We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

4,800
Open access books available

122,000
International authors and editors

135M
Downloads

Our authors are among the

154
Countries delivered to

TOP 1%
most cited scientists

12.2%
Contributors from top 500 universities

WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com

10

Obesity in the Natural History of Type 1 Diabetes Mellitus: Causes and Consequences

Fernando Valente[1], Marília Brito Gomes[2] and Sérgio Atala Dib[1]
[1]*São Paulo Federal University, São Paulo*
[2]*State University of Rio de Janeiro, Rio de Janeiro*
Brazil

1. Introduction

There has been a worldwide epidemic increasing in the prevalence of sedentary, overweight and obesity that comes with modernity and urbanization (Wang et al., 2002). The consequence is the development of insulin resistance (IR) and type 2 diabetes (T2D). This is classically defined as a metabolic disease that occurs due to a higher IR that leads to a slow setting of lower insulin production (more relative than absolute), in general in adult age. T2D is associated also with a genetic predisposition. The majority of T2D individuals are overweight or obese and the ones who do not, at least present increased abdominal adipose mass (ADA, 1997). The rising prevalence of overweight and obesity is happening also in children and adolescents (Pinhas-Hamiel et al., 1996; Willi & Egede, 2000; Rosenbloom et al., 1999). The metabolic syndrome (MS), which physiopathology is based on IR, shows the same trend in children and adolescents (Jago et al., 2008), as well as isolated pre-diabetes (Li et al., 2009).

In parallel, it has been seen an elevation in the number of type 1 diabetes (T1D) cases and its establishment at a younger age (EURODIAB ACE Study Group, 2000). T1D is characterized primarily by a pancreatic beta cell destruction, which may lead to ketosis. It can be classified as autoimmune (with positive anti-islet, anti-insulin, anti-GAD, anti-IA2 and/or anti-IA2 beta antibodies) or idiopathic, in which no autoantibodies can be detected, and occurs more frequently in individuals of African-American or Asian origin. Multiple genetic predisposition and environmental factors are involved with T1D (ADA, 1997). At least one of those autoantibodies is present in 85-90% of T1D on diagnosis. The treatment for T1D consists of multiple insulin injections, known as intensive treatment, to obtain adequate glycemic control and therefore prevent micro (The DCCT Research Group, 1993) and macrovascular (Nathan et al., 2005 and 2003) chronic complications. However, it can be followed by weight gain most of the times (Arai et al., 2008), which can amplify the risk of cardiovascular disease (CVD) in spite of good glycemic control. This weight gain can start on puberty and persist along adulthood (Särnblad et al., 2007). Therefore, some of these patients present clinical features of both T1D and T2D, confounding its classification. This phenotype was initially called double diabetes (DD) (Libman & Becker, 2003; Becker et al.,

2001), and is characterized by positive pancreatic autoantibodies in patients with clinical features of T2D, as IR and overweight and/or obesity (Pozzilli & Buzzetti, 2007; Gilliam et al., 2005; Reinehr et al., 2006), as shown in Table 1 (Pozzilli & Buzzetti, 2007) and in Figure 1.

	T1D	DD	T2D
Age at disease onset	Childhood +++ Adolescence +++ Adult +	Childhood ++ Adolescence ++ Adult (LADA) +	Childhood + Adolescence ++ Adult +++
Major genetics predisposition	MHC class I and II, *InsVNTR*, *CTLA-4*, *PTPN22*	?	*APM1*, *PPARγ 2*, *PtdCho-1*, *TCF7L2*
Environmental factors	Diet, viruses Cow´s milk in infancy	Life style (diet, sedentary life)	Life style (diet, sedentary life)
Circulating antibodies to β cells	+++	+	-
T cell-mediated immunity to β cells	+++	++	-
C-peptide secretion	-	+	+++
IR	-/+	++	+++
Inflammatory markers (cytokines, adipokines)	+	++	+++
Macrovascular complications	+	++	+++

Table 1. Clinical and pathogenic features of DD compared to T1D and T2D (Pozzilli & Buzzetti, 2007).

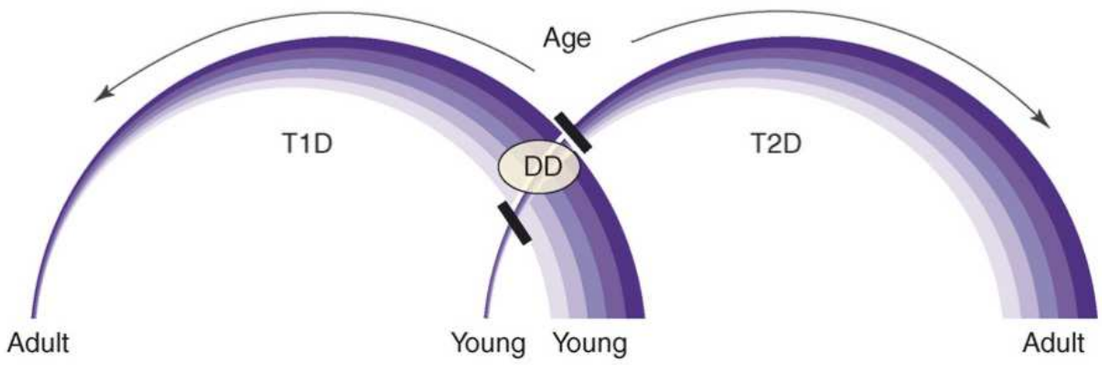


Fig. 1. Schematic representation showing where DD lies in respect to age and the two types of diabetes, as illustrated by two 'rainbows' (Pozzilli & Buzzetti, 2007).

2. Obesity as a accelerate factor to type 1 diabetes mellitus development

Studies with streptozotocin-induced diabetic baboons showed that to have an abnormal glucose tolerance it is necessary an isolated huge loss of beta-cell mass or a moderate loss of these cells associated to an IR (McCulloch et al., 1991), that could be in humans the physiologically IR of adolescence (Acerini et al., 2000) or gestation (Buschard et al., 1987), periods with higher incidence of T1D, or pathological situations like infection (usually one of the triggering factors of T1D) or weight gain.

Others studies suggest that the increase in the body mass index (BMI) and the consequent IR may accelerate the β cell destruction process in individuals predisposed to T1D, due to the release of obesity-related cytokines that show inflammatory and/or immunomodulatory properties (Aldhahi & Hamdy, 2003), triggering diabetes. This hypothesis may be reinforced by one study that correlated high anti-GAD levels with high BMI (Rolandsson et al., 1999). Two interesting data from studies with non-obese diabetic (NOD) mice are that hyperinsulinemia, an IR marker, precede clinical T1D (Armani et al., 1998) and that T1D incidence falls after treatment with rosiglitazone, an insulin sensitizer drug (Beales & Pozzili, 2002).

The IR, autoimmunity and apoptosis of the β cells constitutes the three factors of the called "accelerator hypothesis", proposed by Wilkin (Wilkin, 2001), that contemplate the factors presented in both more common types of diabetes, that is, T2D and T1D. There is a constitucional (intrinsic) high speed of apoptosis of β cells that is necessary to the development of diabetes, but rarely enough. The other two factors, extrinsic, that can speed the apoptosis of beta-cells are IR (result of weight gain and/or physical inactivity) and autoimmunity against beta-cells.

It is known that obese individuals have elevated serum levels of leptin, a cytokine secreted by adipocytes in proportion to adipose tissue mass and that is responsible, among other functions, for regulating food intake and thus BMI. Moreover, leptin controls the cellular immune response and is involved in the pathogenesis of autoimmune diseases (Lord, 2002). Studies have shown that administration of leptin in NOD mice promoted an early inflammatory infiltrate in the pancreatic islets, increased production of interferon gamma (IFN-gamma) by T lymphocytes, which accelerated the establishment of a T1D (Matarese, 2002 e 2005).

