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## Review

# Rising trend of diabetes mellitus amongst the undernourished: State -of- the -art review

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### ABSTRACT

Diabetes mellitus is prevailing in the malnourished populations congruently in well-nourished ones with an escalating trend in the former group regardless of the absence of obesity as an etiologic determining factor as per the studies in underprivileged sectors of the population. Chronic undernutrition across a lifetime may be an imperative stimulator of diabetes in an individual either by progressively reducing beta cell function alongside islet cell volume and increasing the individual predisposition to other genetic or environmental diabetogenic influences with modifying influence on the course of clinical syndrome. Ketosis resistant insulinopenia is irreversible to the sustained vigorous nutritional convalescence in a substantial fraction of malnourished subjects. It also debunks a latent diabetic stage with insulin resistance reflected by greater insulin requirement in comparison to the patients with type I diabetes with the same beta cell failure fraction and obese type II diabetic patients with equivalent glycemic control gauged by HbA1c levels. Current tendency warrants the replacement of conventional therapy by community oriented theranostic approaches and health programs to curb the epidemic.

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## 1. Introduction

The crescendos of diabetes mellitus (DM) have changed aggressively over the past decade. There is an estimated increase by 69% in number of adults with diabetes in developing countries and a 20% increase in developed countries between 2010 and 2030 along with urbanization. 75% of people with diabetes is weighed to be from developing countries by 2025 in comparison to 62% in 1995, with the largest figures from, India, China, and the united states [1]. Diabetes care which accounted for 12% of health expenditures in 2010 (\$376 billion) is expected to come close to \$490 billion by 2030. Augmented prevalence of the disease among the poor, previously acknowledged as “a disease of riches”, alongside health complications burden the economy of developing countries [2]. These findings procured from epidemiological studies project the prevalence of “diabetes epidemic” even if obesity levels remain persistent [3].

Conventionally, a low body weight and energy intake was accredited to decrease the diabetes risk. This perception was based on observations such as the moderate incidence of DM in Europe during the first and second world wars and the prevalence of Non-Insulin Dependent Diabetes Mellitus (NIDDM) in different countries, positively interconnected to the “average fatness” of the population [4–6]. In this context a study by Gupta et al. demonstrated that among urban Indians, rates of diabetes were 3.6% in subjects with a normal body weight and 1.5% in very lean subjects [7]. In 1965, the WHO Expert Committee on Diabetes Mellitus published that “the evidence that under nutrition protects adult populations from diabetes seems unassailable”. In addition, the Committee stated in its second report in 1980 that “in some societies, malnutrition is probably a major determinant of diabetes” [8]. Initial classification by WHO (1985) as malnutrition related diabetes mellitus (MRDM) is revamped by new terminology malnutrition modulated diabetes mellitus (MMDM). MMDM can be subdivided into protein deficient diabetes mellitus (PDDM) and fibrocalculus pancreatic diabetes (FCPD) [9]. It was speculated that whether continued protein deprivation would ultimately result in irreversible damage to  $\beta$ -cells, or would increase their vulnerability to harmful environmental influences [10]. Rao et al. investigated the results of a large study in India in which rates of diabetes were not significantly different between urban and rural subjects as evidence pointing to an association between diabetes and under nutrition, since most rural subjects were undernourished [11]. The objective of this review is to determine the alliance of under nutrition with the pathogenesis of diabetes mellitus.

## 2. Epidemiology of diabetes in undernourished populations

The kinship of diabetes to undernutrition is quite fuzzy. The hypothesis that undernutrition shelters a population from diabetes were inappropriately developed on indirect evidence available from early epidemiologic studies [12]. These studies demonstrated that food scarcity was responsible for the fall in diabetes prevalence, morbidity, and mortality seen during major wars and famine, e.g., the Paris siege of 1870 and the two World Wars [13]. Though dietary factors can clearly alter the prevalence of overt diabetes, several other environmental effects may quite equally be involved, including changes in life-style and in the amount of exercise and stress. As it is almost impossible to isolate the effect of the nutritional changes alone, no specific conjectures are substantiated. Moreover, diabetes mortality data may not exhibit the true prevalence of diabetes at such times [14].

Two studies have been specified which provide the best documentation for supposedly protective effect of undernutrition against DM. In the study of West and Kalbfleisch, the prevalence of

diabetes showed an excellent correlation ( $r=0.89$ ) with the relative body weights of populations from 10 different countries (moderate prevalence rates with the subnormal body weights). The second study in a cohort of subjects in Norway elicited a protective role of undernutrition in diabetes. During a 10-yr follow-up, the study demonstrated no individual with a body weight of less than 90% of the standard developed diabetes. Unfortunately, the number of subjects for the subnormal weight range was inadequate to justify these conclusions [15,16].

The epidemiologic interpretation of the diabetes-undernutrition relation is misidentified by the poor estimates of diabetes prevalence rates in countries with widespread undernutrition. Nationwide multicentric study on the occurrence of diabetes in India (1979) involving 35,000 subjects from all sections of the population (both urban and rural) contemplated absence of discrepancy in the prevalence of diabetes in rural and urban populations (1.9% and 2.4%, respectively) [17,18]. However, amongst a variety of traits that were considered, a poor nutritional status was not found to be collaborated with any minimization in the risk of developing diabetes. Allied findings are also reported in a study carried out in the Philippines in 1980 [19]. In contrast to the colossal prevalence of obesity in patients with NIDDM in the developed world (80–90%), the majority of patients with the same in developing word like India are underweight. Explanation to the query “whether the low body weights head up the onset of diabetes, or occur as a repercussion of it” is still elusive [10,20]. On the other hand surveys by Rao et al. in a chronically malnourished rural population in India concluded that the majority individuals affected by diabetes belonged to traditionally underprivileged category who consumed inadequate diets and is likely to have resulted in metabolic derangement involving DM [21]. In China, on the contrary, rural diabetes prevalence rates are reportedly much lower than those in urban areas and relatively three times higher in obese as compared with lean subjects. This study also highlights the vitality of racial and genetic involvements. The absence of any malnutrition-related syndromes suggests that malnutrition probably is not a dominant factor in the diabetes seen in China [22,23].

In the context of the aforesaid discussion, the high prevalence rate of diabetes in undernourished populations requires broad illustrations to interrogate the overwhelming status of obesity as the single most important environmental determinant of diabetes, ever since the time of Joslin [24]. Despite the virtual elimination of obesity as a significant risk factor in undernourished populations, the risk of developing diabetes is not minimized. These controversies theorize that diabetes is present at least as intermittently in undernourished individuals as it is in well-nourished individuals and obesity is replaced in undernourished populations by some other risk factor that precipitates diabetes [25].

## 3. The influence of undernutrition on the endocrine pancreas

### 3.1. Glucose tolerance and insulin reserve

Chronic undernutrition can significantly impair beta cell function, which is often irreversible permanent despite nutritional rehabilitation and cumulative nutritional insults over a lifetime may lead to overt diabetes. As per the “something inherited, something added” hypothesis for the pathogenesis of diabetes, suggested by Cerasi and Luft, undernutrition might trigger overt diabetes in a genetically predisposed individuals [26]. It can also act indirectly by increasing the susceptibility of the beta cell to the immunological destruction, environmental beta cytotoxic influences and dietary toxins, evidenced by the co-existence in various autoimmune disease conditions. A synopsis of the probable strata of interaction between chronic undernutrition and diabetes is shown in Fig. 1.

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