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# Endocrine and metabolic aspects of dengue syndrome

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**Abstract**

Dengue virus infection is increasing in frequency as well as its complications. Profound/prolonged dengue shock syndrome causes metabolic acidosis leading to different metabolic and electrolyte abnormalities. Endocrine glands may be involved by shock, bleeding, and inflammation and may present with transient abnormalities in hormone levels. These unusual expanded dengue syndrome may require close follow up for proper management. Besides, diabetes mellitus and obesity are risk factors for severe dengue and mortality. This review article summarizes the endocrine and metabolic aspects of dengue infection in brief. *[J Assoc Clin Endocrinol Diabetol Bangladesh, July 2023; 2 (2): 66-70]*

**Keywords:** Dengue, hormones, metabolism

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The flavivirus-dengue is a major healthcare burden for countries residing in tropical and subtropical regions. The dengue virus infection is endemic in Bangladesh with frequent outbreaks. The problem is expected to rise in Bangladesh.[1] Although most of the infections are asymptomatic, the cross-infection between new and previous serotypes causes severe infection and fatality. During the shock syndrome, endocrine glands may be affected. Besides, endocrine diseases may increase the severity of the infection. Various mechanisms may be involved are shown in Figure-1.[2] This review article summarizes the endocrine and metabolic aspects of dengue infection: from available literature (Figure-2).

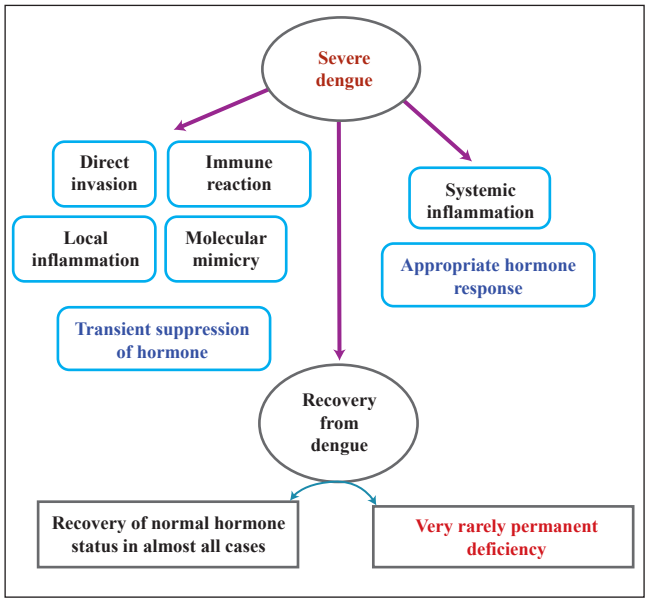


**Figure-1** Possible mechanisms of endocrinopathies with dengue syndrome

## Effects of endocrine and metabolic disorders in the outcome of dengue syndrome

### Diabetes mellitus and hyperglycemia:

The presence of DM is a predictor of severe dengue, dengue hemorrhagic fever, hospital admission, hospital stay, and mortality.[3-5] Suboptimal glycemic control (HbA1c ≥7%) had significantly higher incidences of non-shock DHF and severe dengue.[6]

Diabetes is a chronic meta-inflammatory state that promotes dengue infection. Hyperglycemia increases viral protein expression, translation, and virion release. The progression of dengue is due to increased permeability of vessels and impaired immune response by hyperglycemia.[7,8]

Metformin has several beneficial effects against dengue (decreasing the risk of severe dengue) due to its anti-inflammatory, antioxidant, and helps in vascular endothelial function and increases the size of hemopoietic stem cells.[9]

### Obesity:

The association of obesity (BMI ≥25 kg/m$^2$) as a risk factor for dengue and its severe forms is controversial.[10,11]