On the other hand, adiponectin, another important cytokine produced by adipose tissue, inversely proportional to its fat mass, can decrease the systemic and pancreatic islets inflammatory process, acting as a protective factor in the development of T1D, in addition to reducing IR (Kadowaki et al., 2006; Wellen & Hotamisligil, 2005).

However, development report (OECD, 2009) from 16 countries does not show any obvious relationship between national estimates of childhood obesity prevalence and incidence rates of T1D (Table 2). Therefore, obesity does not account for the wide between-country differences in T1D incidence, which range from 0.57 per 100 000 person-years in China to more than 48 per 100 000 person-years in Sardinia and Finland in the 0- to 14-year age group (Daneman, 2006).

On the other hand, in a meta-analysis of nine studies (eight case–control studies and one cohort study) comprising a total of 2658 cases (Verbeeten et al., 2011), seven reported a significant association between childhood obesity, BMI or %weight-for-height and increased risk for T1D. Four of these studies reported childhood obesity as a categorical exposure and

produced a pooled odds ratio of 2.03 (95% CI 1.46–2.80) for subsequent T1D, but with age at obesity assessment varying from age 1 to 12 years (Figure 2). A dose–response relationship was supported by a continuous association between childhood BMI and subsequent T1D in a meta-analysis of five studies (pooled odds ratio 1.25 (95%CI 1.04–1.51) per 1 SD higher BMI) (Figure 3).

Country	T1D incidence rate in children aged 0-14 years (per 100.000 person-years)	% of children aged 11-15 years overweight or obese
Finland	57,4	15,8
Sweden	41	10,5
Norway	27,9	10
UK	24,5	12
Denmark	22,2	9,7
Canada	21,7	21,3
USA	20,8	29,8
Netherlands	18,8	8
Germany	18	12
Ireland	16,3	14,2
Iceland	14,7	14,5
Spain	13	16,7
Poland	12,9	11,2
France	12,2	10,5
Greece	9,9	18,8
Italy	8,4	18,3

Table 2. Relationship between Type 1 diabetes incidence and prevalence of childhood overweight or obesity in 16 Organization for Economic Co-Operation and Development (OECD) countries, from Health at a Glance 2009: OECD Indicators (OECD, 2009).

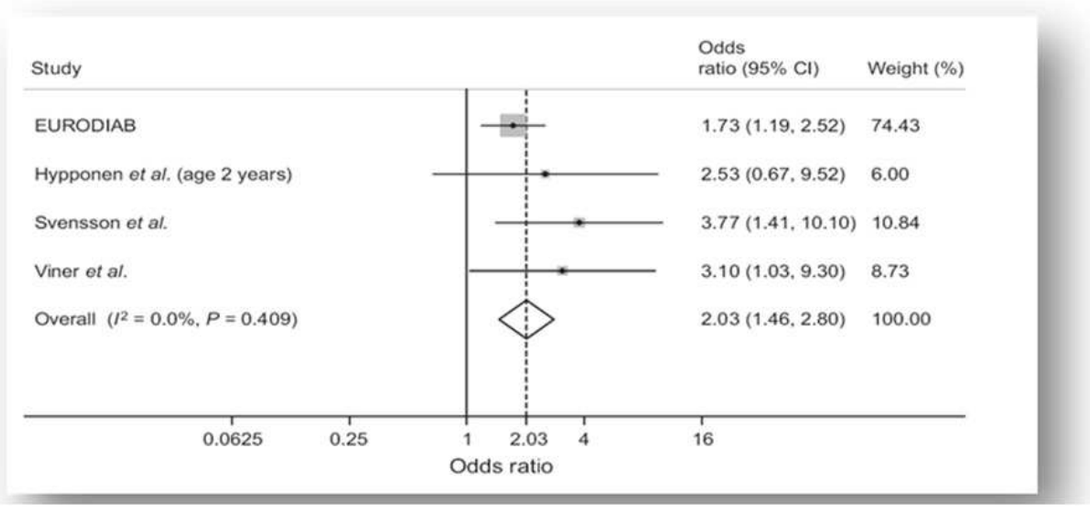


Fig. 2. Meta-analysis (fixed-effects inverse variance model) of studies of childhood obesity as a risk factor for subsequent T1D (Verbeeten et al., 2011).

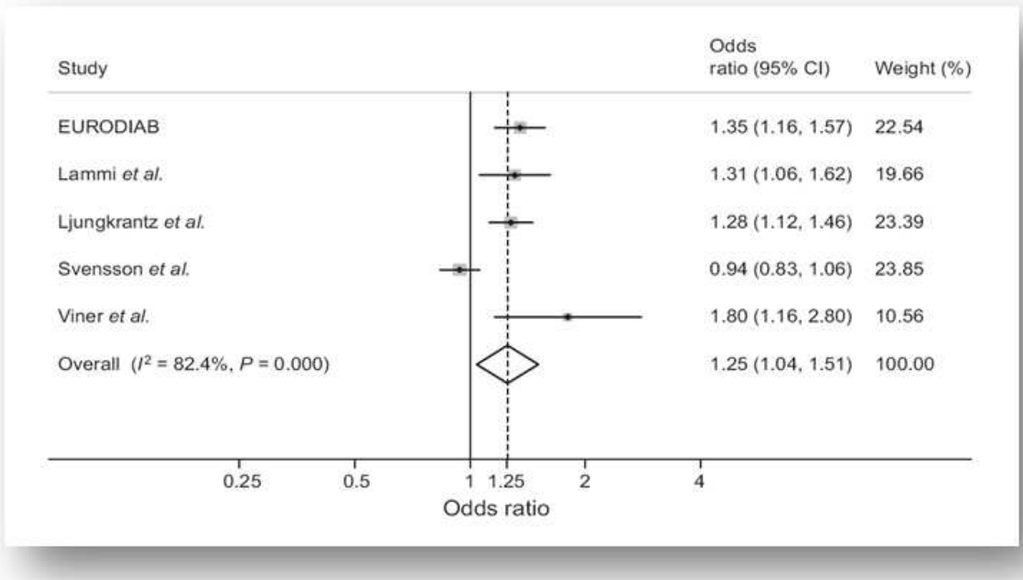


Fig. 3. Meta-analysis (random-effects inverse variance model) of studies of childhood BMI as a risk factor for subsequent T1D. Odds ratios correspond to a 1-unit increase in BMI standard deviation score (SDS)(Verbeeten et al., 2011).

3. Obesity after clinical Type 1 diabetes diagnostic

If on one hand intensive insulin prevents microvascular and macrovascular complications associated with poor glycemic control, the other brings an increased risk of severe hypoglycemia and weight gain, traditionally viewed as a normalization of weight, i.e. the correction of glycosuria, diuresis, and wasting with the initiation of insulin therapy. Insulin stimulates lipogenesis, inhibits protein catabolism, and slows basal metabolism. Other important aspect is the abnormal physiological route of insulin via its peripheral administration in those with T1D, which is also associated with reduced energy metabolism (Charlton & Nair, 1998). Classically normal or underweight, the phenotype of the T1D individuals is thus changing. A follow-up of 18 years of 589 individuals from the Pittsburgh Epidemiology of Diabetes Complications Study (EDC), a cohort of childhood-onset T1D, showed an increase in the prevalence of overweight by 47% (from 28.6% at baseline to 42%) and of obesity by sevenfold (from 3.4% at baseline to 22.7%), concomitantly with the highest prevalence of intensive insulin therapy - 7% and 82% were on intensive insulin therapy (≥ 3 insulin injections per day or on insulin pump) at baseline and 18 years after, respectively (Conway et al., 2010). Although injection frequency increased, total daily insulin dose decreased from 0.76 to 0.62 U/kg/day. Figure 4 shows the temporal patterns in the prevalence of being overweight and obese and the use of intensive insulin treatment, and these data was not influenced by the aging of the cohort and survivorship, as can be seen on Table 3. (age-group-specific prevalence for the 40–49-year-old age group by time period): overweight or obesity were present in 25% of the T1D individuals in 1986–1988 and in 68.2% in 2004–2007 (Conway et al., 2010).

