CAPE NEWS

Newsletter of the Indian Society for Pediatric and Adolescent Endocrinology (ISPAE)

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Contents

From the Editor's desk

Dear members,

The entire Capenews team extends warm wishes to each one of you for the new year! Congratulations to the new Executive Council just elected! This has been an eventful year, including our mid-term meeting being conducted in collaboration with the first international childhood diabetes meeting in India, ISPAD 2018, and we are sure the new team will take ISPAE to further heights.

This issue of CAPENEWS carries a nice summary of the latest Endocrine Society Guidelines on congenital adrenal hyperplasia due to 21-hydroxylase deficiency (21OHD) and mini-reviews on 'genetics of 21OHD' and 'Obesity prevention strategies in the developing world with dual burden of malnutrition'. It also features two interesting case reports and news of meetings past and forthcoming. I am sure all those interested in pediatric endocrinology will find this issue useful. I thank all my team members, Drs Rajni Sharma, Sachin Mittal, Sweta Budyal, and Vani HN for their active participation in designing this issue and for their valuable contributions. My special thanks to Dr Anju Virmani, for her tireless efforts to make this issue a fantastic one.

Dr Vijaya Sarathi, Editor, CAPENEWS

ISPAE 2019 Biennial Meet, Kolkata: Save your dates!!!

ISPAE 2019, the 6th Biennial Conference of our Society, will be held in the historic city of Kolkata on 29th November- 1st December 2019. Please find below online registration link: http://marundeshwara.com/maruncms/user-register.php?conferenceID=177%20-%20ISPAE%202019

There is a choice for registering either for the comprehensive 3-day Pediatric Endocrinology conference, or a one day program, including practical pediatrician-oriented endocrine topics, on 1st December.

Hearty Welcome to New ISPAE Members

Ridha Singh, New Delhi	GD Ramchandani, Kota
Mitrabhanu Satpathy, Jamshedpur	Amit Anil Chaudhari, Palghar, Maharashtra
Lokesh Sharma, Lucknow	Pavithra Nagaraj, Bangalore
Koushik Ural, Lucknow	Praveen Paul George, Vellore
Priyamvada Tyagi, Lucknow	Kaustabh Chaudhuri, Kolkata
Prashant Verma, Dehradun	Avishek Poddar, Kolkata
Mythili Ayyagari, Visakhapatnam	Alok Sardesai, Kolkata
Shrikrishna V Acharya, Mangalore	Agni Sekhar Saha, Kolkata

Dear Friends,

Our two-year term as office bearers of ISPAE Executive Committee comes to an end The current EC was a relatively young council with a good mix of people from the private and service sectors. Each one of us had our own perspectives and opinions to offer and where we lacked in experience, we made up with our sincerity and enthusiasm, and over time, we evolved into a good team that could debate over issues passionately and yet reach an informed decision cohesively.

During our term ISPAE participated in two International meetings - the 10th International Meeting of Pediatric Endocrinology at Washington in Nov 2017, and the 44th Annual Conference of ISPAD in Hyderabad in Oct 2018, as well as hosting the APPES Fellows School along with PET 2017 in Coimbatore in Nov 2017. Several of our team members participated in International Guidelines development: Dr Vandana Jain in neonatal diabetes, Dr Anurag Bajpai and Dr Archana Dayal in use of GnRH analogs, and Drs Anju Virmani, Banshi Saboo, Nikhil Tandon, and Vandana Jain in the 2018 ISPAD Guidelines. Dr Raghupathy was nominated by ISPAE and awarded the prestigious ESPE International Outstanding Clinician award for the year 2018. On the domestic front, ground work has been done to initiate the ambitious project related to diabetes registry, and ISPAE consensus guidelines on diagnosis and management of GH deficiency are being developed, while the ISPAE congenital hypothyroidism screening guidelines have been published.

We would like to thank from the bottom of our hearts, the ISPAE advisors, Dr Meena Desai, Dr Raghupathy, Dr Nalini Shah, Dr PSN Menon, Dr Anju Virmani and Immediate Past President Dr Vijayalakshmi Bhatia for guiding us every step of the way. Thanks to Dr Vijaya Sarathi and his team for the amazing work they have been doing with Cape News, Dr Ravikarnam and his team for revamping the ISPAE website, and to all the members of the ISPAE EC for their active contribution towards ISPAE activities throughout these two years. Their support and participation were instrumental in smooth conduct of our activities during our term.

Now our term comes to an end, and we are happy to hand over the baton to Dr Preeti Dabadghao and her team. We are sure that under their stewardship, our young Society shall continue to be an advocate for furthering the cause of pediatric endocrinology in India as well as nurture our collaborative efforts with other global pediatric endocrine Societies.

On behalf of the outgoing EC of ISPAE we extend our heartfelt thanks to all of you for reposing your confidence in us and extending your full support and guidance throughout our tenure.

Wishing you all a very happy and healthy 2019!
Anju Seth, Anurag Bajpai, Rajni Sharma

ISPAE ELECTIONS: 2019-2020

The following candidates are hereby declared elected:

President: Dr Preeti Dabadghao

Honorary Secretary-Treasurer: Dr Ahila Ayyavoo

Joint Secretary: Dr Leena Priyambada

Executive Members: Dr Aashima Dabas, Dr J Dhivyalakshmi, Dr Kriti Joshi, Dr Ruchi Parikh, Dr Tushar Godbole, Dr Veena Nair, Dr Vijay Jaiswal

Signed: Dr Rajni Sharma (Returning Officer)

Minutes of ISPAE GBM Meeting held on 12th October 2018 (7:00pm-8:00pm), at Hyderabad

Executive Members attended: Dr Anju Seth, Dr Anurag Bajpai, Dr Rajni Sharma, Dr Hemchand Prasad, Dr Preeti Singh.

Advisors attended: Dr Anju Virmani, Dr. Vijaylakshmi Bhatia

Total 34 ISPAE members attended

The meeting was opened by Dr Anju Seth. As per agenda of meeting, the following issues were discussed, and decisions taken

Agenda

1. Ratification of previous Executive meetings
Action: The MOM held on 25.11.17 were read by Dr Anurag Bajpai and unanimously approved by the ISPAE members.

2. Appointment of Auditor and Ratification of Audit Accounts and Activity report
Action:
The process of audit of ISPAE account and filing of ITR for the financial year 2017-18 was still in process. The members were informed of the current status of key components of the ISPAE account by the Secretary with a suggestion that a copy of the audit report would be sent by email to all members once it has been completed. The decision was unanimously agreed upon.
The ISPAE members approved (vote voice) to continue the same chartered accountant Mr Manoj Bhatnagar for looking after the ISPAE accounts for next year (2019-20).
It was advised that the appointed CA for ISPAE conference 2019 work in close collaboration with Mr. Bhatnagar right from beginning of Conference related financial activities.

Annual report and ISPAE activities
Dr Anurag Bajpai read out the annual report. He informed the GBM that ISPAE had conducted 2 programmes at PEDICON 2018 in association with Dr. Harish Mangtani.
Dr Anju Seth shared the good news that Dr. Raghupathy had been awarded the Outstanding Clinician Award 2018 by ESPE at Athens Greece. The whole executive and GBM conveyed their heartiest congratulations to him. The president also shared the news that the ISPAE guidelines for Congenital Hypothyroidism screening were featured in the yearbook of ESPE 2018. Teaching slides from these guidelines would soon be available at ISPAE website. The GBM was informed of the new ISPAE website and the executive appreciated the efforts of Dr Ravikumar Karnam (webmaster), Dr. Ganesh Jevlikar, Dr. Tushar Godbole and Dr Saurabh Uppal for upgrading the website. The GBM was informed that Dr Hemchand had devised moblie apps for Diabetic ketoacidosis management and carbohydrate counting which were freely available for use.
GBM members were encouraged to hold activities on Diabetes day 14 th November and other Pediatric Endocrinology CMEs and workshops at their respective institutes under ISPAE banner with prior permission from the executive.

3. Progress of GH guideline group

Action: The ISPAE members were informed about the formulation of the Growth Hormone guidelines (under process) and the team members working on it. Some groups were yet to submit their final write up and would do so in near future. Then a writing group would be formulated for the same.

4**. ISPAE Diabetes registry progress**

Dr. Anurag Bajpai informed everyone regarding the progress made in the ISPAE diabetes registry. Medtronic along with Sweet Registry had agreed to provide funds to initiate the ISPAE registry on trial basis at 10 centres and Diabetacare had also agreed to provide their software for the next 1 year free of cost. He would be writing to GBM members for expression of interest to be part of the registry in which he would outline the objectives of the registry and terms and conditions to be fulfilled for being part of the registry.

5. Global collaboration: ICPE Global consensus guidelines.

The GBM was informed that Dr Anurag Bajpai and Dr. Archana Dayal Arya would be representing ISPAE in the ICPE consensus group for use of GnRH analogues in precocious puberty and Dr. Vandana Jain for the guidelines for neonatal diabetes.

6. **ISPAE 2019, Kolkata**

Dr Subrata Dey, organizing chair, briefed everyone regarding the progress made in organization of ISPAE 2019 to be held at Kolkata. Dr Tamal Laha (Consultant Pediatrics) would be the organizing secretary and second signatory of the conference along with Dr Dey. Early bird registrations had started for the conference and Dr Dey was in touch with international faculty for invited talks. The venue for main conference would be Marriot/ITC/Hyatt in Kolkata and, for PET school, Vedic Village. The fees for PET school would be Rs 7500 per participant. Dr Dey would be speaking to Novo for a written commitment for PET school.

7. Midterm meeting 2020: The current executive would be sending bids for Mid-term meeting of ISPAE 2020.

8. **Other business**

i) **ISPAE fellowship**: Dr Anurag Bajpai would be circulating letter inviting applications for ISPAE fellowship/observership and extend the last date by 1 month till 15th November 2018. Invitations for ISPAE observership 2019 would be sent by early next year in January.

ii) **ISPAE elections**: The GBM was informed that the process for election of next executive 2019-20 had been initiated. They were invited to stand for various posts. The new executive would send a letter at the beginning of their tenure to all GBM members informing them of various travel grants, charity activities etc.

iii) Dr Vijaylakshmi Bhatia advised that a memorandum of understanding be signed by future conference organizers and the ISPAE executive. It was decided that the executive would formulate guidelines for the same.

The meeting ended with a vote of thanks to the chair.

Summary of Recommendations from Endocrine Society Clinical Practice Guideline on Congenital Adrenal Hyperplasia Due to Steroid 21-Hydroxylase Deficiency

Speiser PW et al, J Clin Endocrinol Metab. 2018;103:4043-88.

Newborn screening Cost-effectiveness

1.1 We recommend that all newborn screening programs incorporate screening for congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21OHD).

1.2 We recommend that first-tier screens use 17-hydroxyprogesterone (17OHP) assays standardized to a common technology, with norms stratified by gestational age.
Technical remark: Clinicians should be aware that immunoassays are still in use and remain a source of false-positive results. Specificity may be improved with organic extraction to remove cross-reacting substances.

1.3 We recommend that screening laboratories employ a second-tier screen by liquid chromatography– tandem mass spectrometry (LC-TMS) in preference to all other methods (e.g. genotyping) to improve the positive predictive value of CAH screening.
Technical remark: Laboratories utilizing LC-TMS should participate in an appropriate quality assurance program. Additionally, clinicians should realize that immunoassays lead to more false-positive results. Thus, if laboratory resources do not include LC-TMS, a cosyntropin stimulation test (CST) should be performed to confirm diagnosis prior to the initiation of corticosteroid treatment.

Prenatal treatment of CAH

2.1 We advise that clinicians continue to regard prenatal therapy as experimental. Thus, we do not recommend specific treatment protocols.

2.2 In pregnant women who are at risk for carrying a fetus affected with CAH and are considering prenatal treatment, we recommend obtaining prenatal therapy only through protocols approved by Institutional Review Boards at centers capable of collecting outcomes from a sufficiently large number of patients, so that risks and benefits can be defined more precisely.

2.3 We advise that research protocols for prenatal therapy include genetic screening for Y-chromosomal DNA in maternal blood to exclude male fetuses from potential treatment groups.

Diagnosis of CAH

3.1 In infants with positive newborn screens for CAH, we recommend referral to pediatric endocrinologists (if regionally available) and evaluation by CST as needed.

3.2 In symptomatic individuals past infancy, we recommend screening with an early-morning (before 8 AM) baseline serum 17OHP measurement by LC-TMS.
3.3 In individuals with borderline 17OHP levels, we recommend obtaining a complete adrenocortical profile after a CST, to differentiate 21OHD from other enzyme defects.

3.4 In individuals with CAH, we suggest genotyping only when results of the adrenocortical profile after a CST are equivocal, or CST cannot be accurately performed (i.e. patient receiving glucocorticoid), or for purposes of genetic counselling.
Technical remark: Genotyping at least one parent aids in the interpretation of genetic test results because of the complexity of the CYP21A2 locus.

Treatment of classic CAH

4.1 In growing individuals with classic CAH, we recommend maintenance therapy with hydrocortisone.

4.2 In growing individuals with CAH, we recommend against the use of oral hydrocortisone suspension and against the chronic use of long-acting potent glucocorticoids.

4.3 In the newborn and in early infancy, we recommend using fludrocortisone and sodium chloride supplements to the treatment regimen.

