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GAVIN PUBLISHERS

Journal of Diabetes and Treatment

Yaqoob K and McCafferty K. J Diabetes Treat 1: 1067.

Mini-Review

DOI: 10.29011/2574-7568.001067

The Relationship Between Low Birthweight, Obesity and Diabetes Mellitus

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Citation: Yaqoob K and McCafferty K (2019) The Relationship Between Low Birthweight, Obesity and Diabetes Mellitus. J Diabetes Treat 1: 1067. DOI: 10.29011/2574-7568.001067

Received Date: 01 June, 2019; **Accepted Date:** 17 June, 2019; **Published Date:** 21 June, 2019

Abstract

Chronic disease has become more prevalent in modern society; and one key reason for this is the increasing life expectancy worldwide. The leading Chronic Non-Communicable Diseases (CNCD) in developed countries include cardiovascular disease, obesity, diabetes, hypertension, cancer and oral health problems. The rising incidence of chronic disease not only has an impact on the individual, but also on society as a whole; as seen in the greater burden on health care systems as well as the negative impact on the economy.

It is therefore essential to find a mechanism to prevent the epidemic of CNCDs that is cost effective and can be applied widely. One such measure would be to identify at-risk individuals so that healthcare systems can work with them to prevent chronic diseases from developing in the first place. One such risk factor that has been suggested is Low Birthweight (LBW). Could LBW be a reliable indicator for chronic disease, particularly diabetes in later life?

Background

LBW is defined as being born weighing less than 2.5 kg [1]. In 2015, it was estimated that approximately 20.5 million (14.6%) of infants were born with a LBW. In addition to high mortality in their early life, those that survived are likely to experience growth retardation, obesity and diabetes, among other CNCDs [2].

Relationship between LBW, obesity and diabetes

Obesity is defined as a Body-Mass-Index (BMI) greater than 30, and is described as an abnormal and excessive accumulation of fat that can impair health. Obesity is the main driver of the current epidemic of diabetes worldwide. A relationship between LBW and the development of obesity in later life could indirectly link LBW with type 2 diabetes. In 2014, more than 39% of adults aged 18 and over were overweight and of these, 13% were obese. Furthermore, this is no longer just a problem in high income countries; in Africa, the number of children who were overweight or obese has more than doubled from 5.4 million in 1990 to 10.6 million in 2014 [3].

However, studies associating LBW and future obesity have shown mixed results. A systematic review and meta-analysis published in 2011 found that a high birth weight was associated with obesity in later life, whilst a LBW was not. Although, these studies measured obesity through BMI scales, a method that does not accurately determine the distribution of fat, particularly around the abdomen (central obesity), which is a better measure of cardio metabolic risk [4].

In 2002 a study was conducted in Shanghai, China that looked at the association between LBW and abdominal adiposity. They found that LBW was an independent risk factor for type 2 diabetes, central obesity and hypertension. Furthermore, the highest prevalence of diabetes (34.5%) was observed among those with the lowest birth weight and central obesity. Therefore, they concluded that birth weight was associated with the risk of type 2 diabetes and abdominal obesity, and that a LBW coupled with abdominal obesity was the strongest predictor for type 2 diabetes [5].

In addition to this, the link between LBW and future obesity may be explained by the finding that nutritionally deprived newborns maybe "Programmed" to eat more because they develop a smaller number of neurons in the region of the brain that controls food intake [6]. Furthermore, there is evidence to suggest that LBW infants have higher circulating levels of leptin and a leptin-

to-fat mass ratio than adults with a normal birthweight. This may be due to nutritional factors during childhood resulting in relative resistance to leptin [3].

Globally, it is estimated that there were approximately 422 million adults living with diabetes in 2014, and Type 2 diabetes accounts for approximately 95% of the global diabetic population. This number is likely to increase significantly over the coming years [7]. Current predictions suggest that as a result of population growth and increasing life expectancy, urbanisation and the adoption of a sedentary lifestyle could lead to a 54% increase in the prevalence of diabetes by 2030 [6].

Studies have demonstrated that it is specifically LBW, measured by a low ponderal index (birthweight-to-length ratio) which was associated with resistance to insulin and its associated disorders such as diabetes in later life [8]. Recently, this observation had been confirmed in a study [9] which demonstrated that infants with a ponderal index in the lowest quintile had the highest prevalence of diabetes at the age of 60, compared to the other four quintiles. Furthermore, these findings were corroborated in a study which found that LBW infants had a 110% increased risk of developing diabetes in later life [10], confirming that reduced foetal growth was associated with an increased risk of diabetes and suggested a specific association with LBW.

However, most of the above studies demonstrate an association and do not prove a cause and effect relationship between LBW and diabetes mellitus. Evidence for the causal effect of LBW on subsequent type 2 diabetes comes from a Mendelian randomisation study, which found that genetic causes for low birth weight were associated with future diabetes. Specifically, for every 1 standard deviation, a lower genetically determined birthweight was associated with an almost doubling the future risk of type 2 diabetes. Crucially the single nucleotide polymorphisms used to score the risk of low birth weight are not known to be associated with diabetes directly, reducing the risk of confounding [11]. The evidence above provides a plausible causal relationship between LBW and the prevalence of obesity and type 2 diabetes in later life.

Studies conducted in high, low and middle-income countries worldwide have shown that there is a strong association between infants born with LBW and their subsequent development of diseases such as coronary heart disease, hypertension, kidney disease, type 2 diabetes mellitus and obesity [2]. These findings can be explained by epigenetic changes in response to adverse conditions for the foetus in utero. However, once born, these infants often no longer face such adverse conditions and so the epigenetic changes result in negative effects in later life. This could result in the chronic diseases listed above.

Recommendations

We recommend the following simple and cost-effective measures to be implemented in order to reduce the incidence of LBW and thus also, the prevalence of chronic disease in the future:

- Educating girls and women on the correct amount of nutritional intake during pregnancy, as well as a healthy diet and smoking cessation to ensure that they and their unborn children remain healthy now and in the future.
- Healthcare providers should monitor a woman's nutritional status throughout her pregnancy, to prevent the foetuses being born with LBWs.
- Promote a greater awareness of the effects of LBW among members of the healthcare profession, so that at-risk patients can be identified sooner and receive support earlier.

The following measures could be implemented at a primary care level, with a view to prevent chronic diseases from developing:

- A formal record of a child's birthweight in their medical records for future reference.
- Children born with a LBW should receive targeted education and support to try and prevent chronic diseases from developing.
- A mandatory health checks every 1-2 years of a child's life when health professionals record simple measurements such as height, weight, waist-hip ratio, BP and urine analysis.

These measures allow health professionals to monitor a child's health status regularly, and identify problems before it becomes too late; allowing them to deliver timely advice, rather than waiting until chronic symptoms begin to present themselves.

Acknowledgements: Professor M. Yaqoob; Barts Health Trust

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