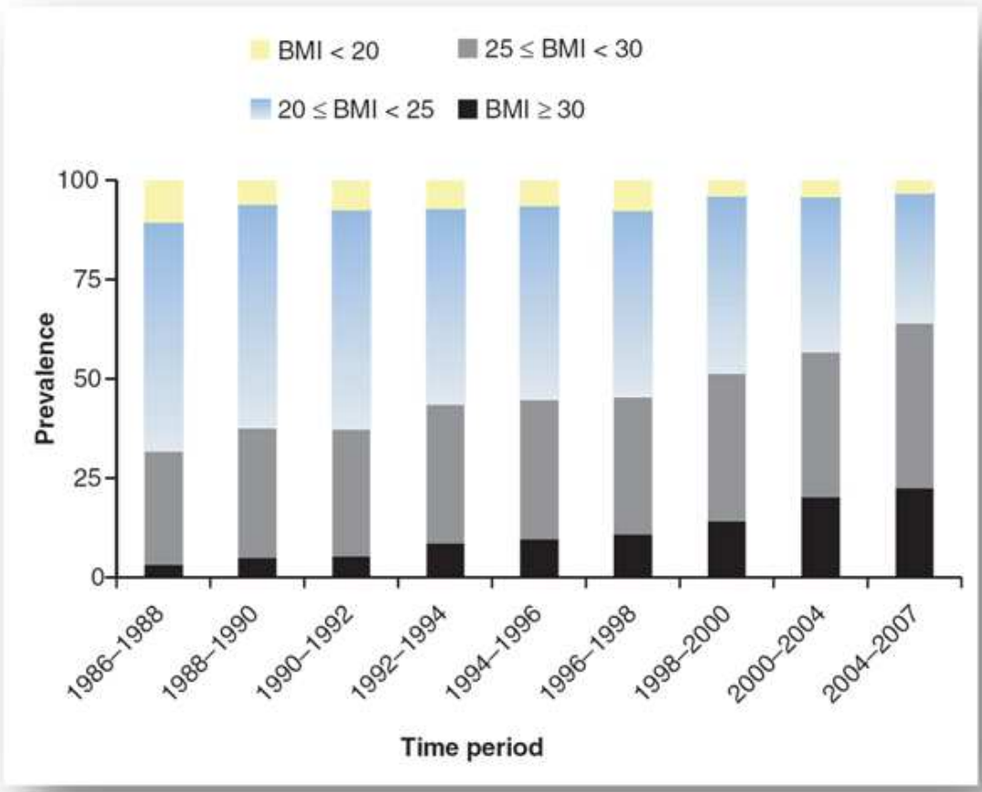


Fig. 4. Temporal patterns in overweight and obesity in Type 1 diabetes (Conway et al., 2010).

	BMI < 20 kg/m² (underweight)	20 ≤ BMI < 25 kg/m² (normal weight)	25 ≤ BMI < 30 kg/m² (overweight)	BMI ≥ 30 kg/m² (obese)
1986–1988	4 (9.1)	29 (65.9)	10 (22.7)	1 (2.3)
1988–1990	3 (5.8)	29 (55.8)	17 (32.7)	3 (5.8)
1990–1992	6 (8.5)	43 (60.6)	18 (25.4)	4 (5.6)
1992–1994	10 (12.2)	39 (47.6)	27 (32.9)	6 (7.3)
1994–1996	14 (11.9)	58 (49.2)	35 (29.7)	11 (9.3)
2004–2007	5 (2.9)	50 (28.9)	79 (45.7)	39 (22.5)

Table 3. Age-specific prevalence of underweight, normal weight, overweight, and obese for those aged 40-49 years in each time period, n (%)(Conway et al., 2010)

The prevalence of overweight/obesity in this T1D population was lower at baseline than general population (31.9 vs. 55.9%), although the incidence in both was similar after a mean of 7 years' follow-up (12%), and after 18 years' follow-up the prevalence of overweight in T1D people appear to have increased at a faster pace than in the general population.
Predictors of weight change were a higher baseline HbA1c, symptomatic autonomic neuropathy (inversely), overt nephropathy (inversely), and going onto intensive insulin therapy during follow-up. By the end of this study, 24% of the T1D people had died. Thus, as overt nephropathy and symptomatic autonomic neuropathy are associated with weight loss, the survivors are biased toward weight gain. The EDC Study also showed that, in T1D with a higher baseline HbA1c, moderate weight gain did not adversely affect the cardiovascular risk profile and favorably influenced the lipid profile in the setting of ameliorated glycemic control, but increased LDL cholesterol levels in the absence of a major improvement in glycemic control (Williams et al., 1999). Subjects who gained the least weight had the lowest LDL cholesterol levels at the follow-up period regardless of changes in HbA1 category. But when the weight gain after insulin was great, case of part of the patients who received intensive treatment in the Diabetes control and complications trial (DCCT) study and placed in the highest quartile of change in BMI, there was unmasking of central obesity or even MS in T1D (Purnell et al, 1998). These patients gained an average of 14 kg during the course of the study, about twice the weight gain equivalent to the third quartile of intensive care and the last quartile of patients on conventional treatment. Patients with the highest weight gain had the highest values of waist-hip ratio, blood pressure and insulin requirements when compared to the group with the same degree of glycemic control and also in intensive care, but who did not gain much weight. These youngsters also had a relatively atherogenic lipid profile, with elevations to levels of triglyceride, LDL cholesterol and apolipoprotein B (apoB) compared to their peers, also intensively treated, but without similar weight gain. The DCCT study (Purnell et al., 2003) also showed that the presence of family history of T2D was one of the strongest predictors for the weight gain in individuals with T1D who underwent intensive insulin therapy in the DCCT. In individuals with a family history of T2D, the weight gain, the final weight, the central fat distribution assessed by waist circumference, the insulin dose (units/kg/day) and degree of dyslipidemia were higher than in those without history familial T2D. Dyslipidemia included increases in triglycerides (TG) in VLDL particles and IDL (intermediate-density lipoprotein), which changes are common in individuals with central adiposity (Terry et al., 1989) and T2D (Brunzell & Chait, 1997). This could correspond to the expression of genes predisposing to T2D in this population. The findings of this study support the hypothesis that insulin treatment allows the expression of various components of MS in individuals with T1D who have family history of T2D, but also suggests that this group should be monitored more closely and earlier in relation to their potential of developing macrovascular complications, which is responsible for most of the increase in mortality found in patients with T1D (Laing et al., 1999), more than three times the general population.