4.4 In adults with classic CAH, we recommend using daily hydrocortisone and/or long-acting glucocorticoids plus mineralocorticoids, as clinically indicated.

4.5 In all individuals with classic CAH, we recommend monitoring for signs of glucocorticoid excess, as well as for signs of inadequate androgen normalization, to optimize the adrenal steroid treatment profile.

4.6 In all individuals with classic CAH, we recommend monitoring for signs of mineralocorticoid deficiency or excess.

Stress dosing

4.7 In all patients with CAH who require glucocorticoid treatment, for situations such as febrile illness (>38.5°C), gastroenteritis with dehydration, major surgery accompanied by general anaesthesia, and major trauma, we recommend increasing the glucocorticoid dosage.

4.8 For every day mental and emotional stress, and minor illness, and/or before routine physical exercise, we recommend against the use of increased glucocorticoid doses.

4.9 In patients with CAH on treatment, we recommend always wearing or carrying medical identification indicating that they have adrenal insufficiency.

4.10 We recommend educating patients and their guardians and close contacts on adrenal crisis prevention and increasing the dose of glucocorticoid (but not mineralocorticoid) during intercurrent illness.

4.11 We recommend equipping every patient with a glucocorticoid injection kit for emergency use and providing education on parenteral self-administration (young adult and older) or lay administration (parent or guardian) of emergency glucocorticoids.

Monitoring therapy

4.12 In patients < 18 months with CAH, we recommend close monitoring in the first 3 months of life and every 3 months thereafter. After 18 months, we recommend evaluation every 4 months.

4.13 In pediatric patients with CAH, we recommend conducting regular assessments of growth velocity, weight, blood pressure, as well as physical examination, in addition to obtaining biochemical measurements to assess the adequacy of glucocorticoid and mineralocorticoid replacement.

4.14 In pediatric patients with CAH < 2 years, we advise annual bone age assessment until near-adult height is attained.

4.15 In adults with CAH, we recommend annual physical examination, including assessment of BP, BMI, and Cushingoid features, in addition to biochemical measurements to assess the adequacy of glucocorticoid and mineralocorticoid replacement.

4.16 In adults with CAH, we recommend monitoring treatment through consistently timed hormone measurements relative to medication schedule and time of day.

4.17 In adults with CAH, we recommend that clinicians do not completely suppress endogenous adrenal steroid secretion, to prevent adverse effects of over-treatment.

Treatment of non-classic CAH (NC CAH)

5.1 In children and adolescents with inappropriately early onset and rapid progression of pubarche or bone age, and in adolescent patients with overt virilization we suggest glucocorticoid treatment of NC CAH.
Technical remark: Risks and benefits of glucocorticoid therapy should be considered and discussed with the patient's family.

5.2 In asymptomatic non-pregnant individuals with NC CAH, we recommend against glucocorticoid treatment.

5.3 In previously treated patients with NC CAH, we suggest giving the option of discontinuing therapy when adult height is attained, or other symptoms resolve.

5.4 In adult women with NC CAH, who also have patient-important hyperandrogenism or infertility, we suggest glucocorticoid treatment.

5.5 In most adult males with NC CAH, we suggest that clinicians generally not prescribe daily glucocorticoid therapy.
Technical remark: Exceptions include infertility, testicular adrenal rest tumors or adrenal tumors, and phenotypes that are intermediate between classic and NC phenotypes.

5.6 In patients with NC CAH, we suggest hydrocortisone stress dosing for major surgery, trauma, or childbirth only if a patient has a suboptimal (>14 to 18 mg/dL) cortisol response to cosyntropin or iatrogenic adrenal suppression.
Technical remark: A range is given for cortisol cut points due to greater specificity of newer cortisol assays (see below).

Long-term management of patients with CAH

Transition to adult care

6.1 In adolescent patients with CAH, we suggest that the transition to adult care begins several years prior to dismissal from pediatric endocrinology.
Technical remark: We advise the use of joint clinics comprised of pediatric, reproductive, and adult endocrinologists and urologist during this transition.

6.2 In adolescent females with CAH, we suggest a gynecological history and examination to ensure functional female anatomy, without vaginal stenosis or abnormalities in menstruation.

Genetic counselling

6.3 In children with CAH, adolescents transitioning to adult care, adults with NC CAH upon diagnosis, and partners of patients with CAH planning a pregnancy, we recommend that medical professionals familiar with CAH provide genetic counselling.

Fertility counselling

6.4 In individuals with CAH and impaired fertility, we suggest referral to a reproductive endocrinologist and/or fertility specialist.

Management of CAH and NC CAH during pregnancy

6.5 In women with NC CAH who are infertile or have a history of prior miscarriage, we recommend treatment with a glucocorticoid that does not traverse the placenta.

6.6 In women with CAH who are pregnant, we advise management by an endocrinologist familiar with CAH.

6.7 In women with CAH who become pregnant we recommend continued pre-pregnancy doses of hydrocortisone/ prednisolone and fludrocortisone therapy, with dosage adjustments if symptoms and signs of glucocorticoid insufficiency occur.

Technical remark: Clinicians should evaluate the need for an increase in glucocorticoid dose during the second or third trimester and administer stress doses of glucocorticoids during labor and delivery.

6.8 In women with CAH who are pregnant or trying to become pregnant, we recommend against using glucocorticoids that traverse the placenta, such as dexamethasone.

6.9 In women with CAH who are pregnant, we advise that the birthing plan includes an obstetric specialist.

Surveillance for long-term complications of CAH and its treatment

6.10 For patients with CAH, we suggest introducing counselling regarding healthy lifestyle choices at an early age to maintain BMI within the normal range to avoid metabolic syndrome and related sequelae.

6.11 In adult patients with CAH, we suggest screening of bone mineral density in anyone subjected to a prolonged period of higher-than-average glucocorticoid dosing, or who has suffered a nontraumatic fracture.

6.12 In adults with classic CAH, we recommend against routine adrenal imaging.
Technical remark: Reserve adrenal imaging for individuals with classic CAH who have clinical evidence of an adrenal mass, poor disease control, lapse in treatment of several years, or lack of response to intensified therapy.

6.13 In males with classic CAH, we recommend periodic testicular ultrasound to assess for the development of testicular adrenal rest tumors.

6.14 In patients with CAH, we recommend against routine evaluation for cardiac and metabolic disease beyond that recommended for the general population.
Technical remark: Clinicians should use their own judgment for the above procedures.

Restoring functional anatomy by surgery in individuals with CAH

7.1 In all pediatric patients with CAH, particularly minimally virilized girls, we advise that parents be informed about surgical options, including delaying surgery and/or observation until the child is older.
Technical remark: Surgeries should be performed only in centers with experienced pediatric surgeons/ urologists, pediatric endocrinologists, pediatric anesthesiologists, behavioral/ mental health professionals, and social work services. Extensive discussions regarding risks and benefits, shared decision-making, review of potential complications, and fully informed consent need to occur prior to surgery. The option to forgo surgery should be considered.

7.2 In severely virilized females, we advise discussion about early surgery to repair the urogenital sinus.

7.3 In the treatment of minors with CAH, we advise that all surgical decisions remain the prerogative of families (i.e. parents and assent from older children) in joint decision-making with experienced surgical consultants.

7.4 In female patients with CAH for whom surgery is chosen, we suggest vaginoplasty using urogenital mobilization and, when chosen, neurovascular-sparing clitoroplasty for severe clitoromegaly.

Experimental therapies and future directions
General considerations and unmet clinical needs

8.1 In patients with CAH, we advise against using experimental treatment approaches outside of formally approved clinical trials. (Ungraded Good Practice Statement)

Adrenalectomy

8.2 In patients with CAH, we suggest that bilateral adrenalectomy not be performed.

Mental health

9.1 For individuals with CAH and their parents, we recommend behavioral/ mental health consultation and evaluation to address any concerns related to CAH.
Technical remark: Clinicians should be aware that individuals with CAH may be at risk for developing mental health problems and should have a low threshold for referral to psychological or psychiatric treatment.
Mental health practitioners should have specialized expertise in assessing and managing CAH-related psychosocial problems.

Genetics of 21-Hydroxylase deficiency (21-OHD)

Srinivasan Vedantham, Associate Director, MedGenome Labs Ltd., Bengaluru, India.

Introduction:

Congenital adrenal hyperplasia (CAH) results from a deficiency in one of the enzymes of cortisol biosynthesis. In almost 95% of cases, 21-hydroxylation is impaired in the adrenal cortex so that 17-hydroxyprogesterone (17-OHP) is not converted to 11-deoxycortisol. Defective cortisol synthesis leads to increase in ACTH levels, resulting in overproduction and accumulation of cortisol precursors, particularly 17-OHP. The elevated 17-OHP results in excessive production of androgens, causing virilization. There are three variants of 21-OHD of which two variants are classic forms, the salt-wasting (SW) and simple virilizing (SV). The third variant is called the non-classic (NC) variant. The SW variant is the most severe, and the NC variant is the least severe form (1). The *CYP21A2* gene codes for 21-OH, which is part of the cytochrome P450 family of enzymes. This brief report discusses the complexities in *CYP21A2* gene, various genetic changes identified in the gene, and technologies available to detect variations in the gene for diagnosis of CAH.

Prevalence and clinical presentation of 21-OHD

The prevalence of classic forms of 21-OHD is 1 in 15,000 newborns, and that of the NC form is estimated to be 1 in 1,000 individuals (2); however, it varies among different ethnic populations. Previous studies on the epidemiology of 21-OHD reported higher prevalence of the SV form of the disease than the SW form (3-6), but in the developed countries, the SW form is more prevalent (5,6). Clinical manifestations of CAH due to 21-OHD are summarised in table 1 (7,8).

Table 1: Summary of common clinical manifestations of 21OHD

<table>
<tr><td colspan="2">Classic CAH</td><td rowspan="2">NC CAH</td></tr>
<tr><td>Salt-wasting</td><td>Simple-virilising</td></tr>
<tr><td>Adrenal crises</td><td>Adrenal crises less common</td><td rowspan="3">No ambiguous genitalia at birth
Premature pubarche
Rarely, advanced bone age and rapid growth in late childhood
Hirsutism, PCOS, and rarely, mild virilisation in adolescents and adults</td></tr>
<tr><td colspan="2">Ambiguous genitalia at birth in females
Normal genitalia in males</td></tr>
<tr><td colspan="2">Pseudo-precocious puberty in children < 6y, with compromised final adult height</td></tr>
</table>

***CYP21A2* gene:**

The *CYP21A2* gene is located in chromosome 6 (6p21.33). The cDNA corresponding to 21-OH is 2 kb long and the encoded protein has 494 amino acids, with a molecular weight of 52kDa. The enzyme is 28% homologous to other cytochrome P450 enzymes that have been studied. The gene encoding 21-OH is 3.4 kb long, contains 10 exons, 9 introns and a 1488 bp open reading frame. There are two 21-OH located adjacent to complement component namely C4A and C4B in the so called 'RCCX complex' in the order of 5'-C4A-CYP21A1P-C4B-CYP21A2-3' (9, 10) (Figure 1). *CYP21A2* is functional whereas *CYP21A1P* is non-functional.

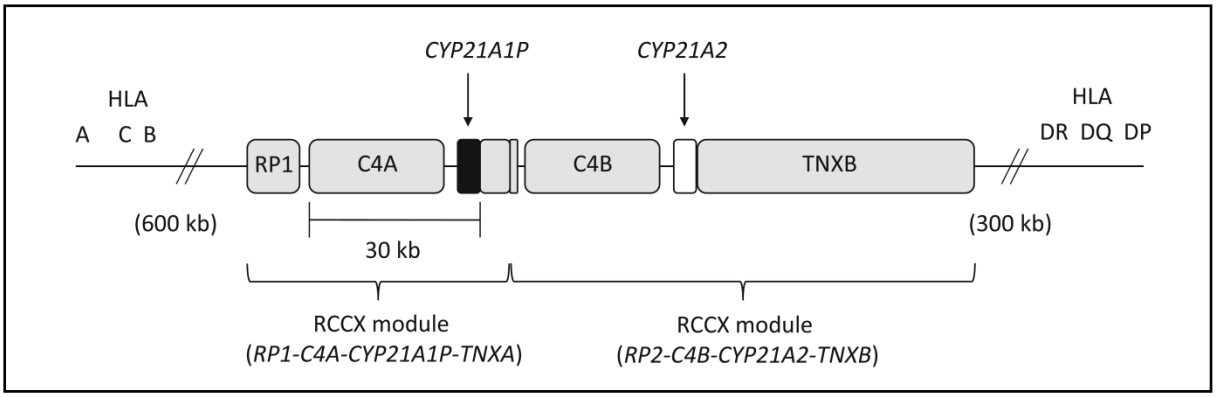


Figure 1: Location of *CYP21A1* on chromosome 6 (Source: ref 11)

Genetic variants in *CYP21A2*:

The active gene *CYP21A2* and its pseudogene *CYP21A1P* differ in approximately 65 nucleotides. There is 98% sequence identity between the two genes, and most of the disease-causing mutations are likely to be an event of gene conversion or non-homologous recombination (11,12). An increasing number of novel mutations have been identified in the disease-causing alleles. In addition, there are reports of compound heterozygotes carrying different mutations in each allele of the *CYP21A2* gene (13).

