

# Pentads and Hexads in Diabetes Care: Numbers as Targets; Numbers as Tools

## INTRODUCTION

Most international organizations accept 7% as a reasonable glycated hemoglobin (HbA1c) value to aim for, while managing diabetes.<sup>[1-3]</sup> These organizations also suggest targets for fasting plasma glucose (FPG) and postprandial plasma glucose (PPG) which should be achieved with optimal glucose-lowering treatment.<sup>[1-3]</sup>

The three parameters, HbA1c, FPG, and PPG, together form the glycemic triad.<sup>[4]</sup> An understanding of the deleterious effects of glycemic variability (GV), mediated in part through oxidative stress, later led to the creation of a unified glucose tetrad concept.<sup>[5]</sup> This helped in improving clinical decision-making and in planning therapeutic interventions.

## THE EARLY PENTAD

Further awareness of the needs of persons with diabetes informed the development of the glycemic pentad.<sup>[6]</sup> To the four glycemic parameters listed above, the pentad added quality of life (QoL). The glycemic pentad highlighted the importance of patient-reported outcomes (PROs) and underlined the relevance of the biopsychosocial model of health to diabetology. This pentad was a person-centered or patient-centered tool, meant to help achieve better outcomes. QoL was included as it is a measurable target, which contributes to long-term outcomes in diabetes care.

## THE GLYCEMIC PENTAD

However, it was felt that QoL was not a glycemic parameter in the strict sense, and its inclusion was not warranted in a list of glycemic targets. Discussion on this topic helped prepare another framework, with five glucose-related variables: HbA1c, FPG, PPG, minimal GV, and minimal hypoglycemia.<sup>[7,8]</sup> This rubric is justified as all five investigations listed are related to glycemia, are independently related to cardiovascular outcomes, and are important targets of glucose-lowering therapy.

## THE GLYCEMIC HEXAD

Fueled by enhanced focus on safety and tolerability of drugs, modern research has revealed subtle differences in the pathophysiology, presentation, and clinical implications of day-time hypoglycemia and nocturnal hypoglycemia. With this in mind, the glycemic pentad has been expanded to the glycemic hexad. The hexad lists three efficacy-oriented targets (HbA1c, FPG, and PPG) along with three safety-oriented goals (hypoglycemia, nocturnal

hypoglycemia and GV). The six-point concept has been published as the Glycemic Sixer,<sup>[9]</sup> a term which resonates with cricket playing nations.

## NUMBERS AS TOOLS

Number-based constructs such as the ones mentioned above are useful pedagogic tools, which also serve as frameworks upon which to plan and evaluate glucose-lowering therapy. Use of these models allows a treating physician to create a glucophenotype<sup>[10]</sup> or glucotype of an individual patient and choose the most appropriate therapy. The chosen treatment modalities help in achieving effective glucose control, in a safe and well-tolerated manner. This process has been facilitated by the development of modern insulin analogs, oral fixed-dose combination, and injectable glucagon-like peptide 1 receptors, which provide effective glucose control with low risk of hypoglycemia.