4. Type 1 diabetes and Metabolic Syndrome

The insulin resistance is a soil to MS development and it is present during T1D evolution, even because of weight gain or because of the glucotoxicity – there was shown a proportion

between fasting glycemic and IR, and improvement of glycemic control is linked to better insulin sensitivity, for example contributing to the so-called period of "honeymoon", the remission phase of diabetes, well known by clinicians, and may occur in up to 50% of patients during the first year of disease (DCCT Research Group, 1987). Yki-Jarvinen et al. (1986), studied insulin sensitivity using the hyperinsulinemic euglycemic clamp in 15 adult patients with T1D and normal BMI during the first 2 weeks, 3 months and 1 year after clinical diagnosis. In the first two weeks of diagnosis, they had a decrease in insulin sensitivity when compared to controls. However, three months after diagnosis, there was an improvement in insulin sensitivity in these patients, and it became similar to that of controls. Importantly, this improvement in insulin sensitivity coincided with the period of "honeymoon" in these patients, and showed a good correlation with HbA1c values and insulin doses in the treatment. Insulin sensitivity of patients who entered clinical remission was 40% greater than those who did not have this condition. Recently, our group performed a cohort and multicenter study (Gabbay et al, 2005; Dib, 2006) to determine the prevalence of MS in a group of patients with T1D and assessing their relation with the time of diagnosis. The study included 524 (276 females) T1D (according to the criteria of the Brazilian Diabetes Society and American Diabetes Association) with an average age of 20 ± 9 years and divided according to the time of T1D in 4 groups: GI, ≤ 5 years (n = 264), G-II, 6-10 years (n = 108), G III, 11-15 years (n = 96) and G IV,> 15 years (n = 56). In these groups were analyzed BMI (kg/m^2), total daily doses of insulin for treatment (U/kg/day), HbA1c values and the prevalence of MS. The criterion used for characterization of MS was the one of the World Health Organization, that is, diabetes mellitus and 2 or more of the following: increase in waist circumference (criterion set for youth) (Freedman et al., 1999), TG ≥ 150 mg/dL or HDL-C < 40 mg/dL (males) and < 50 mg/dL (females), urinary albumin excretion (≥ 20 µg/min) and hypertension (according to criteria adjusted for age and sex) (Brazilian Hypertension, Heart and Nephrology , Societies 2002). The daily insulin dose and HbA1c values were significantly lower in G-I than in other groups (G-I: 0.7 ± 0.3, G-II: 1.1 ± 0.3, G-III: 1.0 ± 0.3 and G-IV: 0.8 ± 0.2 U/kg/day, p = 0.000) and (G-I: 8.7 ± 2.6, G-II: 9.5 ± 2.2, G-III, 9.5 ± 2.3 and G-IV: 9.4 ± 2.8%, p = 0.000), respectively. There was a significant increase in the values of waist circumference (G-I: 71.9 ± 2.2, G-II: 75.7 ± 11.1, G-III: 76.5 ± 8.4 and G-IV: 80.2 ± 7.5 cm, p = 0.000) and BMI (G-I: 20.6 ± 3.8, G-II: 22.4 ± 3.6, G-III: 22.5 ± 3.1 and G- IV: 23.1 ± 4.1 kg/m2, p = 0.000) after 5 years of diagnosis of T1D. However, it is important to note that the BMI values were not superior to classical criteria of obesity or even overweight. The prevalence of MS (G-I: 5.1, G-II: 11.2, G-III: 18.9 and G-IV, 31.5%, p = 0.000) increased with time of diagnosis (Figure 5). The odds ratio (OR) for the development of MS in the other groups in relation to G-I was significant G-III onwards, being equal to 3.59 and 7.18 for this for G-IV in relation to G-I, both with p = 0.001. That is, the odds for the development of MS in patients with T1D and over 15 years of diagnosis is 618% higher than under 5 years of disease. Similarly, the odds for the development of MS for patients with T1D between 11 and 15 years duration is 259% higher than those with less than 5 disease in this group of patients. Other factors related to insulin resistance, such as visceral fat, BMI and TG, even when considered separately, also increased with the duration of the disease.

In another study (Giuffrida et al., 2005), 500 T1D patients [age 19.7 ± 8.9 years (mean ± SD), 52% female], we observe that, also analyzed separately, the prevalence of microalbuminuria (GI: 24.1%, G-II, 25.0%, G-III: 31.0% and G-IV: 55.6%, p <0.05) and hypertension (GI, 8.3%;

G-II: 13.6%, G-III: 28.6% and G-IV: 44.4%, p = 0.000) increased with duration of disease. Data from these studies suggest that chronic glucotoxicity (elevated HbA1c) and factors involved in diabetic nephropathy (microalbuminuria and hypertension) may be one of the mechanisms for the development of MS in T1D, among many others.

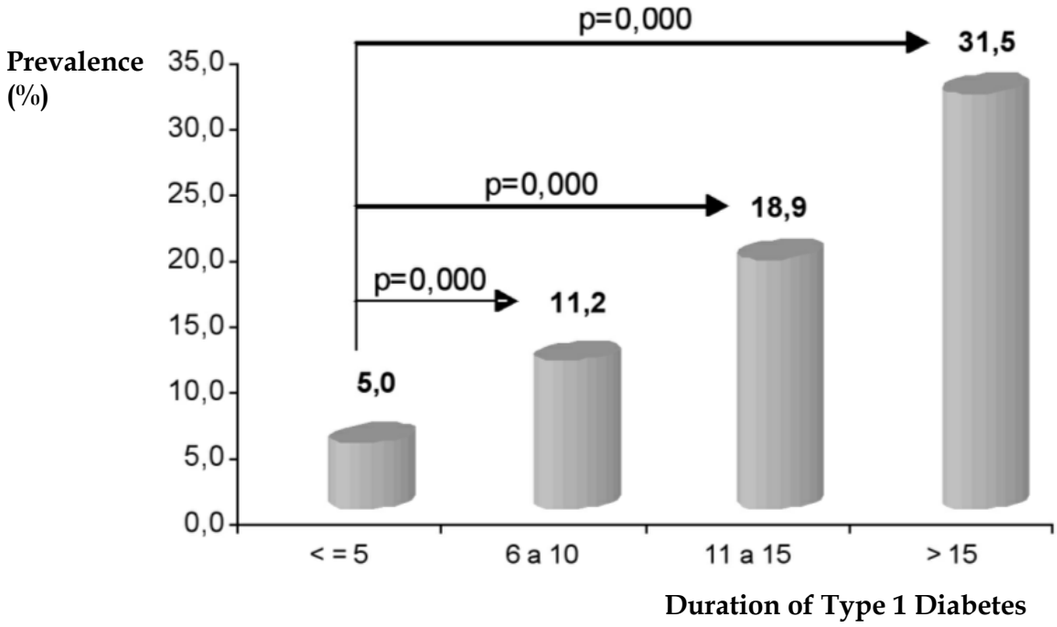


Fig. 5. Prevalence of MS in patients with T1D, according to disease duration. (Dib, 2006)

Aiming to compare the prevalence of MS using the ATP III criteria modified for age in our group of T1D, we studied 521 (51.2% female, age 20 ± 9 years; time of diagnosis of diabetes: 7.7 ± 6.9 years and HbA1c: 9.0 ± 2.4%) and found that this was equal to 12% (unpublished data).

The lowest concentration in the insulin in the liver causes a decrease in the synthesis of GHBP levels (Growth Hormone Binding Protein) (Bereket et al., 1999) that leads to a decrease in GH action, in the values of IGF-1 and in the inhibitory counter-regulation of this hormone, resulting in an exaggerated secretion of GH and increased insulin resistance.

The realization of a strict glycemic control in T1D, according to current guidelines, many often leads to use of supraphysiological doses of insulin, which could result in a stimulation of androgen synthesis, mediated by insulin, as occurs in cases of insulin resistance. Accordingly, the prevalence of Polycystic Ovary Syndrome (PCOS) and other symptoms and signs of hyperandrogenism were evaluated in a group of 85 patients with T1D (Escobar-Morreale et al., 2000). PCOS was defined by the presence of menstrual changes and clinical or laboratory evidence of hyperandrogenism. Other causes of elevated androgen hormones were excluded. Eighteen normal eumenorrheic women served as controls. Thirty-three patients (38%) presented with T1D changes associated with an androgen excess (16 with PCOS and 17 with hirsutism without menstrual abnormalities). The patients with T1D and PCOS had elevated total and free testosterone and androstenedione but normal levels of sex-hormone binding globulin (SHBG) and dehydroepiandrosterone sulfate (DHEAS). However, despite the finding of a high prevalence of hyperandrogenism (including PCOS and hirsutism), there was no difference between clinical variables such as duration of

diabetes, age at diagnosis, conventional or intensive insulin treatment, average daily dose of insulin or glucose control between the T1D patients with and without hyperandrogenism in study.