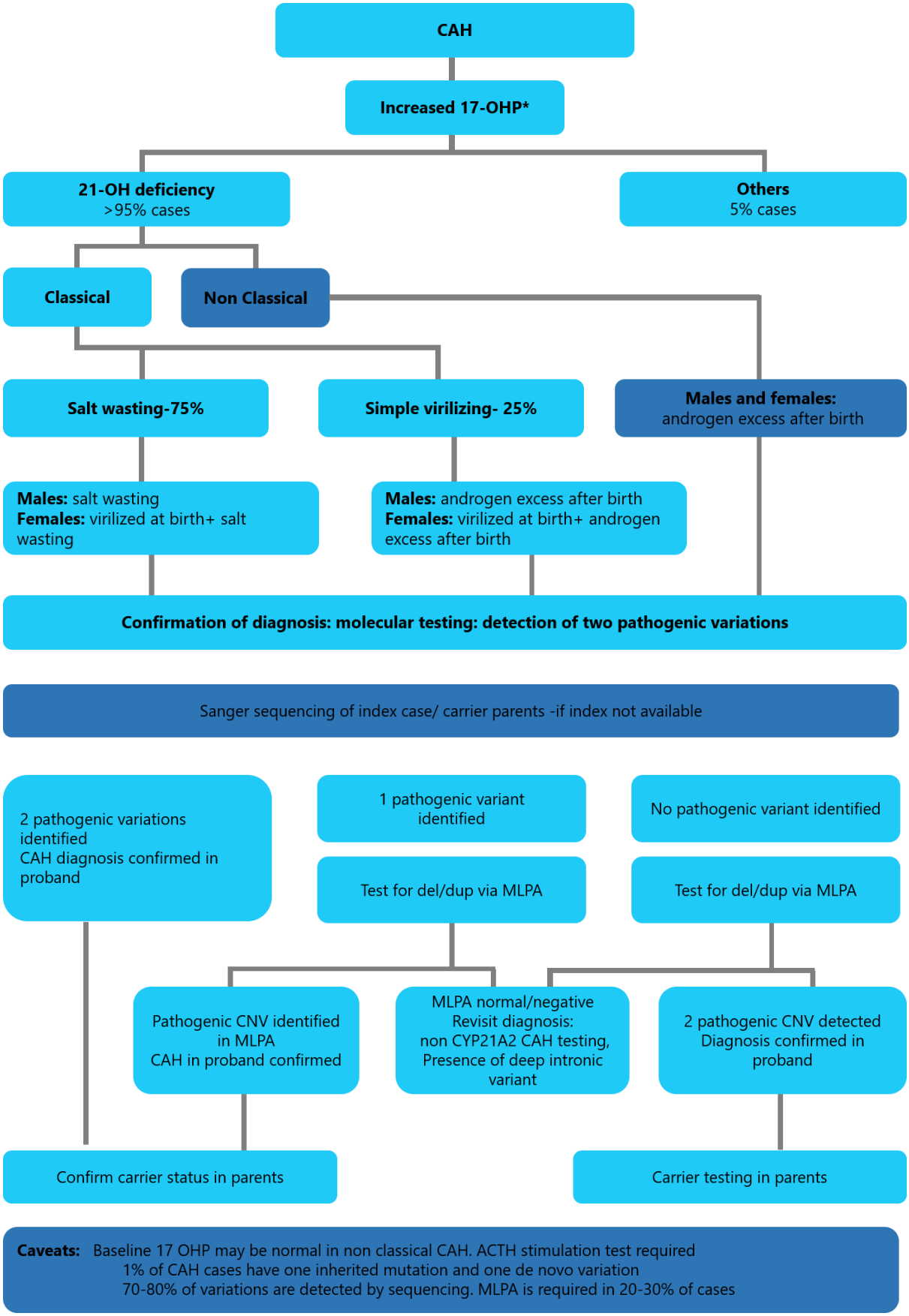
The most comprehensive database containing genetic variants in *CYP21A2* gene associated with phenotypic features is CYP Alleles (https://www.pharmvar.org/gene/CYP21A2).The database contains 169 genetic variants associated with 21-OHD. However, the database has not been updated since March 2011. A recent study compiled 1248 genetic variants comprising of 899 unique variants (14). These variants were compiled from publicly available databases and other publications related to 21-OHD. Among the 899 unique variants, 460 were found to in the translated region and 439 in the non-translated region. Single nucleotide substitutions (includes missense and non-sense variants) were observed in 401 of 460 variants in the translated region. The amino acid change and position determine the degree of disease severity (15). A total of 60 nonsense and frame-shift variations have been described, of which most lead to the classical form of the disease, mainly the SW form (14). Reported in-frame changes comprising the deletions, duplications and indels were found to be 12 in number. Out of the 439 variants in the non-translated region, 19 were reported to affect human health. 290 genetic variants in the intronic regions, 2 variants in the 5' and 3' UTR regions were found to be associated with disease (14). A variant in the promoter sequence (c.-126C>T) has been found to be associated with NC form (16).

Genetic testing algorithm:

An algorithm for genetic diagnosis of CAH due to 21-OHD is given in Figure 2. Genetic testing of variations in 21-OH involves inherited or de novo point mutation detection by Sanger sequencing or identification of larger copy number variation (CNV) like deletion or duplication by multiplex ligation dependent probe amplification (MLPA). Almost 70-80% of genetic variations can be detected by sequence analysis. 20-30% of patients may harbour deletion/duplication in *CYP21A2* that may be detected by MLPA. 1% of cases may report a de novo variation and an inherited variation. It is advisable to perform both the sequencing and MLPA methods simultaneously for detection of genetic variations or CNV (16). An Indian study done by Dubey et al effectively established the use of both MLPA and Sanger sequencing in 15 pregnant women at risk of having an affected offspring with CAH (17). Genetic testing must be followed with genetic counselling for all the affected cases, describing the reason, potential therapeutic options and future management of the disease. Pregnant women with history of earlier previous child diagnosed with 21-OHD require screening of the *CYP21A2* gene in the fetuses of subsequent pregnancies.

Concluding remarks: CAH due to 21-OHD is one of most common autosomal recessive disorders. The gene encoding 21-OH, *CYP21A2* has a functional gene and a non-functional pseudogene. Genetic conversions are reported in the *CYP21A2* gene. Several genetic

Figure 2: Algorithm for Genetic diagnosis for CAH due to 21-OHD



variations are observed in *CYP21A2* and are mostly single nucleotide substitutions. However, there are reports of deletions/ duplications in *CYP21A2*. Genetic testing of the index case for both Sanger sequencing of 21-OH and MLPA for deletion/ duplication is recommended. These tests may be used for screening genetic variations in fetuses of pregnant women with family history and/or earlier child affected with 21-OHD.

References:

1. Galal OM, Rudd, BT, Drayer NM**.** Evaluation of deficiency of 21-hydroxylation in patients with congenital adrenal hyperplasia**.** Arch Dis Child. 43: 410-414, 1968.
2. Pang SY, Wallace MA, Hofman L, et al, Worldwide experience in newborn screening for classical congenital adrenal hyperplasia due to 21-hydroxylase deficiency. Pediatrics. 1988;81:866–74.
3. Rama DAR, Naushad SM et al. Newborn screening in India. Indian J Pediatr. 2004;71:157–60.
4. Jeffcoate TN, Fliegner JR, Russell SH, et al. Diagnosis of the adrenogenital syndrome before birth. Lancet. 1965;2:553–5.
5. Pollack MS, Maurer D, Levine LS, et al. Prenatal diagnosis of congenital adrenal hyperplasia (21-hydroxylase deficiency) by HLA typing. Lancet. 1979;1:1107–8.
6. Kolahdouz M, Mohammadi Z, Kolahdouz P, et al. Pitfalls in molecular diagnosis of 21-hydroxylase deficiency in congenital adrenal hyperplasia. Adv Biomed Res. 2015;4:189.
7. Miller WL. Clinical review 54: Genetics, diagnosis, and management of 21-hydroxylase deficiency. J Clin Endocrinol Metab. 1994;78:241–6.
8. New MI, Abraham M, Gonzalez B, et al. Genotype-phenotype correlation in 1,507 families with congenital adrenal hyperplasia owing to 21-hydroxylase deficiency. Proc Natl Acad Sci USA 2013;110:2611–6.
9. Falhammar H, Wedell A, Nordenström A. Biochemical and genetic diagnosis of 21-hydroxylase deficiency. Endocrine. 2015 Nov;50(2):306-14.
10. White PC, Grossberger D, Onufer BJ et al. Two genes encoding steroid 21-hydroxylase are located near the genes encoding the fourth component of complement in man. Proc Nat Acad Sci. 1985;82:1089-1093.
11. Donohoue PA, Dop C van, McLean RH, et al. Gene conversion in salt-losing congenital adrenal hyperplasia with absent complement C4B protein. J Clin Endocrinol Metab 62:995–1002.
12. Higashi Y, Hiromasa T, Tanae A, et al. Effects of individual mutations in the P-450(C21) pseudogene on the P-450(C21) activity and their distribution in the patient genomes of congenital steroid 21-hydroxylase deficiency. J Biochem. 1991;109:638–44.
13. Speiser PW, New MI, White PC. Molecular genetic analysis of nonclassic steroid 21-hydroxylase deficiency associated with HLA-B14, DR1. N Engl J Med. 1998;319:19–23.
14. Simonetti L, Bruque CD, Fernández CS, et al. CYP21A2 mutation update: Comprehensive analysis of databases and published genetic variants, Hum Mutat. 2018;39(1):5-22.
15. White PC, Speiser PW. Congenital Adrenal Hyperplasia due to 21-Hydroxylase Deficiency. Endocr Rev. 2000;21:245–291.
16. Araújo RS, Mendonca BB, Barbosa AS et al. Microconversion between CYP21A2 and CYP21A1P promoter regions causes the nonclassical form of 21-hydroxylase deficiency. J Clin Endocrinol Metab. 2007;92:4028–34.
17. Dubey S, Tardy V, Chowdhury MR et al. Prenatal diagnosis of steroid 21-hydroxylase-deficient congenital adrenal hyperplasia: Experience from a tertiary care centre in India. Indian J Med Res. 2017;145(2):194-202.

Obesity Prevention Strategies in the Developing World with Dual Burden of Malnutrition

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The Indian population is witnessing an epidemiological and nutritional transition; therefore the problem of malnutrition is of serious concern. Malnutrition refers to deficiencies, excesses or imbalances in a person's intake of energy and/or nutrients. Malnutrition is a spectrum in itself, covering 2 broad groups: undernutrition and overnutrition.

Historically undernutrition has been associated with a higher prevalence of deficiencies of both macronutrients and micronutrients, along with higher prevalence of communicable diseases, whereas overnutrition has been associated with a higher prevalence of noncommunicable diseases (NCDs) such as coronary artery disease, stroke, diabetes and cancer.

After the Second World War, there was scarcity of food in major parts of the world, resulting in malnutrition. After 1980, with the start of automation and computerization, accessibility and availability of food became common in most of the world, with humans retaining the excess energy and thereby increasing in size. With migration from nutritional insufficiency to excess, not only is the prevalence of metabolic disorders increasing, it is also occurring at an earlier age. Much of developing world, including India, is suffering from this nutritional transition. Across the globe, the prevalence of obesity and diabetes is higher in countries in nutritional transition (Africa and Asia) than in the developed world (America and Europe).

In addition to diet and lifestyle, early undernutrition is also linked with overweight in adulthood. This hypothesis, called the "fetal origins of adult disease", which is supported by a number of observational epidemiologic studies, postulates that early (intrauterine or early postnatal) undernutrition causes an irreversible differentiation of metabolic systems. This may, in turn, increase the risks of certain chronic diseases in adulthood. For example, a fetus of an undernourished mother will respond to a reduced energy supply by switching on genes that optimize energy conservation. This survival strategy causes a permanent differentiation of regulatory systems that result in an excess accumulation of energy (and consequently of body fat) when the adult is exposed to an unrestricted dietary energy supply. Because intrauterine growth retardation and low birth weight (LBW) are common in developing countries, they are increasingly facing additional challenges related to rising prevalence of obesity and NCDs like diabetes and hypertension, especially in urban areas.

- India has the second highest number of obese children in the world after China.
- At the same time, India has the highest number of moderately and severely underweight children and adolescents in the world.
- The twin problem of high malnutrition and growing obesity may have a common cause: a high proportion of LBW babies in India.
- In India deaths due to NCDs are rising alarmingly.

Children also suffer from type 2 diabetes mellitus (DM) and hypertension. Our own institution's data reported a high prevalence of prehypertension (33.9%), hypertension (23%), prediabetes (64.3%) and DM (3.8%) and in overweight and obese children (1).

Can we reduce the burden of NCDs of our country? Yes: by diagnosing and managing overweight and obese children and adolescents as well as by screening and tracking the growth of high-risk infants and children.

Screening of high-risk infants and children for development of overweight and obesity

(a) Offspring of mothers with pre-gestational or gestational DM

(b) Infants with birth weight ≤2.5 kg or ≥3.5 kg

(c) Infants who are formula or top fed

(d) Children with a strong family history of DM

(e) Picking up the thin line between catch up growth and accelerated weight gain

(f) Children receiving medications such as long-term glucocorticoids, anticonvulsants and antidepressant drugs, are handicapped, or have other reasons to get obese.