## COMPREHENSIVE THERAPEUTIC APPROACH

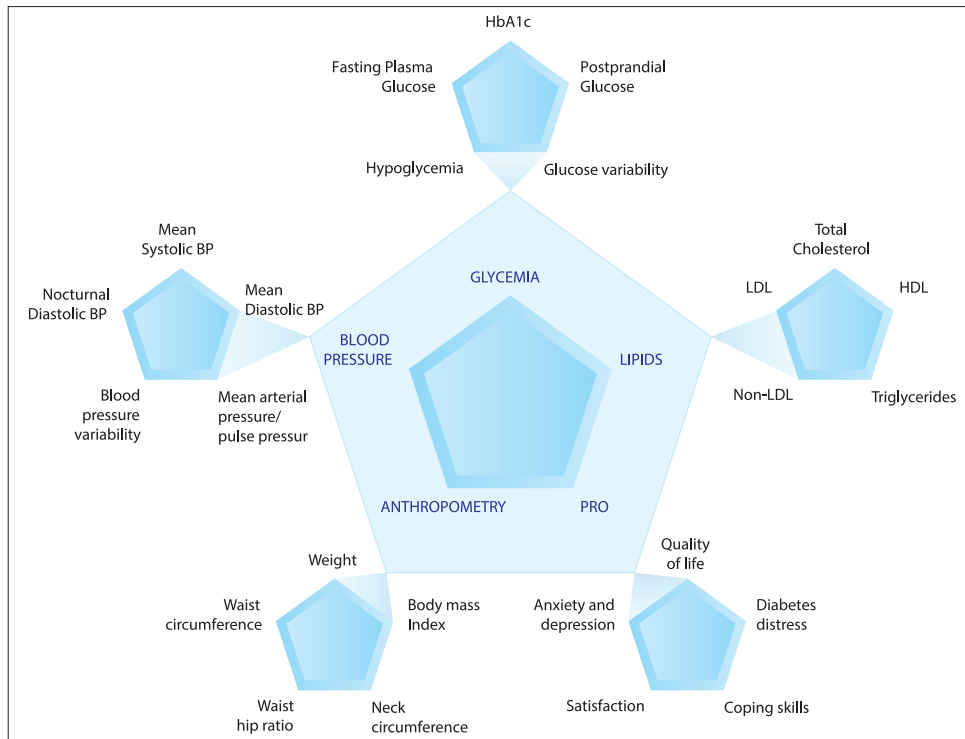
Diabetes management, however, is much more than glucose-lowering alone. The glucocentric approach, in fact, has long been abandoned in favor of a comprehensive one, which targets multiple metabolic pathways and systems. The four main vasculometabolic targets<sup>[11]</sup> in diabetes care can be listed as the Metabolic Quartet (HbA1c, blood pressure, weight, and lipids).

## THE THERAPEUTIC PENTAD

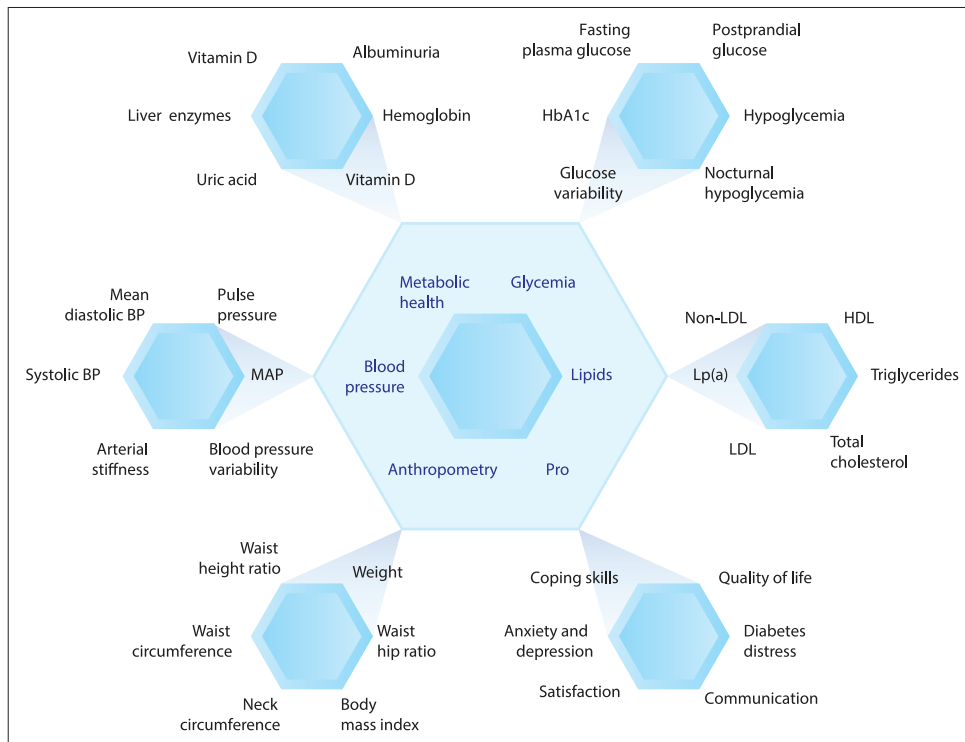
To this quartet, we suggest addition of PROs. Inclusion of PROs to this model reinforces patient-centered or person-centered care as a pillar of diabetes management. It reminds the physician that the person with diabetes care has a right to evaluate treatment regimens. This therapeutic pentad, or pentad of targets, provides guidance to the physician in planning management strategies [Figure 1].

