



Editorial

Women & diabetes: Our right to a healthy future

There are currently over 199 million women living with diabetes, and this is projected to increase to 313 million by 2040¹. Diabetes is the ninth leading direct cause of death in women globally, causing 2.1 million deaths each year, most of them were pre-mature¹. The issue of women and diabetes is important for several reasons.

Diabetes impacts women more severely

Although diabetes affects men and women equally, women are more severely impacted by its consequences. Pre-menopausal women with diabetes lose the protection against heart disease that non-diabetic women have² and are 50 per cent more likely to die from heart disease than men³⁻⁶. A study showed that 36.9 per cent of women with diabetes with a heart attack died within a year, compared to 20.2 per cent of women without diabetes⁷. Compared to men, women are also at a greater risk of blindness due to diabetic retinopathy⁸. Women, with type 1 diabetes, are more likely to suffer from retinopathy and neuropathy⁹. Pregnancy may worsen pre-existing diabetic retinopathy and lead to significant visual impairment. Pregnancy may also worsen pre-existing kidney disease. Elderly women with type 2 diabetes mellitus (T2DM) and end-stage renal disease have a significantly higher risk of death than men with similar problems¹⁰. Women with diabetes are four times more likely to suffer a stroke than women without diabetes¹¹. Cyclical hormonal changes make diabetes control more difficult in pre-menopausal women, and the risk of diabetic ketoacidosis is higher amongst women than men. Women are also consistently more likely to develop depression than men¹². While the higher burden of cardiovascular and other complications in women with diabetes may be due to biological reasons, it is also a fact that, in all countries including the

high-income economies, women tend to receive less intensive care and treatment for diabetes compared to men^{3,13,14}.

Women also develop hyperglycaemia in pregnancy (HIP) which significantly increases the risk of maternal and perinatal morbidity and mortality and pregnancy complications: hypertension and pre-eclampsia, obstructed labour, postpartum haemorrhage, infections, stillbirths, pre-mature delivery, both large and small for gestational age (SGA) infants, congenital anomalies, newborn deaths due to respiratory problems, hypoglycaemia and birth injuries. The risk and number of these complications are directly related to level of maternal hyperglycaemia^{15,16}. Apart from pregnancy complications and poor outcome, HIP increases the vulnerability for future T2DM and is the most reliable marker of future T2DM¹⁷ and cardiometabolic disorders in women¹⁸; with a proven possibility of prevention or delaying onset through appropriate post-partum lifestyle interventions¹⁹⁻²¹.

Gender not only influences the vulnerability to disease but also affects access to health services and health-seeking behaviour for women²² which may amplify both the short- and long-term adverse impact of diabetes. In low-income countries, women suffer disproportionately from economic, political and social discrimination, and consequently from poor health, lack of education and employment²³. Stigmatization and discrimination faced by people with diabetes are particularly pronounced for girls and women, who carry a double burden of discrimination. Lack of education restricts access to information; restriction of free movement or need to be accompanied by an escort or fear of being shunned in marriage or abandonment and divorce if diagnosed with diabetes are important barriers²⁴ which discourage girls and women from

seeking diagnosis and treatment and receiving adequate care, resulting in more complications and less likelihood of achieving positive health outcomes.

Thus, overall, compared to men, women are more vulnerable, have fewer opportunities of being treated, have less access to care and receive less support to deal with the consequences of diabetes. This is true globally but markedly so in low- and middle-income countries, particularly in countries without health insurance and universal health coverage.

Hyperglycaemia in pregnancy (HIP) - A threat to our healthy future

The occurrence of HIP generally parallels the prevalence of pre-diabetes, overweight, obesity and T2DM in a given population. In developing economies that still have considerable levels of undernutrition and hunger, individuals born low birth weight (LBW) or SGA manifest insulin resistance and a higher risk of diabetes at much lower body weight, body mass index (BMI) and central adiposity threshold^{25,26}. In young women born LBW or SGA, these effects may first come into play during pregnancy, resulting in gestational diabetes mellitus (GDM) and/or pregnancy-induced hypertension (PIH). Foetal birth weight <3000 g is significantly associated with higher rates of GDM²⁷. Seshiah *et al*²⁸ reported GDM prevalence rates of 8-10 per cent amongst women of low socio-economic status with pre-pregnancy BMI <19 kg/m² and higher rates at higher BMIs and in urban women.