In addition, prevention and early detection of comorbidities by screening for prehypertension, hypertension, prediabetes and diabetes in overweight and obese children and adolescents is also useful to reverse or appropriately manage them to prevent the negative consequences.

Preventive Strategies

The following preventive strategies will help to tackle this nutrition paradox:

- Public health programs to identify and consider the magnitude and demographic composition of dual-burden households at the local and regional levels, and then develop more targeted interventions
- Educate health care workers about the underweight-overweight phenomenon
- Promotion of breast-feeding
- Improving the nutritional status of women of reproductive age
- Reducing the rates of fetal growth retardation and LBW.

Implementation of these preventive strategies will surely control the rising trends of overweight, obesity and associated NCDs.

Reference

Phatale P, Phatale H. Prevalence of pre-diabetes, diabetes, pre-hypertension, and hypertension in children weighing more than normal. Indian J Endocrinol Metab. 2012;16(Suppl 2):S483-5.

A case of Neonatal Severe Hyperparathyroidism

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Introduction:

The level of extracellular ionized calcium is tightly regulated, principally through the action of parathyroid hormone (PTH), which is secreted in response to signals from membrane bound calcium sensing receptor (CaSR). Heterozygous mutations that impair calcium sensing result in mild to moderate increase in PTH, hypercalcemia and hypocalciuria, a condition termed familial benign hypocalciuric hypercalcemia (FHH). FHH is an autosomal dominant condition due to heterozygous loss of function mutations in the CaSR gene, but autosomal recessive inheritance may also occur. In contrast to FHH, biallelic inactivating CaSR mutations are associated with life-threatening neonatal severe hyperparathyroidism (NSHPT), which results in generalized skeletal demineralization, neurological disabilities, constipation, failure to thrive, respiratory distress and irritability (1). NSHPT can be fatal if not recognised in time, and interventions done. We report a case of a newborn diagnosed with NSHPT, and the challenges faced during diagnosis and treatment.

Case report:

A 19 day old male infant, born at term by caesarean section to consanguineous parents, was hospitalized in the NICU of another hospital, with complaints of lethargy and inability to feed for 2 days. He weighed 2.7 kg at birth, and had no neonatal events. He had been admitted at 7 days of life for fever, but no hospital records were available. On day 25 of life, the baby was referred to our center. At admission, he was ill, dehydrated, weighed 2.23 kg, had bradycardia (98/min), tachypnea (66/min), hypotonia, with no organomegaly or dysmorphic features. There was no history of prenatal drug administration. Laboratory investigations revealed severe hypercalcemia (total calcium 29 mg/dl, ionized calcium 15 mg/dl), hypophosphatemia (1.4 mg/dl), mildly elevated alkaline phosphatase (541.9 U/L), very low Vitamin D (8.6 ng/ml), markedly elevated plasma PTH (1145 pg/ml), with normal blood gas analysis, serum electrolytes, serum magnesium (1.74 mg/dl), blood counts, renal and liver function tests. Spot urine calcium to creatinine ratio was 9.77 (high) (Note: urine sample was inadvertently collected after a dose of furosemide injection). There was no radiological evidence of osteopenia or fractures (figure 1A). ECG was suggestive of sinus bradycardia; parathyroid scintigraphy using Ga-68 DOTANOC (figure 1B) and ^{99m}Tc-sistamibi (figure 1C) and did not reveal any eutopic parathyroid supernumerary or ectopic parathyroid tissue. Both parents had mild hypercalcemia (father's and mother's serum calcium levels were 11.3 mg/dl and 11 mg/dl respectively). The possibility of NSHPT was considered.

He was given normal saline bolus, and 1.5 times maintenance fluid along with IV furosemide @ 1 mg/kg/day. Injection pamidronate was given @ 1 mg/kg/day for 3 days. After the 3rd dose of pamidronate, as the serum calcium was still high, oral cinacalcet (calcimimetic) was started @ 0.6 mg/kg/day in two divided doses. Oral vitamin D drops (400 U/ day) were also

added. After this, the infant started showing improvement, and serum calcium gradually normalised.

Table 1: Showing calcium profile during hospitalization

Date	Treatment given	S. Calcium (mg/dl)	Ionized Ca (mg/dl)	S. Phosphorus (mg/dl)
28-8-18	IV fluids + furosemide	29	15	1.4
29-8-18	Pamidronate (1mg/kg)	25	14.9	1.3
29-8-18		20.7		1.63
30-8-18	Pamidronate (1 mg/kg)	19.4	10.4	1.7
30-8-18		16.4	8.6	1.36
31-8-18	Pamidronate (1 mg/kg)	13.4	7.1	2.59
1-9-18	Cinacalcet	10.7	5.9	2.1
2-9-18		9.7	5.1	1.93
3-9-18		7.2	3.1	2.13

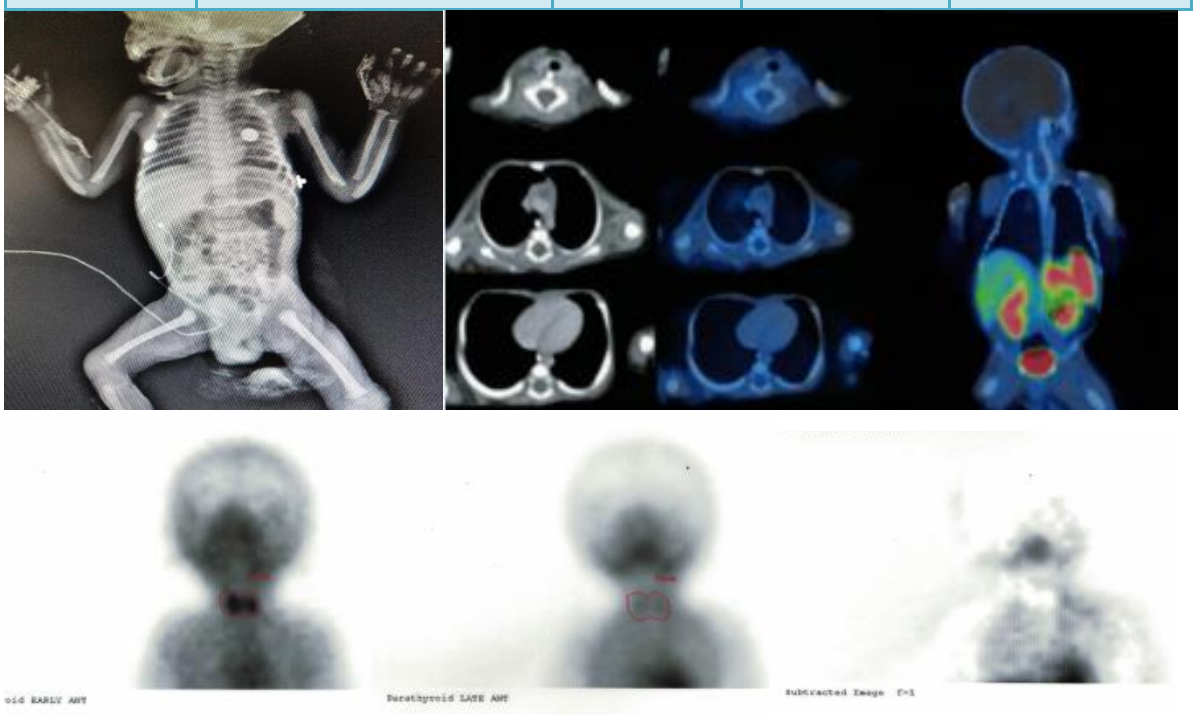

FIGURE 1: Infantogram (1A), Ga-68 DOTANOC PET CT scan – no evidence of abnormal somatostatin receptor expressing lesion anywhere in the body, no evidence of parathyroid adenoma on this study (1B) and ^{99m}Tc MIBI parathyroid scan–normal study, no evidence of parathyroid adenoma (1C).

Parathyroidectomy was planned as the definitive therapy, and the parents counselled in detail regarding this. Genetic evaluation was also planned. Unfortunately, parents deferred further treatment and got the baby discharged against medical advice.

Discussion:

NSHPT is an uncommon, life-threatening disorder that usually results from biallelic loss-of-function mutations in the CaSR gene, although heterozygous dominant negative mutations have also been rarely reported (2). Loss of calcium sensing will lead to parathyroid hyperplasia and increased PTH secretion, leading to decreased renal excretion of calcium. The babies present with failure to thrive, hypotonia, respiratory distress, constipation and bone abnormalities such as demineralisation, rib cage deformity, subperiosteal erosions and metaphyseal widening of long bones (3).

In the case reported here, the baby had failure to thrive, lethargy, poor feeding, hypotonia and respiratory distress, with the highly elevated serum calcium and PTH levels at this age strongly favoring NSHPT.

In NSHPT, medical management is often inadequate, laborious and impractical. Hence total parathyroidectomy is the treatment of choice and is effective in most cases (4). Intravenous bisphosphonates such as pamidronate have often been used in neonates to reduce severe hypercalcemia until surgery is performed. Bisphosphonates are effective in reducing hypercalcemia but have variable duration of effect, lasting from a week to 3-4 weeks in an individual, and may cause side effects during administration (fever, myalgia). The calcimimetic – cinacalcet – has also been used successfully in several cases of NSHPT, wherein a CaSR with loss-of-function mutation or abnormal CaSRs were able to respond. Cinacalcet binds to and activates the membrane CaSR on the parathyroid chief cells, and depresses secretion of PTH (not FDA approved - pending further evaluation of its safety). The drug can be started at a dose of 0.4 mg/kg/day (6 mg/m2/day) in two divided doses (available as 30 mg tablets) and can be increased up to 9.6 mg/kg/day (202 mg/m2/day) in three divided doses (5). In the rare case of absence of any CaSRs on the cell surface, one would not expect any response from calcimimetic therapy (1).

In this case, the improvement in hypercalcemia is largely attributable to the effect of pamidronate; the hypocalcemic effect of cinacalcet is uncertain since it might have been confounded by the continued effect of pamidronate. Most often, a single dose of pamidronate is enough to achieve normal or near-normal calcium levels, but patients with very severe hypercalcemia (serum calcium > 20 mg/dl) may take 3-10 days to reach normocalcemia. Hence, if the fall in serum calcium is adequate (> 10-20% fall per 24h), the next dose of pamidronate can be deferred. However, a few patients may require multiple doses, which should be given cautiously since overzealous treatment may lead to hypocalcemia, as seen in this case.

Total parathyroidectomy is the treatment of choice. 7% of the normal population has supernumerary glands that can be found along the mediastinum, thyroid or thymus, requiring thymectomy or hemithyroidectomy. Preoperative localization tests, including scintigraphy, ultrasonography, and magnetic resonance imaging, are often unrewarding, so the parathyroid tissue must be identified during the surgery (6). Intraoperative methylene blue infusion can be used to identify parathyroid glands during neck exploration (7).

Intraoperative PTH monitoring, with a relative drop in PTH level into the normal range, is suggestive of adequate removal of hyperfunctioning parathyroid tissue (6).

In conclusion, although NSHPT is a rare disorder, it should be considered in the differential diagnosis of neonatal hypercalcemia, as prompt diagnosis and timely intervention will be life-saving.

References:

1. Abeynayake G, EreshaJ, et al. Neonatal severe Hyperparathyroidism: A fatal case. J Endocrinol Diab. 2018;5(1): 1-4.
2. Egbuna OI, brown EM. Hypercalcaemic and hypocalcaemic conditions due to calcium-sensing receptor mutations. Best practice and research Clinical rheumatology. 2008;22(1):129-148.
3. Rodd C, Goodyer P. Hypercalcemia of the newborn: etiology, evaluation, and management. Pediatric nephrology (Berlin, Germany). 1999;13(6):542-547
4. Wilhelm-Bals, Parvex P, MagdelaineC, et al. Successful use of bisphosphonates and calcimimetic in neonatal severe primary hyperparathyroidism. Pediatrics. 2012;129(3):e812-e816.
5. Gannon AW, Monk HM, Levine MA. Cinacalcet monotherapy in neonatal severe hyperparathyroidism: a case study and review. J Clin Endocrinol Metab. 2014;99(1):7-11.
6. Emilio G et al. Intraoperative parathyroid hormone monitoring in Neonatal severe primary hyperparathyroidism. Pediatrics 2014; 134:e1-e3.
7. Kuriloff DB, Sanborn KV. Rapid intraoperative localization of parathyroid glands utilising methylene blue infusion. Otolarygol Head Neck Surg. 2004 Nov; 131(5):616-22

A unique nonendocrine cause of short stature mimicking two endocrine conditions

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Introduction

Short stature is a common abnormality encountered during pediatric or pediatric endocrine practice. However, many nonendocrine disorders lead to short stature whereas few of these may also mimic endocrine conditions. We report a rare nonendocrine condition which mimics two different endocrine conditions.

Case report

An eight yo boy was referred by a pediatric surgeon for evaluation of short stature. He had presented during the neonatal period to a pediatric surgeon with abdominal distension and constipation. He was diagnosed to have Hirschprung's disease on rectal biopsy. He underwent multiple surgeries including two colostomies, but the results were suboptimal.

