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Adrenal Advocacy: Focus on Addison's Disease

The adrenals are a pair of tiny glands, weighing just about 3 grams apiece. Yet these glands pack a powerful punch and are essential for life. Adrenal disorders encompass a wide spectrum of causative factors, clinical presentations, complications, comorbid conditions and concerns related to health. Adrenal medicine is not only relevant to clinical practice, but to public health[1] as well.

In this editorial, we discuss the various aspects of adrenal advocacy, with a focus on Addison's disease.

THE BURDEN OF DISEASE

Addison's disease or primary adrenal insufficiency, is an important, but often under diagnosed, disease. The reported prevalence varies up to 117 cases per million population.[2] This figure seems higher than what is experienced in Indian settings. Prof Kochupillai had calculated over 3 decades ago, a burden of 4 per million of primary adrenal disease related to tuberculosis (TB) in India.[3] Currently, we do not have any definitive estimates of nontubercular Addison's disease in our country. Secondary adrenal insufficiency because of the use of exogenous steroids and disorders of the pituitary is much more common in India. A survey of rural households in North Bihar suggested that 1 out of 3 people had been inappropriately prescribed steroids over a period of 6 months for minor ailments.[4] Studies from Kashmir have suggested a large burden of undiagnosed Sheehan's syndrome (postpartum pituitary dysfunction) among adult women.[5] A more recent study suggested that 14% of patients presenting to the hospital with euvolemic hyponatremia had undiagnosed adrenal insufficiency.[6]

CLINICAL IMPACT

Adrenal insufficiency is an important cause of morbidity (Table 1). Because of its subtle and myriad presentation, the condition often goes unrecognized. This is unfortunate, because this abnormality can be easily managed, in a cost-effective manner.

Adrenal insufficiency should be suspected in conditions such as TB, histoplasmosis, existing autoimmune disease and malignancy. It may coexist with other autoimmune

Table 1. Red Flags Raising Suspicious Adrenal Insufficiency

Symptoms
• Weakness, lack of energy
• Vomiting, nausea
• Darkening of skin, mucous membranes
• Weight loss
• Amenorrhea
Signs
• Hypotension
• Postural hypotension
• Hyperpigmentation of skin
Syndromes
• Tuberculosis, e.g., histoplasmosis, cryptococcosis
• Polyglandular, multiple endocrine neoplasia
• Hypopituitarism
Surrogate laboratory abnormalities
• Hypoglycemia
• Hyponatremia

endocrine diseases, and with other endocrine neoplasia. Sudden cessation of exogenous corticosteroid therapy, whether taken on prescription, or as part of so called "alternative" or over-the-counter medication, can also precipitate adrenal insufficiency.[4] Use of high-dose inhaled steroids or use of steroid-containing creams over large areas of diseased skin can also induce secondary adrenal insufficiency.

Electrolyte and metabolic conditions, such as unexplained euvolemic hyponatremia, recurrent hypoglycemia, hyperkalemia and hypotension, should prompt an evaluation of adrenal function.[5] Physicians must be aware of the common symptoms of adrenal insufficiency, including lethargy, anergy, weight loss and darkening of the skin and mucous membranes.

Sudden change in metabolic and endocrine status (for example, an unexplained reduction in dose requirement of glucose-lowering or blood pressure-lowering therapy) is a red flag that calls for adrenal health assessment. Refractory hypotension and/or hypoglycemia, with greater than- anticipated requirement of inotropes and/or glucose support is another sign of adrenal insufficiency.[6]

PUBLIC HEALTH IMPACT

Adrenal insufficiency is a condition, which deserves attention from a public health perspective as well. Misuse of steroids leading to Cushing's syndrome and sudden cessation of these drugs can precipitate adrenal insufficiency. This calls for steroid stewardship, which is defined as the systematic effort to prescribe and monitor glucocorticoids in a rational manner, while balancing benefit and potential risk in patients who require this therapy. Steroid stewardship includes pre-prescription screening, rational prescription, medical care during corticosteroid use and appropriate monitoring after corticosteroid use has been discontinued.[7]