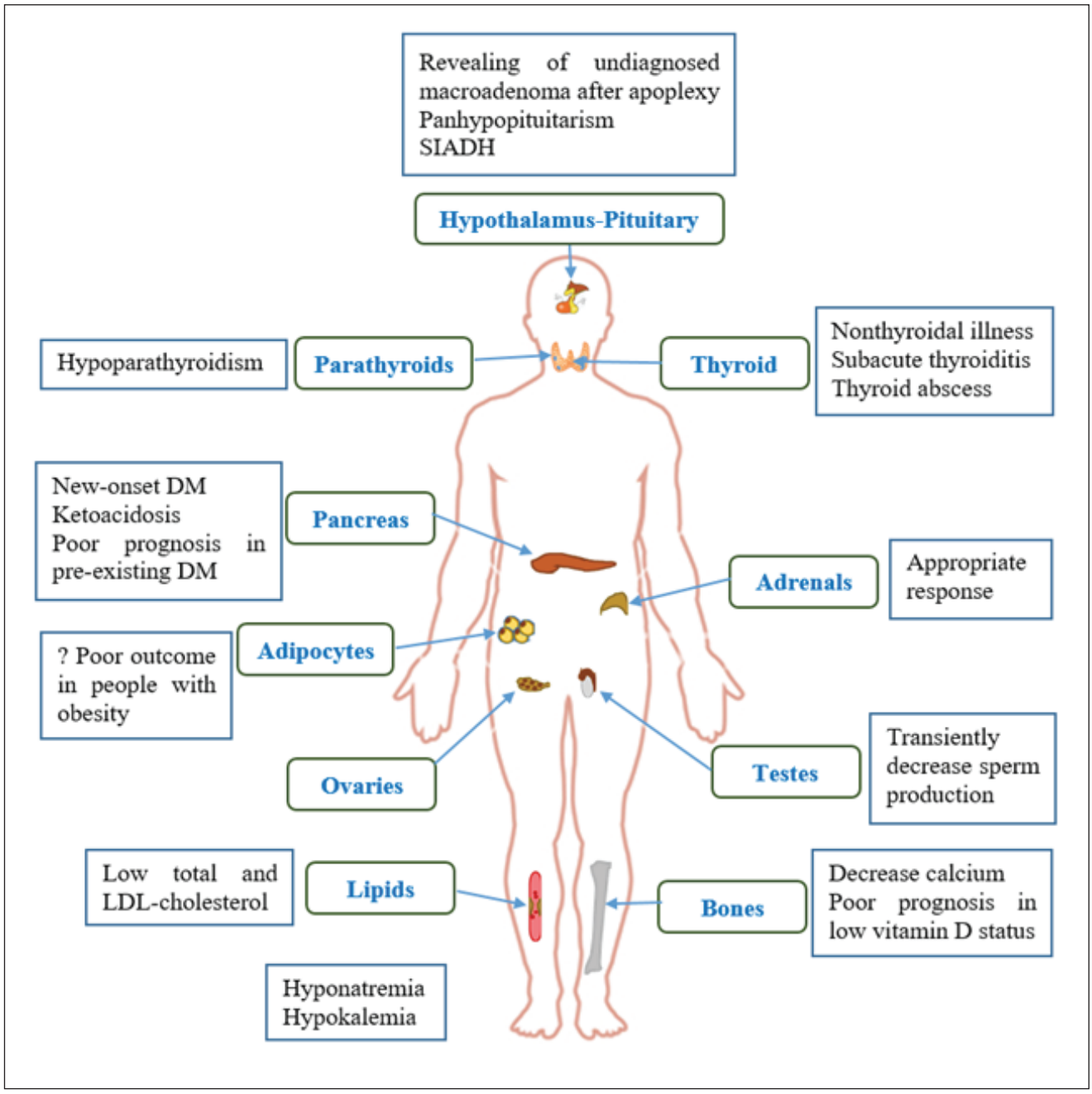


**Figure-2** Endocrine and metabolic involvement of dengue syndrome

Obesity is associated with endothelial, platelet, and immune dysfunction that facilitates viral entry and replication as well as vascular leakage promoting severe dengue.[12]