The gold-standard method for evaluating IR is the hyperinsulinemic euglycemic clamp that directly measures the relationship between blood glucose and insulin levels, but it is difficult to be executed on a large scale since it is an invasive and expensive procedure. For this reason, HOMA-IR is used as a surrogate method to indirectly measure IR, calculated through fasting glycemia and insulinemia relationship. On the other hand, this calculation cannot be used for T1D as these patients do not produce endogenous insulin. So to evaluate the insulin sensitivity in these patients eGDR calculation (Equation 1) was developed that shown a good correlation with hyperinsulinemic euglycemic clamp (Chillarón et al., 2008):

$$eGDR\ (mg.kg\text{-}1.min\text{-}1) = 24{,}4 - 12{,}97\ (W/H) - 3{,}39\ (Hypertension) - 0{,}60\ (HbA1c) \quad (E1)$$

In which W/H is the waist-hip ratio(cm), hypertension is the presence or absence of hypertension (0 = no and 1 = yes) and the value of HbA1c is represented in %. It is also a good predictor of mortality, coronary arterial disease (CAD), microalbuminuria - a precocious hallmark of endothelial dysfunction (Pambianco et al., 2007) – and MS for T1D individuals, according to IDF (International Diabetes Federation), WHO (World Health Organization) and NCEP/ATPIII modified by AHA (American Heart Association).

As we know the insulin resistance is linked to an ectopic store of fat in insulin sensitive tissues like liver and muscle, but it is not clear if this fat accumulation leads to a hyperinsulinemic state or if it is its consequence. In a study with T2D patients, the glycemic control obtained after 67 hours of insulin treatment caused an accrual in intramyocellular and intrahepatic lipid content measured by nuclear magnetic resonance (NMR) spectroscopy, without compromising insulin sensitivity (Anderwald et al., 2002). Like T2D individuals, the intramyocellular lipid content in T1D ones was increased compared to controls and there was a direct relation with the glycemic control (Sibley et al., 2003).

There has been also noted a clear association between IR and visceral fat store, that can take its content extended in consequence of intensive insulin treatment independently of the type of diabetes, aggravating the CVD risk. In the DCCT study, the subgroup of T1D individuals that received intensive insulin treatment had a higher growth in BMI compared to the ones who were treated conventionally and it was noted a stronger correlation of this BMI variation with visceral fat deposit than with subcutaneous fat (Sibley et al., 2003). In this study, there are also demonstrations of direct association between visceral fat content and hepatic lipase, which favors the emergence of atherogenic dyslipidemia in these intensive treated individuals that put on more weight, reaching lipid levels similar to those of the conventionally treated group, suggesting loss of the benefits of intensive insulin therapy on lipids in this group of patients who had an excessive weight gain.

In other study (Nadeau et al., 2010), lean T1D adolescents with short time of disease (average of 7.5 years) without any inflammatory, clinical or lipid abnormalities had a IR - measured by hyperinsulinemic euglycemic clamp - similar to non diabetic obese adolescents and a superior IR than control subjects matched for age, pubertal stage, physical activity level and BMI, despite normal waist and intramyocellular lipid content.

There was also a demonstrated association between fat mass and blood pressure levels in T1D children and adolescents – high fat content, identified by the bioimpedance (BIA), and BMI were related to higher systolic and diastolic blood pressure (Pietrzak et al., 2009). The BIA is an easy, noninvasive, portable, no risk, relatively inexpensive method to measure the percentage of fat and provides results comparable to dual energy X-ray absorptiometry (DXA) (Elberg et al., 2004; Völgyi et al., 2008), that is reliable but expensive, requiring trained operators, individuals exposed to ionizing radiation and is not portable (Thomson et al., 2007).

There are data indicating good correlation between BIA and DXA, including Brazilian (Braulio et al., 2010) and T1D subjects (Leiter et al., 1994). Although overestimating the percentage of fat in lean individuals and underestimate it in obese (Sun et al., 2005), proves useful for predicting metabolic risk (including IR) as well as BMI and waist circumference (Lee et al., 2008). Through the BIA, it is possible to calculate the CDI (central fat distribution index), which assesses the impact of subcutaneous fat in the central fat distribution, and can be measured by dividing the area of abdominal subcutaneous fat mass by total fat (Silva et al., 2009). This measure seems to be relevant in that, according to some studies (Silva et al., 2009; Van Harmelen et al., 1998), the main source of leptin is the abdominal subcutaneous adipose tissue, either by mass effect - the subcutaneous adipose tissue is the major fat depot - as to produce more leptin (larger cell size and leptin gene expression) that omental adipose tissue. However, depending on the impedance (eg the trunk), the results may vary according to position changes, skin temperature, variation in electrode impedance and errors in their placement (Scharfetter et al., 2001).

A new adipokine identified visfatin, increases in proportion to visceral fat mass (Fukuhara et al., 2005) and decreases after gastric band placement (Haider et al., 2006). It is high in individuals with T2D (Chen et al., 2006) and even more in T1D (López-Bermejo et al., 2006), suggesting that its rising is linked to deterioration of pancreatic β cells. In vitro, visfatin activates the insulin receptor regardless of fasting state, increasing glucose uptake in muscle and adipose tissue and reducing hepatic glucose production independently of insulin levels (Fukuhara et al., 2005).

Hyperhomocysteinemia, known risk factor for coronary atherosclerosis (Okada et al., 1999), has also been shown to be detrimental to pancreatic insulin secretion (Patterson et al., 2006).

The C-reactive protein (CRP), an inflammatory marker that confers increased risk for atherosclerosis (Hayaishi-Okano et al., 2002), is increased in T2D patients (Nabipour et al., 2008) and obese subjects (Richardson et al., 2009), and also relates to the control of diabetes (King et al., 2003), i.e. may increase due to the weight gain caused by intensive control of diabetes (Schaumberg et al., 2005).

Ferritin is another acute phase inflammatory marker, correlate positively with CRP and BMI (Richardson et al., 2009), and also more specifically with visceral adiposity and insulin resistance (Iwasaki et al., 2005), leading to increased ferritin levels in T2D patients, concurrent with an augmentation of visfatin (Fernandez-Real et al., 2007).

Recently, several studies have indicated that the gene associated with fat mass and BMI (FTO) has an important genetic effect on BMI and risk of obesity through the rs9939609 polymorphism. This polymorphism is linked to an impaired responsiveness to satiety, ie have an effect on appetite (Wardle et al., 2008). The homozygous AA genotype results in an average gain of 3 kg or 1 unit of BMI over the TT genotype. There is evidence that this

polymorphism is linked to BMI gain in subjects with T1D (Gu et al., 2010) and higher levels of leptin and CRP (Welsh et al., 2010).

5. Conclusion

Obesity may both contribute to the onset of T1D as being a consequence of intensive treatment with insulin, that is, good glycemic control in T1D can lead to excessive weight gain in predisposed individuals (eg relatives of T2D), IR and consequently MS. Thus, the current approach of patients T1D should happen as it is done in T2D, multifactorial with an early and intensive monitoring of lifestyle, blood glucose, blood pressure and lipids, with the aim of identifying, correcting these factors and potentially reduce the high risk for cardiovascular disease in these patients. So gain weight can accelerate the presentation and modify the initial TID phenotype as increase the cardiovascular risk factors during evolution do the disease .