Adrenal insufficiency is also part of congenital adrenal hyperplasia, which can present in various ways. Some individuals present with ambiguous genitalia and may overlap with "transgender" presentations. Transgender healthcare providers should be aware of the anatomic and physiologic impact of adrenal disorders.[8]

ADDISON'S DAY

29th May is observed as International Addison's Day every year. This event has been initiated by the Addison's Disease Self-Help Group, United Kingdom.[9] This is an effort to raise awareness about adrenal disease. The date has been chosen as it is the birthday of John F Kennedy, former US President who self-managed his adrenal insufficiency. This is a suitable platform to come together to support the cause of persons living with adrenal insufficiency.

ADVOCACY AND ACTION

There is a great need to advocate for adrenal health and to take action towards improving suspicion, screening, confirmation and clinical management of adrenal disorders.

Physicians and paramedical professionals should be made aware of the red flags that should prompt evaluation for adrenal insufficiency. Pharmacists must dispense corticosteroids with responsibility, and all cadres of healthcare professionals should own responsibility for steroid stewardship. Sick day rules should be explained and reinforced at each interaction with patients. Persons living with adrenal insufficiency must have continuous access to an emergency kit and their caregivers should be trained in its usage.

The pharmaceutical sector can contribute to adrenal advocacy by providing hydrocortisone, fludrocortisone and adrenocorticotropic hormone at economical rates. We note with pride that the Indian pharmaceutical industry has lived up to this responsibility and Indians have access to economical quality brands of adrenal hormones.[10]

THE WAY AHEAD

Adrenal advocacy is an integral part of health advocacy, and must be propagated at all possible platforms. All stakeholders involved in the diagnosis and care of persons with adrenal disorders should take up this responsibility. Endocrinologists and physicians should take leadership of this campaign, in equal partnership with persons living with adrenal disease, paramedical professionals and policymakers. Adrenal advocacy should be a concerted and continual process, with comprehensive coverage of the entire healthcare community.

Adrenal advocacy should address health policy makers and insurance payers, highlighting the essential nature of treatment for adrenal disease. It is heartening to note that adrenal hormone preparations are part of the World Health Organization Model List of Essential Medicines and the Indian National List of Essential Medicines.[11,12]

The Indian Journal of Clinical Practice hopes to contribute to this cause, through this and other communications. We invite readers to join us in our endeavor to enhance adrenal awareness in our country.

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Children's Development may be Affected by Parental Autoimmune Diseases

A meta-analytical study conducted by a French team links paternal/maternal autoimmune disease with a child's risk of developing a neurodevelopmental disorder such as autism and ADHD. According to the researchers, these connections may be initiated due to exposure to environmental factors such as exposure to pollutants, passive smoking, genetic predisposition, etc. They also proposed that a shared mechanism could be present between the parents and a child, though the maternal route seemed to be riskier.

The neurodevelopmental disorder is caused by a correlation of genes and environmental factors while autoimmune and anti-inflammatory disorders are caused due to activation of the immune system, the circulation of antibodies, cytokines, etc. Several studies have advocated the link between autoimmune disorders and maternal health. However, no data has been provided to indicate the influence of both the parents in a direct way, i.e., during pregnancy.

In the meta-analysis, 14 cases were included with 8.45 lakh mothers and 6 lakh fathers with an autoimmune disorder. Also, 4.98 lakh control mothers and 4.99 lakh control fathers were subjectively recruited. There were 1,82,927 children with neurodevelopmental disorders and 14,168,474 with no such diagnosis or disorder. The results showed that autoimmune diseases in mother and father were associated with a diagnosis of ASD and ADHD in children. Similarly, mothers diagnosed with type 1 diabetes, psoriasis and rheumatoid arthritis increased the risk of ASD and ADHD by the ratio of 1.6, 1.45, 1.38 and 1.36, 1.41, 1.32, respectively. On the other hand, fathers with type 1 diabetes had an increased ratio of ASD and ADHD by 1.42, 1.19 while psoriasis was linked to ADHD at a ratio of 1.18. (*Source: https://www.medscape.com/viewarticle/972960?src=*)

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