IS RENAL INVOLVEMENT RELATED TO BIRTH WEIGHT AND ADULT HEIGHT?

E. VESTBO (1, 2), N. DE F. OLIVARIUS (2), C.E. MOGENSEN (1)

(1) Medical Department M, Århus Kommunehospital, Århus University Hospital, Århus, Denmark.
(2) Central Research Unit and Department of General Practice, University of Copenhagen, Copenhagen, Denmark.

For several years it has been discussed whether birth weight is an independent risk factor for the development of diabetic nephropathy, type 2 diabetes mellitus, and cardiovascular disease [1].

Diabetic patients

Low birth weight has been described as a risk factor for the development of diabetic nephropathy in Type 1 diabetic women, whereas low birth weight did not increase the risk of diabetic nephropathy in Type 1 diabetic men [2]. However, another study of Type 1 diabetic patients found that increased risk of nephropathy was explained by other familial and perinatal factors including maternal smoking during pregnancy, and low-level maternal education [3]. In Pima Indians, Type 2 diabetic subjects with both low and high birth weight had increased risk of elevated urinary albumin excretion [4].

Risk for the development of diabetes

Low birth weight, especially in combination with a family history of diabetes, increases the risk of Type 2 diabetes [5]. Also, in a large study of US men low birth weight increased the risk of diabetes [6]. In a Swedish study the interaction of thinness at birth and high adult body mass index increased the risk of Type 2 diabetes [7]. A study of twin pairs discordant for Type 2 diabetes found that in both monozygotic and dizygotic twins, the twins with Type 2 diabetes had significantly lower birth weight than the non-diabetic twins [8]. However, subjects suffering from intrauterine malnutrition due to siege during the Second World War were not more glucose intolerant than controls [9].

Non-diabetic subjects

In non-diabetic subjects birth weight has been associated to cardiovascular disease. Self-reported low birth weight was associated with increased risk of cardiovascular disease in women [10]. In a large study of Swedish men born 1915 – 29 low birth weight increased the risk of death from ischaemic heart disease [11]. In pregnancy maternal hypertension was increased if the mother herself had been small for gestational age [12]. The low birth weight of the mother could be caused by a genetic predisposition for the development of hypertension. Self-reported low birth weight increased the risk of hypertension in women [13], but self-reported birth weight may be biased.

A more atherogenic pattern of cardiovascular risk factors, including high fasting blood glucose and insulin and low high density lipoprotein was found in women aged 60-71 years with low birth weight compared to women with high birth weight [14]. This study may, however, include a bias of selection as no data were obtained from the women who had died before the age of 60 years. Also school children with low birth weight had relatively high systolic blood pressure and glycated haemoglobin level [15].

However, all these results and hypotheses have been challenged by several groups. Growth retardation due to twin pregnancies did not increase mortality when compared to the general population [16]. Twins had neither increased risk of ischaemic heart disease nor increased risk of deaths from ischaemic heart disease when compared to singletons [17]. In a Danish
population-based study, birth weight was not found to be correlated to known cardiovascular risk factors [18].

**ADULT HEIGHT AS RISK FACTOR**

Birth weight and birth length are predictors of adult height [19]. Also adult height has been described as associated with diabetic nephropathy. A paper of the present volume of this journal presents results based on data from a well-defined background population. Height was inversely related to renal involvement in newly diagnosed middle-aged and elderly diabetic females [20].

The relationship between height and urinary albumin concentration is of special interest because microalbuminuria is a risk marker for several diseases. Microalbuminuria is a predictor for the development of overt proteinuria in Type 1 [21] and Type 2 diabetic patients [22], and several studies have shown that proteinuria predicts cardiovascular mortality in diabetic patients [22-26]. In non-diabetic subjects too, elevated urinary albumin excretion has been associated with preterm death [27], cardiovascular disease [28], and ischaemic heart disease [29].

**Diabetic patients**

An inverse association between height and diabetic nephropathy has also been found in Type 1 diabetic men [30]. The same group found in a prospective study of Type 1 diabetic patients that low height was a risk factor for all-cause mortality when adjusted for confounders, and in men height was inversely related to the severity of albuminuria [31].

**Non-diabetic subjects**

In a 12-year follow-up study, women who developed diabetes were shorter than women who remained non-diabetic [32]. In the Nurses’ Health Study non-diabetic subjects showed an inverse relation between height and the risk of cardiovascular disease [33]. In the shorter women mortality from cardiovascular disease was increased compared with women with average height [34]. Among women who had been hospitalized for cardiovascular heart disease, the patients who had recurrent cardiac events were shorter than women without recurrent cardiac events when followed 3-6 months after hospitalization [35]. This population was highly selected, and the subjects were only followed for a short period. Also in males an inverse trend between height and risk of cardiac heart disease has been described, even after adjustment for confounders including age and smoking status [36]. In a large epidemiological study of males, subjects with cardiac heart disease were shorter than subjects without cardiac heart disease, whereas no difference was found in the height of males with stroke compared to males without stroke [37]. In a highly selected group of students whose fathers had died of cardiac heart disease before the age of 55 years, men, but not women, were shorter than controls [38]. Also in a cross-sectional study, non-diabetic microalbuminuric men were shorter than normoalbuminuric men, whereas no association was found in women [39]. Another group did not find any association between height and urinary albumin excretion in a similar, but larger study [40]. Gunnell et al. found that cardiac heart mortality decreased with increasing childhood leg length in women only. The authors argued that childhood socioeconomic class was an important factor for leg length and for cardiac heart disease [41]. Some of the studies mentioned above did not control for social class [30, 32, 33, 39]. In the NHANES I study, the inverse relation between height and cardiovascular disease disappeared when the analysis was adjusted for age and years of education [42].

**Confounders**

Determinants of adult height are genetic and environmental, including social class [43]. Therefore, social class is an important confounder in these studies. A positive relation between birth weight and socioeconomic status is described [44]. Adult height increased with both educational attainment [45] and (high) social class during a lifetime [46]. Low socioeconomic status in childhood was associated with increased risk of cardiovascular disease in adulthood [47], low educational level was related to a more atherogenic pattern of cardiovascular risk factors [48], and low social class over a lifetime increased the risk of premature death [46].

Also, age is a most difficult confounder to handle because height declines with age. In a longitudinal study of healthy women, the height loss was 0.224 mm/year in the span 43-57 years [49]. The generation effect of increasing adult height over three decades counterbalanced the height loss with aging. The women, however, were followed only to the age of 57 years, and height loss accelerates with increasing age, amounting to 8 cm from age 30 to 80 years for women [50].

In conclusion, many studies find associations between birth weight or adult height and diabetic nephropathy, diabetes, or cardiovascular disease. The underlying mechanism remains unknown. The clinical importance of these relations may be less than other risk factors for the development of these diseases. Birth weight and height cannot be modified by the subjects when first achieved, whereas well-known risk factors such as obesity, hypertension, metabolic control, and smoking can be modified. Based on these results pregnant women should be treated under conditions minimising the risk of growth retardation of
the fetus. However, to prevent the complications of Type 2 diabetes in the clinical work, we have to obtain adequate treatment of hyperglycaemia, hypertension, and dyslipidaemia, and to reduce obesity and smoking.

REFERENCES

20 Olivarius NdeF, Vestbo E, Andreasen AH, Mogensen CE. Renal involvement is related to body height in newly diagnosed diabetic women aged 40 years or over. Diabetes Metab, 2001, xxxxx.