Offspring of mothers with HIP are at a heightened risk of early-onset obesity, pre-diabetes, T2DM and cardiometabolic disorders as a consequence of intrauterine developmental programming^{29,30}. This makes female offspring of mothers with HIP highly vulnerable to hyperglycaemia during pregnancy. Pregnant women with a maternal history of diabetes have significantly raised risk of GDM compared to those with paternal history of diabetes³¹. Worldwide, one in six pregnancies may be associated with hyperglycaemia, 84 per cent of which involve GDM¹. In 2013, 16.8 per cent live births were associated with HIP and 16 per cent of these were due to overt diabetes in pregnancy. This does not account for pregnancies ending in spontaneous abortions, stillbirths or intrauterine deaths that may have been associated with hyperglycaemia proven or otherwise.

South Asia already accounts for 20 and 23 per cent of the global burden of diabetes and pre-diabetes¹ and also for the highest rates of maternal undernutrition,

LBW and SGA infants^{32,33}. In addition, levels of overweight and obesity amongst South Asian women in the reproductive age is rising³³.

The combination of being born small and being overweight as a young adult will continue to provide a continuous stream of young women vulnerable to HIP, and they and their offspring will have a high vulnerability to obesity, T2DM, hypertension, cardiometabolic disorders, polycystic ovary syndrome (PCOS) and other non-communicable diseases (NCDs). Pregnancy maybe considered a multiplier of the unfolding pandemic of diabetes and NCDs, as it provides a crossover or interchange, where undernutrition in the previous generation transits to early life overweight and obesity in the next generation through gestational hyperglycaemia impacting subsequent generations with overweight, obesity, T2DM, cardiometabolic disorders, *etc.*

Whether good control of HIP will prevent or reduce these risks is currently unknown and requires further well-designed studies. Being born full term and normal weight is undoubtedly a good start to life; in addition, early life attention to avoid excess weight and inculcate healthy eating and physical activity behaviour may further help prevent or delay onset of long-term consequences. The foetal environment represented by the mother's periconceptual and gestational health determines whether one starts life with a health 'advantage' or 'handicap', and it is on this 'foundation' that NCD risk factors play out in later life. People starting life with a 'health handicap' may be less able to withstand lifestyle risks and may be vulnerable to developing disease early compared to those starting with a 'health advantage'³⁴. Similarly, lifestyle interventions in adult life to prevent diseases may have variable effects based on early life programming³⁵.

The impact of life conditions on health and the social determinants of health are high on the global development agenda, and it is relevant to consider that these social determinants may get hardwired into the next generation's genome through epigenetic changes³⁴. The recognition that intrauterine and early-life influences play an important role in the causation of chronic diseases does not imply an absolute deterministic process that cannot be overcome by later-life intervention, only that the task becomes more difficult and expensive.

The concept of foetal programming and its consequences is paradigm changing. It highlights

that pregnancy offers a window of opportunity to provide maternal care services, not only to reduce the traditionally known maternal and perinatal morbidity and mortality indicators but also for transgenerational prevention of several chronic diseases³⁶.

Having saved a mother with GDM and pre-eclampsia from dying of obstructed labour or post-partum haemorrhage and her macrosomic infant; or a mother with severe malnutrition and anaemia and her LBW infant, what can be done to ensure their future good health and prevent or delay the onset of hypertension or T2DM? What can be done to ensure that girls born of such pregnancies are given due prenatal attention to prevent further transgenerational risk transmission? This will require transformation in policy and integration of services for maternal and child health, NCD care, prevention and health promotion. It will also require investments in information technology, to identify and track these high-risk mother-child pairs to enlighten, empower and encourage them to adopt healthy living throughout life, as well as empowering local health workers to support and follow their progress. Enrolling, testing, treating, monitoring and tracking women during and after pregnancy and their offspring using information technology may be the most appropriate place to begin this health system transformation to break the ever-rising curve of diabetes and other NCDs³⁷.

Addressing this through focused action on HIP may provide us a safe passage to a healthy future!

Anil Kapur¹ & Veeraswamy Seshiah^{2,3,4,5,*}

¹World Diabetes Foundation, Gentofte, Denmark,

²Distinguished Professor, The Tamil Nadu Dr. M.G.R. Medical University, ³Diabetes in Pregnancy Study Group, India, ⁴Executive Board International

Association of Diabetes & Pregnancy Study Group &

⁵Dr. Seshiah & Dr. Balaji Diabetes Care & Research Institute, Chennai 600 029, Tamil Nadu, India

*For correspondence:
vseshiah@gmail.com

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