On examination, the child had severe short stature (height = 87 cm; height age = 2y). He was much fairer than his parents and siblings. He had fine, hypopigmented, sparse eyebrow hair and scalp hair. His abdomen was distended with multiple scar marks (Fig 1A). Developmental examination revealed a mental age of 4 years. X-ray of left hand revealed a bone age of 1y (Fig 1B). Primary hypothyroidism was suspected, but thyroid function tests were normal (T3 124 ng/ml, T4 10 µg/dl, TSH 3.2 mIU/L). The child was then referred to a pediatric endocrinologist for further evaluation.

A complete anthropometric evaluation revealed an upper segment to lower segment ratio of 1.3, suggestive of short legs; he also had mild widening of the wrists and ankles. X-ray of the long bones revealed mild metaphyseal widening at all long bones, with minimal cupping and fraying (Fig 2). Biochemical evaluation keeping rickets in mind was normal: serum calcium 9.2 mg/dl, phosphorous 4.2 mg/dl and alkaline phosphatase 234 IU/L. He was also evaluated for IGF-1 deficiency syndromes since he had severe bone age delay - serum IGF-1 was 160 ng/ml, and basal growth hormone (GH) 0.8 ng/ml.

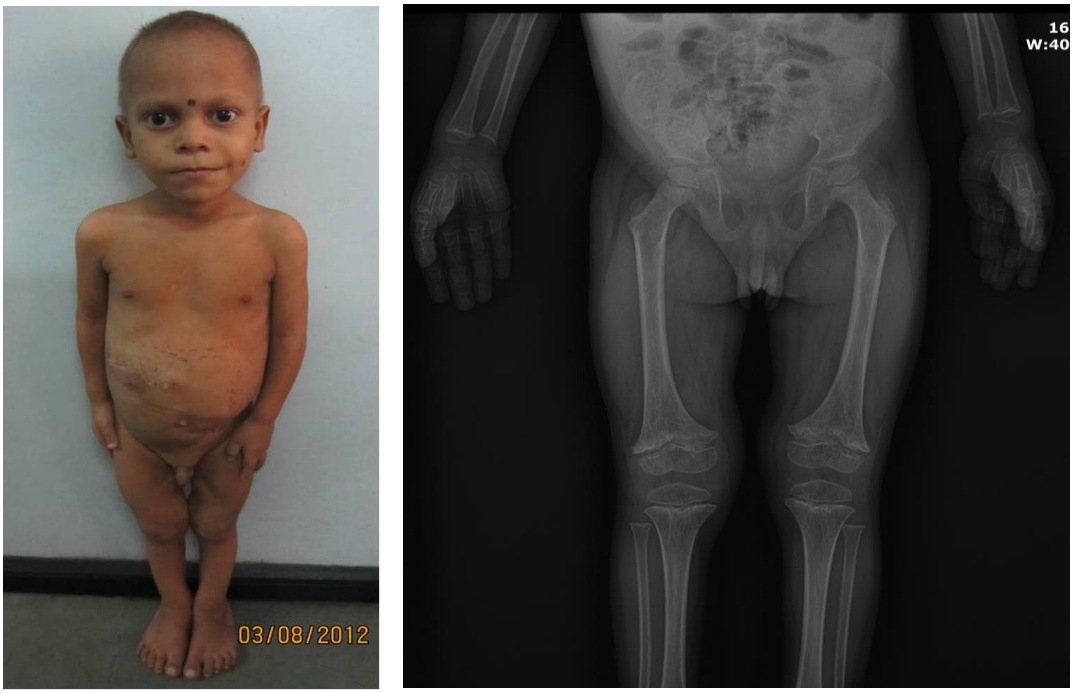


Figure 1: Clinical photograph showing severe short stature with widening of wrists and ankles, fine, hypopigmented, sparse scalp and eyebrow hair, hypopigmented skin, abdominal distension with multiple scar marks on the abdomen (1A) and X-ray showing widening of metaphyses with minimal fraying and cupping of all visualized long bones. The figure also shows bone age of one year and multiple air fluid levels in the abdomen (1B).

In the absence of biochemical abnormalities, radiological findings were suggestive of metaphyseal dysplasia. Combining the key clinical (sparse hypopigmented hair, fair skin), laboratory (normal thyroid function and calcium chemistry), and radiological findings (suggestive of metaphyseal dysplasia), the diagnosis of cartilage hair hypoplasia (CHH) was made, further strengthened by histopathology of the hair, which revealed absent central core. On evaluation for hematological abnormalities, he did not have any evidence of anemia or immunodeficiency (nor was there any history suggestive of recurrent infections in the past).

Discussion

We report an interesting nonendocrine disorder which mimicked two endocrine conditions. At initial presentation to us, the clinical features including severe short stature with sparse scalp and eyebrow hair, abdominal distension, mental retardation and severe bone age delay suggested a diagnosis of congenital hypothyroidism. However, to our surprise the thyroid function was normal. On retrospective review, we realized that the sparse hair was

generalized, unlike hypothyroidism where it is usually restricted to the lateral one third of eyebrows; moreover, the hair was fine, unlike hypothyroidism where it is usually coarse and dry. We then suspected rickets, and based on clinical and radiology findings and normal biochemistry, finally made a diagnosis of metaphyseal dysplasia, as part of CHH. The marked bone age delay, usually indicative of underlying chronic illnesses or hormonal disorders, made the diagnosis of skeletal dysplasia less likely.

CHH, also called as McKusick type of chondrodysplasia, is an autosomal recessive metaphyseal chondrodysplasia. The most important reason not to miss the diagnosis of CHH is to identify the other grave problems associated with the disease. They include defective immunity leading to recurrent infections, abnormal erythrogenesis sometimes requiring blood transfusion, and increased risk of malignancy (non-Hodgkin's lymphoma and basal cell carcinoma) (1-3).

Although CHH is a nonendocrine condition, there are few endocrine aspects of the disease. A single case report found CHH associated with autoimmune hypoparathyoidism. Although no specific association could be put forward between these two conditions, underlying immune dysregulation of CHH may be responsible for this autoimmune process (4).

Marked bone age delay (< -2 SD) has been reported in 14% of children with CHH (5). The reason for this is poorly understood; however, since dysplastic epiphyses are found in 23% of CHH children, primary epiphyseal abnormality seems to be the most probable reason. In our child, since IGF-1 was + 1SD, GH deficiency or insensitivity and even chronic illnesses were unlikely. GH therapy has been tried for management of the short stature, but the studies are limited. In a small study of 4 children with CHH, the benefits of GH were short lasting, somewhat more in those with mild growth failure (6), while in another case report a child with CHH responded well to GH (7).

Hirschprung's disease is seen in 9% of patients with CH (8). Its presence usually indicates a severe form of the disease (9). Children with CHH have poor prognosis for Hirschprung's disease compared to those with non-syndromic Hirschprung's disease (8). The suboptimal response to multiple surgeries may be due to high prevalence of total colonic aganglionosis in CHH subjects.

To conclude, nonendocrine causes of short stature may rarely mimic endocrine disorders. This case report also highlights the need for pediatric endocrinologists to not only rule out endocrine causes of short stature but also to reach the full diagnosis of nonendocrine causes of short stature.

References:

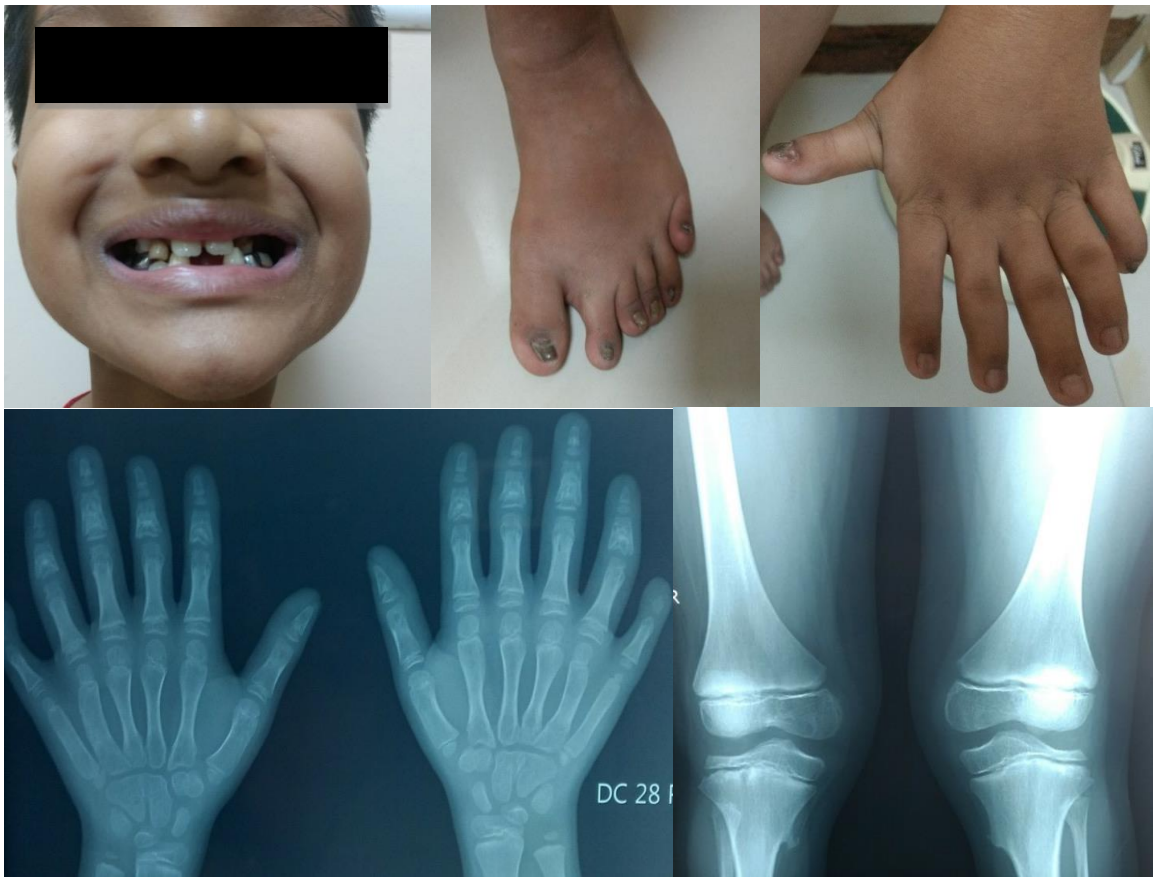
1. Williams MS, Ettinger RS, Hermanns P, Lee B, Carlsson G, Taskinen M, et al. The natural history of severe anemia in cartilage-hair hypoplasia. Am J Med Genet 2005;138:35-40.
2. Taskinen M, Ranki A, Pukkala E, Jeskanen L, Kaitila I, Mäkitie O. Extended follow-up of the Finnish cartilage-hair hypoplasia cohort confirms high incidence of non-Hodgkin lymphoma and basal cell carcinoma. Am J Med Genet 2008;146:2370-5.
3. Mäkitie O, Kaitila I. Cartilage-hair hypoplasia--clinical manifestations in 108 Finnish patients. Eur J Pediatr 1993;152:211-7.

4. Bacchetta J, Ranchin B, Brunet AS, Bouvier R, Duquesne A, Edery P, Fabien N, Peretti N. Autoimmune hypoparathyroidism in a 12-year-old girl with McKusick cartilage hair hypoplasia. Pediatr Nephrol. 2009;24:2449-53.
5. Mäkitie O, Marttinen E, Kaitila I. Skeletal growth in cartilage-hair hypoplasia. A radiological study of 82 patients. Pediatr Radiol 1992;22:434-9.
6. Bocca G, Weemaes CM, van der Burgt I, Otten BJ. Growth hormone treatment in cartilage-hair hypoplasia: effects on growth and the immune system. J Pediatr Endocrinol Metab 2004;17:47-54.
7. Harada D, Yamanaka Y, Ueda K, Shimizu J, Inoue M, Seino Y, et al. An effective case of growth hormone treatment on cartilage-hair hypoplasia. Bone. 2005 Feb;36(2):317-22.
8. Mäkitie O, Heikkinen M, Kaitila I, Rintala R. Hirschsprung's disease in cartilage-hair hypoplasia has poor prognosis. J Pediatr Surg 2002;37:1585-8.
9. Mäkitie O, Kaitila I, Rintala R. Hirschsprung disease associated with severe cartilage-hair hypoplasia. J Pediatr 2001;138:929-31.

Photo Quiz

Kannan S[1], Patil SJ[2], Khadilkar K[1], [1]Department of Endocrinology, Diabetes & Metabolism, [2]Department of Medical Genetics, Narayana Health City, Bangalore, India

An 11 yo boy born to a second-degree consanguineous couple was referred to our Endocrinology OPD with short stature (<3rd centile) and an abnormal Growth Hormone (GH) stimulation test. Clinical exam revealed disproportionate short limbs with genu valgus deformity at the knee, abnormal teeth and hypoplastic nails. He was also noted to have polydactyly in both hands and feet. There was no evidence of mental subnormality. Cardiac examination was normal. What is the diagnosis?