## THE FIVE PENTUPLETS

Each angle of this pentad can further be expanded, to serve as a teaching tool. This taxonomic structure is similar to that used by the ancient Indian physician, Atreya, who propounded Atreya's quadruple.<sup>[12]</sup> His quadruple lists four components, which are essential for optimal medical outcome. These are the physician, patient, drug, and attendant. For each stakeholder, Atreya describes four properties, thus creating four equipowerful quadruplets. Similarly, we can embellish the therapeutic pentad and create five quintuplets, to provide a comprehensive list of



**Figure 1:** The therapeutic pentad and pentuplets. BP: Blood pressure, HDL-C: High-density lipoprotein-cholesterol, LDC-C: Low-density lipoprotein-cholesterol



**Figure 2:** The therapeutic hexad and hexuplets. BP: Blood pressure, HDL-C: High-density lipoprotein-cholesterol, LDC-C: Low-density lipoprotein-cholesterol, LP (a): Lipoprotein (a), MAP: Mean arterial pressure, PRO: Patient-reported outcome

targets that must be addressed in diabetes management. This serves as an exhaustive list of evidence-based end-points, which contribute toward improving both biomedical and psychosocial, health, in persons with diabetes.

### THE THERAPEUTIC HEXAD

Diabetology is an ever-evolving science<sup>[13]</sup> and its complexity is bound to grow. Insights into pathophysiology and salutogenic

**Table 1: Various glyceemic and therapeutic models in diabetes care**

Model	Component
Glyceemic triad	HbA1c, FPG, PPG
Glucose quartet	Triad + GV
The early glyceemic pentad	Quartet + QoL
Glyceemic pentad	Quartet + hypoglycemia
Glyceemic sixer/hexad	Quartet + hypoglycemia + nocturnal hypoglycemia
Therapeutic quartet	HbA1c, BP, cholesterol, body weight
Therapeutic pentad	HbA1c, BP, cholesterol, body weight, QoL
Therapeutic pentad, with quintuplets	Glycemia, BP, lipids, anthropometry, PROs
Therapeutic sixer/hexad, with sextuplets	Pentad + nonglyceemic metabolic health

HbA1c: Glycated hemoglobin, FPG: Fasting plasma glucose, PPG: Postprandial glucose, GV: Glyceemic variability, QoL: Quality of life, PROs: Patient-reported outcomes, BP: Blood pressure

factors of diabetes, coupled with pharmaceutical developments, will increase the range of targets in diabetes management. We therefore propose a therapeutic hexad, or sixer, with six accompanying sextuplets. The sixth angle that we add is metabolic health, which includes nonglyceemic investigations related to renal, hepatic, and metabolic parameters. The relationship of these “numbers” to cardiovascular outcomes is well documented and backed by evidence [Figure 2].

## FROM TOOLS TO TARGETS

The rubrics discussed in this editorial are not ends in themselves. Rather, they utilize a numerophile strategy to prepare teaching tools which are easy to understand, teach, and learn [Table 1]. We note, with appreciation, usage of these models at national level across South and Southeast Asia and efforts of experts to achieve concordance of existing therapies with our models.<sup>[14]</sup> The models convert complex theory into simple (but not simplistic) knowledge, which informs pragmatic clinical decision-making. This, in turn, helps achieve optimal health for persons living with diabetes.

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