GUEST EDITORIAL

The Jarasandha Syndrome

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Jarasandha, King of Magadha, was a character in the Mahabharata. Born as two lifeless halves of a baby, Jarasandha was brought together when Jara, an asuri (demon), inadvertently joined the halves.

Jarasandha dueled with Bhima, who could not defeat him initially. Lord Krishna took a leaf and tore it into two. Bhima then ripped Jarasandha into two parts, but they rejoined again and again. Krishna then took another leaf, tore it into two, and threw each half on opposite sides. Bhima got the hint, broke Jarasandha's body, and flung the right half towards the left side, and vice versa. This ensured victory for the Pandavas[1].

A similar situation occurs in type 2 diabetes and obesity. Overweight and hyperglycemia are two halves of the same syndrome, inseparable from each other. Disordered energy intake and energy expenditure, too, are facets of the same dysfunction. Just as Jarasandha regrows, obesity and type 2 diabetes present with multiple comorbidities and complications. These continue to appear during the natural trajectory of disease, and need to be managed by treating the root cause, i.e., adiposopathy and insulin resistance[2].

The challenge that clinicians face is managing dysglycemia and heavy body weight together, as well as decoupling energy intake and energy expenditure. The KgA1c paradox[3] describes the potential increase in weight (kg) when HbA1c is lowered using conventional therapies such as sulfonylureas, pioglitazone, and insulin. The metabolic setpoint alludes to the homeostatic mechanisms, which prevent excessive weight loss by modifying energy balancing pathways[4]. These phenomena, together, may be described as the Jarasandha challenge. This challenge poses a significant public health burden, and must be tackled at the primary care level[5].

Modern pharmacotherapeutics now offers the possibility of resolving this situation. Peptide agonists such as glucagon-like peptide 1 receptor agonist (GLP-1RA) and GLP-1RA/GIPRA (Glucose-dependent insulinotropic polypeptide receptor agonist) have been approved for use in type 2 diabetes and chronic weight management. Currently approved include liraglutide, semaglutide, and tirzepatide. These drugs are able to optimize glycemia, while reducing body weight as well[6]. They also maintain weight loss over prolonged periods of time, thus decoupling the two Jarasandha halves of metabolic dysfunction. Long-term use of tirzepatide and semaglutide is associated with sustained charges in appetite and energy expenditure, which allow the metabolic setpoint to be reset at a lower level. Along with intensive behavioral therapy, lifestyle modification, and dietary management, these drugs are effective in managing both diabetes and obesity[7].

The Jarasandha syndrome is an allegory, which represents not only the pathophysiology of obesity, but also the challenges associated with its management. More importantly, the story reminds us that with strategic planning and determination, we can defeat these diseases.

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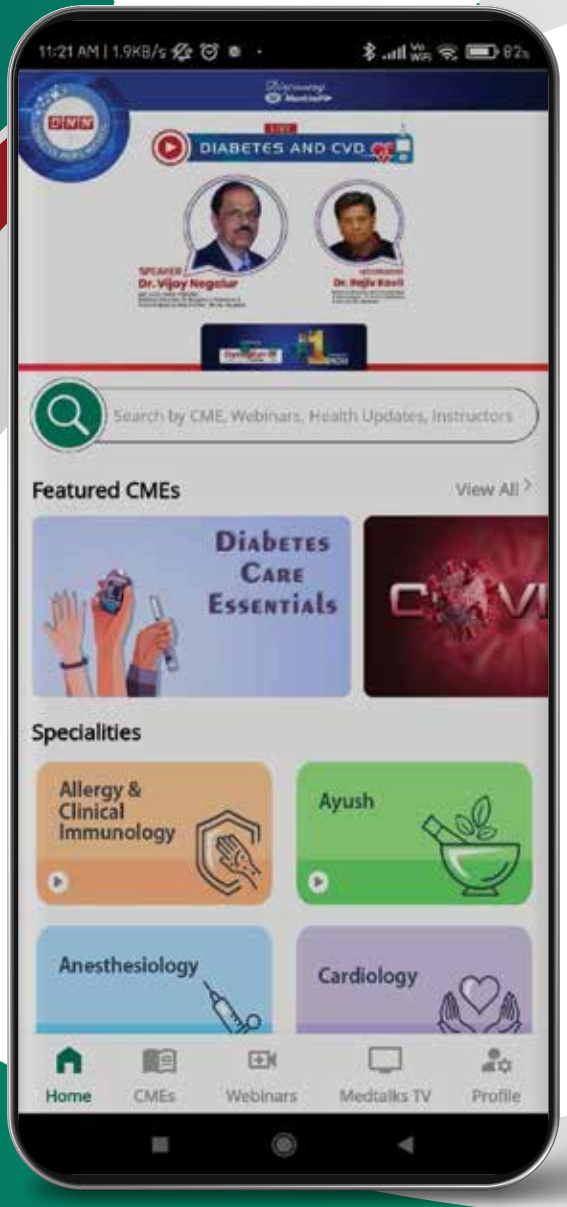

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