6. References

Acerini CL, Vheetham TD, Ege JA, Dunger DB. Both insulin sensitivity and insulin clearance in children and young adults with type 1 (insulin-dependent) diabetes vary with growth hormone concentrations and with age. *Diabetologia* 2000; 43: 61-8.

Aldhahi, W. and Hamdy, O. Adipokines, inflammation and the endothelium in diabetes. *Curr. Diab. Rep.*2003, 3, 293-298.

American Diabetes Association. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 1997; 20: 1183-97.

Anderwald C, Bernroider E, Krššák M, Stingl H, Brehm A, Bischof MG, Nowotny P, Roden M and Waldhäusl W. Effects of Insulin Treatment in Type 2 Diabetic Patients on Intracellular Lipid Content in Liver and Skeletal Muscle. *Diabetes* 2002, 51: 3025–3032.

Arai K, Yokoyama H, Okuguchi F et al. Association between Body Mass Index and Core Components of Metabolic Syndrome in 1486 Patients with Type 1 Diabetes Mellitus in Japan (JDDM 13). *Endocrine Journal*, 2008, vol 55 (6), 1025-1032.

Armani A, Durant S, Throsby M, Coulad J, Dardenne M, Homo-Delarche F. Glucose homeostasis in the nonobese diabetic mouse at the pre-diabetic stage. *Endocrinology* 1998; 139: 1115-24.

Beales PE, Pozzili P. Thiazolidinediones for the prevention of diabetes in the non-obese diabetic (NOD) mouse: implications for human type 1 diabetes. *Diabetes Metab Res Rev* 2002; 18: 114-7.

Becker DJ, Libman I, Pietropaolo M, Dosch M, Arslanian S, LaPorte R. Changing phenotype of IDDM: is it type 1 or type 2? *Pediatr. Res*. 2001, 49, 93A.

Bereket A, Lang CH, Wilson TA. Alterations in the growth hormone-insulin-like growth factor axis in insulin dependent diabetes mellitus. *Horm Metab Res* 1999; 31: 172-81.

Braulio VB, Furtado VC, Silveira MG, Fonseca MH, Oliveira JE. Comparison of body composition methods in overweight and obese Brazilian women. *Arq Bras Endocrinol Metab*. 2010; 54/4.

Brunzell JD, Chait A. Diabetic dyslipidemia: pathology and treatment. In: Porte D, Sherwin J (eds.). *Ellenberg and Rifkin's Diabetes Mellitus*. 5th ed. Norwalk: Appleton and Lange; 1997. p.1077-98.

Buschard K, Buch I, Molsted-Pedersen L, Hougaard P, Kuhl C. Increased incidence of true type I diabetes acquired during pregnancy. *Br Med J (Clin Res Ed)* 1987; 294 (6567): 275-9.

Charlton M, Nair K. Role of hyperglucagonemia in catabolism associated with type 1 diabetes. Effects of leucine metabolism and the resting metabolic rate. *Diabetes* 1998; 47: 1748–1756.

Chen M-P, Chung F-M, Chang D-M, Tsai JC-R, Huang H-F, Shin S-J and Le Y-J. Elevated plasma level of visfatin/PBEF in patients with type 2 diabetes. *JCEM*, 2006, 91: 295-299.

Chillarón JJ, Goday A, Pedro-Botet J. Síndrome metabólico, diabetes mellitus tipo 1 y resistencia a la insulina. *Med Clin (Barc)* 2008, 130(12): 466-71.

Conway B, Miller RG, Costacou T, Fried L, Kelsey S, Evans RW and Orchard TJ. Temporal patterns in overweight and obesity in Type 1 diabetes. *Diabet. Med*. 27, 398–404 (2010).

Daneman D. Type 1 diabetes. Lancet 2006; 367: 847–858.

Dib, SA. Insulin Resistance and metabolic syndrome in Type 1 Diabetes Mellitus. *Arq Bras Endocrinol Metab* vol 50 nº 2 Abril 2006

Elberg J, McDuffie JR, Sebring NG, Salaita C, Keil M, Robotham D, Reynolds JC and Yanovski JA. Comparison of methods to assess change in children's body composition. *Am J Clin Nutr*. 2004 July; 80 (1): 64–69.

Escobar-Morreale HF, Roldan B, Barrio R, Alonso M, Sancho J, de Calle H, et al. High prevalence of the polycystic ovary syndrome and hirsutism in women with type 1 diabetes mellitus. *J Clin Endocrinol Metab* 2000; 85: 4182-7.

EURODIAB ACE Study Group. Variation and trends in incidence of childhood diabetes in Europe. EURODIAB ACE Study Group. *Lancet* 2000, 355, 873-876.

Fernandez-Real JM, Moreno JM, Chico B, López-Bermejo A and Ricart W (2007). Circulating Visfatin Is Associated With Parameters of Iron Metabolism in Subjects With Altered Glucose Tolerance. Di*abetes Care* 30: 616–621, 2007.

Freedman D, Serdula MK, Srinivasan SR, Berenson GS. Relation of circumference and skin fold thicknesses to lipid and insulin concentrations in children and adolescents: the Bogalusa Heart Study. *Am J Clin Nutr* 1999; 69: 308-17.

Fukuhara A, Matsuda M, Nishizawa M, Segawa K, Tanaka M, Kishimoto K, Matsuki Y, Murakami M, Ichisaka T, Murakami H, Watanabe E, Takagi T, Akiyoshi M, Ohtsubo T, Kihara S, Yamashita S, Makishima M, Funahashi T, Yamanaka S, Hiramatsu R, Matsuzawa Y, Shimomura I.Visfatin: a protein secreted by visceral fat that mimics the effects of insulin. *Science* 2005, 307, 426-430.

Gabbay MAL, Gomes MB, Pires AC, Dib SA. Prevalence and trends of metabolic syndrome in type 1 diabetes according to duration of the disease. *Diabetes* 2005; 54 (suppl.1): A176.

Gilliam LK, Brooks-Worrell BM, Palmer JP, Greenbaum CJ, Pihoker C. Autoimmunity and clinical course in children with type 1, type 2 and type 1.5 diabetes. *J Autoimmun*. 2005, 25, 244-250.

Giuffrida FMA, Gabbay MAL, Pires AC, Brito M, Dib SA. Desenvolvimento dos sinais da síndrome metabólica em pacientes com diabetes mellitus tipo 1 de acordo com o tempo de duração da doença. *Arq Bras Endocrinol Metab* 2005; 49: S96.

Gu HF, Alvarsson A and Brismar K. The Common FTO Genetic Polymorphism rs9939609 is Associated with Increased BMI in Type 1 Diabetes but not with Diabetic Nephropathy. *Biomarker Insights* 2010:5 29–32.

Haider DG, Schindler K, Schaller G, Prager G, Wolzt M and Ludvik B. Increased plasma visfatin concentration in morbidly obese subjects are reduced after gastric banding. *JCEM*, 2006, 91: 1578-1581.

Hayaishi-Okano R, Yamasaki Y, Katakami N, Ohtoshi K, Gorogawa S-I, Kuroda A, Matsuhisa M, Kosugi K, Nishikawa N, Kajimoto Y, Hori M. Elevated C-reactive protein associates with early-stage carotid atherosclerosis in young subjects with type 1 diabetes. *Diabetes Care* 2002, 25: 1432–1438.

Iwasaki T, Nakajima A, Yoneda M, Yamada Y, Mukasa K, Fujita K, Fujisawa N, Wada K and Terauch Y (2005). Serum Ferritin Is Associated With Visceral Fat Area and Subcutaneous Fat Area. *Diabetes Care* 28: 2486–2491, 2005.