Pearls from ISPAD 2018

Ganesh Jevalikar, Medanta Medicity Hospital, Gurugram, Haryana

Newer insulins, glucagon

- Faster acting aspart (FiAsp) is non-inferior to aspart; ultra-rapid lispro being studied.
- Afreeza (inhaled insulin) is likely to be available by next year in India. It has quicker onset and higher peak than SC lispro. Disadvantages include higher and relatively fixed dosing. Efficacy is affected in case of lung parenchymal disease.
- Intradermal lispro injected with a very small steel needle has faster action than SC route
- U300 glargine is non-inferior to degludec.
- Nasal glucagon has similar profile compared to IM glucagon.

Type 2 diabetes in children

- Beta cell depletion and reduction of insulin secretion is faster in children with T2DM compared to adults, leading to higher rates of therapy failure.
- Metformin is the most important drug in T2DM treatment and nearly 50-60% children respond, however additional therapy may be needed if HbA1c is not controlled with metformin.
- Rising HbA1c indicates the need for escalating therapy, regardless of its absolute value.
- Therapy considerations include metformin alone if HbA1c < 6.5%; metformin + additional OAD if between 6.5-7%; metformin, OAD + additional OAD/injectable GLP1 if between 7-9%; insulin is needed if HbA1c> 9%.
- No single test is superior for diagnosis of prediabetes. Tests like fasting glucose, post meal glucose and HbA1c may pick up different types of dysglycemia.

Bariatric surgery in adolescents

- Diet and lifestyle modification alone often fail to control obesity.
- It is important to address obesity before significant complications set in.
- Sleeve gastrectomy is emerging as the surgery of choice for obesity. It is relatively easier to perform and has less complications.
- The extent of weight loss after any bariatric surgery procedures follow a normal distribution.
- Cosmetic problems post-surgery due to excess redundant skin need to be addressed adequately and need to be covered by insurance agencies.
- Obese children have multiple co-morbidities that need to be addressed, including diabetes, fatty liver, dyslipidemia, sleep abnormalities and psychiatric abnormalities.

Diabetic ketoacidosis

- Irrespective of the protocol used, frequent and adequate monitoring is very important.
- Both SC and IM rapid acting insulin injected every 2h have been used in DKA treatment (especially mild), and are associated with lower hospitalization cost, most likely because of fewer days of ICU admission for IV insulin infusion.
- SC and IM insulin is associated with initial rise followed by decline of ketones; the time taken for resolution may be slightly longer.
- Absorption of SC insulin may be erratic if the peripheral circulation is poor.

- A recent randomized control trial published in NEJM showed that the neurological outcomes were not different, irrespective of type and rate of fluid administration. However, since the patients included in this trial were mostly mild or moderate DKA, conclusions can't be generalized.
- In case of DKA due to pump failure, serum ketones rise faster than the blood glucose.
- Impaired mental state during DKA predicts lower IQ 6 months later.

Fat and proteins in diet

- Fats and proteins have additive impact after 90 minutes.
- High protein reduces hypos better than high fat, with a dose-response trend per gram of protein.
- 30 grams of protein with a meal needs additional insulin.
- Dose response to fat occurs 5 hr later; 20 gm of fat needs additional insulin.
- 60/40 dual wave bolus is needed for high fat and high protein diet, and should be administered over 2-3 hr.
- Add 20-60% of the ICR.
- With MDI, be more conservative than with pumps.

Hemchand Prasad, Mehta Children's Hospital, Chennai

IAP Chennai city Branch and the Department of Pediatrics, Mehta Hospital, Chennai - have developed a mobile app for the management of pediatric DKA.

This is a free mobile application for non-Apple devices and can be downloaded freely from Google Play Store. The link for download is as follows: http://play.google.com/store/apps/details?id=com.hopebusinesssolutions.pediatricdka

Kuppermann N et al. Clinical trial of fluid infusion rates for pediatric diabetic keto-acidosis. N Engl J Med. 2018 Jun 14;378(24):2275-2287.

To find the effect of intravenous fluids (IVF) on brain injuries in children with diabetic ketoacidosis (DKA), a 13-center RCT examined the effect of the rate of administration and the sodium chloride content of IVF on neurologic outcomes. Children were randomly assigned to one of 4 treatment groups in a 2-by-2 factorial design (0.9% or 0.45% sodium chloride content, and rapid or slow rate of administration). A total of 1389 episodes of DKA were reported in 1255 children. The Glasgow Coma Scale (GCS) score declined to less than 14 in 48 episodes (3.5%), and clinically apparent brain injury occurred in 12 episodes (0.9%); these parameters were not significantly different among the treatment groups. Memory and IQ scores obtained after the children's recovery from DKA also did not differ significantly among the groups. Serious adverse events other than altered mental status were rare and occurred with similar frequency in all treatment groups. The study concluded that neither the rate of administration nor the sodium chloride content of IVF significantly influenced neurologic outcomes in children with DKA.

Carpenter TO et al. Burosumab therapy in children with X-linked hypophosphatemia. N Engl J Med. 2018;378(21):1987-1998.

To investigate burosumab, a monoclonal antibody that targets FGF-23, in patients with X-linked hypophosphatemia, an open-label, phase 2 trial, randomly assigned 52 children with the disease, in a 1:1 ratio, to receive subcutaneous burosumab either every 2 weeks or every 4 weeks. The burosumab dose was adjusted to achieve a serum phosphorus level at the low end of the normal range. The mean Thacher rickets severity total score decreased significantly at week 6 in both dose groups (P<0.001) and persisted at week 64. The mean serum phosphorus level increased after the first dose in both groups, and more than half the patients in both groups had levels within the normal range by week 6. Renal tubular phosphate reabsorption increased from baseline in both groups. Across both groups, the mean serum alkaline phosphatase level decreased from baseline to week 64. The mean standing-height z score increased in both groups, with greater improvement seen at all time points with the every-2-week dosing than with the every-4-week dosing. Physical ability improved, and pain decreased. Nearly all the adverse events were mild or moderate in severity.

Sharma R et al. Long-acting intramuscular ACTH stimulation test for the diagnosis of secondary adrenal insufficiency in children. J Pediatr Endocrinol Metab 2018 Dec 7. doi: 10.1515/jpem-2018-0330

Short Synacthen test (SST) is the most recommended test for the diagnosis of patients with adrenal insufficiency (AI). However, injection Synacthen is not easily available in some countries, and endocrinologists often use Acton-Prolongatum (intramuscular [IM] long-acting adrenocorticotropic hormone [ACTH]) in place of Synacthen. There are no studies validating the use of IM-ACTH in children with suspected AI. Hence, to evaluate the diagnostic value of the IM-ACTH test against the ITT for the diagnosis of secondary AI (SAI) in 48 (36 boys/12 girls, age range: 5-14y) children with suspected growth hormone deficiency were evaluated using both the ITT and the IM-ACTH test. 28 patients had a normal cortisol response (≥18 µg/dL) in the ITT and 20 had low values. In patients with a normal cortisol response on the ITT, the peak value obtained after the IM-ACTH test was higher than that on the ITT (28.7±8.8 vs. 23.8±4.54 µg/dL, p=0.0012). Compared to the ITT, the sensitivity and specificity of the IM-ACTH test for the diagnosis of SAI at cortisol cut-offs <18 µg/dL and <22 µg/dL were 57.1% and 92.8%, and 100% and 73.5%, respectively. The study concluded that peak cortisol value <18 µg/dL on the IM-ACTH test is highly suggestive of SAI, whereas a value >22 µg/dL rules out SAI.

Huffnagel IC et al. The natural history of adrenal insufficiency in X-linked adrenoleukodystrophy: an international collaboration. J Clin Endocrinol Metab 2019;104:118-126.

Primary adrenal insufficiency (AI) is an important clinical manifestation of X-linked adrenoleukodystrophy (ALD). To delineate the natural history of AI in male patients with ALD, a retrospective review of medical records of male patients with ALD followed at two inter-national tertiary referral Centers of Expertise for ALD between 2002 and 2016 was conducted. Data on 159 male patients was available. Lifetime prevalence of AI in male patients with ALD was ~80%. Median time until AI was 14y (95% CI: 9.7-18.3 years). The cumulative proportion of patients who developed AI was age-dependent and highest in early childhood [0-10y: 46.8% (SEM 0.041%); 11-40y, 28.6% (SEM, 0.037%); >40y, 5.6% (SEM, 0.038%)]. No association between clinical manifestations and plasma ratios was detected. The authors suggested a minimum of adrenal testing every 4-6 months for patients age ≤10y, annual testing for those aged 11-40y, and solely on-demand testing for those aged >40y.

Child CJ et al. Safety outcomes during pediatric GH therapy: final results from the prospective GeNeSIS observational program. J Clin Endocrinol Metab 2019 Feb 1;104(2): 379-389.

To assess the association of GH therapy with premature mortality, diabetes and neoplasia, a prospective, multinational, observational study (1999 - 2015) including a total of 22,311 GH-treated children from 827 investigative sites in 30 countries was conducted. The predominant short stature diagnoses were GH deficiency (63%), idiopathic short stature (13%), and Turner syndrome (8%), with follow-up of 4.2 ± 3.2y (∼92,000 person-years [PY]). 42 deaths occurred with a standardised mortality ratio (SMR) of 0.61 (95% CI: 0.44-0.82); the SMR [5.87 (3.21-9.85)] was elevated for patients with cancer-related organic GH deficiency. Based on 18 cases, T2DM risk was elevated [standardised incidence ratio (SIR): 3.77 (2.24-5.96)], but 72% had risk factors. In patients without cancer history, 14 primary cancers were observed [SIR: 0.71 (0.39-1.20)]. Second neoplasms occurred in 31 of 622 cancer survivors [5.0%; 10.7 (7.5-15.2) cases/1000 PY] and intracranial tumor recurrences in 67 of 823 tumor survivors [8.1%; 16.9 (13.3-21.5) cases/1000 PY]. All three hemorrhagic stroke cases had risk factors. To conclude, GeNeSIS (Genetics and Neuroendocrinology of Short Stature International Study) data support the favorable safety profile of pediatric GH treatment.

Wasserman JD et al. DICER1 mutations are frequent in adolescent-onset papillary thyroid carcinoma. J Clin Endocrinol Metab. 2018 May 1;103(5):2009-2015.

Papillary thyroid carcinoma (PTC) is a common malignancy in adolescence and is molecularly and clinically distinct from adult PTC. To characterize the prevalence of DICER1 variants in pediatric PTC, specifically in tumors without conventional PTC oncogenic alterations, 40 patients who were <18y of age at the time of surgery who underwent partial or total thyroidectomy (30 malignant, 10 benign) were selected. Their thyroidectomy specimens underwent genotyping for 17 PTC-associated variants, as well as full sequencing of the exons and exon-intron boundaries of DICER1. Conventional alterations were found in 12 of 30 (40%) PTCs (five BRAFV600E, three RET/PTC1, four RET/PTC3). Pathogenic DICER1 variants were identified in 3 of 30 (10%) PTCs and in 2 of 10 (20%) benign nodules, all of which lacked conventional alterations and did not recur during follow-up. DICER1 alterations thus constituted 3 of 18 (16.7%) PTCs without conventional alterations. To conclude DICER1 is a driver of pediatric thyroid nodules, and DICER1-mutated PTC may represent a distinct class of low-risk malignancies.

REPORT OF ISPAD 2018

Banshi Saboo, Anju Virmani, Archana Sarda, Shuchy Chugh

It was our privilege and honor to organize the 44th annual meeting of ISPAD, in Hyderabad, coming to India for the first time, with the theme "Reaching the Unreached". ISPAD 2018 was a meeting with many other firsts also. "Diabetes 101" was a series aimed to reach the unreached health professionals, especially in developing countries, with international experts covering the basics of childhood diabetes care, apart from plenaries on other relevant issues like reaching disadvantaged patients, and coping with under-nutrition and over-nutrition. For the first time, dieticians, nurse educators, and young doctors from SAARC countries could attend, as registration rates were kept specially low and in Indian rupees. For the first time, there was a separate category of abstracts which aimed to reach the unreached patients and family members - these were displayed on the last day for families. For the first time, a troupe of 22 T1D children travelled nearly 600 km across the country, from Aurangabad to Hyderabad, to present a cultural program during the inaugural function – they were doing this for the first time (some even traveling by train for the first time)! The ISPAD 2018 Guidelines released during the meeting, have a dedicated section on the needs of resource constrained situations for the first time. Being in India, there was a lec-dem Yoga session. The Charity Run had a record number of participants, and an overwhelming response. Finally, the buzz around this meeting took the ISPAD membership to an all-time high, with 185 new members from the SAARC region (an exciting nearly 120% increase in SAARC membership) in the past year, with 95% of them 3y memberships. ISPAD 2018 ended up being attended by 1113 delegates, from 69 countries, including almost 400 from India. There were 355 regular and 17 late breaking abstracts accepted. The four outstanding ISPAD Prize Winners for 2018 were Moshe Phillip**,** ISPAD Prize for Achievement; Ragnar Hanas, Lestradet Prize for Education and Advocacy; Bruce Buckingham**,** ISPAD Prize for Innovation in Pediatric Diabetes Care; and Martin Tauschmann, Young Investigator Prize. The Hyderabad Convention Center was a much-appreciated venue, with its well-arranged halls, tranquil environs, and excellent food.

