

Between 1983 and 1987, Food and Drug Administration (FDA) approved 16 new systemic antibiotics, but since then antibiotic approvals have been on the decline. Since 2008, only two systemic antibiotics have been approved [2]. As time went on and the idea of antimicrobial resistance still had not caught on with mainstream medicine, the drying pipeline of antimicrobial agents along with increasing resistance got the Infectious Disease Society of America (IDSA) up in arms. The IDSA set forth their "Bad Bugs, No Drugs" campaign in 2004 [3]. Along with a series of papers, the IDSA and Society of Healthcare Epidemiology of America (SHEA) came out with the current antimicrobial stewardship guidelines that were published in 2007[4].

Antibiotics continue to save lives every day. This ability to control infection is critical to other advances in medicine be it neonatal care, organ transplantation, chemotherapy for malignancy, immunosuppression, safe surgery and obstetric care or intensive care interventions. But sadly antibiotic resistance has now become a major public health crisis. It is a common scenario to have a very sick patient with infection and the laboratory reports listing every single drug as resistant. The greater the volume of antibiotics used, the greater the chances that antibiotic-resistant populations of bacteria will prevail in the contest for survival of the fittest at the bacterial level.