Jago, R. et al. Studies to Treat or Prevent Pediatric Type 2 Diabetes (STOPP-T2D) Prevention Study Group * Prevalence of the metabolic syndrome Among a Racially/Ethnically Diverse Group of U.S. Eighth-Grade Adolescents and Associations With Fasting Insulin and Homeostasis Model Assessment of Insulin Resistance Levels. *Diabetes Care* 2008, 31(10): 2020-2025.

Kadowaki T, Yamauchi T, Kubota N, Hara K, Ueki K, Tobe K. Adiponectin and adiponectin receptors in insulin resistance, diabetes, and the metabolic syndrome. J. *Clin. Invest.* 2006, 116: 1784–1792.

King DE, Mainous AG, Buchanan TA and Pearson WS. C-reactive protein and glycemic control in adults with diabetes. *Diabetes Care* 2003, 26: 1535–1539.

Laing SP, Swerdlow AJ, Slater SD, Botha JL, Burden AC, Waugh NR, et al. The British Diabetic Association Cohort Study II: cause-specific mortality in patients with insulin treated diabetes mellitus. *Diabet Med* 1999;16:466-71.

Lee K, Song Y-M and Sung J. Which Obesity Indicators Are Better Predictors of Metabolic Risk? Healthy Twin Study. *Obesity* (2008) 16, 834–840.

Leiter LA, Lukaski HC, Kenny DJ. The use of bioelectrical impedance analysis (BIA) to estimate body composition in the diabetes control and complications trial (DCCT). *Int J Obesity* 1994; 18: 829–835.

Li C., Ford ES, Zhao G, Mokdad AH. Prevalence of Pre-Diabetes and Its Association With Clustering of Cardiometabolic Risk Factors and Hyperinsulinemia Among U.S. Adolescents National Health and Nutrition Examination Survey 2005–2006. *Diabetes Care* 2009, 32: 342–347.

Libman, I.M. and Becker, D.J. (2003). Coexistence of type 1 and type 2 diabetes mellitus: 'double' diabetes? *Pediatr. Diabetes* 2003, 4, 110-113.

López-Bermejo A, Chico-Julià B, Fernàndez-Balsells M, Recasens M, Esteve E, Casamitjana R, Ricart W, Fernández-Real JM Serum visfatin increases with progressive beta cell-deterioration. *Diabetes* 2006, 55, 2861-2875.

Lord, G. Role of leptin in immunology. *Nutr. Rev.* 2002, 60, S35-S38.

Matarese G, Moschos S, Mantzoros CS. Leptin in immunology. *J. Immunol*. 2005, 174, 3137-3142.

Matarese G, Sanna V, Lechler RI, Sarvetnick N, Fontana S, Zappacosta S, La Cava A. Leptin accelerates autoimmune diabetes in female NOD mice. *Diabetes* 2002, 51, 1356-1361.

McCulloch DK, Kahn SE, Schwartz MW, Koerker DJ, Palmer JP. Effect of nicotinic acid-induced insulin resistance on pancreatic B cell function in normal and streptozotocin treated baboons. *J Clin Invest* 1991; 40: 166-80.

Nabipour I, Vahdat K, Jafari SM, Beigi S, Assadi M, Azizi F, Sanjdideh Z. Elevated High Sensitivity C-Reactive Protein Is Associated with Type 2 Diabetes Mellitus: The Persian Gulf Healthy Heart Study. *Endocrine Journal*, 2008, vol 55 (4), 717-722.

Nadeau KJ, Regensteiner JG, Bauer TA, Brown MS, Dorosz JL, Hull A, Zeitler P, Draznin B. and Reusch JEB. Insulin Resistance in Adolescents with Type 1 Diabetes and Its Relationship to Cardiovascular Function. *Clin Endocrinol Metab*, February 2010, 95 (2): 513–521.

Nathan DM, Lachin JM, Cleary P., Pomar T., Brillon DJ, Backlund JY, O'Leary DH, Genuth SM. Diabetes Control and Complications Trial / Epidemiology of Diabetes Interventions and Complications Study Research Group. Intensive Diabetes therapy and carotid intima-media thickness in type 1 diabetes mellitus. *NEJM* 2003, 348: 2294-2303.

Nathan DM et al. Diabetes Control and Complications Trial / Epidemiology of Diabetes Interventions and Complications Study Research Group. Intensive Diabetes treatment and cardiovascular disease in patients with type 1 diabetes. *NEJM* 2005, 353: 2643-2653.

OECD. Health at a Glance 2009: OECD Indicators. Paris: Organization for Economic Co-Operation and Development Press, 2009: 38–51.

Okada E, Oida K, Tada H, Asazuma K, Eguchi K, Tohda G, Kosaka S, Takahashi S and Miyamori I. Hyperhomocysteinemia Is a Risk Factor for Coronary Arteriosclerosis in Japanese Patients With Type 2 Diabetes. *Diabetes Care* 1999, 22: 484–490.

Pambianco G, Costacou T, Orchard TJ. The Prediction of Major Outcomes of Type 1 Diabetes: a 12-Year Prospective Evaluation of Three Separate Definitions of the metabolic syndrome and Their Components and Estimated Glucose Disposal Rate - The Pittsburgh Epidemiology of Diabetes Complications Study experience. *Diabetes Care* 2007, 30: 1248–1254.

Patterson S, Flatt PR, Brennan L, Newsholme P, McClenaghan NH. Detrimental actions of metabolic syndrome risk factor, homocysteine, on pancreatic B-cell glucose metabolism and insulin secretion. Journal of Endocrinology 2006, 189: 301-10.

Pietrzak I, Mianowska B, Gadzicka A, Młynarski W, Szadkowska A. Blood pressure in children and adolescents with type 1 diabetes mellitus – the influence of body mass index and fat mass. *Pediatric Endocrinology, Diabetes and Metabolism* 2009, 15 (4): 240-5.

Pinhas-Hamiel O, Dolan LM, Daniels SR, Standiford D, Khoury PR, Zeitler P. Increased incidence of non-insulin-dependent diabetes mellitus among adolescents. *J Pediatr* 1996, 128, 608-15.

Pozzilli,P. and Buzzetti, R. A new expression of diabetes: double diabetes. *TRENDS in Endocrinology and Metabolism* 2007, 18 (2), 52-57.

Purnell JQ, Hokanson JE, Marcovina SM, Steffes MW, Cleary PA, Brunzell JD. Effect of excessive weight-gain with intensive therapy of type 1 diabetes on lipid levels and blood pressure: results from the DCCT. Diabetes Control and Complications Trial. *JAMA* 1998; 280: 140-6.

Purnell JQ, Dev RK, Steffes MW, Cleary PA, Palmer JP, Hirsch IB, et al. Relationship of family history of type 2 diabetes, hypoglycemia, and auto antibodies to weight gain and lipids with intensive and conventional therapy in the Diabetes Control and Complications Trial. *Diabetes* 2003; 52: 2623.

Reinehr T, Schober E, Wiegand S, Thon A, Holl R. DPV-Wiss Study Group. B-Cell autoantibodies in children with type 2 diabetes mellitus: subgroup or misclassification? *Arch. Dis. Child.* 2006, 91, 473-477.

Richardson MW, Richardson MW, Ang L, Visintainer PF, Wittcopp CA.The abnormal measures of iron homeostasis in pediatric obesity are associated with the inflammation of obesity. *Int J Pediatr Endocrinol*.; 2009:713269. Epub 2009 Oct 8.

Rolandsson O, Hägg E, Hampe C, Sullivan EP, Nilsson M, Jansson G, Hallmans G, Lernmark A. Glutamate decarboxylase (GAD65) and tyrosine phosphatase-like protein (IA-2) autoantibodies index in a regional population is related to glucose intolerance and body mass index. *Diabetologia* 1999, 42, 555-559.