ISPAD 2018 was jointly supported by ISPAE, and Diabetes India. The annual GBM of ISPAE was held on Friday 12th October evening. Details of the GBM are elsewhere in this newsletter.

Our theme was amply reflected in the inaugural event, with the Udaan t1d troupe of 22 T1D children belonging to remote villages around Aurangabad, presenting a 30-minute performance. There was a Ganpati Vandana, invoking the blessing of the Ganapati the Remover of obstacles, with a Bharatanatyam dance by 9yo Swanandi Joshi, and several folk dances showcasing the bright colors of India. They traversed not just 600 km, but a much longer journey of using education and camaraderie to deal with Type1 l, poverty, illiteracy, isolation. There were many wet eyes in the auditorium, when they sang "We are the Children" and "Jai Ho".

The ISPAD Charity 5k Run on the last day, was from 7-9 am, followed by a Q&A session for the families with experts, and a walk through the "Family" posters. Registration had to be closed after 350, though there were several more enquiries. This was a unique group, because along with two professionally trained T1D athletes, more than 150 T1Ds, from Hyderabad and across the country, ranging in age from 5y to 40y, ranging from pumpers to children from economically underprivileged status, participated and ran together. There were over 110 children from different centers of Changing Diabetes in Children (CDiC) in Hyderabad. There were the T1D family members, there were doctors and educators, all united in one cause. Then there were Gavin Griffiths, from London, UK – founder of DiAthletes – who has set a record by running 25 marathons in 30 days earlier this year; and Brais Dacal from Coruna, Spain - Professional Cyclist diagnosed at age

7y, whose motto is “Diabetes will only slow you down if you let it”. Walkers included Lakshmi Narayana who is blind (and T1D) - he later gave a moving little speech about how he manages his diabetes, but a little differently from others because he cannot see. Rainbow Hospitals kindly provided 2 ambulances, nurses, and emergency supplies to manage any crisis. They began by eating a banana (!) each, and warmed up under the guidance of Gavin Griffiths, who taught them how important a proper warm up before sports is. Brais Dacal circled continuously around the route to spot if anyone was in trouble. The parents and doctors who were scared of letting the kids exercise, got inspired by the little ones (under 10y) completing the 2.5k half Run – indeed some of them wanted to run the entire 5 km! After the Run, they came in to test sugars and take insulin - and learnt the concept and importance of correction doses. Then breakfast, again a teaching moment – we had deliberately included fruit. Prizes were given to the first 3 winners in the categories under 10y (ran 2.5 km) and 10-18y (ran 5 km). It was awesome that little Aditya the winner of the under 10 group, came first despite running in loose chappals!

Injected and fed, the entire group of over 500 people sat down to ask questions of the panel of experts from across the world: Dr Carmel Smart (Australia), Dr Carine de Beaufort (Luxembourg), Gavin (UK), Dr Lori Laffel, Dr Philip Zeitler (USA) Dr Leenatha Jakkidi, and Dr Apoorva Gomber (India). Some were surprised to get the same answers their own doctors always gave: no substitute for insulin, important to check sugars daily, important to keep good control. Shravani and Aditya were given prizes for the best question. All the children went off in their event T-shirts, happy and motivated. Though there were 2 ambulances (Rainbow Hospitals), plenty of candies and 5 Glucagon injections for emergencies, there was not a single hypoglycemia, or other problem. Dr Laffel's winding up words were moving: "You are all heroes, and your parents are wonderful! Look after yourselves, so when the permanent cure comes, you would be ready." In the words of a CDIC child, “I am so happy to be here at this event, as I learnt I can play sports, including cricket, and grow with diabetes.” We feel we all grew a little with this meeting.

Activities by ISPAE Members

World Diabetes Day 2018

Meena Mohan, PSG Institution of Medical Sciences and Research, Coimbatore

WDD celebrations were conducted at the PSG Institution of Medical Sciences and Research auditorium on Sunday, 28th October. The day started with Hba1c testing, and providing measurement cups for use in the kitchen and puncture proof container for sharp disposal. It was followed by "Your Questions Answered" session by Ms Srihari, diabetes educator from Sanofi. A lec-dem on "Hands on experience on carb counting with South Indian food items" was delivered by our dietician Ms Vijaya Lakshmi. After this, Maheswar, a 22 yo with T1D, shared his experience on his nine-day trip to Chandrakani pass at Manali, North India. Dr Jayalakshmi, HOD of MSR discussed "Safe disposal of sharps in the community" and its importance. Lunch was provided to all the attendees.
In the afternoon, workshop stations were held on the following topics.
1. Hypo/hyper glycemia
2. Sick day management
3. Insulin technique and storage
4. Diet in greater detail
5. Blood glucose monitoring at home

40 children and their families, with a total of 150 members, graced the occasion.

Amarnath Kulkarni, Lotus Hospital, Lakdikapool, Hyderabad, & SVS Medical College, Mahaboobnagar

WDD celebrations were conducted at 3 places in Telangana state:
1. Lotus Hospital, Lakdikapool, Hyderabad - for urban children. Drawing, fancy dress, and games competitions were held. Thirty children with their families (total 70) participated.
2. At ESI Medical College, Sanathnagar, Hyderabad – A workshop on “Advances in technology: I-port and insulin pump” was conducted, which trained 20 doctors. In addition, 20 patients’ families also participated.
3. SVS Medical College Mahaboobnagar – for rural children, in which 30 children participated.

Shaila Bhattacharyya, Manipal Hospital, Bangalore.

On the occasion of WDD, we organized a “Sweet 1 India” Diabetes Camp in association with Shivajoyti, at Cubbon Park, Bengaluru. In keeping with this year’s theme “The Family and Diabetes”,

we asked the families to come up with exciting ideas. Our main aim was to bring together families so they learn and share their experiences. The dress color code was **lemon yellow,** depicting the abundant shine each child has, because of the parents' constant support in living with diabetes. Parents came up with some innovative games like "Sorting out the healthy from the unhealthy foods", "Pictionary", "Shooting the unhealthy food" and "Passing the hoop". Every game played had a message which educated the child to eat healthy, play well and live happy. Apart from the games, we had an amazing talent show where the children demonstrated their unique abilities in dancing, singing, yoga, elocution, drawing and making best out of waste. The cherry on the icing was the skit enacted by children, showing how to face, handle and later live with diabetes in a healthy way! As a token of our appreciation, and in keeping with the theme, we gifted all the families a plant, signifying "Growth of life in a healthy way".

All in all, we were happy with the enthusiasm shown and talent portrayed by all the families and their children, which made our day, leaving us with a broad smile and many memories to be cherished.

Santhosh Olety, Consultant Pediatric Endocrine and Diabetes, Karnataka Institute of Endocrinology and Research, Bengaluru

A half day event was organized at the Karnataka Institute of Endocrinology and Research (KIER) on 11th November, with the objectives of raising awareness about childhood diabetes, creating a platform for interaction of parents and children, to empower them and increase psychological well-being. We took this opportunity to entertain them through drawing and various age appropriate educational, fun filled, and team building activities. It was well attended by 130 members, which included 45 children. The event also included a mini walkathon by children and parents carrying placards displaying diabetes awareness and regular monitoring for a better health outcome. The event ended by getting parents' feedback, a talent show by children in the form of folk dances, Bharatanatyam, chanting shlokas, and singing, and of course relishing the healthy meals by all the attendees.




Ashok Venkatanarasu, Consultant Endocrinologist, Yashoda Hospital, Secunderabad

We conducted awareness programs on healthy life style at different times, for school children and for the teachers of St. Ann's School, Hyderabad, on the occasion of WDD.




We also conducted a Walk for diabetes awareness in the community, as part of the celebrations.

Subramanian Kannan, Narayana Health City

• We kicked off the WDD 2018 Program with a diabetes awareness skit for the public in the Lobby
• We then had about 25 children with Type1 Diabetes attending educational fun activities
• Our dietician emphasized carbohydrate counting, our child psychiatrist gave tips on how to cope with common problems at home related to food and insulin
• A Magic show for the kids sent ripples of laughter in the crowd
• All kids were given a Glucagon injection kit and taught about hypoglycemia management
• Fundus examination and Neuropathy testing were done for appropriate patients
• The show ended with Lunch.

Anbezhil Subbarayan, Consultant Pediatric Endocrinologist & Diabetologist, Apollo Children's Hospital, Chennai.

A Workshop was conducted in our center for Nurses and Dietitians, on 14th November, on the occasion of WDD.


Deepa Anirudhan, Asst Prof, Pediatrics & Pediatric Endocrinology, Govt Medical College, Thrissur

WDD was actively celebrated on 14 Nov 2018 at the Dept of Pediatrics, GMC, Thrissur, attended by 37 children with T1D. The function was inaugurated by Prof Purushothaman, HOD, Pediatrics. Prof Mohankumar gave the felicitation. There was a session by Dr Deepa on "How to control diabetes optimally", and another on Insulin injection Techniques by Mr Janardhanan, Diabetes Counsellor, Sanofi. Diabetic log books and injection grids were distributed to all patients. There were various cultural programs by children and parents and a magic show. Dr Keerthy, PG Pediatrics, conducted a Quiz program for parents also.

Hemchand Prasad, Mehta Hospital, Chennai.

For WDD, we at Mehta Hospital conducted a CME attended by 50 pediatricians and PGs. There was a guest lecture by Prof Timothy Barrett from Birmingham on Rare Diabetes in children, followed by case presentations by PGs on rare causes of DM. The cases discussed included mitochondrial diabetes, Seckel syndrome, DIDMOAD, Roger syndrome, and pancreatic diabetes. The meeting was appreciated by all. An app for management of diabetic ketoacidosis which has been developed in house was also released.

Veena V Nair, Consultant Pediatric and Adolescent Endocrinologist, Ananthapuri Hospitals and Research Institute, Thiruvananthapuram, Kerala.

A walkathon was organized at St Johns School, Nalanchira, Thiruvananthapuram, flagged off by Padmasri Dr Marthanda Pillai, Chairman, Ananthapuri Hospital, and past National President IMA. This was followed by an awareness session on “Lifestyle and Diabetes” by Dr Veena and “Healthy Eating Habits” by Ms Jaziya, Chief Dietician, Ananthapuri Hospital. Students of class 11 and 12 were checked for weight, height, BP, and signs of insulin resistance (IR); family history of diabetes was enquired for; and BMI calculated. A group of 20 high-risk adolescents - obese/ overweight + family history of diabetes or signs of IR - were identified; they and their parents were called for detailed metabolic screening.

Ravindra Kumar, Senior Specialist, Hindu Rao Hospital & North Delhi Municipal Medical College, Delhi.

On the occasion of WDD, the North Delhi Municipal Corporation organized a three-day function from 14-16 Nov 2018 at Hindu Rao Hospital, along with a Diabetes Detection Drive on all days. On the 14th, after the Inauguration, there was a 2h Panel Discussion on Diabetes by Experts. On the 15th morning, after a Nukkad Natak, there were post-lunch lectures on Type 1 and Type 2 DM, and Diabetes in Pregnancy; and Yoga and Alternative medicine. On the last day, we held a Quiz for MBBS students and Interns on diabetes.

Vijay Jaiswal, Head, Pediatric Endocrine Unit, LLRM Medical College, Meerut.

WDD celebrations at LLRM Medical College were inaugurated by the Honorable Principal, Dr RC Gupta, and attended by all HODs and undergraduates, nurses, the sweet children and their parents in good number. The program consisted of a 20 minutes PowerPoint presentation on diabetes; a Quiz on diabetes for undergraduate students; thoughts by the T1D children and their parents; Prize distribution; and the vote of thanks.

Devi Dayal, Prof & Head, Endocrinology & Diabetes Unit, Dept of Pediatrics, Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh.

To commemorate WDD, PGIMER organized a "Type 1 diabetes education day" on 14th November at the auditorium. It was attended by about 50 families of children with T1D. Prof Devi Dayal emphasized the theme this year, i.e. "Families and Diabetes" and the need for parents and other family members to support these children. Dr Jaivinder Yadav spoke on day-to-day management of T1D. There were interactive sessions on needle use, newer insulins, pen devices, newer modalities of insulin delivery and glucose monitoring, and nutritional management of T1D.

Sandeep Julka, Consultant Endocrinologist, CHL Hospitals, Indore

For WDD, under the banner **Defeat Diabetes Premier League**, we had a series of sporting events at the Residency Club, Indore. The players were all T1Ds, ages ranging from 7-60y! The sports included table tennis, badminton, squash, skating, hula hoop and aerobics. The winners were Fiza Rafi Sheikh and Dhanjaya Baweja (badminton), Fiza (TT), Sidhant Khanchandani (skating), Mouli Arora (hula hoop), and Vansh Kasturi (squash). Eminent sportspersons Meer Ranjan Negi and Lt Gen BS Sisodia gave away the prizes.

