

The metabolic syndrome in a global perspective

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ABSTRACT

The term “metabolic syndrome” refers to the clustering of a number of cardiovascular risk factors (obesity, hypertension, dyslipidemia and hyperglycaemia) believed to be related to insulin resistance. The prevalence of each of these diseases as well as the metabolic syndrome is increasing world wide. Obesity, hypertension, dyslipidemia and diabetes are no longer diseases of the wealthy. By 2025, three out of four people with diabetes will be living in third world countries, and similar trends are likely for the other components of the syndrome. Preventive action is urgently needed, and studies in China and India have proven to be effective.

A global transition in the disease pattern has been observed, where the relative impact of infectious diseases is decreasing while chronic diseases like cardiovascular disease, cancer and diabetes are increasingly dominating the disease pattern. Based on estimates from the World Health Organisation, chronic diseases were responsible for as many deaths as infections, malnutrition, perinatal death and death during pregnancy in [1]. Chronic diseases are no longer diseases of the western world only. As of today, four out of five deaths due to chronic diseases will occur in low and middle income countries.

Europe and North America have experienced a gradual modification of lifestyle over several centuries, where a diet based on high intake of carbohydrate replaced the traditional hunter-gatherer diet with high protein intake. Similar changes have occurred in third world countries, but in many cases the transition has taken place over decades – not centuries. A combination of increased access to food and decreasing demands with respect to physical activity has led to increasing prevalence of obesity, dyslipidemia, hypertension and hyperglycaemia/diabetes, a combination of features often referred to as the metabolic syndrome. This clustering of risk factors in certain individuals has been known since the late 1800's while insulin resistance was first described in 1936 [2]. In his Banting lecture in 1988 Reaven [3] described the metabolic syndrome as a clustering of cardiovascular risk factors in individuals with insulin resistance, and he suggested that insulin resistance was the trigger of the syndrome. Following his definition, numerous groups of researchers world wide identified a long list of factors and features associated with the metabolic syndrome characterised and this led to considerable confusion and uncertainty with respect to the definition. Over the last ten years numerous attempts have been made to reach an agreement on a common, internationally accepted definition of the syndrome. This process, however, also led to a change in concept with respect to the common denominator in the syndrome. Where Reaven had insulin resistance as the central and hypothetically causal factor tying the syndrome together, the more recent definitions including the most recent definition by International Diabetes Federation (IDF) from 2006 [4] see obesity or central obesity as the central factor defining the syndrome if at least to other elements of dyslipidemia, hypertension and hyperglycaemia are present, and

where insulin resistance is no longer even a part of the syndrome. The somewhat paradoxical consequence is, that while the metabolic syndrome is attracting increasing awareness from not least the pharmaceutical industry, the uncertainty with respect to definition and not least to the pathophysiological determinant(s) of the syndrome is increasing [5]. Despite the fact that more than 17,000 scientific papers with the Mesh-term metabolic syndrome or insulin resistance have been published over the last ten years, a recent review clearly demonstrates the need for a critical analysis of the components of the syndrome – and even the mere existence of the syndrome is highly needed.

The main reason why the metabolic syndrome is attracting scientific and commercial interest is that the factors defining the syndrome (however defined) are all factors associated with an increased morbidity and mortality in general and from cardiovascular disease (CVD) in particular. It is nevertheless highly questionable whether the inclusion of presence or absence of the metabolic syndrome improves the prediction of risk of developing CVD over and above a prediction based on the individual risk factors in a multifactorial model [6]. Consequently, and because of the lack of good, global data on the prevalence of the metabolic syndrome, this paper will focus primarily on the individual risk factors rather than on the full syndrome.

BLOOD PRESSURE/HYPERTENSION

Hypertension is the most important single, modifiable risk factor for stroke and an important risk factor for atherosclerosis and ischaemic heart disease. Obesity, lack of physical activity and modification of diet in a “Westernised” direction are all associated with increasing blood pressure. In accordance with this, urbanisation is also associated with increasing blood pressure as demonstrated in migration studies from e.g. India, Africa, Australia and Greenland. Studies from Chennai in India have shown similar or even higher blood pressure levels in slum-areas as in middle and high income areas, demonstrating that the increasing blood pressure is not just a consequence of increasing wealth but rather a consequence of (yet unidentified) components associated with urbanisation [7].

DYSLIPIDAEMIA

Dyslipidaemia is generally characterised by increased total cholesterol in combination with increased levels of low density lipoprotein (LDL)-cholesterol and is associated with an increased risk of atherosclerosis and CVD. People living characterised by a traditional life style in rural areas in third world countries generally have low total and LDL cholesterol levels, and populations with high intake of fish and marine mammals generally have high HDL-cholesterol levels. Migrant studies moving from rural to urban areas in third world countries or moving from third world countries to Europe or North America systematically show atherogenic changes in the lipid profile as a consequence of migration. This is likely to be one important contributory factor to the high morbidity and mortality from CVD in e.g. immigrant Indian or Pakistani groups in UK.

OVERWEIGHT AND OBESITY

The prevalence of obesity and overweight is increasing world wide to a level where WHO is using the term “obesity epidemic”. Based on the European standards defining obesity (body mass index) (BMI) 27-30 kg/m² and obesity (BMI >30 kg/m²) both obesity and overweight are relatively uncommon conditions in major parts of the third world countries. Several studies have however shown that the association between BMI and morbidity or cardiovascular risk factors varies considerably by region and ethnicity [8]. In Europe, the risk of developing diabetes really starts to increase at BMI-levels in the range 25-27, while for females from India the entire increase in risk is found in the BMI-interval from 18-25 [8]. The same is true for the association between BMI and blood pressure or dyslipidemia with global positive associations between BMI and blood pressure

or lipids but with considerable differences with respect to level of the associations where populations from Asia or Africa in general have higher levels of BP or lipids for a given level of BMI when compared to European and North American populations. There are populations not following this pattern. Recent studies of the Inuit population in Greenland have shown that they tolerate markedly higher levels of BMI and waist circumference without developing metabolic derangement in the form of hypertension, dyslipidemia, hyperglycaemia and hyperinsulinaemia [9].