Rosenbloom A, Joe JR, Young RS, Winter WE. Emerging Epidemic of Type 2 Diabetes in Youth. Diabetes Care 1999, 22: 345–354.

Särnblad S., Ingberg CM, Åman J, Schvarcz E. Body composition in young female adults with Type 1 diabetes mellitus. A prospective case-control study. *DIABETIC Medicine*, DOI: 10.1111/j.1464-5491.2007.02144.x

Scharfetter H, Schlager T, Stollberger R, Felsberger R, Hutten H and Hinghofer-Szalkay H. Assessing abdominal fatness with local bioimpedance analysis: basics and experimental findings. *International Journal of Obesity* (2001) 25, 502 ± 511.

Schaumberg DA, Glynn RJ, Jenkins AJ, Lyons TJ, Rifai N, Manson JE, Ridker PM, Nathan DM (2005). Effect of Intensive Glycemic Control on Levels of Markers of Inflammation in Type 1 Diabetes Mellitus in the Diabetes Control and Complications Trial. *Circulation* 2005; 111; 2446-2453.

Sibley SD, Palmer JP, Hirsch IB and Brunzell JD. Visceral Obesity, Hepatic Lipase Activity, and Dyslipidemia in Type 1 Diabetes. *J Clin Endocrinol Metab*, July 2003, 88 (7): 3379–3384.

Silva EA, Flexa F, Zanella MT. Impact of abdominal fat and insulin resistance on arterial hypertension in non-obese women. *Arq Bras Endocrinol Metab*. 2009; 53/3.

Sociedade Brasileira de Hipertensão. Sociedade Brasileira de Cardiologia e Sociedade Brasileira de Nefrologia 2002 IV. Diretrizes Brasileiras de hipertensão arterial. p.5-7.

Sun G, French CR, Martin GR, Younghusband B, Green RC, Xie Y, Mathews M, Barron JR, Fitzpatrick DG, Gulliver W and Zhang H. Comparison of multifrequency bioelectrical impedance analysis with dual-energy X-ray absorptiometry for assessment of percentage body fat in a large, healthy population. *Am J Clin Nutr* 2005; 81: 74–8.

Terry RB, Wood PDS, Haskell WL, Stefanick ML, Krauss RM. Regional adiposity patterns in relation to lipids, lipoprotein cholesterol, and lipoprotein subfraction mass in men. *J Clin Endocrinol Metab* 1989; 68: 191-9.

The Diabetes Control and Complications Trial (DCCT) Research Group. Effects of age, duration and treatment of insulin-dependent diabetes mellitus on residual betacell function: observations during eligibility testing for the Diabetes control and Complications Trial (DCCT). *J Clin Endocrinol Metab* 1987; 65: 30-6.

The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *NEJM*, 1993, 329 (14): 977-986.

Thomson R, Brinkworth GD, Buckley JD, Noakes M and Clifton PM. Good agreement between bioelectrical impedance and dual-energy X-ray absorptiometry for estimating changes in body composition during weight loss in overweight young women. *Clinical Nutrition* (2007) 26, 771–777.

Van Harmelen V, Reynisdottir S, Eriksson P, Thörne A, Hoffstedt J, Lönnqvist F and Arner P. Leptin Secretion From Subcutaneous and Visceral Adipose Tissue in Women. *Diabetes*, Vol. 47, June 1998.

Verbeeten KC, Elks CE, Daneman D, Ong KK. Association between childhood obesity and subsequent Type 1 diabetes: a systematic review and meta-analysis. *Diabetic Medicine* 2011 Jan: 28 (1): 10-8.

Völgyi E, Tylavsky FA, Lyytikäinen A, Suominen H, Alén M and Cheng S. Assessing Body Composition With DXA and Bioimpedance: Effects of Obesity, Physical Activity, and Age. *Obesity* (2008) 16, 700–705.

Wang, Y., Monteiro C., Popkin B.M. Trends of obesity and underweight in older children and adolescents in the United States, Brazil, China, and Russia1–3. *Am J Clin Nutr*; 75:971–7, 2002.

Wardle J, Carnell S, Haworth CMA, Farooqi IS, O'Rahilly S and Plomin R. Obesity Associated Genetic Variation in *FTO* Is Associated with Diminished Satiety. *J Clin Endocrinol Metab* 93: 3640–3643, 2008.

Wellen K., Hotamisligil G. Inflammation, stress, and diabetes. *J. Clin. Invest*. 2005, 115:1111–1119.

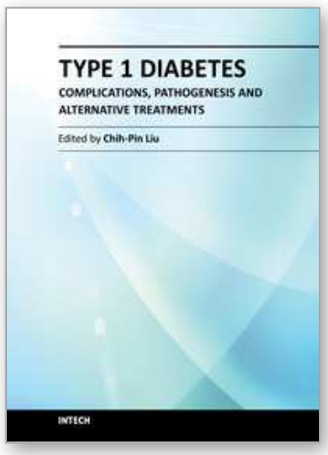
Welsh P, Polisecki E, Robertson M, Jahn S, Buckley BM, Craen AJM, Ford I, Jukema JW, Macfarlane PW, Packard CJ, Stott DJ, Westendorp RGJ, Shepherd J, Hingorani AD, Smith GD, Schaefer E and Sattar N. Unraveling the Directional Link between Adiposity and Inflammation: A Bidirectional Mendelian Randomization Approach. *J Clin Endocrinol Metab* 95: 93–99, 2010.

Wilkin TJ. The accelerator hypothesis: weight gain as the missing link between Type I and Type II diabetes. *Diabetologia* 2001;44:914-22.

Willi SM, Egede LE. Type 2 diabetes mellitus in adolescents. *Current Opinion in Endocrinology & Diabetes*, 2000, 7:71–76.

Williams KV, Erbey JR, Becker D, Orchard TJ. Improved glycemic control reduces the impact of weight gain on cardiovascular risk factors in type 1 diabetes. The Epidemiology of Diabetes Complications Study. *Diabetes Care* 1999; 22: 1084–1091.

Yki-Jarvinen H, Koivisto VA. Natural course of insulin resistance in type 1 diabetes. *N Engl J Med* 1986; 315: 224-30.



Type 1 Diabetes - Complications, Pathogenesis, and Alternative Treatments

Edited by Prof. Chih-Pin Liu

ISBN 978-953-307-756-7
Hard cover, 470 pages
Publisher InTech
Published online 21, November, 2011
Published in print edition November, 2011

This book is intended as an overview of recent progress in type 1 diabetes research worldwide, with a focus on different research areas relevant to this disease. These include: diabetes mellitus and complications, psychological aspects of diabetes, perspectives of diabetes pathogenesis, identification and monitoring of diabetes mellitus, and alternative treatments for diabetes. In preparing this book, leading investigators from several countries in these five different categories were invited to contribute a chapter to this book. We have striven for a coherent presentation of concepts based on experiments and observation from the authors own research and from existing published reports. Therefore, the materials presented in this book are expected to be up to date in each research area. While there is no doubt that this book may have omitted some important findings in diabetes field, we hope the information included in this book will be useful for both basic science and clinical investigators. We also hope that diabetes patients and their family will benefit from reading the chapters in this book.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Fernando Valente, Marília Brito Gomes and Sérgio Atala Dib (2011). Obesity in the Natural History of Type 1 Diabetes Mellitus: Causes and Consequences, Type 1 Diabetes - Complications, Pathogenesis, and Alternative Treatments, Prof. Chih-Pin Liu (Ed.), ISBN: 978-953-307-756-7, InTech, Available from: http://www.intechopen.com/books/type-1-diabetes-complications-pathogenesis-and-alternative-treatments/obesity-in-the-natural-history-of-type-1-diabetes-mellitus-causes-and-consequences

INTECH
open science | open minds

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

IntechOpen