फिजा ने हासिल की दोहरी सफलता

इंदौर। शुगर (डायबिटीज) की बीमारी का सामना कर रहे सैकड़ों खिलाड़ी रेसीडेंसी क्लब में एकत्रित हुए। मौका था प्रदेश में पहली बार आयोजित डिफीट डायबिटीज प्रीमियर लीग का, जहां खेल के मैदान में बच्चों से लेकर बुजुर्गों ने अपने खेल से जीत हासिल की और डायबिटीज को हराने का संदेश दिया।

यूथ डायबिटीज डे के उपलक्ष्य में टीम रेडियन्स और सीएचएल अपोलो द्वारा रेसीडेंसी क्लब में आयोजित स्पर्धा में टाइप वन और टाइप टू डायबिटीज के साथ जीवन जी रहे खिलाड़ियों ने टेबल-टेनिस, बैडमिंटन, स्क्वॉश, स्केटिंग जैसे खेलों में चुनौती पेश की। इसके अलावा खिलाड़ियों के लिए हुलहूप, एरोबिक्स का भी आयोजन हुआ।

आयोजक एंडोक्राइनोलॉजिस्ट डॉ. संदीप जुल्का ने बताया कि बैडमिंटन बालिका वर्ग में फिजा रफी शेख पहले स्थान पर रहीं जबकि प्रांजल मिश्रा को दूसरा स्थान हासिल हुआ। बैडमिंटन के बालक वर्ग में धनंजय बवेजा ने जीत हासिल की जबकि प्रियांश वासवानी उपविजेता रहे। टेबल-टेनिस स्पर्धा में फिजा रफी शेख ने खिताब हासिल करते हुए दोहरी उपलब्धि अपने नाम की। स्केटिंग में सिद्धांत खनचंदानी, हुलाहूप में भौली अरोरा और जान्हवी जुल्का, स्क्वॉश में वंश कम्तूरी ने सफलता प्राप्त किया। स्पर्धा में 7 वर्ष से लेकर 60 वर्ष तक के खिलाड़ियों ने हिस्सा लिया। कार्यक्रम के अतिथि पूर्व अंतरराष्ट्रीय हॉकी खिलाड़ी मीर रंजन नेगी, पूर्व रणजी क्रिकेटर लेफ्टिनेंट जनरल बीएस सिसौदिया और वरिष्ठ पत्रकार सुधाष सालातकर थे।

Anil Vedwal, Yog Dhyan Foundation, Delhi

"If you don't believe Super Heroes are real, I will show you a Type 1 Diabetic." – Robin Arzon

Putting together an exciting event can be a great way to generate widespread interest around WDD and engage diabetic young minds, their families and members of the community happily together. With this aim in mind, YDF combined WDD and Diwali celebrations with 200+ T1D children and their families on 4th November. The event started with a Rangoli Making Competition, with the children divided into 8 groups; beautiful rangolis depicted Diwali, Yoga and Diabetes. We then welcomed our honored guests, Dr Anju Virmani (Pediatric Endocrinologist), Ms Bindiya Chhabra (Executive President, Sant Nirankari Trust), and Ms Shubhda Bhanot (Chief Diabetes Educator, Medanta). Dr Virmani and some children shared ideas and experiences about eating during festivals. Then things got more exciting, with a Balloon Bursting Competition – the brightly colored balloons being a perfect substitute for Diwali crackers. Groups of children were given different colored balloons – each group had to burst only their own color! This was followed by a Fashion Show Competition where the beautifully dressed children "walked the ramp". Finally, the prize distribution, and this quarter's HbA1c and blood glucose testing, with little gifts for all the children there. And of course, the day can't be complete with an empty stomach, so a delicious lunch was served to all children and families. The function concluded with a speech of thanks. This fun, happy and meaningful day was possible only with the help of our Volunteers, Supporters and Mentors, who worked really hard to make this event a grand hit.

Meghna Chawla, Consultant Pediatric Endocrinologist, Ruby Hall Clinic, Pune

On the occasion of WDD, Ruby Hall Clinic in association with Lions Club International had organized the ***"15th WDD & Organ Donation Program"*** at Pune. It started with a rally with hundreds of school students carrying placards displaying information on prevention of diabetes. This was followed by a public awareness program, in which Dr Meghna Chawla, spoke on awareness of signs and symptoms of diabetes in children; Dr Harshal Ekatpure, Consultant Endocrinologist, educated people on

preventive measures of diabetes; and Dr Sanjay Pathare, Director- Medical Services, Ruby Hall Clinic, spoke on myths and facts of organ donation.

Tushar Godbole, Pediatric Endocrinologist, Nashik

Harmony Health Hub, Nashik organized a trekking activity for families of children with T1D on 21st October 2018, in which 25 children with their families participated. They were given breakfast with a demonstration on carb counting and dose adjustments for the carbs and the scheduled activity. This was followed by a trek for 1 km up-hill. There was a yoga session by Ms Sarika, followed by discussion on healthy snack options by nutritionist Ms Ketaki Pujare. Dr Godbole organized the event and thanked the participants.

J Dhivyalakshmi, Consultant Pediatric Endocrinologist, Sri Ramachandra Institute of Higher Education & Research, Chennai

1. On 30.06.2018 "Growth Module for Postgraduates" was organized, in which 40 PGs in and around Chennai participated. Dr Kavitha Bhat, Consultant Pediatric Endocrinologist, Rainbow Children's Hospital, Bengaluru, and Dr Hemchand Krishna Prasad, Consultant Pediatric Endocrinologist, Mehta's Children's Hospital, Chennai, were the invited speakers. Following the talks, there was a hands-on session on "Growth charts as a diagnostic tool" highlighting growth charts plotting and identifying disorders of growth. All sessions were highly appreciated by the participants.

2. On 09.10.2018, a half-day CME on "Pediatric Endocrinology in office practice" was organized for practicing pediatricians and physicians in Kanchipuram, Tamil Nadu, in association with Indian Academy of Pediatrics (IAP) - Kanchipuram branch and Indian Medical Association - Kanchipuram Branch, and attended by about 50 delegates. The program was well appreciated by all delegates.

3. The following activities were conducted as part of the WDD program:

i) On 20.10.2018, a CME on "Insulin Therapy and Insulin delivery devices" was conducted in association with IAP - Chennai city branch, and attended by about 50 delegates. Dr Anbezhil Subbarayan, Consultant Pediatric Endocrinologist, Apollo Children Hospital, Chennai, was the invited speaker. There was a workshop on insulin pumps and other insulin delivery devices following the scientific session.

ii) On 17.11.2018, this year's second Nurses' education program on pediatric diabetes was conducted, attended by about 50 nurses in and around Chennai. The program highlights were the workshops on insulin injection technique, glucometers and case scenarios. The first program was organized on 23.01.2018.

iii) On 24.11.2018, a T1D children meet was organized, in which about 15 children and their family members were taken for a short trip to Birla Planetarium, Kotturpuram, Chennai. The program highlights were the release of "My journey with Diabetes" – a patient information booklet, and distribution of Diaversary Medals for children.


Shalmi Mehta, Pediatric Endocrinologist, Ahmedabad

A CME on Pediatric Endocrinology was organised by Endokids Clinic and Academy of Pediatrics, Ahmedabad on 5th August, 2018, attended by more than 100 pediatricians. The faculty, including Drs Vaman Khadilkar, Sudha Rao, Hemchand Prasad, Shalmi Mehta and Ruchi Shah, shared their knowledge and experience in handling the common pediatric endocrine conditions seen in office practice.




Publications

Rakesh Kumar, PGIMER, Chandigarh

1. Chaudhary N, **Kumar R**, Sachdeva N, Dayal D. Vitamin D levels in children with Hashimoto's thyroiditis: Before and after L-thyroxine therapy. Thyroid Res Pract 2018; 15:23-8.
2. **Kumar R**, Raviteja KV, Sachdeva N, Dayal D. Feasibility and Acceptability of Professional Continuous Glucose Monitoring System in Children with Type 1 Diabetes Mellitus: an observational study. J Diabetol 2019;10:15-20.
3. Harikrishnan V, **Kumar R**, Sachdeva N, Dayal D. Low plasma ghrelin levels in children with severe protein-energy malnutrition. International J Contemporary Pediatrics 2018; 5(4): 1527-1532.
4. Venkatesh V, **Kumar R**, Varma DK, et al. Changes in platelet morphology indices in relation to duration of disease and glycemic control in children with type 1 diabetes mellitus. J Diabetes Complications. 2018;32(9):833-838.
5. **Kumar R**, Pilania RK, Bhatia A, Dayal D. Acquired generalized lipodystrophy and type 1 diabetes mellitus in a child: a rare and implacable association. BMJ Case Rep. 2018;2018. pii: bcr-2018-225553.
6. Paul M, Badal D, Jacob N, et al. Pathophysiological characteristics of preproinsulin-specific CD8+ T cells in subjects with juvenile-onset and adult-onset type 1 diabetes: A 1-year follow-up study. Pediatr Diabetes. 2018;19(1):68-79.
7. Tan TSE, Manfredonia C, **Kumar R** et al. Retrospective review of Synacthen testing in infants. Arch Dis Child. 2018 Oct;103(10):984-986.

Anju Virmani, Max, Pentamed & Rainbow Hospitals, Delhi

1. Pihoker C, Forsander G, Fantahun B, **Virmani A,** et al. The Delivery of ambulatory diabetes care to children and adolescents with diabetes. Pediatric Diabetes 2018; 19 (Suppl. 27): 84–104.

2. Laffel LM, Limbert C, Phelan H, **Virmani A** et al. Sick day management in children and adolescents with diabetes. Pediatric Diabetes 2018; 19 (Suppl. 27): 193–204.

Awards and Fellowships

Dr Hari Mangtani from Nagpur has been awarded ESPE fellowship for a period of 3 months which he will be pursuing under Dr Senthil Senniappan at Alder Hey Children's hospital, Liverpool, UK.

Dr J Dhivyalakshmi from Chennai has received the ISPAD Allan Drash Clinical Fellowship for 2018 at the Lucile Packard Children's Hospital, Stanford University, California, USA.

Dr Priti Phatale received the "Best Paper Award" in AIAAROCON 2018 (All India Association for advancing research in obesity conference) for the paper 'Tri-Ponderal mass index (TMI): A better tool to correlate total body fat in children weighing more than normal'.

Answer to Photo Quiz

Ellis van Crevald Syndrome or Chondroectodermal dysplasia is an autosomal recessive disorder caused by homozygous or compound heterozygous mutations in the EvC ciliary complex subunit 1 (*EVC*) or *EVC2* gene. It is characterized by a narrow chest, short ribs, postaxial polydactyly with a complete extra metacarpal, ectodermal dysplasia with hypoplastic nails and teeth, and structural heart disease (most commonly an atrial septal defect).

Registration link: http://marundeshwara.com/maruncms/user-register.php?conferenceID=177%20-%20ISPAE%202019

ACCOUNT DETAILS
Branch Name- Axis Bank Ltd, Sarat Bose Road, Kolkata; A/C No- 918010081461829
A/c Name- Indian Society For Pediatric and Adolescent Endocrinology A/c Conference 2019
IFSC Code- UTIB0000411

ISPAE PET Fellows School 2019

at The Vedic Village, Kolkata
Tuesday, 26 November to Thursday, 28 November 2019

ISPAE PET Fellows' School is a 3 day intensive residential training program for young entrants in pediatric endocrinology, and a refresher course for those already working in the field of pediatric endocrinology. This residential course is conducted in a secluded quiet environment with a student to faculty ratio of 5:1, aiming to promote maximum interactions between the trainees and the faculty members, both national and international. Registrations are limited to 30 seats only.

Course registration fees is Rs.7500/- **(to be paid only after selection)**

Please complete the application form and return by email to **Dr Sudha Rao** (ISPAE - PET Convener) at c_sudha@hotmail.com **AND Dr Sarah Mathai** (ISPAE – PET Co convener) at sarjomat@yahoo.co.in with a detailed CV (not more than 2 pages) and a reference letter from the Head of the Division/ Department before **Friday , 19th April 2019**.

Application format enclosed herewith.

It is mandatory that all applicants become member of ISPAE.

Selected candidates will be notified by 21st July 2019.

Dr Sudha Rao	***Dr Sarah Mathai***	***Dr Subrata Dey***
Convener ISPAE-PET	***Co-Convener ISPAE PET***	***Org Chair ISPAECON2019***

APPLICATION FORM

Please complete the form and return by email to

Dr Sudha Rao c_sudha@hotmail.com AND Dr Sarah Mathai sarjomat@yahoo.co.in

DEADLINE FOR APPLICATION – FRIDAY, 19 APRIL 2019

Title:	Surname:	First Name:
Gender: MALE ☐ FEMALE ☐	Date of birth:	
Present Position:		
Institution/		
Department:		
Postal Address:		
City	Postcode	Country:
Telephone (work):	Fax:	
Email:		
Address and contact phone no. in case of emergency:		

Degrees (please state nature of degree e.g. MD/PhD; subject e.g. Medicine / Pediatrics, year of passing, and University):

Degree	Year	Institution / Place

Have you had formal training in Pediatric Endocrinology? If yes, please give details:

Clinical (duration): _____ Place: _____

Research (duration): _____ Place: _____

Have you attended PET school before: Yes/ No; If Yes, place & year _____

Description of your interest / activities in pediatric endocrinology: _____

_____

Publications (may attach in the brief CV)

a) List of original publications (peer reviewed):

b) Original publications in Pediatric Endocrinology:

Summarize briefly your career plans:

_____

_____

Expectations from this training program:

_____

_____

Date: **Signature:**

Please attach a brief CV (maximum of 2 pages) including publications and other details.

A separate recommendation letter from your Head of Department should accompany this application.

It is mandatory that all applicants become members of ISPAE