**Endocrine and metabolic manifestations of dengue syndrome**

**Pituitary:**

Clinically significant cases of pituitary involvement are very rare. Patients mostly presented with neurological features rather than endocrine manifestations following acute hemorrhage due to thrombocytopenia (apoplexy). Various hormone abnormalities (Excess- prolactin, growth hormone; Deficiency- all anterior pituitary) were discovered during presentation as a result of macroadenoma, indicating negligence.[13,14] Panhypopituitarism with empty sella after a long duration of infection suggests under-reporting.[15]

**Thyroid:**

Dengue may have a central suppressing effect on thyroid

functions without clinical manifestations and complete recovery (nonthyroidal illness).[16] However, a few cases reports showed subacute thyroiditis and it may happen in the background of autoimmunity.[17,18] Besides, dengue may precipitate thyroid storm and secondary infection with abscess formation may also occur.[19,20]

**Parathyroids:**
Primary hypoparathyroidism may be revealed during dengue infection.[21]

**Pancreas:**
Rarely, dengue causes DM by acute pancreatitis (including the destruction of beta-cells) by several mechanisms like- inflammation and its consequences, and molecular mimicry.[22] Even patients may present with diabetic ketoacidosis with hyperglycemia with normal glycemic status after recovery.[23]

**Adrenals:**
Appropriate cortisol responses occur according to the severity of the infection.[24,25] There is no benefit of corticosteroids in the prevention of disease progression, hospital admission, or mortality.[26]

**Testes:**
Sperm production may transiently reduce due to the reduction of the testosterone/LH ratio (subtle Leydig cell dysfunction).[27]

**Ovaries:**
No articles were found to describe the dengue infection on the ovaries. Menstruation during the infection may present with menorrhagia and dysmenorrhea.[28]

**Dyslipidemia:**
Blood and membrane lipids play important roles in the pathogenesis of dengue. The virus induces PCSK9 which may be associated with vascular leakage.[29] Several studies showed a negative association between the severity of dengue with total as well as LDL-cholesterol levels. The association with other lipid fractions is controversial.[30,31] Despite the reported antiviral properties of anti-lipid drugs in animal and in vitro studies, clinical benefits are not significant.[32]

**Bone metabolism:**
**Vitamin D:**
Vitamin D may be used as a marker of the severity of dengue. Due to its antiviral and immunomodulatory effects, vitamin D supplementation may be a possible therapeutic drug.[33] Genetic variants of the vitamin D receptor (VDR) are also associated with disease severity.[34] Similarly, VDR agonist may be another anti-dengue agent.[35]

**Calcium:**
Calcium has a role in immunity and platelet function. Hypocalcemia, although asymptomatic in most cases, has a negative association with the severity of dengue and mortality. Hypocalcemia may occur as a result of different mechanisms including reduced $Na^+$-$K^+$ ATPase and $Ca^{2+}$-ATPase activity, acquired parathyroid hormone deficiency, renal one-alpha hydroxylase insufficiency, reduced dietary vitamin D intake, and reduced dietary calcium intake.[36] The role of calcium supplementation in dengue is not well studied.[37]

**Electrolyte imbalance:**
Around one-third and one-fourth of patients may present hyponatremia and hypokalemia at admission respectively without any significant association with hospital stay or mortality.[38] The prevalence of electrolyte imbalance is higher in children.[39] The abnormalities occur at distribution levels which may be influenced by different hormones or endocrine-related drugs.[40]

## Conclusions
In conclusion, DM and hyperglycemia are the most relevant endocrine involvement in dengue syndrome. However, other glands may also be rarely involved and require a close follow-up to detect early for proper management.

**Conflict of Interest**
The author have no conflicts of interest to disclose.
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**Data Availability**
Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

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