Due to this ethnic variability in response to BMI and waist circumference, WHO is now recommending the use of ethnicity specific cut points defining overweight and obesity. The most recent definition of the Metabolic Syndrome by IDF [4] is following this recommendation but at the same time defines obesity based on waist circumference only. The rationale for this is that the metabolic activity of intraabdominal fat differs from that of subcutaneous fat. Furthermore BMI is not an optimal measure of obesity as individuals with high muscle mass and low fat mass may have the same BMI as individuals with large fat mass and low muscle mass. A word of caution may be needed here. Virtually all studies of the association between fat mass or fat distribution have been performed in white Caucasian populations from Europe or North America. In general these results are uncritically extrapolated to other populations and ethnic groups despite the fact that body composition is modified by ethnicity.

HYPERGLYCAEMIA/DIABETES

The number of individuals with diabetes is increasing worldwide, but most rapidly so in third world countries. This increase in total number of cases is primarily due to demographic factors (general population growth and increasing mean age and survival time), to a decreasing mortality in patients with diabetes, but also to a true incidence increase, induced by obesity, physical inactivity and urbanisation. Several studies from India, China, Pacific islands, USA, Africa and South America concordantly demonstrate that urbanisation is associated with a doubling of the underlying diabetes prevalence.

CONSEQUENCES OF THE GLOBAL INCREASE IN THE "METABOLIC SYNDROME"

As already discussed, all components in the metabolic syndrome are closely associated with an increased risk of developing CVD. During the last decades most countries have experienced a systematic decrease in the incidence of CVD. With the current temporal trends in the CVD risk factors included in the metabolic syndrome stagnation or even increase in the incidence of CVD are to be expected. One study from India has demonstrated an increasing prevalence of CVD in low-income groups [7]. As presence of the metabolic syndrome is also associated with increased risk of developing diabetes, an increased prevalence not only of diabetes but also of the following late diabetic complications must be expected.

The changing disease pattern from infectious diseases to chronic diseases is a major challenge in relation to organisation as well as funding of the future health care system in all parts of the world. The chronic diseases typically require lifelong treatment involving life style modification as well as pharmacological treatment. In the global perspective, very few countries are prepared to face this challenge. Very few countries have a health care system organised in a way that can face the challenge, and the costs will in major parts of the world grossly exceed the resources currently set aside for health care by countries as well as by individual patients and their families. The only possible solution will be an increased focus on targeted prevention in combination with a gradual reorganisation and restructuring of the health care service moving from a solely treatment oriented activity to a combined treatment and preventive effort. Here the increasing focus on trends in chronic, non-communicable disorders by non-governmental institutions, the WHO

and national as well as international aid-organisations must be positive and encouraging [1].

WHY IS THE PREVALENCE OF THE METABOLIC SYNDROME INCREASING?

Demographic changes combined with the increasing prevalence of obesity and physical inactivity are generally assumed to be the driving forces, but as discussed above, urbanisation is one of the most important factors explaining the increasing problem with the metabolic syndrome in a global perspective. This has been general knowledge for decades, but despite this only very few studies have focused on the actual changes in life style related factors, living conditions, social structures etc. associated with and induced by urbanisation, and probably contributing to the health problems related to urbanisation. Without this type of research it will still be impossible to set up a rational prevention strategy. The strategy is *not* to prevent urbanisation, as this is probably an unavoidable consequence of the global development. Thus the strategy must be to identify the effects of urbanisation and specifically to try to modify the negative effects through targeted prevention programmes.

GLOBAL PREVENTION OF THE METABOLIC SYNDROME

Prevention of chronic non-communicable diseases may seem impossible in countries where access to food, clean water and high infant mortality rates have top priority (health-related) political issues. Nevertheless the non-communicable disorders do compose a real and overwhelming threat to possibilities within health care, and not least so in third world countries. WHO has estimated that by year 2025 more than 300 million people world wide will suffer from diabetes. Three out of four of these will live in third world countries, countries with very limited resources to manage this problem. This in itself demonstrates that prevention is no longer an intellectual exercise or theoretical possibility but a must. All efforts should be combined in the process of integrating existing knowledge related to prevention and early treatment of chronic diseases into any future programme for health care organisation in any part of the world. In this case international organisations like WHO and the World Bank, national and international aid organisations like DANIDA, NORAD etc. as well as non-governmental organisations (NGO's) play an important role. All these organisations have the potential to combine scientific evidence with their experience in health programmes to make the local modifications and adjustments that will be essential for the success, and at the same time to influence political priorities through funding as well as political incentives. On this background it is interesting and encouraging that programmes preventing chronic diseases are not always developed in westernised countries. The first study to show that lifestyle modification (physical activity and diet) is efficient in preventing diabetes was planned and conducted in China [10]. The study was subsequently repeated in Finland, USA, Canada and India, and all these studies confirmed the original results. Based on the experiences from China and India it ought to be possible to develop prevention programmes and strategies that are not only effective, but also locally acceptable and feasible. It is not going to be easy, but history has shown that it is possible.

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